Department of Defense **Smallpox Response Plan**
Washington, DC 29 September 2002

Unclassified version 3.1

Summary. This publication provides implementing instructions and accompanying planning guidance to Department of Defense activities to prepare for and respond to a smallpox outbreak.

Distribution: Unlimited

DoD Smallpox Response Plan.

Planning Guidance:

Annex A. Surveillance, Contact Tracing, & Epidemiological Investigation.

Annex B. Vaccination Guidelines.

Annex C. Isolation & Quarantine Guidelines.

Annex D. Specimen Collection Guidelines.

Annex E. Communications Plans & Activities.

Annex F. Decontamination Guidelines.

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Annex I. Medical Logistics & Product Distribution.

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Summary. This publication provides implementing instructions to Department of Defense activities to prepare for and respond to a smallpox outbreak. This document amplifies and implements the Smallpox Response Plan & Guidelines issued by the Centers for Disease Control & Prevention (CDC). This DoD Smallpox Response Plan provides for response to smallpox outbreaks on military installations and contingency operations around the world, as well as military support to civil authorities. This publication applies to uniformed departments of the Air Force, Army, Navy, Marine Corps, and Coast Guard (Active and Reserve), nonmilitary persons under military jurisdiction, selected Federal employees, and family members and other people eligible for care within the military health care system. Technical revisions will be issued by DASG-HCA. Send comments and suggested improvements to DASG-HCA, 5111 Leesburg Pike, Suite 401, Falls Church, VA 22041.

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1. Situation.

a. General.

(1) Purpose. This plan provides implementing instructions and accompanying planning guidance to prepare for and respond to a smallpox outbreak. A single case of smallpox outside of an approved laboratory constitutes a smallpox outbreak. This document amplifies and implements the Smallpox Response Plan & Guidelines issued by the Centers for Disease Control & Prevention (CDC). This DoD Smallpox Response Plan provides for response to smallpox outbreaks on military installations and contingency operations around the world, as well as military support to civil authorities.

(2) Applicability. This plan applies to uniformed departments of the Air Force, Army, Navy, Marine Corps, and Coast Guard (Active and Reserve), nonmilitary persons under military jurisdiction, selected Federal employees, and family members and other people eligible for care within the military health care system.

(3) Summation. Appendix 1 summarizes this document on one page. Similarly, the first appendix to each of the annexes summarizes that annex. Appendix 4 provides a summary of tasks specified in this plan and its accompanying planning guidance.

b. Contagious Disease. Smallpox is a contagious, sometimes-fatal infection that can be prevented by vaccination with live vaccinia virus (Appendix 3). Although a World Health Organization (WHO) global campaign eradicated naturally occurring smallpox by the late 1970's, there remains concern that clandestine stores of smallpox virus could be used as a biological weapon (BW). If an outbreak of smallpox occurred, several factors could contribute to a more rapid spread of smallpox than seen before this disease was eradicated (e.g., fewer people with immunity, delay in recognizing an eradicated disease, more immunodeficient individuals, greater individual mobility). Because of these factors, a single case of smallpox would require an immediate and coordinated public-health and medical response to contain the outbreak.

(1) Effect on Readiness. A smallpox outbreak would significantly affect military readiness. An outbreak would degrade combat-mission capability among vulnerable troops; stress military medical operations to maximum capacity; restrict military operations; limit transit of international boundaries; and divert military manpower for health care or crowd control.

(2) Smallpox Disease. Smallpox is a contagious disease caused by the variola virus. Historically, smallpox killed 30% of those infected, on average. Smallpox involves sudden fever, malaise, headache, vomiting, and eruption of a deep-seated rash. The lesions of this rash contain live variola virus. The hemorrhagic and flat (confluent) forms of smallpox killed nearly all those who developed those forms. Survivors of smallpox can be severely scarred, especially on the face. Rarely, smallpox causes blindness.

(3) Transmission of Smallpox. Variola virus causes a strictly human disease that spreads naturally only from one person to another. There are no natural animal or insect reservoirs or vectors. The most common way of being infected with smallpox is to inhale the virus on droplets during face-to-face contact ($\leq$ 6 feet) with a contagious person. Direct contact with infected skin lesions would also transmit the virus. Indirect transmission, such as contact with inanimate objects (e.g., contaminated bed linens) carrying smallpox scabs, was uncommon. Deliberate transmission by aerosol may be possible.

c. Threat Assessment. Smallpox has been eradicated; the last natural case occurred in 1978. However, smallpox remains a biological threat, because of remaining viral stocks. Smallpox virus could be released in either military or civilian settings, or both. The appearance of one case of confirmed smallpox (other than an accidental exposure in one of the two internationally approved storage facilities) indicates probable use of smallpox as a

BW agent. Release of smallpox as a biological weapon constitutes an outbreak. The release could be from a point source or in a multifocal manner. The outbreak could begin with index cases in many locations within a nation or within multiple nations, resulting in a pandemic (a widespread epidemic).

(1) Smallpox Stocks. By international agreement, only two repositories are approved for stocks of smallpox virus, one at the CDC in Atlanta and one at the Research Institute for Viral Preparations in Moscow (later moved to the State Center for Virology and Biotechnology) in Koltsovo, Russia.

(2) The Soviet Union weaponized tons of smallpox viruses. Several countries are suspected of trying to develop smallpox as a biological weapon.

(3) Intentional release of smallpox (variola) virus as a bioweapon could result in widely dispersed smallpox cases. Disease could cross population lines, from military to civilian communities, and vice versa. Major disruptions in civil, political, medical, and economic order could follow.

d. Smallpox Vaccine. Historically, smallpox vaccine protected more than 95% of healthy people who received it. Studies published in 2002 by Frey and colleagues showed that ~98% of people who received either full strength Dryvax-brand smallpox vaccine or Dryvax diluted 1:5 developed the classic pox lesion at the vaccination site that signifies vaccine "take." Smallpox vaccine contains live vaccinia viruses, which evokes an immune response that protects against variola virus, the virus that causes smallpox. The WHO's use of smallpox vaccine was key to eradicating natural smallpox. Current supplies of smallpox vaccine are limited because production ceased in the early 1980's. Additional supplies of smallpox vaccine are being produced now, using more modern production methods.

(1) Adverse Reactions After Smallpox Vaccination. Like all vaccines, smallpox vaccine can cause rare but serious adverse reactions. However, smallpox vaccine causes an unusual set of potential adverse reactions, unlike other vaccines. These characteristics will warrant additional education, screening, and monitoring before, during, and after smallpox vaccination. For every 1,000,000 doses of smallpox vaccine given to previously unvaccinated adults, several serious adverse reactions can be expected, based on historical experience. The side-effect rates that follow are based on data collected in the United States during the 1960s, when about 300,000 adults got their first smallpox vaccination and over 4 million adults got repeat smallpox vaccinations (re-vaccinations).

(a) 600 cases of auto-inoculation (also called accidental infections, i.e., touching the vaccination site and then transferring vaccinia viruses to eyes, genitals, or other itchy body sites). Vaccinia virus can also spread to contacts of vaccine recipients by touch.

(b) 60 serious skin reactions (e.g., progressive vaccinia, eczema vaccinatum).

(c) 8 serious neurologic reactions (e.g., post-vaccinal encephalitis).

(d) 1 to 5 deaths due to vaccination reactions (usually due to progressive vaccinia, post-vaccinal encephalitis, or severe eczema vaccinatum).

(e) Treatment of patients with some of these disorders with an antibody preparation called vaccinia immune globulin (VIG) or an antiviral compound called cidofovir may be of value (Annex H).

(2) Groups Susceptible to Adverse Vaccine Reactions. Several groups of people are known to be more likely to develop the adverse reactions listed above than the general population, but the relative risk is unknown. During pre-outbreak vaccination programs, these people would generally receive a medical exemption from smallpox vaccination. During a smallpox outbreak, however, the benefit-risk balance would shift, and public-health authorities would recommend that many of these people be vaccinated (Annex B). Some of the clinical conditions warranting caution with smallpox vaccination include: atopic dermatitis (including history of it), other chronic skin conditions, altered immune states (e.g., AIDS, cancers), and pregnancy.

e. Friendly Forces. An integrated, effective response to a smallpox outbreak will require extensive coordination between diverse Federal agencies (e.g., DoD, DHHS, CDC, Federal Emergency Management Agency (FEMA), FBI), as well as state, territorial, and local public-health activities. DoD is unique in that it has both national healthcare policy responsibilities (similar to DHHS/CDC) and the equivalent of state and local healthcare delivery responsibilities. Thus, the DoD Smallpox Response Plan must outline the critical activities at the installation, regional, national, and international levels. The Department of Defense adopts the CDC Smallpox Response Plan as the foundation for DoD's response to a smallpox outbreak. This document provides specific detail for planning, implementation, and execution of military actions in response to an outbreak of smallpox in either US or overseas theaters of operation. The DoD response will be rapid, scalable, modular, and in support of the CDC Smallpox Response Plan.

f. Assumptions.

(1) If smallpox virus is intentionally released as a biological weapon, it will not have been genetically modified to evade protection offered by current or future smallpox vaccines.

(2) Global mixing of population. Assume uneven, but widespread, mixing of infected and uninfected personnel in and between the US and its allies during the early, uncontrolled phase of a smallpox outbreak via modern mass transportation systems.

(3) Given the 7- to 17-day (typically 12- to 14-day) incubation period between exposure and symptoms, generations of smallpox cases will arise at intervals of roughly 2 to 3 weeks. A smallpox outbreak could persist for months or years before public-health officials regain control over the disease. In other words, a smallpox outbreak would not spread peak over a few days (as inhalational anthrax cases might). Rather, smallpox cases would appear over the course of weeks, with the outbreak evolving over months.

(4) Routine vaccination of US military recruits against smallpox was intermittent after 1984 and discontinued in 1990. Routine vaccination of US civilians ceased in about 1972. Thus, susceptibility to smallpox is universal among children and young adults, and widespread among older adults.

(5) People vaccinated more than 10 years ago retain some partial immunity against smallpox (Mack, 1972), but they warrant revaccination to increase their immunity. Military personnel (now senior officers and senior NCOs) vaccinated in the 1980s have an estimated 7% chance of death, if infected with smallpox. Military personnel vaccinated in the 1970s would have an ~ 11% case-fatality rate. These rates are high enough to warrant re-vaccination to protect them.

(6) Response to the malicious release of variola virus may be required while military forces are simultaneously engaged in armed conflict.

g. Legal Considerations.

(1) Military commanders' actions regarding isolation or quarantine on a military installation of infected or possibly infected DoD and non-DoD personnel will be determined by the nature of the outbreak and the laws, regulations and policies concerning those specific types of situations, especially regarding people other than military personnel. Commanders must obtain legal and medical advice on individual situations from their legal and medical staffs. Local legal advice will reflect state law and coordination with civilian authorities.

(2) The Robert T. Stafford Disaster Relief and Emergency Assistance Act, P.L. 93-288, 42 USC 5121. Under the Stafford Act, a Governor may request that the President declare a major disaster or emergency if an event is beyond the combined response capabilities of the affected state, territorial, and local governments. Based on the severity and magnitude of the situation, the President may issue a major disaster or emergency declaration. Following a declaration, the President may direct any federal agency to use its authorities and resources in support of state and local assistance efforts. If an emergency involves an area or facility for which the federal government exercises exclusive or primary responsibility and authority, the President may unilaterally direct the provision of emergency assistance. The Governor of the affected State will be consulted if possible. Under the Stafford Act and DoD Directive 3025.1, commanders retain their "immediate response" authority.

(3) Law Enforcement. Under the Posse Comitatus Act (18 USC 1385 and other federal law, e.g., 10 USC chapter 18), and under DoD policy, military personnel in a Title 10 duty status (as distinguished from Title 32 National Guard duty status) generally may not participate in law-enforcement activities within the United States, except as otherwise authorized by statute or the Constitution. Consequently, military personnel acting under Title 10 shall not collect evidence; interrogate witnesses or suspects; engage in searches for or seizure of evidence; seize, arrest, or apprehend civilians; or otherwise operate as law-enforcement officers, unless specifically authorized by law. Law-enforcement assistance is

not ordinarily part of consequence-management operations. The National Guard, when performing state active duty under Title 32, is not bound by the prescriptions of the Posse Comitatus Act.

(4) Quarantine Enforcement. Title 42 United States Code section 97 (42 USC 97; Appendix A-5) authorizes military officers commanding any fort or station upon the seacoast to enforce quarantines or other restrains established by the health laws of any State respecting vessels and ports, and "all such officers of the United States shall faithfully aid in the execution of such quarantines and health laws, according to their respective powers and within their respective precincts, and as they shall be directed, from time to time, by the Secretary of Health and Human Services."

(5) Use of Weapons. Military personnel do not typically carry weapons when operating in a consequence-management role. If ordered, units may deploy to sites of BW attacks with their weapons in storage, in case the unit is subsequently authorized to carry arms by the Secretary of Defense or is deployed from the site to an assignment where weapons are authorized. The military on-scene commander is responsible to ensure that weapons and ammunition are adequately stored and physically secured at the site of the BW attack. In an emergency situation and then only when expressly authorized by the Secretary of Defense, in consultation with the Attorney General, units providing consequence-management support may be authorized to carry arms.

(6) Guidance on Intelligence Collection/Sharing. In a domestic consequence-management environment, DoD may have limited or no authority or responsibility for the collection of intelligence. In the context of a terrorist threat or acts of terrorism, the FBI, as the lead federal agency (LFA), has the overall responsibility for assembling, analyzing, and disseminating intelligence, whether of domestic or foreign origin, on the operating environment. Effective DoD consequence-management support will require obtaining information concerning the operational environment in which specific consequence-management tasks are to be conducted. Most of this information on the operational environment is unclassified data, available from open sources, passive observation, and liaison. DoD collects and shares information to support consequence-management operations in accordance with the Federal Response Plan (FRP).

2. Mission. DoD will immediately prepare to respond to a smallpox outbreak in accordance with this document. In case of smallpox outbreak, DoD will conduct response operations in accordance with this document to contain and halt the outbreak, preserve combat readiness, save lives, and prevent human suffering. When authorized by the Secretary of Defense, DoD will provide support to civil authorities in accordance with the Federal Response Plan.

3. Execution.

a. DoD Intent.

(1) General. US military forces must remain dominant across the full spectrum of military operations, able to engage adversaries in any theater concurrent with support to the civil authorities who will lead our national response to a smallpox outbreak. The desired end state for this military response will be achieved with the smallpox outbreak is contained, designated personnel have been vaccinated, and further consequence-management activities have transitioned to civil authorities.

(2) Response of US Military Forces. For a smallpox outbreak on a military installation, commanders will take immediate action to counter a biological attack under provisions of applicable laws and directives. For a smallpox outbreak outside a military installation, DoD support to civil authorities will follow DoD Directive 3025.15 (Appendix 2), and subparagraph (3) below. DoD will provide administrative and medical responses (e.g., a search-and-containment strategy), as well as minimizing operational impact through vaccination of targeted subpopulations (i.e., wide-area vaccination, Appendix 5). Wide-area vaccinations are more likely to be needed if a smallpox outbreak occurs while military forces are simultaneously engaged in armed conflict, to preclude restrictions of movement. DoD will act in support of the Federal Response Plan.

(3) Support to Civil Authorities. US military forces will support DoD-approved requests for military assistance and provide DoD capabilities to respond to the consequences of a consequence-management situation in the US, its territories, and possessions. While maintaining command and control of DoD assets, commanders will ensure close coordination with civil authorities and the effective use of military capabilities to satisfy validated requests. Local military commanders and responsible officials of the DoD components located in the vicinity of the smallpox outbreak may, upon a civilian request, execute an immediate response within their unit capability to save lives, prevent human suffering, and mitigate great property damage (see also Appendix 2).

(4) The operational priorities of search and containment will be:

(a) Intense medical surveillance for people manifesting fever and rash consistent with early smallpox symptoms.

(b) Timely identification and vaccination of appropriate contacts of potential smallpox cases.

(c) Delineation of functional or geographic boundaries around cases or outbreaks (i.e., wide-area vaccination).

(d) Appropriate isolation of potential smallpox cases.

(e) Identification of contacts of potential smallpox cases.

(f) Other steps appropriate to the situation, including restriction of movement and/or use of personal protective equipment.

(5) After an outbreak begins, the key to stopping the outbreak lies in vaccinating the right people (i.e., those who otherwise would spread the disease to others), rather than large numbers of people at random. Determining the "right" people will be a professional challenge. DoD will conduct wide-area vaccination when appropriate to maximize retention of military capabilities. Educating, isolating appropriate individuals after fever develops and providing appropriate personal protective equipment are other important tasks (Annex C).

b. Concept of Operations. A smallpox response operation will consist of six phases scoped by tasks to be accomplished. These phases, while generally sequential, may overlap in execution.

(1) Phase I. Deliberate Planning & Preparedness. Combatant commanders with responsibilities for conducting consequence-management operations in response to chemical, biological, radiological, nuclear, or high-yield explosive (CBRNE) incidents will initiate deliberate planning to support implementation of this Smallpox Response Plan. Most planning for implementation takes place at the installation and military treatment facility (MTF) level. Preparedness is the aggregate of all measures and policies taken before the event occurs, reducing the damage caused by the event. Preparedness relies upon deliberate planning activities. Preparedness involves ongoing medical surveillance for generalized febrile vesicular or pustular rash illness (GFVPRI, Annex A).

(2) Phase II. Situation Assessment & Notification. Phase II begins with the notification of a confirmed case of smallpox anywhere in the world. At that time, all military commanders and responsible officials of DoD are authorized to execute immediate response, within their capability and authority, to save lives, prevent human suffering, and limit spread of the disease on DoD installations and bases. In addition, upon a civilian request, execute an immediate response within their organic capability.

(3) Phase III. Consequence-Management Deployment. Phase III begins with the CJCS Deployment/Execute Order establishing formal command relationships, and directing deployment of forces. Phase III ends when identified forces have completed movement to the designated incident location.

(4) Phase IV. Military Consequence-Management Support. Phase IV begins with the arrival of smallpox response teams (e.g., epidemiological teams described in Annex A, specialized treatment teams described in Annex G and Annex H) at appropriate locations and ends with the determination that support is no longer required. As the scope and magnitude of any required support to civil authorities diminishes, DoD forces will coordinate with FEMA and the primary agencies under the FRP while planning for transition. Coordination will include the FEMA Disaster Field Office (DFO), Federal Coordinating Officer (FCO), and state-level DFOs.

(5) Phase V. Transition to Civilian Agencies. Although planning for transition of consequence management begins as soon as practical following the initial response, Phase V begins with formal implementation of the transition plan for those tasks and responsibilities being accomplished by US military forces to the appropriate civilian agencies.

(6) Phase VI. Redeployment. Phase VI begins with the redeployment of the US military forces involved in the smallpox consequence-management operation and is complete when identified forces have returned to their previous military postures. After completing the mission, after-action reports and lessons learned will be documented in the Joint Lessons Learned Program and as otherwise directed.

c. Tasks. Appendix 4 provides a summary of tasks specified in this plan and its accompanying planning guidance.

(1) Supporting Plans. Commanders will undertake appropriate medical-contingency planning to be able to detect smallpox cases and to prepare to implement post-outbreak measures described in this document. The Combatant Commands, Services, Directorate of Military Support (DOMS), and the Joint Task Force for Consequence Management (JTF-CM) will develop and exercise DoD-specific contingency plans for response to a smallpox outbreak, building on existing DoD medical command and control assets. DoD will coordinate with allies and coalition members on smallpox-response programs.

(2) Training. Commanders will schedule, conduct, and evaluate training to meet requirements of this document. The military medical departments will train health-care providers in smallpox surveillance and response.

(3) Smallpox Response Teams. The Services will develop, train, and exercise various smallpox response teams: epidemiologic teams (Annex A), IND support teams (Annex B), and specialized treatment teams (Annex G and Annex H).

(4) Medical Surveillance. Military Treatment Facility (MTF) commanders will institute surveillance for generalized (febrile) vesicular-pustular rash illness (Annex A). The military medical departments will enhance and improve detection and surveillance programs.

(5) Biological Detectors. Biological detectors have a limited capacity to identify orthopox viruses. These detectors are in short supply and do not render warnings quickly enough to allow donning of protective equipment before exposure to the virus (i.e., they aren’t quick enough to “detect to warn” locally). However, detection in one location may provide "early warning" at more distant locations in time to take preventive measures. Currently, the primary means of recognizing a smallpox outbreak will likely be the clinical diagnosis of smallpox. Earlier detection would require implementation of a near-real-time medical surveillance program monitoring patient symptoms and/or environmental sample testing. Preventive medicine teams should collaborate with any nearby reconnaissance or surveillance teams for sample collection of medical importance (i.e., food, water, soil) and referral testing.

d. Coordinating Instructions.

(1) Post-Outbreak Assessment. If a smallpox outbreak is confirmed anywhere around the world, commanders will be informed via command channels, augmented by

reports in the news media. Upon notification, military commanders will evaluate their installations and units, to determine the needed intensity of medical surveillance for smallpox cases among these personnel. First, the installations and units will be categorized as “distant” or “near” to the diagnosed case(s) of smallpox. The threshold between “distant” and “near” is 1-hour ground travel time or 1 air leg from the diagnosed case(s). Next, military commanders will determine the status of their forces as either Certainly Unexposed, Probably Unexposed, or Potentially Exposed (using definitions below). Leaders then report through higher headquarters for consolidation and subsequent reporting to the Command’s Smallpox Coordination Cell. To preserve the presumed safety and health of the unexposed population, commanders will restrict nonessential movement until this assessment is completed. See Appendix J-5 and Appendix J-6 for additional discussion of restriction of movement.

(a) “Area of Interest.” The area of interest for a command includes the population and territory within 1 hour ground travel distance of the installation or territory, as well as, all locations within a single leg of air transport for airports within 1 hour of the installation.

(b) “Distant.” An operational area is distant relative to a smallpox outbreak, if the commander’s area of interest does not yet have one or more confirmed cases of smallpox among the total population in that area (i.e., military, civilian, host nation).

(c) “Near.” An operational area is near a smallpox outbreak, if the commander’s area of interest does include one or more confirmed cases of smallpox among the total population in that area (i.e., military, civilian, host nation).

(d) Certainly Unexposed. People completely isolated from *any* external contact for 18 or more days before recognition of the smallpox outbreak; e.g., naval forces at sea for greater than 18 days.

(e) Probably Unexposed. People sufficiently isolated or distant that the commander finds it unlikely that any of the population will develop smallpox (e.g., military forces that have mixed only with populations distant from currently known cases of smallpox).

(f) Potentially Exposed. Groups of people who have mixed with populations “near” to currently known cases of smallpox. Enhance fever-rash medical surveillance among these groups. These people need to be interviewed as per contact-tracing procedures described in Annex A, to assess risk of exposure on an individual basis.

(2) Medical Planning & Response.

(a) IND Planning. Pre-outbreak planning focuses on obtaining sufficient smallpox vaccine to protect the Force and our beneficiaries. As of September 2002, the Food & Drug Administration (FDA) regulates the use of all available forms of smallpox vaccine as Investigational New Drugs (INDs). This situation may change in coming months. IND protocols require extensive education, documentation, and informed consent before

administration (Annex B). Distribution of smallpox vaccine and related materials will be coordinated by the US Army Medical Materiel Agency (Annex I).

(b) DoD Response Teams. As a smallpox outbreak develops, epidemiologic investigation teams (i.e., Epi-Teams, Annex A) to augment current capabilities at military treatment facilities (MTFs) will travel to the site(s) to confirm the diagnosis, trace contacts, and assist with local control measures. If needed, Epi-Teams will be supplemented with IND Support Teams (IND Teams, Annex B) and Specialized Treatment Teams (T-Teams) to augment local resources (Annex G and Annex H).

(c) Facilities. After outbreak confirmation, patient-care plans must address patient movement and evacuation requirements, decontamination, isolation, treatment, stress management, and pain management. As a smallpox outbreak expands, installation commanders will need to provide separate places to lodge and care for smallpox cases and their contacts, outside of hospitals, while taking preventive measures to contain the spread of infection. The CDC plan refers to these as Type C, X, and R facilities (Appendix C-4). Type C facilities are intended for people with contagious smallpox. Type X facilities are intended for people whose diagnosis is uncertain ("X" for unknown). Type R facilities are residences or similar facilities for people potentially exposed to smallpox while under fever surveillance. Education, training, and communications, before an outbreak, will be critical for a prompt, disciplined, and effective response.

(d) Vaccination Policy. DoD response teams will be vaccinated against smallpox, similar to preparations for CDC and state-level response teams. Civilian authorities are currently developing policies for offering pre-outbreak vaccination to health-care workers or the public. DoD's pre-outbreak smallpox vaccination policy is currently under development. If smallpox vaccine is administered under IND conditions, vaccination must be voluntary, with education, documentation, and informed consent. The only permissible exception would require the President of the United States to waive requirements for individual consent of Service Members under 10 USC 1107 and 21 CFR 50.23(d). The President may not waive requirements for education or documentation.

(e) Mental Health and Chaplain Services. Plan for mental health and chaplain services for emergency workers and their families, especially when these workers are deployed away from their home base. Plan for mental health and chaplain services for smallpox casualties, their contacts, and their families. Depending on the size of an outbreak, it may be appropriate for the installation community activities center to act as a family support center, in coordination with personnel from the American Red Cross, to assist the military family. Stress management teams will be used as appropriate.

(3) Force Protection. Commanders shall institute appropriate force protection measures, and coordinate with local law-enforcement officials to provide for the security of DoD personnel and equipment.

(a) Commanders whose units or installations qualify as "distant" from diagnosed smallpox cases will move to FPCON BRAVO or CHARLIE, based on specific

circumstances, and initiate the appropriate response measures, Annex A. Changes in Force Protection Condition will be determined locally or by other authority.

(b) Commanders whose units or installations qualify as “near” diagnosed smallpox case will move to FPCON CHARLIE, and initiate enhanced medical surveillance for unusual fever with rash (Annex A). Commanders may to distribute brochures (Appendix A-6) describing symptoms of generalized febrile vesicular or pustular rash illness (GFVPRI, Annex A) to all personnel entering the installation. Based on local conditions, Commanders may upgrade to FPCON DELTA. Changes in Force Protection Condition will be determined locally or by other authority.

(c) Smallpox transmission can be stopped by isolating people capable of infecting others. Isolate people with smallpox symptoms as soon as fever develops. But there is no infectious-disease value in isolating people who do not have symptoms. They are not contagious. While it may initially seem desirable to close installation gates to keep contagious people out, people exposed up to 18 days earlier may already be within the installation’s boundaries. As a result, restrictions imposed today will have little value until 2 or more weeks in the future. Restrictions rarely can be implemented stringently enough to be completely protective. Nonetheless, reducing the number of people visiting an installation may reduce the total number of person-to-person interactions, which may contribute to infection-control. Public-health workers will trace the contacts of smallpox cases, vaccinate them, and place them under fever surveillance. To limit the further spread of smallpox, encourage people to voluntarily limit their movements. See also Appendix J-5 and Appendix J-6.

(d) To manage large numbers of people arriving at vaccination sites, the main strategy of security personnel should be to secure a limited-access perimeter at a designated distance from the physical plant; and secure the clinic itself (interior perimeter, e.g., main and secondary entrances, front drive, parking area) and maintain order within the facility. To avoid disrupting operations at military hospitals and clinics, it may be appropriate to administer vaccinations at an alternate location (e.g., recreation center, school). Security personnel can adopt procedures by which people seeking medical care can identify themselves (e.g., signs requesting those with fever or contacts of smallpox patients to flash their cars’ hazard lights).

(e) Air Operations. In coordination with US Transportation Command (USTRANSCOM) and the Combatant Command(s), military air traffic between installations should be minimized upon notification of a confirmed case of smallpox, until the extent of the outbreak is determined and medical personnel can interview affected aircrew for presence of fever or rash, travel history and plans, and smallpox vaccination status (Annex A). Medical personnel will provide information to aircrew about personal protective equipment and other measures to reduce disease transmission. USTRANSCOM will coordinate with Combatant Commands for strategic-lift requirements, with appropriate priority given to DoD smallpox response requirements.

(4) Operational Constraints. The scope of the DoD smallpox response will depend upon the geographic distribution of smallpox cases.

(a) Intelligence. In a domestic consequence-management situation, DoD has little or no authority or responsibility for the collection of intelligence domestically. In the context of a terrorist threat or acts of terrorism, the FBI, as the lead federal agency for crisis management, has the overall responsibility for assembling, analyzing, and disseminating intelligence, whether of domestic or foreign origin, on the operating environment. However, appropriate DoD medical experts may be consulted for technical advice and support, including the Armed Forces Medical Intelligence Center (AFMIC).

(b) Media Impact. The media will play an important role in reporting and shaping public opinion concerning a smallpox outbreak and consequence-management response. Any DoD response must take into account media coverage. The lead federal agency (i.e., DOJ/FBI or FEMA) is the lead agency for public-affairs guidance under the Federal Response Plan. The interagency Joint Information Center (JIC), using health risk communication, will provide information to the media. The OASD(PA) is the point of contact for all media inquiries concerning DoD support. See Annex E.

(c) Medical. During a BW attack, medical and public-health needs will be significant factors. The National Disaster Medical System (NDMS), which includes DoD coordination of participating nonfederal-fixed hospitals and DoD-provided patient evacuation, is the primary federal-level medical-response element. Other DoD medical capabilities external to NDMS may be requested, if necessary to augment or sustain the NDMS/local response to save lives and minimize human suffering. The time-sensitive nature of such requirements requires early and rapid interagency coordination. Restrictions on the use of military medical stocks and on military personnel vaccinating civilians may need to be addressed in mission planning. DoD unit commanders, upon notification of deployment in support of the lead federal agency, will need to ensure full implementation of appropriate force health protection measures.

(d) Mortuary Affairs. Despite efforts to save lives and prevent injury, BW attacks may create mass fatalities. DoD may be requested to assist in mitigating the potential health risks posed by mass fatalities. See also Joint Publication 4-06, Joint Tactics, Techniques, and Procedures for Mortuary Affairs in Joint Operations, 28 August 1996 (www.dtic.mil/doctrine/jel/new_pubs/jp4_06.pdf).

(e) Domestic Transportation Assets. Transportation of DoD and other federal personnel and assets to a domestic BW attack will be critical to a successful response. DoD transportation assets are in high demand and require advanced planning. All transportation modes should be considered to support domestic consequence-management operations. Unlike overseas deployments, ground transportation is an option in a domestic situation. Under FRP Emergency Support Function (ESF) #1, Department of Transportation's Movement Coordination Center will coordinate deployment of federal resources, including DoD resources, to support consequence-management operations.

(f) Communications with Other Agencies. Planners should ensure interoperability with the interagency Joint Operations Center, as established by the lead federal agency (i.e., FBI), and take the potential requirement into account and ensure communications with all agencies are sufficient to accomplish the mission (Annex E).

(g) Noncombatant Evacuation Operations (NEO). Standard procedures for NEO operations will be followed. People evacuated may be isolated at port of entry (i.e., return to the United States), with appropriate attention to human needs, until interviews establish likelihood of exposure to smallpox (Annex A). If appropriate to the circumstances, evacuated people may be offered the choice of smallpox vaccination or isolation for 18 days, to prevent spread of disease within the United States. See also Joint Publication 3-07.5, Joint Tactics, Techniques, and Procedures for Noncombatant Evacuation Operations.

(5) Operational Security (OPSEC).

(a) Federal, state, territorial, and local agencies conduct consequence-management operations in an unclassified forum. To ensure consistency and expeditious flow of information, DoD will be an active participant in the unclassified forum. As required, commanders will develop Critical Information Lists (CIL) containing specific information requiring protection that relate to DoD deployments and consequence-management operations. Once the CIL is developed, the threat and our vulnerability to the threat are identified and analyzed; a risk assessment of potential exploitation is made; and countermeasures are developed and executed.

(b) Notification of Strategic Forces. If a smallpox outbreak is confirmed, the Joint Staff or Combatant Commanders will notify strategic forces, with instructions to preserve the unexposed status of unit personnel, using the highest levels of OPSEC available.

4. Administration and Logistics.

a. Medical Materiel. See Annex I.

b. Reports. See Annex A.

5. Command and Control. As a smallpox outbreak develops, the Combatant Commander responsible for conducting consequence-management operations (e.g., Northern Command for the United States) in response to CBRNE incidents may designate a Smallpox Coordination Cell to augment the usual crisis-action process. The Smallpox Coordination Cell will consist of medical, logistics, and other relevant subject-matter experts. The Smallpox Coordination Cell will receive reports of smallpox cases and provide advice for medical and logistical support. The Smallpox Coordination Cell will coordinate with smallpox-response staff at the Military Services, the CDC, and other agencies, synchronize information exchange for military chains of command, coordinate communication with local, state, territorial, national, and international public-health authorities, and coordinate activities of DoD smallpox response teams. For example, the Cell will coordinate with the Federal

Emergency Management Agency's Disaster Field Office (DFO), Federal Coordinating Officer (FCO), and state-level DFOs.

DoD APPENDIX 1
DoD Smallpox Response Plan – Summary.

1. Before a smallpox outbreak, DoD will develop, exercise and improve its smallpox response plans at command and installation levels.
   a. Installation commanders will identify:
      (1) Facilities other than normal hospital or clinic locations at which mass vaccinations can be effectively delivered (CDC Guide B, CDC Annex 2).
      (2) Facilities suitable for Type C, X, or R facilities (Annex C), including plans for laundry, food service, and medical waste disposal.
   b. Medical commanders will establish programs and policies to:
      (1) Train healthcare providers in smallpox recognition and response (Annex A, Annex B, Annex C, Annex D, Annex F, Annex G, Annex H).
      (2) Institute medical surveillance for general vesicular-pustular rash illness (Annex A).
      (3) Develop, exercise plans for active surveillance during an outbreak (Annex A). Set up triage clinics to evaluate people concerned they may have early smallpox.
      (4) Train and exercise response teams (Annex A, Annex B, Annex G, Annex H).
      (5) Maintain a supply of shipping materials for smallpox-infected specimens.
      (6) Report cases of fever-rash illness (defined in Annex A) via reportable-disease chain, as Serious Incident Report, to CDC, and to state or host nation.
2. Once a smallpox outbreak is confirmed:
   a. Military commanders will evaluate their installations as “distant” or “near” to the diagnosed case(s) of smallpox. The threshold between “distant” and “near” is 1-hour ground travel time or 1 air leg from the diagnosed case(s).
   b. Military commanders will next evaluate their units as:
      (1) Certainly Unexposed (isolated for previous $\geq$ 18 days, e.g., naval forces at sea).
      (2) Probably Unexposed. People sufficiently isolated or distant so exposure unlikely.
      (3) Potentially Exposed. Groups of people who mixed with other known “near” cases. Do fever-rash surveillance and contact tracing to assess individual risk (Annex A).
   c. Aircrew: Minimize military air traffic between installations upon confirmation of a case of smallpox, until extent of outbreak is determined and medical personnel can interview affected aircrew regarding fever, rash, travel, and vaccination (Annex A).
   d. Military Treatment Facility commanders will:
      (1) Conduct active surveillance to identify other potential smallpox cases (Annex A), augmented with epidemiologic teams (Epi-Teams).
      (2) Isolate potential cases during evaluation, to reduce spread (Annex C).
      (3) Identify contacts of potential cases (Annex A).
      (4) Vaccinate contacts and their contacts (Annex B) and monitor fever (Annex C).
      (5) Vaccinate non-contact high-risk personnel (Annex B).
      (6) Care for smallpox patients (Annex G), with treatment teams (T-Teams).
      (7) Care for people who develop adverse reactions after vaccination (Annex H).
   e. Military commanders will communicate with their communities (Annex E).
3. As a smallpox outbreak develops, Combatant Commanders may designate one or more Smallpox Coordination Cells to coordinate the DoD response and provide a focal liaison with CDC smallpox response coordinators.

DoD APPENDIX 2
Military Assistance to Civil Authorities.

DoD Directive 3025.15, Military Assistance to Civil Authorities, dated 18 February 1997 (http://www.dtic.mil/whs/directives/corres/pdf/d302515_021897/d302515p.pdf), governs military assistance during times of civil emergency. It states that the "Department of Defense shall cooperate with and provide military assistance to civil authorities as directed by and consistent with applicable law, Presidential Directives, Executive Orders, and this Directive."

DoD Directive 3025.15 also states "All requests by civil authorities for DoD military assistance shall be evaluated by DoD approval authorities." The directive designates the Secretary of the Army as the "approval authority for emergency support in response to natural or man-made disasters…." The Secretary of the Army exercises this responsibility through the Directorate of Military Support (DOMS).

"Requests for immediate assistance (i.e., any form of immediate action taken by a DoD Component or military commander to save lives, prevent human suffering, or mitigate great property damage under imminently serous conditions) may be made to an Component or Command. The DoD Components that receive verbal requests from civil authorities for support in an exigent emergency may initiate informal planning and, if required, immediately responds as authorized in DoD Directive 3025.1 (reference (g))."

DoD APPENDIX 3
Information Paper on Smallpox Infection and Smallpox Vaccine.

1. Smallpox. Smallpox is a contagious viral disease that spreads from one person to another. Smallpox usually spreads by exhaled droplets at close contact, usually face-to-face (≤ 6 feet) or household contact. Smallpox symptoms (e.g., high fever, fatigue, headache, backache) begin 7 to 17 days (typically 12 to 14 days) after exposure. A characteristic rash follows in 2 to 3 days. See Appendix G-2 for a timeline from date of exposure or onset of symptoms. Smallpox kills about 30% of those infected. Survivors are often permanently scarred or, rarely, blinded. Animals and insects do not harbor nor transmit smallpox (i.e., act as reservoirs or carriers).

2. Controlling Transmission. To stop smallpox transmission, isolate people capable of infecting others. The two most important ways to stop the spread of smallpox are (a) early diagnosis and (b) cooperating with workers tracing the contacts of smallpox cases. Isolate people with smallpox symptoms as soon as fever develops. But there is no infectious-disease value in isolating people who do not have symptoms. They are not contagious. While it may initially seem desirable to close installation gates to keep contagious people out, people exposed up to 18 days earlier may already be within the installation's boundaries. As a result, restrictions imposed today will have little value until 2 or more weeks in the future. Restrictions rarely can be implemented stringently enough to be completely protective. Public-health workers will trace the contacts of smallpox cases, vaccinate them, and place them under fever surveillance. Limit installation access, but do not expect gates and fences to keep viruses outside. To limit spread of smallpox, encourage people to voluntarily limit their movements. See Appendix J-5 and Appendix J-6.

3. Contacts Defined. Face-to-face contact with a suspected, probable, or confirmed case of smallpox. Risk increases with close contact (< 6 feet), increasing time of exposure (e.g., > 1 hour), and presence of rash or cough. Consider cases potentially contagious from date of onset of fever > 101.0°F (38.3°C). Cases will infect about half of their household contacts. On average, each case is likely to infect 1 to 10 people.

4. Smallpox Vaccine. Smallpox vaccine protects more than 95% of healthy people who receive it. Smallpox vaccine contains live vaccinia viruses, which cross-protect against variola virus, the virus that causes smallpox. Unfortunately, smallpox vaccine causes rare, but serious adverse reactions after vaccination. Current supplies of smallpox vaccine are limited because production ceased in the early 1980's. Additional supplies of smallpox vaccines are being produced now, using purer, more modern production methods. While smallpox vaccine is very effective, personal protective equipment will be used to augment protection for the individual worker.

5. Cautions Before Vaccination. Some people are more likely to develop adverse vaccine reactions. During pre-outbreak vaccination, the following diseases would bar (contraindicate) smallpox vaccination: atopic dermatitis (and history of it), other chronic skin conditions, altered immune states (e.g., AIDS, cancers), and pregnancy. During a smallpox outbreak,

however, the benefit-risk balance would shift, and public-health authorities would recommend that many of these people be vaccinated (see also Annex B). In post-outbreak situations, household members of contacts with these bars should either be vaccinated or isolate themselves away from vaccinated household members until the vaccination site heals.

DoD APPENDIX 4
Summary of Specified Tasks.

1. Installation And Unit Commanders.

a. Pre-Outbreak.

(1) Initiate deliberate planning for implementation of the DoD Smallpox Response Plan. Plan, paragraph (para) 3b(1)(a).

(2) Schedule, conduct and evaluate training for smallpox response. Plan, para 3c(2).

(3) Identify facilities other than normal hospital or clinic locations at which mass vaccinations can be effectively delivered. Plan, Appendix 1, para 1a(1).

(4) Identify facilities suitable for Type C, X, or R facilities, including plans for laundry, food service, and medical waste disposal. Plan, Appendix 1, para 1a(2).

b. Post-Outbreak.

(1) Implement post-outbreak control measures. Plan, para 3c(1).

(2) Perform post-outbreak assessment of forces, then report to higher headquarters. Plan, para 3d(1).

(3) Coordinate with civil authorities for effective use of military capabilities. Plan, para 3a(2).

(4) Coordinate with law-enforcement officials to provide security of DoD personnel and equipment. Plan, para 3d(2).

2. Military Treatment Facility (MTF) Commanders.

a. Pre-Outbreak.

(1) Initiate deliberate planning for implementation of the DoD Smallpox Response Plan. Plan, para 3b(1)(a).

(2) Undertake appropriate planning and education to detect smallpox cases. Plan, para 3c(1).

(3) Provide for education of primary-care providers, regarding recognition of adverse events after smallpox vaccination. Annex B, para 2b(3)(g)(i).

(4) Identify facilities other than normal hospital or clinic locations at which mass vaccinations can be effectively delivered. Plan, Appendix 1, para 1a(1).

(5) Identify facilities suitable for Type C, X, or R facilities, including plans for laundry, food service, and medical waste disposal. Plan, Appendix 1, para 1a(2).

(6) Identify Airborne Infectious Isolation Rooms. Annex C, para 3c(3).

(7) Consult with industrial hygiene and facilities management personnel regarding HVAC systems. Annex C, para 3c(4).

(8) Provide for smallpox specimen-collection team. Annex D, para 2b(1)(b). Maintain smallpox specimen collection kit. Annex D, para 3a.

(9) Develop procedures for emergency credentialing of healthcare workers to assist with outbreaks. Annex G, para 1c(6).

(10) Develop/enhance Respiratory Protection Program. Annex C, para 4b(1).

(11) Refine plans for providing Personal Protective Equipment. Annex C, para 3e(4)(a).

(12) Coordinate security requirements. Annex C, para 4b(4).

(13) Identify sources for increased requirements of medical supplies. Annex C, para 6a(3).

b. Post-Outbreak.

(1) Promptly report cases of GFVPRI. Annex A, para 3a(2).

(2) Designate vaccination coordinator responsible for vaccine administration. Annex B, para 2b(3)(a).

(3) Set up triage clinics to evaluate people concerned they may have early symptoms of smallpox. Plan, Appendix 1, para 1b(3).

(4) Coordinate with local health departments to provide for contact tracing of civilians who are not DoD beneficiaries. Annex A, para 3a(7).

(5) Establish an appropriate procedure for notifying and obtaining access to contacts. Annex A, para 6b(2)(g)

3. Vaccination Site Coordinators.

a. Institute prevaccination screening to identify contraindications. Annex B, para 2b(3)(b).

b. Provide verbal and written counseling to vaccine recipients before vaccination. Annex B, para 2b(3)(h)(ii).

c. Administer smallpox vaccinations. Annex B, para 1a.

d. Document vaccinations in electronic Immunization Tracking System. Annex B, para 2b(3)(e)(i).

e. Report daily smallpox vaccinations to higher headquarters and to CDC reporting system. Annex B, para 2c(1).

4. Military Medical Departments.

a. Pre-Outbreak.

(1) Train healthcare providers in smallpox recognition, surveillance and response. Plan, para 3c(2).

(2) Institute surveillance for generalized vesicular-pustular rash illness. Plan, para 3c(4). Plan, Appendix 1, para 1b(2).

(3) Develop and exercise plans for active surveillance during an outbreak. Plan, Appendix 1, para 1b(3).

(4) Train and exercise response teams. Plan, Appendix 1, para 1b(4).

b. Post-Outbreak.

(1) Promptly report cases of GFVPRI. Plan, Appendix 1, para 1b(6).

(2) Be prepared to augment clinical staff of any hospital or clinic overwhelmed with smallpox patients. Annex G, para 1c(5).

(3) Manage adverse-event programs after vaccinations, including detailed adverse event reporting. Annex B, para 1a.

(4) Each MTF will periodically train laboratory staff in collection, handling, and shipping smallpox specimens. Annex D, Appendix D-1, para 2.

(5) The MTF will provide training on workplace hazards and the emergency preparedness plan. Annex F, para 2c(6).

(6) Provide administrative support for IND protocol implementation. Annex G, para 4a.

5. Combatant Commanders.

a. Pre-Outbreak. Develop and exercise DoD-specific contingency plans for response to a smallpox attack. Plan, para 3c(1).

b. Post-Outbreak.

(1) Receive reports of smallpox cases and coordinate logistical efforts. Plan, para 3b(2).

(2) Coordinate with smallpox-response staff at CDC and other agencies, synchronize information exchange for military chains of command. Plan, para 3b(2).

(3) Coordinate communications with local, state, territorial, national and international public health authorities. Plan, para 3b(2).

(4) Coordinate activities of DoD smallpox response teams. Plan, para 3b(2).

6. Military Services.

a. Pre-Outbreak

(1) Develop, train, and exercise various smallpox response teams. Plan, para 3c(3).

(2) Identify, train, prepare, and equip at least two rapidly deployable Smallpox Epi-Teams. Annex A, para 6c(2)(c).

b. Post-Outbreak. Establish medical surveillance for GFVPRI through existing disease-reporting channels. Annex A, para 3a(2).

7. Office of the Secretary of Defense.

a. Pre-Outbreak.

b. Post-Outbreak.

(1) Approve requests for military assistance to Civil Authorities. Plan, para 3a(3).

(2) Authorize DoD forces to provide civil support IAW Federal Response Plan. Plan, para 2.

(3) Collect and share information to support consequence-management operations IAW Federal Response Plan. Plan, para 1d(5).

DoD APPENDIX 5

Public-Health Actions to Limit Spread of Smallpox.

	Value of Smallpox Vaccine	Contagious Period	Medical Surveillance	Isolation to Prevent Spread	Isolate Until … (see Appendix C-10)
Cases: People infected with smallpox	None after disease develops. Consider cidofovir to treat.	From fever to scab separation.	Ask about contacts.	Yes. Hospital or type C facility (Appendix C-4).	… all scabs fall off.
Suspected case	Only if symptoms not due to smallpox.	If smallpox, from onset of fever > 101°F (38.3°C).	Ask about contacts.	Yes. Hospital or type C facility.	… diagnosis established.
Contact: Fever, no rash	Only if symptoms not due to smallpox, and then only within 4 days of exposure.	If smallpox, from onset of fever > 101°F (38.3°C).	Ask about contacts.	Yes, type C or type X facility.	… smallpox diagnosed, or 18 days after last contact with case, or 14 days after successful vaccination.
Contact: Rash, no fever	Only if symptoms not due to smallpox, and then only within 4 days of exposure.	If smallpox, from onset of fever > 101°F (38.3°C).	Twice-a-day temp, daily telephone contact.	Yes, type C or type X facility.	… 18 days after last contact with case, or 14 days after successful vaccination.
Contact: No rash, no fever	Perhaps, best within 4 days of exposure.	n/a	Twice-a-day temp, daily telephone contact.	Home (type R) with daily telephone contact. Daily activities within ~ 20 mi of home.	… 18 days after last contact with case, or 14 days after successful vaccination.
Contacts of contacts	Yes. If vaccine barred, isolate away from contact until contact isolation ends or vaccine scab separates (14 to 21 days).	n/a	Twice-a-day temp, daily telephone contact.	Home (type R) with daily telephone contact. Daily activities within ~ 20 mi of home.	… 18 days after last contact with contact, or 14 days after successful vaccination.
No known contact -- "near"	Yes, if within 4 days after exposure, with usual cautions.	n/a	Active search for fever > 101°F (38.3°C).	Avoid unvaccinated people.	Free movement 7 to 14 days after successful vaccination.
No known contact -- "distant"	Yes, with usual cautions.	n/a	Active search for GFVPRI.	Limit contact with unvaccinated people.	Free movement 6 to 8 days after successful vaccination.

Definitions

Contact – Prolonged face-to-face contact. Risk increases with close contact (< 6 feet), increasing time of exposure (e.g., > 3 h), and presence of rash or cough.

"Near" if one or more confirmed cases of smallpox among the population within 1-hour ground travel or 1 air leg.

"Distant" if no confirmed cases of smallpox among the population within 1-hour ground travel or 1 air leg.

Type C facility - (C for confirmed) Mode of shelter and care for people diagnosed with smallpox.

Type X facility - (X for Uncertain) Mode of shelter for medical surveillance of contacts of smallpox cases with fever, but without symptoms of smallpox.

Type R facility - Residential mode of housing for surveillance of vaccinated contacts of smallpox cases.

ANNEX A TO SMALLPOX RESPONSE PLAN 29 September 2002
SURVEILLANCE, CONTACT TRACING, AND EPIDEMIOLOGIC INVESTIGATION.

REFERENCES.

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http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideA/Guide-A.doc.

b. CDC Smallpox Response Plan, Annex 5, Suggested Pre-Event Activities for State & Local Health Authorities, 23 September 2002.
http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-5.doc.

c. CDC Smallpox Response Plan, Annex 8, Checklists for State/Local/CDC Personnel Actions in a Smallpox Emergency, 23 September 2002.
http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-8.doc.

d. Department of Defense. Triservice Reportable Events Guidelines & Case Definitions, version 1.0. Washington, DC, July 1998.
http://amsa.army.mil/documents/DoD_PDFs/Jul98TriServREGuide.pdf.

1. General. This DoD Annex augments CDC Guide A. Appendix A-1 summarizes CDC Guide A and this DoD Annex on one page.

2. Mission. DoD personnel will conduct surveillance, contact tracing, and epidemiologic investigations of smallpox outbreaks that affect DoD units and installations, anywhere in the world. For outbreaks that span the borders between federal and local property or territory, DoD personnel will support and assist disease-control efforts, taking advantage of the resources in references a and b. On order, DoD personnel will provide support to civil authorities.

3. Pre-outbreak Rash Medical Surveillance.

a. Generalized Febrile Vesicular-Pustular Rash Illness (GFVPRI).

(1) GFVPRI is submitted for addition to the Tri-Service Reportable Medical Event List (reference c).

(2) The Services and the Joint Staff will establish medical surveillance for GFVPRI through existing disease-reporting channels. Military treatment facilities (MTFs), both hospitals and clinics, will use ICD9 code 057.9 (viral exanthem unspecified) to report GFVPRI and generalized vesicular-pustular rash illness (GVPRI) patient encounters in automated data systems, unless a more specific ICD9 code is appropriate clinically. Surveillance systems currently operated by the military track health-care visits related to

potential bioterrorist agents through the Ambulatory Data Set (ADS) (e.g., Electronic Surveillance System for the Early Notification of Community Based Epidemics, ESSENCE). This medical surveillance can detect simultaneous outbreaks at different locations, so it is important that MTF staff enter ADS information precisely and promptly.

(3) Each military treatment facility (MTF) will periodically train its staff in the clinical recognition of GFVPRI and smallpox, and the application of the CDC GVPRI protocol for evaluating patients for smallpox (including how to differentiate smallpox from chickenpox). Such training programs can focus on documents listed in Appendix B-5.

(4) Each MTF will post the CDC "Generalized Vesicular or Pustular Rash Illness Protocol" Poster [www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-4-rash-color.pdf or .ppt] in appropriate locations, adding specific MTF telephone numbers for reporting a suspicious case.

(5) Within an MTF, any illness consistent with GFVPRI will be evaluated per CDC guidelines and GVPRI protocol (see references a and b). MTFs will develop internal procedures for notification of the preventive-medicine or public-health service, infection-control service, dermatology service, and the command group regarding patients with GFVPRI. DoD medical personnel will expeditiously seek specialist consultation for assistance with diagnosis of smallpox cases. Telemedicine capabilities will be useful for remote consultations.

(6) Consultation will require dermatology and/or infectious disease specialists. Additionally, laboratory testing of specimens will likely be required in the early stages of a smallpox outbreak (Annex D). Because these assets are not readily available, obtain assistance via CDC. As explained in Annex D, CDC will coordinate with the US Army Medical Research Institute of Infectious Diseases (USAMRIID) and the Laboratory Response Network for the appropriate laboratory asset to support. Overseas units will receive support through military channels.

(7) If a smallpox case is recognized within an MTF, secure the entrances and exits of the affected unit, until a roster of names, addresses, and telephone numbers can be created of all people present, including degree of exposure (e.g., face-to-face contact) with the suspected smallpox case (CDC Form 8). After this roster is completed, these people may be released, with instructions that they will be contacted by preventive-medicine or public-health personnel about the possible need for smallpox vaccination within the next few days. Advise these people not to travel more than 20 miles from their city of residence. In the case of an individual considered likely to flee and be uncooperative regarding medical follow-up, seek legal counsel and consider possible individual detention. When communicating this request, use someone skilled in health risk communication. There is little need to close installation gates, unless this effort would be useful to find named face-to-face contact(s) ($\leq$ 6 feet) of a suspected smallpox case. The MTF should then prepare to isolate the case (Appendix C-4) and initiate

contact tracing (Appendix A-3). MTFs will coordinate with local health departments to provide for contact tracing of civilians who are not DoD beneficiaries.

b. Reporting a Suspected Case of Smallpox.

(1) In the civilian sector, CDC requires immediate reporting of a suspected case of smallpox. DoD activities will comply with similar requirements, in the following sequence:

(a) MTF personnel will use the CDC GVPRI protocol to evaluate unusual clinical cases, synchronizing medical and infection-control expertise with the command group.

(b) After ruling out more plausible explanations, submit GFVPRI report immediately through established Service disease-reporting systems (Appendix A-2), regardless of time of day. These reporting systems typically begin with the local preventive-medicine or public-health service.

(c) Also submit Serious Incident Report (SIR) to higher military headquarters (i.e., operational forces command communications channels), regardless of time of day. Operational forces command communications will be the primary/only means of reporting in certain situations (e.g., deployed forces).

(d) Also notify CDC Emergency Preparedness & Response Branch, 770-488-7100, if within the United States, its possessions, or its territories.

(e) Also notify State Health Department (see http://www.cdc.gov/other.htm#states), as applicable.

(f) Also notify other appropriate authorities (e.g., local health department; host nation public-health authorities), as applicable.

(2) As a smallpox outbreak develops, the Combatant Commander with responsibility for conducting consequence-management operations (e.g., Northern Command for the United States) in response to CBRNE incidents may designate a Smallpox Coordination Cell to augment the usual crisis-action process. Specific instructions to clarify and focus reporting expectations and requirements across the global Military Health System (MHS) will be issued according to the specific circumstances encountered. The Smallpox Coordination Cell will:

(a) Consist of medical, logistics, and other relevant subject-matter experts.

(b) Coordinate smallpox response efforts for that Unified Command.

(c) Receive reports of smallpox cases and advise on medical and logistical support.

(d) Coordinate with smallpox-response staff at the Military Services, the CDC and other agencies. For example, the Cell will coordinate with the Federal Emergency Management Agency's Disaster Field Office (DFO), Federal Coordinating Officer (FCO), and State-level DFOs.

(e) Arrange headquarters-level consultations with designated military preventive-medicine and infectious-disease subject matter experts.

(f) Synchronize information exchange for military chains of command.

(g) Coordinate communication with local, state, national, and international public-health authorities.

(h) Coordinate activities of DoD smallpox response teams.

(i) Coordinate with Disaster Medical Assistance Teams.

4. Smallpox Clinical Presentations and Differential Diagnosis. See Appendix A-7.

5. Smallpox Case Definitions and Case Classification.

a. DoD adopts CDC definitions and classifications without change, to assure DoD consistency with CDC (Appendix A-8, Appendix A-12).

b. Case definitions are likely to change with time, especially as an outbreak develops. Such change is consistent with good public-health practice. DoD will follow evolving CDC guidance to assure currency, quality, and compatibility.

c. Case classification as confirmed, probable, or suspected carry national, international, and military implications.

(1) DoD headquarters will exert no effort to constrain reporting by local military clinicians or MTFs. Nonetheless, it is prudent to assure that the clinician and the MTF coordinate and consult with DoD subject-matter experts ***before*** independently reporting the possibility of a case outside of professional channels. Subject-matter experts include: Infectious-disease (ID) physicians, dermatologists, preventive-medicine (PM) centers (i.e., USACHPPM, NEPMU), or members of Smallpox Epidemiologic Response Teams (i.e., smallpox-specific "Epi-Teams"). The contradictory needs for timely diagnosis and minimizing false-positive alerts must be balanced.

(2) MTFs may initially classify a potential case as suspected or probable. Classification of a first case in a geographic area as "confirmed" requires consultation with DoD and/or CDC infectious disease experts (e.g., DoD or CDC smallpox Epi-Team), including laboratory confirmation. Outside the United States, host nation and/or WHO experts may provide confirmation.

(3) ICD9 code 050 (smallpox) or 050.0 (variola major) will be used to report smallpox cases in automated data systems, unless another ICD9 code is more appropriate clinically.

6. Post-Outbreak Response — Epidemiological Investigation.

a. Concept of Operations.

(1) Upon recognition of any probable or confirmed case of smallpox, established with expert consultation, initiate a case investigation immediately. Coordinate investigation with local officials, seeking expert consultation as needed. A case investigation may also be initiated for suspected cases (in conjunction with expert consultation), depending upon probability of smallpox diagnosis and level of suspected threat.

(2) Local or regional medical personnel will complete most case investigations (e.g., community health nurses). Regional preventive-medicine or public-health personnel, MTFs, and DoD Smallpox Epi-Teams will provide consultative and logistical support.

(3) Case investigations (as detailed in Appendix A-3 and Appendix A-13) will serve to establish smallpox diagnoses, identify contacts of the case for vaccination and medical surveillance, identify the most likely source of infection, monitor outcomes, and conduct epidemiologic analysis.

b. Case Investigations.

(1) Establish the diagnosis (if not already confirmed). Responders will begin case investigations by establishing (confirming) the diagnosis.

(a) Case investigations can be initiated for cases based on clinical presentation. However, obtain consultation from infectious-disease physicians, dermatologists, preventive-medicine physicians, CDC experts, or other subject-matter experts.

(b) Refer to Annex D for disposition of clinical specimens for laboratory confirmation.

(2) Identify Close Contacts. Once a suspected, probable, or confirmed case is identified, the highest priorities are to reduce risk of transmission by (a) promptly identifying, placing under fever surveillance, and vaccinating close contacts of cases and (b) isolating the cases.

(a) Begin contact tracing within hours of identifying a case of smallpox. Conduct contact tracing as detailed in Appendix A-3 and Appendix A-13.

(b) All individuals conducting case interviews should be vaccinated before initiating their first face-to-face interviews with suspected, probable, or confirmed smallpox cases or contacts. Personal protective equipment will provide an additional layer of protection (Annex C).

(c) There are significant ethical issues in asking unvaccinated personnel to conduct interviews with smallpox cases or their contacts. In the absence of force-wide vaccination, consider these options for initiating case investigations before arrival of a smallpox Epi-Team. Personal protective equipment is especially important until vaccine becomes available (Annex C).

(i) In the United States, use vaccinated state or county response personnel for case investigation.

(ii) Designate a small number of local or regional personnel (worldwide) for initiating the case investigation (e.g., EPMU-7 personnel for Southern Italy). These case investigators would need pre-outbreak vaccination and initial training.

(iii) Designate one or more smallpox responders at each major MTF. These case investigators would need pre-outbreak vaccination and initial training.

(iv) Use vaccinated CDC/WHO response teams, if available.

(v) Use volunteer interviewers who understand the risks and who agree to be vaccinated as rapidly as possible, ideally within 3 days of exposure, if smallpox is not ruled out. Preference may be given to people vaccinated against smallpox in the past, as they may respond to repeat vaccination more quickly. Examples include health-care providers already in contact with the case or other unvaccinated personnel. These people should use personal protective equipment, as discussed in Annex C.

(d) DoD adopts all CDC Forms (Appendix A-14) for use in case investigations, including expected revisions issued by CDC, to promote interoperability between DoD and civilian agencies.

(e) Certain military-specific demographic information may be useful to simplify location of contacts. Specific items may include, but are not limited to: Social Security numbers with family-member prefix (FMP), personal Social Security number, military unit name, military service, and personnel status (e.g., active-duty, Reserve/Guard, retiree, family member). Other data fields that may be useful include unit identification codes (UICs), reporting unit codes (RUCs), installation name, APO or FPO address, DSN telephone number, immediate supervisor, and commanding officer. These items may be added as “write-ins” on the existing CDC Forms. In addition to Appendix A-14, forms may be obtained via Internet at http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/index.asp. Forms 1A, 1B, 8, 9, 10-1 and 10-2 are provided with DoD overlays to collect Service-specific information. Once

CDC finalizes its current form-redesign program, DoD will modify the CDC Forms to add the DoD-specific fields on readily distributable templates. MTFs will coordinate with local health departments to provide for contact tracing of civilians who are not DoD beneficiaries.

(f) Under CDC guidance, people performing case interviews and follow-up will assign each case and each contact a specific case/contact identification number. Cases and contacts will be differentiated based on state. DoD will adopt a case/contact identification system to avoid duplicate case-identification numbers. The numbering system will include two parts, a prefix and a suffix. The prefix will be the 5-digit zip code of the installation conducting the contact tracing. The suffix will be a serial number.

(g) MTFs will establish an appropriate procedure for notifying and obtaining access to contacts. For example, a case investigator could notify the installation or unit commander, or the case investigator would notify local medical personnel who make appropriate linkages.

(h) Contacts of smallpox cases should be vaccinated and/or isolated, as per guidance in Annex B and Annex C.

(3) Identify most likely source of initial exposure.

(a) Attempt to complete this step within 24 hours.

(b) Provide timely notification of where initial exposure or virus release may have occurred to appropriate authorities (e.g., commander of installation, Service medical operations center, local or nearest MTF).

(4) Identify or estimate the population at risk, as described in reference a. Be especially aware of close contact conditions typical in military communities (e.g., recruit barracks, shipboard, group dining facility).

(5) Compare epidemiologic features of outbreak with expected features of smallpox and varicella (chickenpox) (Appendix A-7, Appendix A-9). Identify unexpected epidemiologic features of the outbreak.

(a) Note health status and vaccination status of affected population.

(b) With an intentional release of smallpox as a terrorist event or as part of a military conflict, MTFs will report any unexpected or unusual presentation, morbidity, mortality, incubation period, or transmission to higher medical headquarters.

(6) Develop effective containment strategies, by evaluating the characteristics and extent of the outbreak.

(a) Control methods may include installation closure, isolation of personnel, restriction of travel, ban on use of large transport vehicles (e.g., buses, airplanes), closure of crowded central facilities (e.g., gym, dining facilities, shopping center).

Note: Installation closures and restrictions of movement have limited value, because the installation may already harbor people incubating a smallpox infection but who do not yet manifest symptoms. See the DoD Smallpox Response Plan and Annex C for additional considerations for restriction of movement.

(b) Installation and unit smallpox response plans will include methods for notifying security personnel for assistance with implementing control measures.

c. Levels of Response. Responses to a smallpox outbreak will be delivered in three levels of response: Local, Regional, and Global. Responsibilities and actions for each level are delineated below.

(1) Local Response.

(a) Local commands and/or operational units will maintain primary responsibility for conducting case investigations. Installation commanders or operational commanders (e.g., joint task force commander) will be responsible for rapid execution of smallpox response plans. Local responders will be responsible primarily for establishing the diagnosis, contact identification and tracing, and identification of the source of infection.

(b) Immediate reporting of suspected, probable, or confirmed cases via established Service disease-reporting systems and Serious Incident Reports (SIRs) to higher military headquarters are required. In addition, US facilities will promptly notify local and state health departments. Overseas facilities will promptly notify the appropriate host-nation health authority.

(c) Smallpox Response Coordinator. Local commands will identify a Smallpox Response Coordinator, to function as the local coordinator for case investigations. This coordinator will also serve as a liaison between the local command, local response personnel, Smallpox Epi-Teams, and DoD and civilian authorities.

(d) Because external support (e.g., Smallpox Epi-Teams) may not arrive on-site for 24 to 48 hours or longer, local personnel and resources will be required to initiate case investigations.

(e) Case investigators will report all findings to Smallpox Epi-Teams once they arrive. Smallpox Epi-Teams will be attached under the operational control (OPCON) of the Joint Task Force, Combatant Command, or installation commander, as applicable, who may delegate OPCON to subordinate commanders. The Epi-Teams will communicate with the local senior military medical authority and higher medical headquarters without restriction.

(2) Regional Response.

(a) Regional Smallpox Epidemiologic Response Teams (Smallpox Epi-Teams), MTFs, and preventive-medicine centers (e.g., NEPMU, CHPPM) will provide consultative and logistical support to local event responders. Within the US, consultative and logistical support may also be obtained from CDC and the state health department.

(b) Regional responders will provide key support for identifying the population at risk, identifying unexpected epidemiologic features, and developing containment and control strategies.

(c) Smallpox Epidemiologic Response Teams (Smallpox Epi-Teams). Each Service will identify, train, prepare, and equip at least two rapidly deployable Smallpox Epi-Teams. Proposed capabilities and composition of Epi-Teams is detailed in Appendix A-4 of this DoD Annex.

(i) All Smallpox Epi-Team members will be vaccinated before conducting face-to-face case interviews, contact tracing, or handling specimens (Annex B).

(ii) Smallpox Epi-Teams will be attached under the operational control (OPCON) of the Joint Task Force, Combatant Command, or installation commander, as applicable, who may delegate OPCON to subordinate commanders. The Epi-Teams will communicate with the local senior military medical authority and higher medical headquarters without restriction.

(iii) Smallpox Epi-Teams and regional PM assets will assist with notification of CDC, state health department, host-nation public-health authorities, WHO, or other appropriate entities.

(iv) Smallpox Epi-Teams will have capability (i.e., organic training and supplies) to administer smallpox vaccine.

(d) Regional MTFs.

(i) MTFs located in the region of smallpox outbreak will provide logistical support, consultative assistance, and medical-care assets as appropriate and available.

(ii) MTFs with infectious-disease specialists will provide consultative assistance with diagnosis and treatment and laboratory support.

(iii) Larger MTFs may provide a number of pre-vaccinated personnel to assist with early case investigative efforts before arrival of a smallpox Epi-Team.

(iv) If available, MTFs may also have a limited supply of smallpox vaccine for rapid distribution to local responders and contacts.

(3) Global Response.

(a) As a smallpox outbreak develops, the Combatant Commander responsible for conducting consequence-management operations (e.g., Northern Command for the United States) in response to CBRNE incidents may designate a Smallpox Coordination Cell to augment the usual crisis-action process. This Smallpox Coordination Cell will receive reports of smallpox cases and direct logistical efforts. The Smallpox Coordination Cell will provide a focal liaison with CDC and other smallpox response coordinators, synchronize information exchange for military chains of command, coordinate communication with local, state, national, and international public-health authorities, and coordinate activities of DoD smallpox response teams.

(b) Command Smallpox Response Coordinator. In the event of a smallpox case, a single person within the Unified Command, skilled in health risk communication, located at the Smallpox Coordination Cell, shall be designated to oversee Command-wide coordination of contact identification, tracing, vaccination, medical surveillance, and other response activities.

(c) The Smallpox Coordination Cell will coordinate with CDC (United States) and host nation or WHO (overseas), to ensure proper execution of epidemiologic responses for both DoD personnel and civilians in the local area or host-nation of an outbreak.

(d) DoD will provide support to the lead federal agency (under the Federal Response Plan) for contact tracing, medical surveillance, and epidemiologic investigation.

7. Post-Outbreak Surveillance.

a. Under normal circumstances, disease reporting in the Services is passive. After a smallpox case or outbreak, Services will shift to active medical surveillance to ensure rapid and complete case ascertainment. Appendix A-6 can be used to assist nonmedical members of a military community in distinguishing illnesses of concern from routine illnesses. The Services and Joint Staff will develop plans for active medical surveillance of GFVPRI.

(1) Such plans will be coordinated among the Services and Joint Staff.

(2) Such plans will incorporate guidance found in Appendix A-11.

b. The Services and Joint Staff will initiate daily active medical surveillance immediately after a confirmed case of smallpox.

c. Enhanced Hospital-based Surveillance (EHBS). Service plans will incorporate EHBS, based on guidance in Appendix A-11.

d. Reporting. During an outbreak, MTFs will report smallpox cases periodically (e.g., daily) to Service disease-reporting centers (typically beginning with local preventive-medicine or public-health service), their higher military headquarters, the state health department, the CDC, and other appropriate public-health authorities (e.g., host nation, if overseas) (Appendix A-10).

8. Contact Identification, Tracing, Vaccination, and Surveillance.

a. Planning Conditions.

(1) MTFs will follow CDC recommendations for public health and clinical processes and practices of these functions, unless doing so conflicts will operational requirements. DoD medical units may need to conduct contact identification, tracing, vaccination and medical surveillance functions in United States or overseas locations.

(2) Whenever possible, DoD will employ definitions, protocols and forms developed by CDC, adjusting as the CDC definitions evolve.

(3) DoD may work with other federal, international, state and local agencies and non-governmental organizations to accomplish these functions.

(4) Pre-established Smallpox Epi-Teams will have skills, preparation (including recent vaccination), equipment, and resources to perform contact identification, tracing, vaccination, and medical surveillance functions on short notice.

(5) DoD's local investigators and Smallpox Epi-Teams will cooperate with law enforcement, intelligence, and security operations.

b. Responsibility.

(1) The local commander responsible for smallpox response will assign a single person (Smallpox Response Coordinator) to oversee functions of contact identification, tracing and medical surveillance.

(2) The MTF will follow the CDC GVPRI protocol, seeking infectious disease or dermatology consultation as clinically indicated. Laboratory confirmation is important for a first case in a geographic area (Annex D).

(3) The local response coordinator, skilled in health risk communication, will establish liaison and coordination with local, state, other federal, and international response agencies.

(4) The local response coordinator will direct all local activities of the team(s) assigned to these functions.

c. Team members assigned to identify, trace, and monitor contacts will:

(1) Be recently vaccinated (within 3 to 10 years) before initiating contact interviewing, tracing or medical surveillance functions.

(2) Receive at least the minimum training required to perform these functions.

(3) Follow procedures outlined in Appendix A-3 and Appendix A-13.

(4) Be able to identify symptomatic contacts with fever or rash (i.e., suspected cases), for their immediate transport for medical evaluation.

(5) Prioritize contacts for vaccination, in accordance with Appendix A-3.

(6) Make arrangements for immediate vaccination of contacts.

(7) Conduct active medical surveillance of contacts in accordance with Appendix A-3 and Appendix A-13.

(8) Assess contacts and their household contacts for vaccine “take” and for adverse events (Annex B). Refer those with adverse events for medical evaluation, as appropriate.

(9) Conduct impromptu training for local personnel who unexpectedly take on the role of contact-tracer or interviewer (Appendix A-3).

d. Guidance for Identification of Close Contacts.

(1) Identify people who had close personal contact with the smallpox case (confirmed or probable) since the date fever began.

(2) Since smallpox is a contagious disease, once a case is confirmed, the highest priorities for case investigators are to reduce risk of ongoing transmission by (a) immediately identifying and vaccinating close contacts of cases and (b) isolating the cases.

(3) DoD will use CDC Forms 1 thru 11 in case investigations, adapting as CDC issues any subsequent changes (Appendix A-14). DoD overlays for several of these forms appear at that appendix.

(4) Under CDC guidance, each case and each contact is assigned a specific case/contact identification number. Cases/contacts are also differentiated based on state. DoD will adopt a case/contact identification system to avoid duplicate case-identification numbers. The numbering system will include two parts, a prefix and a suffix. The prefix will be the 5-digit zip code of the installation conducting the contact tracing. The suffix will be a serial number.

(5) In addition to Appendix A-14, local or regional responders and case investigators who are initiating the investigation may obtain forms via the Internet at www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/index.asp. Local responders may also obtain forms, technical consultation, and other assistance from the Unified Command's Smallpox Coordination Cell, a DoD or CDC smallpox response team, or other regional infectious-disease or preventive-medicine centers (e.g., USACHPPM, NEPMUs).

(6) MTFs will establish an appropriate procedure for notifying and obtaining access to contacts. For example, a case investigator could notify the installation or unit commander, or the case investigator would notify local medical personnel who make appropriate linkages.

(7) Case investigators will report all findings to Smallpox Epi-Teams once they arrive. Smallpox Epi-Teams will be attached under the operational control (OPCON) of the Joint Task Force, Combatant Command, or installation commander, as applicable, who may delegate OPCON to subordinate commanders. The Epi-Teams will communicate with the local senior military medical authority and higher medical headquarters without restriction.

e. If team functions include vaccinating contacts, team members assigned will:

(1) Assess contacts for contraindications to vaccination.

(2) Vaccinate contacts according to Annex B.

f. The contact identification, tracing and surveillance team will provide daily reports to the commanding DoD authority (and other authorities as directed by commanding DoD authority) summarizing information on contacts found and those not found, as outlined in Appendix A-3 and Appendix A-13.

9. Special Situations.

a. Ships Underway. If a suspected smallpox case breaks out on board ship, the commanding officer will contact higher headquarters immediately.

b. Air Crews on Missions Away From Home Base. In coordination with US Transportation Command and the Combatant Command, military air traffic between installations should be minimized upon notification of a confirmed case of smallpox, until the extent of the outbreak is determined and medical personnel can interview affected aircrew for presence of fever or rash, travel history and plans, and smallpox vaccination status. Surveillance and clearance will be coordinated between medical authorities and installation and aviation commanders, recognizing the risk of spreading infection to the crews' destination(s). If appropriate, aircrews will begin daily fever surveillance until 14 days after successful vaccination, promptly reporting fever > 101°F (38.3°C).

c. Title 42 United States Code section 97 (42 USC 97; Appendix A-5) provides that quarantines and other restraints established by the health laws of any State, respecting any vessels arriving in any port shall by duly observed by coastal military installations. And “all such officers of the United States shall faithfully aid in the execution of such quarantines and health laws, according to their respective powers and within their respective precincts, and as they shall be directed, from time to time, by the Secretary of Health and Human Services.”

APPENDIX A-1
Surveillance, Contact Tracing, & Epidemiology – Summary.

1. Training. Each military treatment facility (MTF) will periodically train its staff in the clinical recognition of smallpox. Post CDC "Generalized Vesicular or Pustular Rash Illness Protocol" Poster [www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-4-rash-color.pdf or .ppt], in MTFs, adding specific telephone numbers to report GFVPRI.

2. Reporting. Promptly report cases of "Generalized Febrile Vesicular-Pustular Rash Illness" (GFVPRI) (cases of fever with blistery or pus-filled blistery rash) as follows:

a. Submit report immediately through Service disease-reporting systems, beginning with local preventive-medicine or public-health service.
b. Submit Serious Incident Report (SIR) to higher headquarters.
c. Notify CDC Emergency Preparedness & Response Branch, 770-488-7100.
d. Notify State Health Department (see http://www.cdc.gov/other.htm#states).
e. Notify other appropriate authorities. If overseas, coordinate with host nation.

3. Source. Initially, the most critical information about cases to report to headquarters may be facts about visits to transportation hubs (e.g., airports) or large congregations (e.g., arenas, malls) in the interval ~ 7 to 17 days before smallpox diagnosis.

4. Coordination. MTF appoints Response Coordinator. MTF follows GVPRI protocol, seeking infectious-disease or dermatology consultation as indicated. Laboratory confirmation is important for a first case in a geographic area. Begin contact tracing.

5. Specimens. MTF coordinates with CDC regarding specimen collection (Annex D). Headquarters support deployment of DoD Smallpox Epidemiologic Response Team(s). Local staff and Epi-Team(s) investigate case(s) to confirm the diagnosis of smallpox.

6. Priorities. Once a suspected, probable, or confirmed case is identified, the highest priorities are to reduce risk of transmission by (a) isolating the cases and (b) promptly identifying and vaccinating close contacts of cases. Transport contacts with fever or rash to Type C facility to rule out smallpox (Annex C, DoD Appendix 7).

7. Contacts. Conduct contact tracing if case suspected or confirmed. Use detailed CDC Forms 1-4 at first. For ongoing outbreaks, use CDC Forms 5A and 5B. Key goals of contact tracing are identification, vaccination, and describing distribution of outbreak. Report medical surveillance data daily to higher headquarters and to CDC (method to be provided by CDC). Contacts remain under active medical surveillance (e.g., telephone acceptable, CDC Forms 10 and 11) for 18 days after last contact with case or 14 days after successful vaccination.

8. Medical Surveillance. Investigation may warrant additional active surveillance, Forms 10 through 13. Compare outbreak's epidemiologic features with expectations of smallpox and varicella (chickenpox).

APPENDIX A-2
Service Reportable-Disease Surveillance Centers.

Army Medical Surveillance Activity
Building T-20, Room 213 (Attn: MCHB-EDS)
6825 16th Street, NW
Washington, DC 20307-5000
Phone: 202-782-0471 (DSN 662)
Fax: 202-782-0612
http://amsa.army.mil/AMSA/amsa_home.htm

Navy Environmental Health Center (for both US Navy and US Marine Corps)
620 John Paul Jones Road
Portsmouth, VA 23708
Phone: 757-953-0763 (DSN 377), after hours 757-621-1967
Fax: 757-953-0680
http://www-nehc.med.navy.mil/

Air Force Force Health Protection and Surveillance Branch
Institute for Environment, Safety and Occupational Health (ESOH) Risk Analysis
2513 Kennedy Circle
Brooks AFB, TX 78235-5123
Phone: 210-536-5454 (DSN 240)
Fax: 210-536-6841
http://iera.satx.disa.mil/iera/index.html

Coast Guard Headquarters Directorate of Health and Safety
Commandant (G-WKH)
2100 Second Street SW
Washington, DC 20593
Phone: 202-267-1098
Fax: 202-267-4338

APPENDIX A-3
Impromptu Training Curriculum for Contact Tracers And Interviewers.

SITUATION: Smallpox cases have been diagnosed in our community. When you finish this training, you will be helping find possible contacts, people who might have been exposed to smallpox. Before you begin interviews, you will receive smallpox vaccine for your own protection.

1. Goal. Your job is to help find the people who had face-to-face contact with smallpox cases and their contacts. Once you find them, you will help them get vaccinated to avoid contracting smallpox themselves. By finding them, you help slow and stop the spread of smallpox in the community. As you work with these individuals, listen well and use words and phrases that get your message across clearly. You will be assigned one or more of the following jobs:

a. Identification and tracing (asking about and finding) the contacts of people infected with smallpox, as well as the people who are contacts of those contacts.

b. Interviewing these people about their travels, their symptoms, and their own contacts.

c. Arranging for vaccination of these people. And

d. Helping with fever surveillance of these contacts, in case they go on to develop symptoms of smallpox themselves.

2. You will notice how often the word "contact" is used in the sections above. The definition of contact is "face-to-face contact with a suspected, probable, or confirmed case of smallpox. Risk of disease transmission increases with close contact ($\leq$ 6 feet), increasing time of exposure (e.g., >1 hour), and presence of rash or cough."

3. The Centers for Disease Control & Prevention (CDC) developed a set of forms to help perform this work. The purpose and master copies of each form appear in Appendix A-14, including several with DoD overlays. Master copies are also available at http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/index.asp.

4. Interview Case to Identify Contacts.

a. Using CDC Forms 2, 2A, 2B, 2C and 2D (the contact-identification module), interview each suspected, probable, or confirmed smallpox case. The forms collect detailed name and contact information for all people with whom case had face-to-face contact (within 6 feet) from onset of fever until the time of the interview. Enter how long the cases were exposed to non-household contacts, if that information is known. List the names of household and non-household contacts on the appropriate forms.

b. Obtain as much locating information as possible (e.g., names, addresses, telephone numbers) for each person with whom the case had known face-to-face contact after onset of fever. Ask the cases what they did and who they saw each day; beginning with the day their fever began. Include specific questions in the interview to help the case remember various types of contacts (e.g., work-related activities, social activities). For example, “Who did you have lunch with that day?”

c. Ask for detailed information about places visited since the fever began. This will help identify places where unknown people may have been exposed to an infectious case. These include physician offices, hospital emergency departments, health clinics, work and school locations, regular activities, and occasional activities.

d. This module also requests in-town and out-of-town travel history since onset of fever.

e. If time or personnel constraints permit, or if the case is unable to answer questions because of illness, interview the case’s family, close friends, and work associates to verify the case’s travel and contact history since onset of fever.

f. If only contacts in one state are involved, give all the information obtained to the people responsible for tracing, interviewing, and medical surveillance of contacts within the state. Provide the names of the contact and household members of contacts to personnel or clinics responsible for completing contact information (e.g., name, address, phone number) and for vaccinating contacts.

g. If the case names out-of-state contacts or places of travel, arrange for the information to be given to the CDC Coordination Group.

h. After listing all contacts, group the contacts into priority categories for vaccination, based on duration of exposure. Use the following guidelines:

(1) Highest priority. Household contacts, immediate family members, and people who work full time in the household.

(2) Second priority. Named contacts who spent time in the case’s home, but who do not live there (e.g., close friends who visited, any person who spent the night).
Named non-household contacts with > 3 hours of exposure.
People exposed in a physician office or other medical facility.

(3) Third priority. Named non-household contacts with 1-3 hours of exposure.

(4) Fourth priority. Named non-household contacts with < 1 hour of exposure.

(5) Fifth priority. Non-household contacts with < 1 hour of exposure at a designated location.

i. Other factors for contact tracers to consider when assigning contacts to priority groups include case's status (e.g., fever, rash, presence of cough, closeness of exposure). For example, did the contact sit next to a potentially infectious case for 2 hours at a meeting versus sitting across the room for the same meeting?

5. Tracing and Interviewing Contacts.

a. Staff assigned to trace contacts will receive names and any known address, telephone number(s), or other locating information for these contacts from people who interview the cases.

b. Contact-tracing personnel should:

(1) Find locating or contact information for each contact of each smallpox case. If contact information is incomplete or unknown, use work and school contact numbers, telephone directories, voting lists, neighborhood interviews, site visits, "hangouts," and similar methods. If contacts cannot be found through these mechanisms, other means of notifying potential contacts, such as media announcements, may be appropriate.

(2) Locate each contact.

(3) Interview each contact to confirm contact with the suspected, probable, or confirmed smallpox case, the presence or absence of symptoms in the contact (e.g., fever and/or rash) and to identify additional contacts who may not have been listed by the case. Record this information on CDC Form 8.

(4) Make arrangements for immediate vaccination of the contact and his or her household contacts. If this is not performed at the household by the contact tracer, provide a form that documents names and identifying information of all people in the household referred for vaccination on CDC Form 9.

(5) If the contact has symptoms of fever > 101ºF (38.3ºC) or rash, immediately transport the contact to a Type C facility or other designated site for medical evaluation to rule out smallpox (Annex C). Interview the person as a suspected case using the Smallpox Case Investigation Form (CDC Forms 1A and 1B). Identify, interview, and vaccinate his or her contacts while the evaluation for smallpox is being undertaken.

(6) If the contact does not have fever or rash, place the contact under fever surveillance, so that if he or she develops fever or rash, the contact can be immediately isolated to prevent exposure to other people.

(7) Identify household contacts (including regular household visitors and people who work in the home) of the contact of the smallpox case. Record their names, ages, relationship to the case, and other information on CDC Form 8 or 10 (page 2, Secondary Contact Information).

(8) If household members cannot be vaccinated due to valid contraindications, they should be housed separately from the contact, until the end of the contact's isolation period, or until all vaccination scabs of people in the household separate (14 to 21 days after vaccination).

(9) Notify the person responsible for reporting out-of-state contacts to the CDC Coordination Group, if a contact has left the state.

3. Monitoring for Fever and Vaccine Take of Contacts.

a. Contacts who do not have fever or rash at the time of interview must remain under active fever surveillance for 18 days after their last contact with the smallpox case, or for 14 days after successful vaccination. The contact-tracer and the contact will agree on a method for daily communication. Creative solutions may be needed if the contact does not have access to a home telephone.

b. Contacts must monitor and record their temperature in the morning and early evening each day (using CDC Form 10). Each day before 8 p.m., the contact must call or be called by health staff to report daily temperatures, health status, and any unexpected adverse reaction after vaccination.

c. During medical surveillance, the contacts may continue their usual daily activities, going to work or attending school, as long as no temperatures > 101ºF (38.3ºC) occur. The contacts should not, however, travel away from their city of residence (not more than ~ 20 miles from city of residence).

d. If contacts develop a temperature > 101ºF (38.3ºC), they must remain in their own homes. If they have two temperature readings in a row > 101ºF, the contacts must contact health-department personnel immediately, and remain at home. The contacts should have contact only with their vaccinated household members, until further evaluated by health-department personnel.

e. Seven days after vaccination, depending on local arrangements and staff availability, contacts must either visit the health department or report the status of their vaccine site, and the status of the vaccination sites of their household members. The question for vaccinated people is this: Does the area of their arm where they were vaccinated look like the picture they were given when they were vaccinated? In other words, does the site involve a pus-filled blister or an area of hardened swelling (i.e., induration or congestion) around a central lesion? For telephone conversations, it will generally be better to ask the contact to describe the vaccination site, rather than asking a yes/no question, such as "Does the site look like the picture?" More useful questions might include: "Does the site have any blister or pus-filled white area?" "Don't touch it, but tell me if it looks soft and squishy." Successful smallpox vaccination results in a pustular lesion in previously unvaccinated people 6 to 8 days after vaccination (Appendix B-13). In previously vaccinated people, either a pustular lesion or an area of

definite induration or congestion around a central lesion develops by 6 to 8 days after vaccination.

f. Using CDC Form 10, personnel assigned to monitor the health status of contacts will:

(1) Record daily temperature readings and health status,

(2) Record information on vaccine take and severe adverse reactions after vaccination among contacts and their household members,

(3) Refer for in-home follow-up any contacts who fail to report in and cannot be contacted by telephone, and

(4) Answer questions of contacts who are under fever surveillance.

(5) If resources permit, visit the household on day 6 to 8 after vaccination to record vaccine “take.”

g. Maintain CDC Form 10 for each contact. Record information on the date and type of follow up (i.e., in person or by telephone), recorded temperature, other symptoms of illness, and vaccination-site reaction on day 6 to 8.

h. Obtain information on the vaccine take of other people in the household and record it on CDC Form 10 or 11.

i. In addition, use CDC Form 11 as a daily tracking form to record summary information from all contacts monitored.

j. If personnel are limited, state and Federal health authorities may institute a passive system of monitoring health status [may use CDC Form 12, in development]. In this approach, contacts only call health department personnel if any of the following occur:

(1) They have 2 consecutive temperatures > 101º F (38.3ºC) or develop a rash.

(2) They have no reaction at the vaccine site on day 6 to 8.

(3) They developed a serious adverse reaction to vaccination.

(4) They completed the period of monitoring (i.e., 18 days from last contact with the case or 14 days after successful vaccination) and request to be officially released from monitoring.

k. For coordination of contact tracing with vaccination, personnel should:

(1) Using CDC Form 8 or 9, make a list of names and Social Security numbers (or driving license numbers) of contact and household members referred for vaccination. Provide this list to the vaccination clinic site where the contacts/household members will be sent.

(2) Provide a daily Master Report (CDC Form 13, in development) to the person responsible for coordinating contact tracing that includes:

__ Contacts found
__ Contacts not found
__ Disposition of found contacts
__ Interviewed and vaccinated/referred for vaccination
__ Interviewed and referred for illness evaluation
__ Isolated if fever or rash develops
__ Status of contacts not found
__ Whereabouts known but unable to contact for interview
__ Whereabouts unknown
__ Number of contacts' household members
__ Number of contacts' household members vaccinated/referred for vaccination

l. Refer to Appendix C-10 for flow charts for recommended contact identification and tracing activities.

APPENDIX A-4
Characteristics of Smallpox Epidemiologic Response Teams ("Smallpox Epi-Teams").

1. Purpose. To describe the composition, capabilities, activation, and activities of Smallpox Epidemiologic Response Teams (Smallpox Epi-Teams) that would respond to any report of possible exposure or occurrence of cases of smallpox.

2. Background. Smallpox is unique as a bioterrorist weapon in its high case-fatality rate and ability to spread from person-to-person in an open society such as the United States. Routine vaccination of US military recruits against smallpox was intermittent after 1984 and discontinued in 1990. Routine vaccination of US civilians ceased in about 1972. Thus, susceptibility to smallpox is universal among children and young adults, and widespread among older adults (Appendix 7).

3. Assumptions.

a. Smallpox virus may be used in a terrorist attack against US civilian or military targets anywhere in the world. Such attacks may occur silently, with case appearance as the first evidence of such an attack. Other attacks may be associated with detectable events, in which case a suspicious substance and potentially exposed personnel would be the immediate issues of concern.

b. DoD will be expected to respond with its own resources to any such incidents that occur on its own installations in the United States or on other bases around the world. Some assistance may be possible from civilian authorities when an attack involves a community near a military installation. Civilian resources may be overwhelmed and civilian authorities will likely be unable to fully support activities on military installations.

c. In the event of an attack in the US that does not directly involve military installations, civilian resources may be overwhelmed and civilian authorities could call upon DoD resources to assist in providing response support.

d. In the event of an outbreak, early compilation of accurate information to confirm and define the scope of the problem will be a critical element in any response effort.

e. Early recognition and definition of a possible smallpox attack may be the deciding factor in how quickly the spread of disease can be contained.

4. Possible Scenarios.

a. There are several types of events that may occur:

(1) Reports of one or more clinical cases suspected to be smallpox.

(2) An incident occurs in which one or more people are exposed to a substance suspected to be smallpox.

b. There are several types of civilian-military interaction that may occur:

(1) Within the borders of the United States, an attack occurs that initially appears to involve only personnel and locations entirely on a military installation.

(2) Within the borders of the United States, an attack occurs that initially appears to involve only civilian personnel and locations outside of military installations.

(3) Within the borders of the United States, an attack occurs that initially appears to involve both civilian and military personnel or to involve locations both within and outside of military installations.

(4) Outside of the borders of the United States, an attack occurs that appears to involve military personnel or military installations.

(5) Outside of the borders of the United States, an attack occurs that appears to involve only US civilian personnel and locations outside of military installations (e.g., Embassies and their staffs).

5. Concept.

a. Depending on the nature of the attack, a DoD Smallpox Epi-Team may be assigned under the operational control of a Unified Command, a medical command authority of one of the US Armed Services (e.g., a regional medical command, Military Treatment Facility), or an installation commander. Alternatively, after a request from civilian authorities, the team could be assigned under the operational control of FEMA, CDC, state health officer, or other designated authority.

b. Number of Smallpox Epi-Teams. DoD will establish at least six teams, two from each Service, to provide the necessary global response capability to DoD. One or two will be located in the Pacific region, at least two in the United States, and one or two in Europe.

c. Smallpox Epi-Team Composition. Epidemiologic response teams will be trained with materials developed by the DoD and the CDC. Each full team will consist of approximately 6 to 12 members. DoD may field smaller teams with sufficient capability where local support can be expected from host organizations or installations. Sufficient members will be identified to allow team function despite members taking personal leave. Team members will typically serve terms of 24 or more months. Teams will arrange for replacement of a portion of the team on an annual cycle, according to personnel turnover. The core members of the teams will typically include the following:

(1) Team leader (1 per team). A senior officer in the medical branch responsible for all activities of the team. This individual will serve as the lead coordinator with military and civilian authorities and oversee communication between the team and command-and-control elements.

(2) Operations officer or public-health advisor (1 to 2 per team). Medical Service Corps, Medical Corps, or other medical-branch officer with training in public health (e.g., community health nurses) who assists the team leader with communications, logistics, inter-agency coordination, mission tracking, reporting to high headquarters, vaccination activities, contact tracing, training, and related functions. Also serves as primary adviser for operations and disease-response activities, including recommendations for quarantine, isolation, and hospital infection control.

(3) Epidemiologist (1 per team). Medical corps officer or other medical branch officer with advanced degree in epidemiology who serves as technical consultant and primary leader of investigation activities, medical surveillance, data collection, analysis, and definition of the scope of disease occurrence.

(4) Infectious-disease physician and/or dermatologist (1 to 2 per team). Serves as primary consultant in diagnosing and monitoring possible cases of disease. Also assists with diagnosis of adverse events after vaccination and monitors and analyzes vaccine safety data. Serves as the primary consultant on matters of infection control in medical facilities. An Infection Control Officer could fulfill some roles in this category.

(5) Laboratory scientist (1 per team). Medical service corps officer with laboratory expertise who advises team leader on specimen collection, handling, shipping, and related procedures. Serves as liaison with military and civilian laboratories to support the investigation and disease-control plan.

(6) Preventive-medicine, public-health, or environmental-health technician (1 to 2 per team). Provides logistical and administrative support to team, to meet requirements for equipment, supplies, transportation, meals, and quarters. As time allows, augments the activities of other team members, to assist in accomplishing critical tasks.

(7) Communication specialist (0 to 1 per team). Public affairs or medical branch officer or senior noncommissioned officer with excellent writing and speaking skills and experience in media relations and risk communication. Serves as the communication link between the team and local health departments, press offices, and other outside agencies requesting information on team activities. In the absence of a specific member assigned to the team, the team will request local support from the host command.

(8) Occupational-medicine specialist (0 to 1 per team). An occupational-medicine physician who provides consultation and recommendations relating to protecting health-care workers, health department staff, emergency responders, and others with occupational risk in the outbreak.

(9) Community health nurse (0 to 1 per team). Community health nurse who provides expertise in performing case investigations, contact tracing, teaching, and home visits.

(10) Immunization technician (1 or more per team). A medic trained in screening for contraindications, vaccination, and management and reporting of adverse events after vaccination.

d. Smallpox Epi-Team Capabilities. Epi-Teams will be on-call to travel within 6 to 12 hours upon activation. The team will provide initial problem definition and assessment capabilities to senior authorities. After an initial in-brief with the host command authority, the team will complete an initial assessment within 24 hours and provide updates on assessment activities at least daily thereafter. The Smallpox Epi-Team will serve in the capacity of a field investigative team and will have at least the following capabilities:

(1) Confirm or refute the existence and number of smallpox cases.

(2) Confirm or refute the presence of a substance that may contain smallpox virus (subject to more definitive testing facilities elsewhere in the Laboratory Response Network).

(3) Upon confirmation of cases or an exposure, estimate the immediate threat of disease spread in the affected population.

(4) Serve as advisors to local authorities on immediate response activities, to include vaccination, quarantine, medical care, and safety precautions.

(5) Rapidly identify additional resources required to support response to an outbreak and coordinate an appropriate civilian or DoD response package.

(6) Administer smallpox vaccine.

6. Required Training and Preparation.

a. All team members will be vaccinated against smallpox.

b. All team members will attend smallpox training provided by the CDC and/or DoD. Examples include the DoD Emergency Preparedness Course, Health-Risk Communication Course, Combined Humanitarian Assistance Response Training.

c. All team members will be knowledgeable experts on the CDC Smallpox Response Plan and Guidelines, as well as this DoD Smallpox Response Plan.

d. Teams will complete 1-day planning and practice sessions at least quarterly.

7. DoD Implementation.

a. Team development and support will be coordinated by the US Army Medical Department, as lead agent for the DoD Immunization Program for Biological Warfare Defense. Nonetheless, individual team composition and the various teams will be constituted and supported by each of the military Services. The Services and the Joint Staff will develop agreements to ensure that Unified Combatant Commands and other command authorities develop plans to support this response capability.

b. Prior planning and coordination with Unified Commands is critical to ensure that senior commanders know of and are prepared to request the Smallpox Epi-Team capability as needed. Also, hosting commands will provide the logistical, transportation, and other support requirements the team will need.

c. Initial team training and preparation will focus on the smallpox threat. However, as team capabilities mature, the team will develop expertise in responding to other bioterrorist events or to epidemics of contagious disease that result from natural, as well as deliberate, causes.

APPENDIX A-5
State Health Laws Observed by US Officers (42 USC 97).

42 US Code Section 97.

“The quarantines and other restraints established by the health laws of any State, respecting any vessels arriving in, or bound to, any port or district thereof, shall be duly observed by the officers of the customs revenue of the United States, by the masters and crews of the several Coast Guard vessels, and by the military officers commanding in any fort or station upon the seacoast; and all such officers of the United States shall faithfully aid in the execution of such quarantines and health laws, according to their respective powers and within their respective precincts, and as they shall be directed, from time to time, by the Secretary of Health and Human Services.”

APPENDIX A-6
Handout to Identify Symptoms of Smallpox.

Signs of Smallpox: a sudden fever of 101°F (38.3°C) or higher followed 1 to 4 days by a rash of blisters or firm pus-filled blisters. Unlike chickenpox, all the bumps of the rash should be at about the same stage as it develops. Fever may drop once rash begins.

High Risk for Smallpox: If you have **ALL THREE** of these symptoms, come in for medical evaluation right away.

Check: ☑

☐ Sudden fever above 101°F (38.3°C), blistery rash 1 to 4 days later **AND** at least one of the following: exhaustion, headache, backache, chills, vomiting, or severe abdominal pain.

All 3 boxes checked = High Risk

☐ Blisters or pus-filled blisters with clear borders.
Blisters that are firm/hard, round, and deep.
Blisters may contain a sunken center or join together.

☐ Blisters at the same stage on all areas: all blisters, or all pus-filled blisters.

Moderate Risk of Smallpox: If you check **BOTH** boxes in group A or if you check **BOTH** big boxes in group B, come in for medical evaluation.

GROUP A

☐ Sudden fever above 101°F (38.3°C), rash 1 to 4 days later **AND** at least one of the following: exhaustion, headache, backache, chills, vomiting, or severe abdominal pain.

Both boxes checked = Moderate Risk

☐ Blisters or pus-filled blisters with clear borders.
Blisters that are firm/hard, round, and deep.
Blisters may contain a sunken center or join together.

Check: ☑ ----------

GROUP B

☐ Sudden fever above 101°F (38.3°C), rash 1 to 4 days later **AND** at least one of the following: exhaustion, headache, backache, chills, vomiting, or severe abdominal pain.

First Box + 4 other symptoms checked = Moderate Risk

☐ Four or more of the following symptoms:
- ☐ Blisters appearing thickest on the face, arms, legs, and head.
- ☐ First blisters appear on roof of mouth, inside nose, face, or forearms.
- ☐ Blisters changed from spots to bumps to pus-filled blisters.
- ☐ Blisters appearing on palms and soles of feet.
- ☐ Patient appears really sick.

Low Risk for Smallpox: If you don't have the symptom combinations listed above, you probably don't have smallpox. If you get a fever above 101°F, follow the directions above. If you have other symptoms, seek routine or appropriate medical care.

APPENDIX A-7
Smallpox Clinical Case Description and Differential Diagnosis.

1. Smallpox is characterized by both an enanthem (internal rash) with lesions in the mouth and on the posterior pharynx, as well as an exanthem (external rash). Constitutional symptoms before onset of rash (exanthem) include fever (100%), which generally occurs about 1 to 3 days before rash onset, headache (90%), backache (90%), chills (60%), and vomiting (50%). Less common symptoms include pharyngitis and severe abdominal pain. The hallmark of the ordinary (or classic) type of smallpox is a generalized vesiculopustular rash with lesions found more densely on the face and extremities (centrifugal pattern), including the palms and soles of the feet. All lesions on any one part of the body are at a similar stage of development and are about the same size. Rash progresses from sparse macules (day 1), to papules (day 2), vesicles (days 3 to 4), pustules (days 5 to ~ 12), and scabs (days 13 to 18) for a total duration of 2 to 3 weeks.

2. Less common presentations of the smallpox rash include flat, or hemorrhagic lesions. A rash that progresses through the stages more rapidly and has fewer lesions characterizes modified smallpox, which occurs more commonly among previously vaccinated people. Infection via cutaneous inoculation also has a shorter course with appearance of one or several vesicles at the site of inoculation after about 3 days. Asymptomatic cases are very uncommon and their role in transmission is unclear, but likely to be minimal.

3. Because routine childhood vaccination in the United States stopped in 1971, people currently < 30 years old are susceptible to smallpox. If exposed, they are expected to exhibit classic or atypical presentations. People > 30 years old may have been vaccinated during childhood or as adolescents or adults for travel or occupational reasons. Vaccination of health-care workers and people traveling overseas continued until the late 1970s and U.S. military personnel were vaccinated until 1990. Epidemiological studies showed that a high level of protection against smallpox persists for ≤ 5 years after primary vaccination and substantial but waning immunity can persist for ≥ 10 years. Antibody levels after revaccination can remain high longer, conferring a greater period of immunity than occurs after primary vaccination alone. Although some assume that adults > 30 years old in the United States have little or no immunity to smallpox, there is evidence that vaccination during infancy results in long-term reduction in mortality. Therefore, it is possible that if smallpox virus were introduced into the U.S. population, some vaccinated adults -- especially those who received two or more doses of smallpox vaccine -- may develop modified smallpox following exposure and that mortality would be markedly lower than among unvaccinated people.

4. The most likely condition to consider in the differential diagnosis of vesiculopustular rash is varicella (chickenpox). Major and minor distinguishing characteristics are listed in the following table:

	Smallpox: Clinical Features	Varicella (Chickenpox): Clinical Features
Major Distinguishing Features	Febrile prodrome: temperature > 101°F and systemic symptoms (e.g., prostration, severe headache, backache, abdominal pain, vomiting) 1 to 4 days *before* rash onset.	No or mild prodrome before rash onset.
	Lesions are deep, firm, well-circumscribed pustules; may be confluent or umbilicated.	Lesions are typically superficial vesicles.
Other Distinguishing Features	Rash concentrated on face and distal extremities (centrifugal pattern).	Rash concentrated on trunk and proximal extremities (may involve face or scalp) (centripedal pattern).
	Rash in same stage of evolution on any one part of the body	Rash appears in crops so lesions are in different stages of evolution (i.e., mixed papules, vesicles, or crusts) on any one part of the body.
	First lesions on oral mucosa/palate (enanthem), followed by exanthem (rash) on face or forearm.	First lesions on trunk (occasionally face).
	Lesions on palms and soles of the feet (seen in > 50%).	Lesions very uncommon on palms and soles.
	Lesions may itch at scabbing stage.	Lesions generally itch intensely.
	Lesions slowly evolve from papule to pustule in days.	Lesions generally evolve from macules to papules to vesicles to crusts in < 24 hours.
	Illness lasts 14 to 21 days.	Illness lasts 4 to 7 days.

5. In herpes zoster, lesions are usually localized to 1 or 2 dermatomes (i.e., an area of the surface of the body attached to the same spinal nerve), but can become generalized, especially among immune-compromised people. The lesions in localized herpes zoster are painful and could be differentiated from smallpox based on their appearance.

6. Other diagnoses include drug eruptions, erythema multiforme, impetigo, disseminated herpes simplex, and enteroviral infections associated with a vesicular rash.

APPENDIX A-8
Smallpox Case Definitions and Case Classification.

Note: Preliminary CDC case definitions appear below, but may require revision by public-health personnel conducting the epidemiological investigation, depending upon the specifics of the epidemic.

1. Clinical Case Definition of Smallpox. An illness with acute onset of fever > 101ºF, followed by a rash characterized by vesicles or firm pustules in the same stage of development without other apparent cause.

2. Laboratory Criteria for Confirmation. To be conducted in Laboratory Response Network (LRN) Level C or D laboratories only. LRN Level D laboratories include CDC and USAMRIID. Initial confirmation of a smallpox outbreak requires testing in a Level D laboratory. Level C laboratories will assist with testing of clinical specimens after initial confirmation of an outbreak by CDC.

a. Isolation of smallpox (variola) virus from a clinical specimen (Level D laboratory only), or

b. Polymerase chain reaction (PCR) identification of variola DNA in a clinical specimen, or

c. Negative-stain electron microscopy (EM) identification of variola virus in a clinical specimen (Level D laboratory or approved Level C laboratory).

3. Case Classification.

a. Confirmed. A case of smallpox that is laboratory confirmed.

b. Probable. A case that meets the clinical case definition that is not laboratory confirmed, but has an epidemiological link to another confirmed or probable case.

c. Suspected.

(1) A case that meets the clinical case definition, but is not laboratory confirmed and does not have an epidemiological link to a confirmed or probable case of smallpox, or

(2) A case that has an atypical presentation that is not laboratory confirmed, but has an epidemiological link to a confirmed or probable case of smallpox. Atypical presentations of smallpox include (a) hemorrhagic lesions or (b) flat, velvety lesions not appearing as typical vesicles nor progressing to pustules.

4. Definition of Contact. A person who has had contact with a suspected, probable, or confirmed case of smallpox. A contact's risk of contracting smallpox increases with close contact (6 feet or less), increasing length of exposure to a case and the stage and severity of clinical case (increasing with onset of rash and/or cough.) Thus, close contact is defined as any face-to-face contact ($\leq$ 6 feet, able to reach out and touch) with a smallpox case and duration of contact should be quantified, if possible.

5. The importance of case confirmation using laboratory diagnostic tests differs depending on the epidemiological situation. Laboratory confirmation is important for a first case in a geographic area, leading to release of vaccine as part of a response. In a setting where multiple cases are identified, laboratory capacity may soon be overwhelmed. In such instances, priority for laboratory resources will include:

a. Testing of clinical or environmental specimens that will provide information about a potential source of exposure, facilitating law-enforcement activities and case detection. And

b. Testing of clinical specimens from cases with an unclear presentation but who are suspected as cases following expert consultation.

APPENDIX A-9
Expected Epidemiological Features of Smallpox.

1. Incubation period: typically 12 to 14 days (range: 7 to 17 days).

2. Person-to-person spread by droplet transmission (most common), contact with material from pustules/rash lesions or contaminated clothing or bedding (less common), or small-particle aerosol (least common).

3. Although smallpox cases are generally not infectious to others until the onset of rash (about 7 to 17 days after exposure), because exact date of rash onset may not be noted accurately and because the infectious enanthem may precede rash onset by 1 to 2 days, consider cases potentially infectious from date of onset of fever.

4. Period of highest transmission is during the first 7 to 10 days after onset of rash. But a person is considered infectious until all scabs have separated. Risk of contracting disease increases with length and environment of contact.

5. People at greatest risk for disease are household and face-to-face contacts to cases after the onset of rash.

6. During the smallpox era, the seasonal transmission of disease was highest during winter and early spring.

7. Currently, the age distribution of cases would be expected to mimic the age distribution of the population, due to the lack of immunity among many people in the community.

8. An expected case-fatality rate of up to 30%. This proportion may be greater due to (a) lack of natural immunity, (b) a high percentage of non-vaccinated people in the U.S. population, (c) waning immunity against smallpox in previously vaccinated people, and (d) a larger immune-compromised population compared to the smallpox era. The case-fatality rate may be lower due to (a) better intensive care and medical treatment options than 30 years ago and (b) partial immunity among the adult population.

9. Smallpox does not spread like wildfire. A smallpox outbreak would evolve over the course of months. Given the typical 12- to 14-day incubation period between exposure and symptoms, generations of smallpox cases will arise at intervals of roughly 2 to 3 weeks. On average, each person infected with smallpox will infect 3 to 5 other people. In hospital settings, where more serious cases of disease are taken and where workers have closer contact with cases, the average smallpox case will infect 10 to 12 people.

10. The likelihood of a susceptible household contact of a smallpox case contracting smallpox is about 58% (range: 38% to 88% in 8 studies).

11. Epidemiological features of **varicella** (chickenpox) that are similar to smallpox:

a. Incubation period: typically 12 to 14 days (range 7 to 17 days).

b. Person-to-person spread of varicella occurs by (a) direct contact, droplet or aerosol from vesicular fluid of skin lesions or (b) secretions from the respiratory tract.

c. Varicella cases may be infectious several days before rash onset until lesions scab, but the period of highest transmission is the first 2 to 3 days after rash onset. Scabbed varicella lesions are not infectious. Although these transmission features are different from smallpox, they will probably not be helpful in distinguishing between the two diseases.

d. The seasonal transmission of varicella is highest during winter and early spring though in the United States, in areas where varicella vaccine coverage is high, the spring seasonality is becoming attenuated.

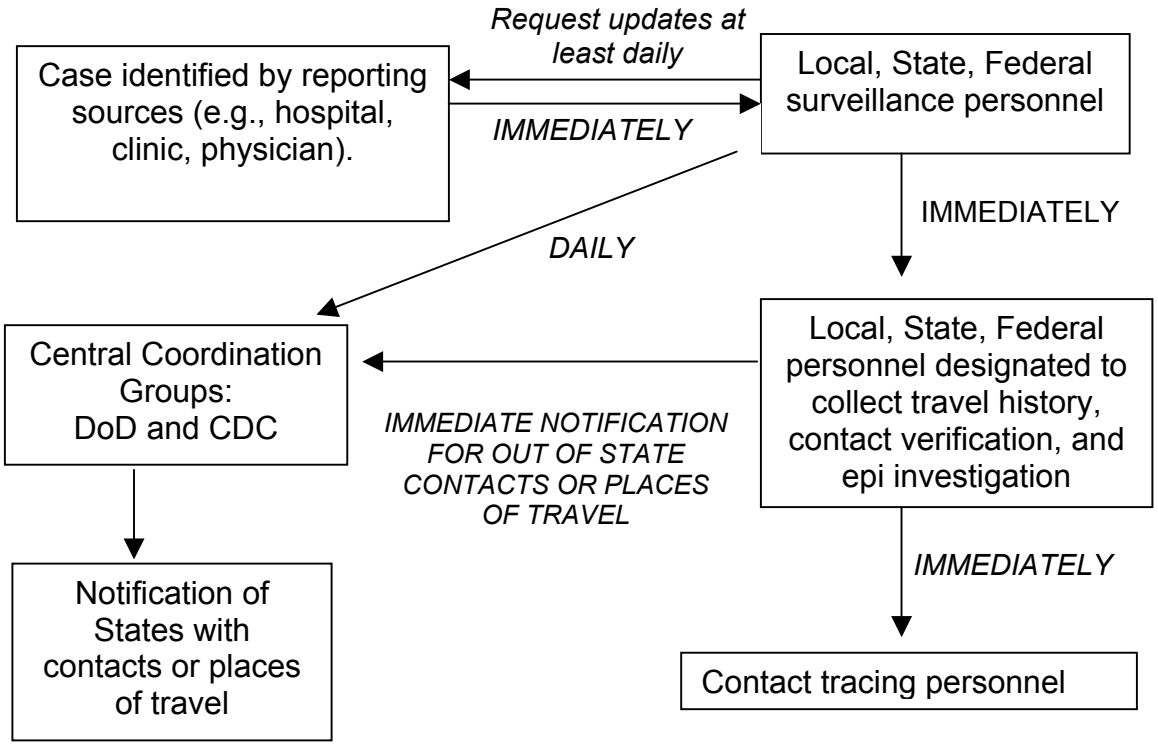
12. Epidemiological features of **varicella** (chickenpox) useful in distinguishing it from smallpox:

a. Most varicella cases occur in children. Only 5% of adults 20 to 29 years of age are susceptible and only 1% of adults 30 to 39 years are susceptible. Thus, varicella in adults is uncommon. However, adults from tropical climates are more likely to be susceptible than their U.S. counterparts. Although varicella cases have declined dramatically in areas with moderate to high vaccine coverage in the United States, varicella cases have declined in all age groups and about 90% of cases still occur among children < 15 years old.

b. Varicella has an expected case-fatality rate of 2 to 3 deaths per 100,000 cases, much lower than smallpox.

c. A secondary attack rate among susceptible household contacts of about 80% (range 65% to 90%), higher than smallpox.

APPENDIX A-10
Surveillance Reporting and Information Flow.



1. MTF personnel will use the CDC GVPRI protocol to evaluate unusual clinical cases, synchronizing medical and infection-control expertise with the command group.

2. After ruling out more plausible explanations, submit GFVPRI report immediately through established Service disease-reporting systems (Appendix A-2), regardless of time of day. These reporting systems typically begin with the local preventive-medicine or public-health service.

3. Also submit Serious Incident Report (SIR) to higher military headquarters (i.e., operational forces command communications channels), regardless of time of day. Operational forces command communications will be the primary/only means of reporting in certain situations (e.g., deployed forces).

4. Also notify CDC Emergency Preparedness & Response Branch, 770-488-7100, if within the United States, its possessions, or its territories.

5. Also notify State Health Department (see http://www.cdc.gov/other.htm#states).

6. Also notify other appropriate authorities (e.g., local health department; host nation public-health authorities), as applicable.

APPENDIX A-11
Enhanced Hospital-Based Surveillance.

1. Once a case of smallpox has been confirmed in a community, patients with febrile rash illnesses will be directed to seek evaluation and care at a small number of facilities (e.g., clinics, hospitals) where physicians and health professionals familiar with smallpox and similar rash illnesses will see, diagnose, and triage patients. Precautions to prevent spread of possible smallpox will be implemented. In addition, other area hospitals will be asked to initiate active medical surveillance for cases to identify patients admitted with compatible illnesses. Installations should identify these facilities in advance and make plans for the evaluation of sizeable numbers of patients with rash illnesses.

2. Active Surveillance in Hospitals.

a. Each hospital in the active medical surveillance network will identify one person (i.e., hospital surveillance officer) responsible for daily active surveillance at that institution (e.g., infection-control practitioner, ICP). Patients will be evaluated and assigned a risk category: high, medium or low. The ICP will notify the health department immediately of any high-risk patient for transfer to the designated type C facility for isolation of smallpox cases (Annex C). All patients identified as medium risk will be reported to the health department and transferred to a type X facility (Annex C). In the event there are no suspected smallpox patients, a report will still be sent to notify the health department that surveillance was conducted and yielded no suspect patients (i.e., “zero reporting”). Smallpox surveillance forms will be completed on all suspect cases. Line lists will be maintained and updated daily, including both new patients and previously reported patients until smallpox is ruled out (CDC Form 6 and CDC Form 7).

b. Prospective Surveillance. Active surveillance for possible cases of smallpox currently hospitalized will be performed prospectively from first report of an index case in the emergency room (and any other unit that could accept patients directly without having ER evaluation), intensive care units, pathology and laboratory departments. Whenever possible, potential cases will be seen by an infectious-disease (ID) consultant, dermatologist, or smallpox consultant to clarify the diagnosis. Surveillance in each department is described below.

c. Retrospective Surveillance. To identify cases that may have been admitted before the outbreak was recognized, but once transmission in the community was theoretically possible, conduct retrospective screening of patients admitted with compatible syndromes from the date determined by local health department personnel. If resources are available, review records for all patients who were seen in the ER and discharged home, admitted, or transferred to another hospital. Review charts of patients with a non-lab-confirmed diagnosis of varicella (chickenpox), or generalized herpes zoster (shingles) or herpes simplex virus (HSV), or those described to have a diffuse vesicular or pustular rash with fever and no lab-confirmed diagnosis, to determine if the illness may have been smallpox. Evaluate patients currently in the hospital. Report those

transferred to another facility, discharged or expired to preventive-medicine or public-health channels, or gaining MTF for follow-up.

3. Strategies for Conducting Active Surveillance.

a. Emergency Departments, Intensive Care Units (ICUs), Wards. The ICP will visit or contact each hospital ward or unit to identify any hospitalized patient who could have smallpox.

b. Any patient with diagnosis of varicella (chickenpox), generalized herpes zoster (shingles), or HSV or “rule out (R/O) smallpox” will be evaluated. Any cases not already lab-confirmed will have infectious disease and/or dermatology consultation and rapid laboratory testing for varicella-zoster virus (VZV) (with HSV or other testing, if clinically indicated). Those considered high risk will be reported to the local or state health department as suspected or probable smallpox cases and be referred to the designated type C facility for isolation (Annex C). Moderate-risk patients will be entered on a separate line list (CDC Form 7, page 2) kept by the ICP with status updated at least daily (CDC Form 6). If a non-smallpox diagnosis is made, the patient is no longer on the active moderate-risk list. If the patient’s illness evolves and he or she meets criteria for high risk, the patient is reported as a new high-risk case and reported and transferred accordingly.

c. Pathology Department (for hospitals where autopsies are performed).

(1) Prospective. ICP will contact the chief pathologist daily to identify any previously unreported patients who died with a diagnosis of varicella (chickenpox), disseminated herpes zoster (shingles), or HSV, R/O smallpox, hemorrhagic or petechial or confluent/flat rashes, and any patient with a rash who died within 48 hours of admission. All these cases will have autopsies requested to confirm cause of rash, with a record review by an infectious-disease consultant. Report high-risk cases to preventive-medicine or public-health channels and complete smallpox surveillance form (CDC Form 1A and Form 1B).

(2) Retrospective. Review all deaths that occurred since smallpox transmission began in the community (as determined by local health officials), using the same criteria as above. All these patients will have autopsies requested to confirm cause of rash, with record review by the infectious-disease consultant. The physician of record may be contacted to provide additional information. Report high-risk cases to preventive-medicine or public-health channels. Complete a smallpox surveillance form.

d. Laboratory.

(1) Prospective. Review lab requests and results daily for tests ordered for orthopox viruses, varicella-zoster (excluding serology), herpes simplex (excluding serology), Rocky Mountain spotted fever, rickettsial pox, coxsackie viruses or echoviruses (excluding serology) or blood cultures ordered with diagnosis of possible

meningococcemia. Cross-check patients with newly ordered tests that have negative or pending results against a list of reported smallpox cases and the hospital's daily line list of cases for continued monitoring (CDC Form 6 and CDC Form 7). Record those not on either list on the lab surveillance list and perform chart review, to determine if patients have a clinically compatible illness. The infectious-disease consultant will determine risk category of patients in these groups. Report high-risk patients to preventive-medicine or public-health channels as suspected or probable smallpox cases, then transferred to a type C isolation facility. Follow results on low-risk hospitalized patients daily via line list until a diagnosis is confirmed. Review previously ordered tests with negative results in the same manner.

(2) Retrospective. If resources are available, review lab requests over the previous 7 days for the above tests with negative or pending results. Cross-check them against the list of reported smallpox cases and daily line list for continued monitoring. Record those not on either list on the lab surveillance list and perform chart review and infectious-disease consultation as above.

e. List Updates. ICP will maintain two lists (i.e., high-risk list, moderate-risk list) of cases and continually update lists with new cases.

(1) All high-risk cases are considered suspected or probable smallpox cases and will be reported immediately to the preventive-medicine or public-health surveillance officer, with arrangements made for immediate transfer to the designated type C isolation facility (Annex C). Report people whose illnesses evolve and who move from moderate- to high-risk as suspected or probable smallpox cases. Update patient location, status and lab results daily (CDC Form 6). Deliver the smallpox surveillance forms and updated high-risk list to the preventive-medicine or public-health surveillance officer once daily.

(2) The ICP will maintain daily line list of patients at moderate risk for smallpox but who are still under investigation. Update patient location, status and lab results daily. Deliver this updated list to the preventive-medicine or public-health surveillance officer once daily.

APPENDIX A-12
Classification of Evaluated Patients.

1. High Risk ("Epi-Linked").

a. Patients epidemiologically linked to a confirmed case of smallpox who have a history of a febrile prodrome (early symptoms with fever) and on examination had a maculopapular (red, bumpy) rash with predominantly face or distal-extremity distribution OR involvement of the palms and/or soles. "Epidemiologically linked" means a known connection in time and space with a source of infection. Or

b. Patients epidemiologically linked to a confirmed case of smallpox who have a viral syndrome with fever > 101°F and systemic symptoms (e.g., prostration, headache, backache, chills, vomiting, abdominal pain) for < 4 days but who do *not* have a generalized rash on examination.

2. High Risk (Not Epi-Linked). Patients with a severe prodromal illness with temperature > 101°F 1 to 4 days before rash onset, and at least one of the following: prostration, headache, backache, chills, vomiting, or abdominal pain, AND either (a) or (b):

a. Generalized rash of acute onset that is either: comprised of deep, round, dermal lesions characteristic of smallpox; maculo-papular rash involving the palms and/or soles OR distributed more densely on the face and distal extremities than the trunk AND no other lab-confirmed diagnosis that would adequately explain the illness. Or

b. Prostration or shock AND either maculo-papular rash, hemorrhagic rash, or rash with flat, velvety lesions that may be confluent AND no other lab-confirmed diagnosis that would adequately explain the illness.

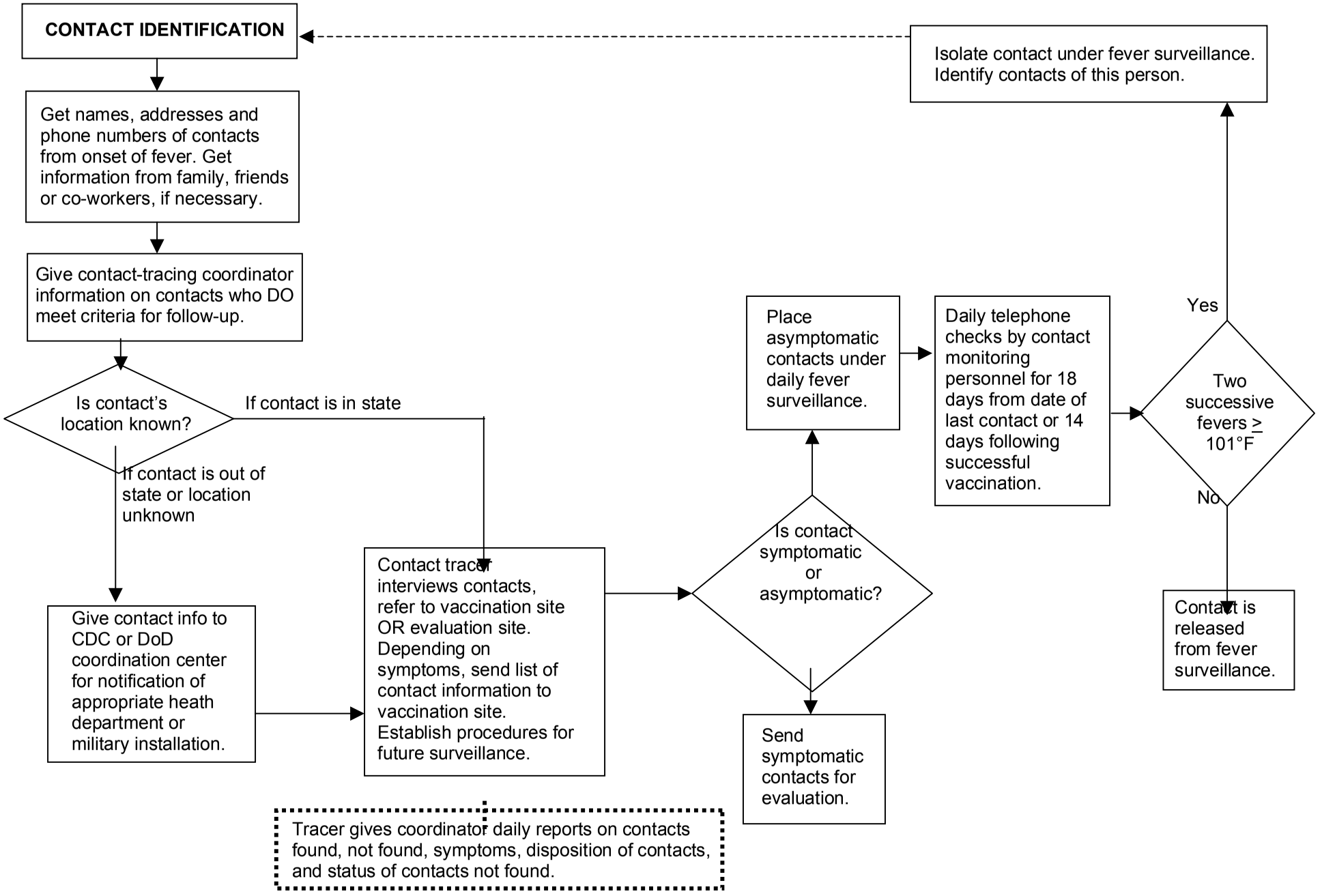
3. Moderate Risk (Not Epi-Linked). Patients with no known contact, or brief or uncertain contact, with a smallpox case with a prodromal illness consisting of temperature >101°F and at least one of the following: prostration, headache, backache, chills, vomiting, or abdominal pain AND a generalized rash of acute onset that is atypical for smallpox (e.g., lesions on oral mucosa only, maculo-papular rash with localized distribution to face, or face and forearms, hemorrhagic/petechial rash) AND no other lab-confirmed diagnosis that would adequately explain the illness.

4. Low Risk (Not Epi-Linked). Patients who are not epidemiologically linked to a smallpox case AND

a. Lack a history of a febrile prodrome,

b. Do not have classic smallpox lesions, OR

c. Have a laboratory confirmed non-smallpox diagnosis compatible with their illness.


CONTACT IDENTIFICATION
Get names, addresses and phone numbers of contacts from onset of fever. Get information from family, friends or co-workers, if necessary.
Give contact-tracing coordinator information on contacts who DO meet criteria for follow-up.
Is contact's location known?
If contact is in state
If contact is out of state or location unknown
Give contact info to CDC or DoD coordination center for notification of appropriate heath department or military installation.
Contact tracer interviews contacts, refer to vaccination site OR evaluation site. Depending on symptoms, send list of contact information to vaccination site. Establish procedures for future surveillance.
Is contact symptomatic or asymptomatic?
Send symptomatic contacts for evaluation.
Place asymptomatic contacts under daily fever surveillance.
Daily telephone checks by contact monitoring personnel for 18 days from date of last contact or 14 days following successful vaccination.
Two successive fevers ≥ 101°F
Yes
No
Isolate contact under fever surveillance. Identify contacts of this person.
Contact is released from fever surveillance.
Tracer gives coordinator daily reports on contacts found, not found, symptoms, disposition of contacts, and status of contacts not found.

APPENDIX A-14
Forms for Contact Identification, Tracing, and Surveillance.

Note. This appendix ignores obsolete CDC Forms and refers only to the CDC Form numbers in the numbering scheme of 23 January 2002. The CDC Forms are being extensively revised and will change again. Consult CDC website for current form versions: http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/index.asp.

Form	Purpose	Comment
Forms 1-4	*Detailed smallpox case investigation*	*4 modules**
Form 1 module	"Case Investigation Form Module." Patient, medical history and clinical case information (4 pages total) Form 1A. Intake history of the smallpox case (2 pages). Form 1B. Clinical course of disease (2 pages)	
Form 2 module	"Contact Identification Module" (5 pages total) Form 2. Contact information/interviewer checklist (2 pages). Form 2A. Case Travel/Activity Calendar, for recording daily events, names, and contact information for household contacts (1 page). Form 2B. Interview Contact/Site Summary Worksheet, for recording names, contact information, and exposure risks (1 page). Form 2C. Contact Transportation, for recording information on transportation and places visited outside of work or residence (1 page). Form 2D – Out of Area Travel Log, for recording names of places visited outside of home/work area (1 page).	
Form 3 module (previously Form 4)	"Source of Exposure Module" Form 3. Source of Exposure Interview Form (7 pages). Form 3A. Exposure Source Site Visit Form, for listing sites visited during period of possible exposure (1 page)**.** Form 3B. Exposure Source Transportation form, for listing sites (cities, states, countries) where case traveled during period of exposure and modes of transportation (1 page).	

* Note. The modules represented by the series of CDC Forms 1 through 4 are intended for the initial stages of a smallpox outbreak investigation. The investigation will require two or three staff members working concurrently. Using CDC Forms 1A and 1B, a medical epidemiologist should abstract information from admitting medical record or ER record, while another epidemiologist or public-health advisor interviews the case (or family member/friend if case is too ill for the interview) starting with CDC Form 2A, 2B, 2C, and 2D (contact identification module) and then CDC Forms 3A and 3B (source of

exposure module). Obtain information needed for CDC Form 1A or 1B that is not available from the medical record from the case or a close family member or friend.

Form 6 Daily Case Status Tracking form, used for updating case information that affects case classification (e.g., lab results, epi linkage) (1 page).

Form 7 Smallpox Hospital Surveillance Daily Tracking form.
Page 1 of 2 is used to line list high-risk patients.
Page 2 of 2 is used to line list medium-risk (sick) patients.

Form 8 Contact Interview, form for interviewing each contact and identifying household contacts of contacts (1 page).

Form 9 Contact Vaccination Referral form, roster for recording referral of contacts and household members for vaccination at a fixed site (1 page).

Form 10 Individual Contact Surveillance form, to record vaccine take and serious adverse events among household members of contacts (for use by contact tracer)
Page 1 of 2 is used for recording contacts.
Page 2 of 2 is used for secondary contact information (household contacts of case contacts).

Form 11 Contact Tracing form, master form for daily tracking of contact list (1 page).

CDC Forms under development.

Form 12 Form for contact to record daily temperatures, health status, vaccine take, and serious vaccine adverse events and vaccine take and serious vaccine adverse events of household contacts. *(This could be the same form as form 10 or with minor modifications.)*

Form 13 Daily master form to summarize contacts found/not found, symptoms of contacts, disposition of found contacts (vaccinated/referred for vaccination, referred for illness evaluation, isolated if fever or rash develops, status of contacts not found, number of contact's household members and those vaccinated or referred for vaccination. *(This may not need to be a form but rather a computer generated report from contact form data.)*

CDC Forms follow on successive pages. Forms 1A, 1B, 8, 9, 10-1 and 10-2 are provided with DoD overlays to collect Service-specific information.

Smallpox Case Investigation (Form 1A) (DOD OVERLAY)

STATE Case Report # _____

Patient Information

1. DATE OF CASE INTERVIEW: Month Day Year

2. NAME OF PERSON FILING THIS CASE:
Last: _____ ___ ___First: _____

Copy to Individual Military Health Record_____ Copy to CDC/State/Military Smallpox
Copy to Local/Base Military Health Office_____ Surveillance Center_____

3. PATIENT'S NAME: Last:_____ First: _____ Middle Name: _____ Suffix: _____ Nickname: _____

4. DATE OF BIRTH: Month Day Year

5. AGE: _____

6. GENDER: ☐ Male ☐ Female

7. RACE: Mark all that apply:
☐ White
☐ Black/African America
☐ Asian/Pacific Islander
☐ Native American/Alaskan
☐ Other, Please Specify: _____

8. ETHNICITY: ☐ Hispanic ☐ Non-Hispanic

3a. FMP-Sponsor-Social Security Number

3b. Personal Social Security Number

(Information on this form is subject to the Privacy Act of 1974.)

3c. Status:
☐ Active
☐ Guard/Reserve
☐ Retired
☐ Family Member

3d. Service_____ 3e. Unit Name_____

9. HOME ADDRESS:
_____
Street Address, Apt No. City State Zip Code

10. TELEPHONE: Home: Area Code Number Work: Area Code Number Other: Area Code Number

11. INTERVIEW LANGUAGE: _____ 12. COUNTRY OF BIRTH: _____

13. INFORMATION PROVIDED BY: ☐ Case ☐ Household Member ☐ Other Family Member ☐ Other (Specify):_____

IF NOT CASE, NAME: Last: _____ ___ First: _____ Middle Initial: _____

TELEPHONE: Home: Area Code Number Work: Area Code Number

14. ADMITTED TO HOSPITAL? ☐ Yes ☐ No ☐ Unknown IF YES, DATE OF ADMISSION: Month Day Year

HOSPITAL NAME:
_____
City State

MEDICAL RECORD #: _____

Vaccine and Medical History

15. SMALLPOX VACCINATION PRIOR TO OUTBREAK? ☐ Yes ☐ No ☐ Unknown
Note: Routine childhood smallpox vaccinations stopped in the United States in 1971; however, health care workers were vaccinated until the late 1970s and new military recruits not previously vaccinated were vaccinated until 1990.

DATE OF LAST VACCINATION: Month Day Year OR AGE AT VACCINATION: _____

16. IS A SMALLPOX VACCINATION SCAR PRESENT? ☐ Yes ☐ No ☐ Unknown
Note: This may be confused with BCG scars in immigrants.

17. SMALLPOX VACCINATION DURING THIS OUTBREAK? ☐ Yes ☐ No ☐ Unknown

DATE OF VACCINATION: Month Day Year

18. VACCINATION RECORD: ☐ Yes ☐ No ☐ Unknown

19. VACCINE "TAKE" RECORDED: ☐ Yes ☐ No ☐ Unknown

20. HISTORY OF VARICELLA DISEASE? ☐ Yes ☐ No ☐ Unknown

21. HISTORY OF VARICELLA VACCINATION? ☐ Yes ☐ No ☐ Unknown

VACCINE DATE, IF KNOWN:
Note: Varicella vaccine available in 1995. Month Day Year

22. PRE-EXISTING IMMUNOCOMPROMISING MEDICAL CONDITIONS, INCLUDING LEUKEMIA, OTHER CANCERS, HIV/AIDS? ☐ Yes ☐ No ☐ Unknown

IF YES, PLEASE SPECIFY: _____

23. FOR FEMALES OF 15-44 YEARS OF AGE, PREGNANT? ☐ Yes ☐ No ☐ Unknown

24. DURING THE PAST MONTH, ANY PRESCRIBED IMMUNOCOMPROMISING/IMMUNOMODULATING MEDICATIONS INCLUDING STEROIDS? ☐ Yes ☐ No ☐ Unknown

IF YES, PLEASE SPECIFY: _____ FOR WHAT MEDICAL CONDITION? _____

Smallpox Case Investigation (Form 1A – page 2)

STATE ☐☐ Case Report # _____

Current Illness

25. DATE OF CASE INTERVIEW: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

26. HAVE YOU HAD A FEVER AS PART OF THIS ILLNESS? ☐ Yes ☐ No ☐ Unknown IF YES, DATE OF ONSET OF FEVER: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

DID YOU MEASURE YOUR TEMPERATURE WITH A THERMOMETER: ☐ Yes ☐ No ☐ Unknown

MAXIMUM FEVER TEMPERATURE TO DATE: _____ F / C

DATE OF MAXIMUM FEVER: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

IF TEMPERATURE NOT MEASURED, DESCRIBE: ☐ Very Hot ☐ Hot ☐ Warm ☐ Unknown

27. DATE OF RASH ONSET: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

28. COUGH PRIOR TO RASH ONSET: ☐ Yes ☐ No ☐ Unknown

29. DATE OF COUGH ONSET: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

30. COUGH WITH RASH: ☐ Yes ☐ No ☐ Unknown

31. OTHER SYMPTOMS PRIOR TO RASH ONSET: (CHECK ALL THAT APPLY)

Headache: ☐ Yes ☐ No ☐ Unknown Backache: ☐ Yes ☐ No ☐ Unknown
Chills: ☐ Yes ☐ No ☐ Unknown Vomiting: ☐ Yes ☐ No ☐ Unknown
Other, Specify: _____

32. TYPE OF LESIONS ON THE DATE OF 1ST CASE INTERVIEW:
☐ Papules ☐ Vesicles
☐ Pustules ☐ Hemorrhagic
☐ Scabs ☐ Flat, confluent
☐ Unknown

33. DISTRIBUTION:
☐ Generalized, predominantly face and distal extremities (centrifugal)
☐ Generalized, predominantly trunk (centripetal)
☐ Localized, not generalized
☐ Other, specify: _____

Case Classification

34. IS THIS CASE LABORATORY-CONFIRMED: (SEE SMALLPOX CASE DEFINITION AND CLASSIFICATION BELOW) ☐ Yes ☐ No ☐ Pending ☐ Unknown

IF YES, BY WHAT METHOD: _____

35. IS THIS CASE EPIDEMIOLOGICALLY-LINKED TO A CONFIRMED OR PROBABLE CASE: ☐ Yes ☐ No ☐ Unknown

IF YES, WHICH TYPE OF CASE: ☐ Confirmed ☐ Probable

36. IS THIS CASE: ☐ Confirmed ☐ Probable ☐ Suspect

Smallpox Case Definition and Classification

Clinical Case Definition: An illness with acute onset of fever >101 F followed by a rash characterized by vesicles or firm pustules in the same stage of development without other apparent cause.

Case Classification
Confirmed case = A case that meets the above case definition and is laboratory confirmed.
Probable case = A case that meets the clinical case definition that is not laboratory confirmed but has an epidemiological link to another confirmed or probable case.
Suspect case = A case that meets the clinical case definition but is not laboratory confirmed and does not have an epidemiological link to a confirmed or probable case of smallpox, OR a case that has an atypical presentation that is not laboratory confirmed but has an epidemiological link to a confirmed or probable case of smallpox. Atypical presentations of smallpox include a) hemorrhagic and b) flat, velvety lesions not appearing as typical vesicles nor progressing pustules.

DATA MANAGEMENT USE ONLY:

DATE ENTERED IN SYSTEM: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

ENTERED BY (INITIALS): _____

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Smallpox Case Investigation Supplementary (Form 1B) (DOD OVERLAY)

STATE ☐☐ Case Report # _____

Patient Information

1. DATE OF FOLLOW-UP: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

3d. Service_____ 3e. Unit Name_____

2. NAME OF PERSON FILING THIS CASE:
Last: _____ ___ ___First: _____ Middle Initial: ____

3. PATIENT'S NAME:
Last: _____ First: _____
Middle Name: _____ Suffix: _____ Nickname: _____

3a. FMP-Sponsor-Social Security Number ☐☐ ☐☐☐ ☐☐ ☐☐☐☐

3b. Personal Social Security Number ☐☐☐ ☐☐ ☐☐☐☐

(Information in this form is subject to the Privacy Act of 1974.)

3c. Status: ☐ Active ☐ Guard/Reserve ☐ Retired ☐ Family Member

3d. Service_____ 3e. Unit Name_____

4. ADMITTED TO 2ND HOSPITAL OR ISOLATION SITE? ☐ Yes ☐ No ☐ Unknown

IF YES, DATE OF ADMISSION: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

HOSPITAL NAME: _____
City State

2nd HOSPITAL MEDICAL RECORD #: _____

Clinical Course

5. SMALLPOX TYPES*: RASH (MOST SEVERE STAGE):

☐ Ordinary Type: ☐ Confluent – Face and other site ☐ Semi-confluent – Face only ☐ Discrete lesions
☐ Modified Type
☐ Flat Type
☐ Hemorrhagic Type: ☐ Early ☐ Late

*Ordinary type:	Raised, pustular lesions with 3 sub-types:	Flat type:	Pustules remain flat; usually confluent or semi-confluent, usually fatal
Confluent	Confluent rash on face and forearms	Hemorrhagic type:	Widespread hemorrhages in skin and mucous membranes
Semi-confluent	Confluent rash on face, discrete elsewhere	Early	With purpuric rash, always fatal
Discrete	Areas of normal skin between pustules, even on face	Late	With hemorrhage into base pustules, usually fatal
Modified type:	Like ordinary type but with an accelerated course		

6. DATE LAST SCAB FELL OFF: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

7. COMPLICATIONS (Check all that apply).

Skin Secondary bacterial infection:	☐ Yes	☐ No	☐ Unknown
Ocular corneal ulcer or keratitis:	☐ Yes	☐ No	☐ Unknown
CNS encephalitis:	☐ Yes	☐ No	☐ Unknown
Respiratory: ☐ Bronchitis	☐ Yes	☐ No	☐ Unknown
Respiratory: ☐ Pneumonia	☐ Yes	☐ No	☐ Unknown
Joint/Bones: ☐ Arthralgia	☐ Yes	☐ No	☐ Unknown
Joint/Bones: ☐ Osteitis	☐ Yes	☐ No	☐ Unknown
Hemorrhagic:	☐ Yes	☐ No	☐ Unknown
Shock:	☐ Yes	☐ No	☐ Unknown

Other, please specify: _____

8. ANTIVIRAL MEDICATION: CIDOFOVIR ☐ Yes ☐ No ☐ Unknown

OTHER ANTIVIRAL MEDICATIONS, SPECIFY: _____

9. SMALLPOX VACCINATION HISTORY

WAS THE CASE VACCINATED SINCE THE COMPLETION OF FORM 1A? ☐ Yes ☐ No ☐ Unknown

DATE: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

VACCINE "TAKE" RECORDED AT 7 DAYS? ☐ Yes ☐ No ☐ Unknown

Clinical Course Disposition

10. DATE OF HOSPITAL DISCHARGE: ☐☐ Month ☐☐ Day ☐☐☐☐ Year

COMPLICATIONS AT DISCHARGE: ☐ Yes ☐ No ☐ Unknown

IF YES, PLEASE SPECIFY: _____

Smallpox Case Investigation Supplementary (Form 1B- page 2)

STATE Case Report # _____

Clinical Course Disposition

11. OUTCOME: ☐ Survived ☐ Died

12. DATE OF DEATH: ☐☐ ☐☐ ☐☐☐☐ (Month Day Year)

13. AUTOPSY PERFORMED: ☐ Yes ☐ No ☐ Unknown

DATE: ☐☐ ☐☐ ☐☐☐☐ (Month Day Year)

14. SITE AUTOPSY PERFORMED:

_____
Site/Institute

_____
City State

NAME OF PATHOLOGIST: _____

TELEPHONE: ☐☐☐ ☐☐☐ ☐☐☐☐ (Area Code Number)

Laboratory Information

15. LAB TESTING FOR SMALLPOX: ☐ Yes ☐ No ☐ Unknown

Mark those that apply:	DATE SPECIMEN TAKEN	RESULT	TYPE OF SPECIMEN* (SKIN LESION, SEROLOGY, OTHER (SPECIFY))
PCR:	___/___/_____	☐ Positive / ☐ Negative / ☐ Indeterminate	_____
Culture:	___/___/_____	☐ Positive / ☐ Negative / ☐ Indeterminate	_____
Electronic Microscopy:	___/___/_____	☐ Positive / ☐ Negative / ☐ Indeterminate	_____
IgM:	___/___/_____	☐ Positive / ☐ Negative / ☐ Indeterminate	_____
IgG Acute:	___/___/_____	☐ Positive / ☐ Negative / ☐ Indeterminate	_____
IgG Convalescent:	___/___/_____	☐ Positive / ☐ Negative / ☐ Indeterminate	_____

16. FINAL CASE STATUS: ☐ Confirmed ☐ Probable ☐ Suspect ☐ Not Smallpox

17. LAB CONFIRMED? ☐ Yes ☐ No ☐ Unknown

TYPE OF TEST: _____

IF NOT SMALLPOX, SPECIFY CORRECT DIAGNOSIS: _____

Smallpox Case Definition and Classification

Clinical Case Definition: An illness with acute onset of fever >101 F followed by a rash characterized by vesicles or firm pustules in the same stage of development without other apparent cause.

Laboratory Criteria for Diagnosis*
1. Isolation of smallpox (Variola) virus from a clinical specimen, or
2. Polymerase chain reaction (PCR) identification of variola DNA in a clinical specimen, or
3. Negative stain Electron microscopy (EM) identification of Variola virus in a clinical specimen

Case Classification
Confirmed case = A case that meets the above case definition and is laboratory confirmed.
Probable case = A case that meets the clinical case definition that is not laboratory confirmed but has an epidemiological link to another confirmed or probable case.
Suspect case = A case that meets the clinical case definition but is not laboratory confirmed and does not have an epidemiological link to a confirmed or probable case of smallpox, OR a case that has an atypical presentation that is not laboratory confirmed but has an epidemiological link to a confirmed or probable case of smallpox. Atypical presentations of smallpox include a) hemorrhagic and b) flat, velvety lesions not appearing as typical vesicles nor progressing pustules.

DATA MANAGEMENT USE ONLY:

DATE ENTERED IN SYSTEM: ☐☐ ☐☐ ☐☐☐☐ (Month Day Year)

ENTERED BY (INITIALS): _____

Draft Version 4.0 20 Dec 01

Smallpox Case Investigation

Form 2 –Instructions for Obtaining Contact Tracing Information

Form 2 - Contact information/interviewer checklist

Form 2A – Case Travel/Activity Calendar: for recording daily events names and contact information for household contacts

Form 2B – Interview Contact/Site Summary Worksheet: for recording names, contact information, and exposure risks

Form 2C – Contact Transportation: for recording information on transportation and places visited outside of work or residence

Form 2D – Out of Area Travel Log: for recording names of places visited outside of home/work area

Introductory Script for Contact Module for Case Interview

It is very important that we ask you questions now because (you/your child/other) may have smallpox infection. If you are the suspected case, the questions relate to you. If we are interviewing you about your child or another family member or a close friend who may have smallpox, these questions relate to that person. The more information thatwe get from you now, the more chance we have of stopping the spread of this very serious illness.

We will be asking you lots of questions about people (you or insert name for child/other_____) have been around, places (you or insert name for child/other_____) have been including regular activities such as work and school and occasional activities or trips (you/your child/other) might have taken, in different periods of time. Firstly we need to know who (you or insert name for child/other_____) have been in close contact with and where you have been since you became sick starting with the first day of your fever. These people may have caught smallpox from (you or insert name for child/other_____) and we can prevent them from coming down with smallpox or make the illness less serious if we vaccinate them as soon as possible. Every hour counts.

We will show you a calendar to help you remember this information. After that, we will talk with you about a different time period before you got sick to try and find out where you caught this infection.

We will start by looking at the calendar.

Instructions for interviewer: Please record date of fever onset, date of rash onset and date of interview on the calendar. Mark the days from fever onset until today (date of interview) in blue and refer to the calendar as you review activities each day. The interview period starts on the day of the interview and goes back to the day of fever onset. It may be helpful to list activities for each day as that day is discussed. Keep in mind that we are interested in the "Who, what, where, how, and when".

Interview Checklist

□ Accurately identify appropriate interview period (when patient could have been contagious)

□ Begin with overview of entire interview period using the Case Travel/Activity Calendar addressing activities below and getting a preliminary list of contacts (named, unnamed or groups) in the following priority order:

1st - HH contacts; immediate family members and others with >3 hours in house since rash
2nd - contacts with close contact to rash (<6 ft) for >3 hours
3rd - contacts with close contact to rash (<6 ft) for 1-3 hours
4th - contacts with close contact to rash (<6 ft) for < 1 hour
5th - contacts with >6ft contact to rash for >1 hour
6th - contacts with >6ft contact to rash for <1 hour

- Case Travel/Activity
  - Type of Residence; single detached house, apartment with separate entrance; apartment or dormitory with shared entrance or other areas, shelter or other

  - Routine Activity
    - work
      - name and address; # of companies in bldg; setting (office, cube); # employees; # in office; schedule; work outside the office; contact with public or others from outside
    - school
      - name & address; classes; schedule; other school activities; off-campus activities
    - shopping (gas, groceries, mall, video store)
    - exercise
    - church
    - laundry (either at the laundromat or cleaned by someone else or sent out)
    - picking up or taking others (children etc) to places
    - other
    - mode of travel to and from routine activities

  - Health Care Provider visit
    - name & address of provider(s), clinic(s), or facilities visited; locations visited within facility (i.e. emergency room, outpatient waiting area, etc)

  - Group Events (Was there assigned seating? Did case cough or have close contact with any other attendees?)
    - sporting events
    - theater
    - family gathering
    - holiday event
    - festivals
    - work parties
    - other
    - mode of travel

  - Visitors
    - overnight
    - family
    - friends
    - mailman, UPS, repairmen
    - hosting a party
    - other

  - Out of Town Travel
    - alone or with a group
    - airplane (including airports)
    - car (gas stations, rest stops, restaurants/fast food)
    - train, boat, bus other
    - hotels
    - restaurants
    - tours
    - sightseeing
    - other

- After overview, start back from date of interview and go back day by day until day of fever onset accounting for any gaps in time

- Obtain detailed information for each person and group:
  - name, age, sex, description, address, phone number(s), time and place of contact

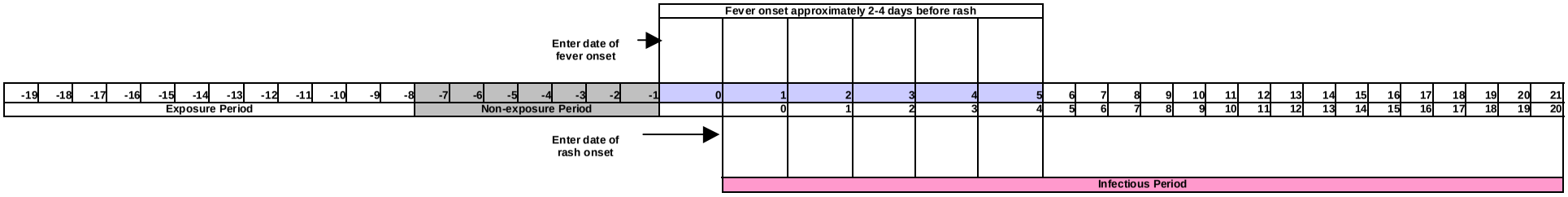
  - for unnamed contacts or groups, obtain as much information as possible on their description, locating information or other information that may assist in locating them.

  - obtain enough information on the duration and proximity of contact to assign contacts to the appropriate risk category (i.e. beginning and end time for each exposure, distance between patient and contact during exposure, accurate symptom history of patient to verify if contacts were during infectious period)

Name of Interviewer: _____ Case #_____ Date Interviewed:_____

[DRAFT (12/31/01)] CASE TRAVEL/ACTIVITY CALENDAR (FORM 2A)

SUNDAY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY
DATE:	DATE:	DATE:	DATE:	DATE:	DATE:	DATE:
DATE:	DATE:	DATE:	DATE:	DATE:	DATE:	DATE:
DATE:	DATE:	DATE:	DATE:	DATE:	DATE:	DATE:
Week fever onset DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C
DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C
DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C	DATE: ☐F☐R☐C



Interviewer Contact/Site Summary Worksheet (Form 2B)

Case ID# _____ **Date Interviewed:** ____/____/____

Name of Interviewer: _____ **Date of Rash Onset:** ____/____/____

	Exposure			Contact				
Name of Person (Last, First) and/or Name of Site	First Date	Last Date	Distance (Circle)	X, A, B, C, D, E	Date Field Record Initiated	Field Record #	# of Days Since Rash Exposure	Notes:
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			
			<6ft or >6ft		___/___/___			

Case Contact Priority Categories:
X = (highest priority) Case Household contacts: all immediate family members; others spending >3 hours in the household since case's onset of rash
A = Non household contacts with close contact (less than 6 feet) with Case with rash for >3 hours
B = Non household contacts with close contact (less than 6 feet) with Case with rash for 1-3hours
C = Non household contacts with close contact (less than 6 feet) with Case with rash for <1hour
D = Non household contact with contact greater than 6 feet with Case with rash for >1 hour
E = Non household contact with contact greater than 6 feet with Case with rash for <1hour OR Non household contact with Case with Fever only (no rash)

Smallpox Case Investigation

Form 2C – Contact Transportation **Case ID: _____**

Complete as much information on worksheet as possible for each type of transportation used since onset of fever of case Date: _____/_____/_____

Interstate or international travel								
Date mm/dd/yyyy	**Time AM/PM**	**Type of transport Bus, train, plane, car**	**Company name**	**Flight/route number**	**Origin City**	**Origin State**	**Destination City**	**Destination State**

Travel within city and state including commuting to and from work/other regular activities						
Date mm/dd/yyyy	**Time AM/PM**	**Type of transport Bus, train, plane, carpool or taxi**	**Company name**	**Route number/flight**	**Origin City**	**Destination City**

OUT OF AREA TRAVEL LOG (Form 2D)

Smallpox Case ID: _____ **Interviewer(s): _____** **Date Interviewed: ____/____/____**

Travel Date	Mode of Travel	Carrier Information	Origin		Destination		Notes
			City	State/Country	City	State/Country	

Smallpox Case Investigation

Form 4 -- Source of Exposure **ID:** _____

The second time period we need to ask you about, is from one to three weeks before your rash. This will help us learn where you may have caught this infection. We will ask you about sick people you or (_____insert name of family member/other) may h ave been around over the last 3 weeks and places that you have been.

1. Do you know whom you caught this illness from? 1 □ Yes 2 □ No (if no, go to Question 5)

2. Name of person: Diagnosis:

3. Home Address

City: State: Zip:

Telephone Home Cellular

4. Do you know where you caught this illness? 1 □ Yes 2 □ No (if no, go to Question 6)

5. If yes, Name of place

Address (if known)

City: State: Zip:

Date Phone (if known)

Time

Number of persons potentially exposed

6. During the dates from (insert date 1, 21 days before rash onset) to (insert date 2, 7 days before rash onset) before your rash onset, were you in contact with anyone who appeared to have:

Chickenpox 1 □ Yes 2 □ No 2 □ Unknoown

A severe rash on the face and/or arms 1 □ Yes 2 □ No

Smallpox Case Investigation

Form 4 -- Source of Exposure **ID:** _____

7. If yes, Name of person: Dignosis:

_____

Address

_____

City: State: Zip:

_____

Telephone Home Cellular

_____

8. Date of exposure: / /

_____

Interviewer: Please use clinical and exposure data to classify the case to one of the categories below.

9. Smallpox Case classification 1 □ Confirmed 2 □ Probable 3 □ Suspected

_____

Case classification:

Confirmed	A case of smallpox that is laboratory confirmed
Probable	A case that meets the clinical case definition that is not laboratory confirmed but has an epidemiological link to another confirmed or probable case
Suspected	A case that meets the clinical case definition but is not laboratory c onfirmed and does not have an epidemiological link to another confirmed or probable case of smallpox OR a case that has one of the following atypical presentations (hemorrhagic or flat, velvety lesions) that is not laboratory confirmed but has an epidemiological link to a confirmed or probable case of smallpox.

If case does not know source of infection, continue with the following questions.

Now we need to think back to try to find out where you may have caught this illness. We will start by looking at the calendar. The interviewer should record date of rash onset then count back 7 day and 21 days. Mark the 14 day time period clearly on the calendar in red..

Smallpox Case Investigation

Form 4 -- Source of Exposure **ID:** _____

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Insert month e.g. December	Insert month	Insert month	Insert month	Insert month	Insert month	Insert month

For the next questions, I'd like you to think back to the 14 day period between 1 and 3 weeks ago that we have marked on the calendar. Lets start with weekdays. Offer dates, holidays, etc., as available to anchor the case's recall to this time period.

What is your usual weekday routine? Do you work? Go to school? Volunteer on a regular basis? Have another every day activity?

Interviewer: Consider routine weekday activities in a systematic way going either back from day 7 or forwards from day 21 from fever onset depending on what seems easier to do.

For weekends, ask about usual routines and then occasional activities. Prompt especially for attendance at public events. A question to capture this type of attendance follows after questions regarding usual activities.

10. During this 14 days time period designated above (**show the calendar**), did you spend any time regularly (3 or more times a week) in the following places? (Check all that apply)

Work 1 □ Yes 2 □ No

School 1 □ Yes 2 □ No

A restaurant 1 □ Yes 2 □ No

Your child's school or day care center? 1 □ Yes 2 □ No

Grocery Store 1 □ Yes 2 □ No

Smallpox Case Investigation

Form 4 -- Source of Exposure **ID:** _____

Other i.e. place of worship, gym, restaurant, volunteer work, etc, specify

If yes to any of the above, please complete **Form 4A -- Exposure Source Site Form. For daily activities such as work, dropping child off at day care center, indicate range of days.**

11. If you work, go to school, or transport your children or other family members to school and/or day care or other regular activities, how do you travel to and from these places?

Car–alone, bicycle, walk 1 □ Yes 2 □ No

Car–with other people in the car at least sometimes 1 □ Yes 2 □ No

If yes, complete **Form 4B -- Exposure Source Transportation Form**

Bus, train or subway 1 □ Yes 2 □ No

If yes, complete **Form 4B -- Exposure Source Transportation Form**

Taxi 1 □ Yes 2 □ No

If yes, complete **Form 4B -- Exposure Source Transportation Form**

Other, specify (e.g, plane) 1 □ Yes 2 □ No

If yes, complete **Form 4B -- Exposure Source Transportation Form**

Note: for regular travel schedule e.g. to and from work, indicate range of days and times if this is the same each day.

12. During the 14 day time period designated above, did you travel out of town (if city, out of urban area, if rural, our of county)?

1 □ Yes 2 □ No

If yes, please complete **Form 4B -- Exposure Source Transportation Form**

13. During the 14 day time period designated above, did you visit any of the following activities at least once: (read each description)

Hotel or convention center 1 □ Yes 2 □ No

Shopping mall or large store 1 □ Yes 2 □ No

Church, temple, mosque or other place of worship 1 □ Yes 2 □ No

Doctor's office, emergency department, clinic or hospital? 1 □ Yes 2 □ No

Airport 1 □ Yes 2 □ No

Smallpox Case Investigation

Form 4 -- Source of Exposure **ID:** _____

Bus, train or subway station	1 □ Yes	2 □ No
Theater (e.g., movies or play)	1 □ Yes	2 □ No
Concert	1 □ Yes	2 □ No
Public sporting event	1 □ Yes	2 □ No
Fair, festival or carnival	1 □ Yes	2 □ No
Any other gathering with more than 100 other people	1 □ Yes	2 □ No

If yes to any of the above, please complete for each place visited **Form 4B -- Exposure Source Transportation Form**

Smallpox Case Investigation

Form 4 -- Source of Exposure **ID:** _____

Form 4A -- Exposure Source Site Visit Form

List all sites that you (insert name if interviewing regarding child or other person) visited in the 1-3 weeks before the rash onset: Date: _____/_____/_____

Day of week	Date mm/dd/yyyy	Time	Site code	Type of site	Name of site	Street address	City	County	State	Zip

Smallpox Case Investigation

Form 4 -- Source of Exposure **ID:** _____

Form 4B Exposure Source Transportation

Complete as much information as possible for each type of transportation you (insert name if interviewing regarding other person) have used for travel or commute in the 1-3 weeks period before rash

onset: Date: _____/_____/_____

Interstate or International travel

Date mm/dd/yyyy	Time AM/PM	Type of transport Bus, train, plane, carpool, Taxi	Company name	Flight/route number	Origin City	Origin State	Destination City	Destination State

Travel and commute within city and state

Date mm/dd/yyyy	Time AM/PM	Type of transport Bus, train, plane, carpool, Taxi	Company name	Flight/route number	Origin City	Destination City

Draft 2 - Guide A: Form 6 -- Daily Case Status Tracking

DRAFT

Smallpox Daily Followup Sheet

Date ____________

State ________ **Local Health Department** ________

							Current Status			Updated Status?		
Case ID	**Last Name**	**First Name**	**DOB**	**Sex**	**Hospital**	**Chart No.**	**Case Status**	**Lab Status**	**Epi Link**	**Case Status**	**Lab Status**	**Epi Link**

Shaded area above is printed daily from existing surveillance data

Area above for updates

Draft 2 - Guide A: Form 7 -- Smallpox Hospital Surveillance Daily Tracking

LINE LIST: HIGH RISK PATIENTS (Suspected or probable smallpox cases)

Hospital:_____ Date: ___ / ___ / 200__

Completed by: _____ Contact phone number _____

Name	Medical Record Number	DOB	Sex	Epi-linked?	Date of Rash Onset	Date of admission	Attending Physician/Location	Date of Isolation	Date reported to health dept.	Date transferred to type C facility	Type C facility Name

LINE LIST: MEDIUM RISK PATIENTS

Name	Medical Record Number	DOB	Sex	Epi-linked?	Date of Rash Onset	Date of admission	Attending Physician/Location	Diagnosis	Lab Tests Resulted (Specimen:Test:Result)	Lab Tests Pending	Comment/Disposition

Lab Tests:
Varicella-zoster: DFA, PCR, IgG, EM, Tzanck, culture
Herpes simplex: DFA, PCR, Tzanck, EM, culture
Blood culture
Other viral culture
Orthopox virus testing
Serology
Biopsy/Pathology

Interview information

(DOD OVERLAY)

Date _____/_____/____ Time: _____AM/PM Place_____
Interviewer: Name_____ Phone: _____

Case information
Name: Last _____First_____ SSN_____ Case ID#_____

Contact information

(Information on this form is subject to the Privacy Act of 1974.)

Name	Service
Status Active Guard/Reserve Retired Family	Unit Name
SSN	Home Phone
FMP – Sponsor SSN	Work phone
Address	Cell phone
City	Other phone
Birth date	Email
Date of exposure	Duration of exposure
Place of exposure	Confirmation of exposure yes no dk
Were other persons who you can identify exposed at the same time you were?	

Household contacts of the contact. Include household-like contacts (nanny, neighbors or relatives who visit frequently, etc.)

Number	Name	Relationship	Birth date	Age (years)	Present (Y/N)
1					
2					
3					
4					
5					

For household members not present, how/when/where to contact them:

Name	Contact information (phone number, address)

(DOD OVERLAY)

(DOD OVERLAY)

Contact and Household Member Identification for Referral to Vaccination Site

Name of Contact Tracer:_____

Date of referral (mm/dd/yyyy): _____/_____/_____

Vaccination Site referred to: _____

Vaccination Site Address: _____ Phone:_____

(Information on this form is subject to the Privacy Act of 1974.)

Name (Last, first, MI)	**Status: Active/ Guard Reserve Retired Family**	**Service/ Unit Name**	**Contact (C) or Household Member (H)**	**SS# or other identification (driver's lic. #, passport #)**	**FMP – Sponsor SS#**

(DOD OVERLAY)

Draft 2 – Guide A – Form 10 **- Individual Contact Surveillance** **DOD OVERLAY** **29 Sep 02** 1 of 2

CITY ________________ COUNTY______________ STATE ______________ (DOD OVERLAY)

DATE VACCINATED: _____/_____/_____ VACCINE LOT # ________________VACCINATED BY _______________

CONTACT TRACER: Name ____________________________ PHONE: _______________________

CONTACT NAME ___________________________ DATE BIRTH ________________SEX ______ SSN ________________

STATUS: ☐ACTIVE ☐GUARD/RESERVE ☐RETIRED ☐FAMILY FMP - SPONSOR SSN ________________

SERVICE______________ UNIT NAME ____________________

HOME ADDRESS ____ HOME PHONE ______________

OCCUPATION ____ BUSINESS PHONE __________________

BUSINESS ADDRESS ____

EXPOSURE TO CASE ID#__________________ CASE SSN#_______________

DATE OF 1ST EXPOSURE: ______/_____/______ DATE OF LAST EXPOSURE: _______/______/_______

(Information on this form is subject to the Privacy Act of 1974.)

Date	**Type of Contact**	**Time of Contact**	**Signs and Symptoms**					**Vaccination Site***	**Meds taken since last contact**	**Contacted By**
			Temp °F	**Yes or No**						
				Head-ache	Back-ache	Malaise	Rash			
	Visual									
	Phone									
	Visual									
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*From the following list, choose the letter closest to the bottom of the list that describes the vaccination site. For example, if the vaccination site is read and indurated on a particular day, you would write only the letter "I."

O – No Reaction
R – Redness
I – Induration
P – Papule, Pustule
U – Ulcer
S – Scab

(DOD OVERLAY)

Secondary contact Information (household contacts of case contacts)

List all secondary contacts including family members, visitors, workers in household since date that contact was exposed to case

(Information on this page is subject to the Privacy Act of 1974.)

No.	Last Name/ First Name	Age yrs	Sex M/ F	Relation	Other Phone #	Social security #	FMP-Sponsor Social Security #	Status: Active Guard/Reserve Retired Family	Service/ Unit Name	Address (if different from contact) #/Street/Apt City State Zip	Vacc date	Day7VaccSiteStatus **Y**:like photo card **OR N**:other status, **and RV:**need revaccination, or **NRV**: no revac need, (**N / RV** referred to:)	**Severe Reaction Y/N:** describe **Type, Onsetate Referred to:**

Draft 2 - Guide A: Form 11 – Contact Tracking

CONTACTS UNDER SURVEILLANCE – DAILY RECORD MASTER FORM

City_____County_____State_____

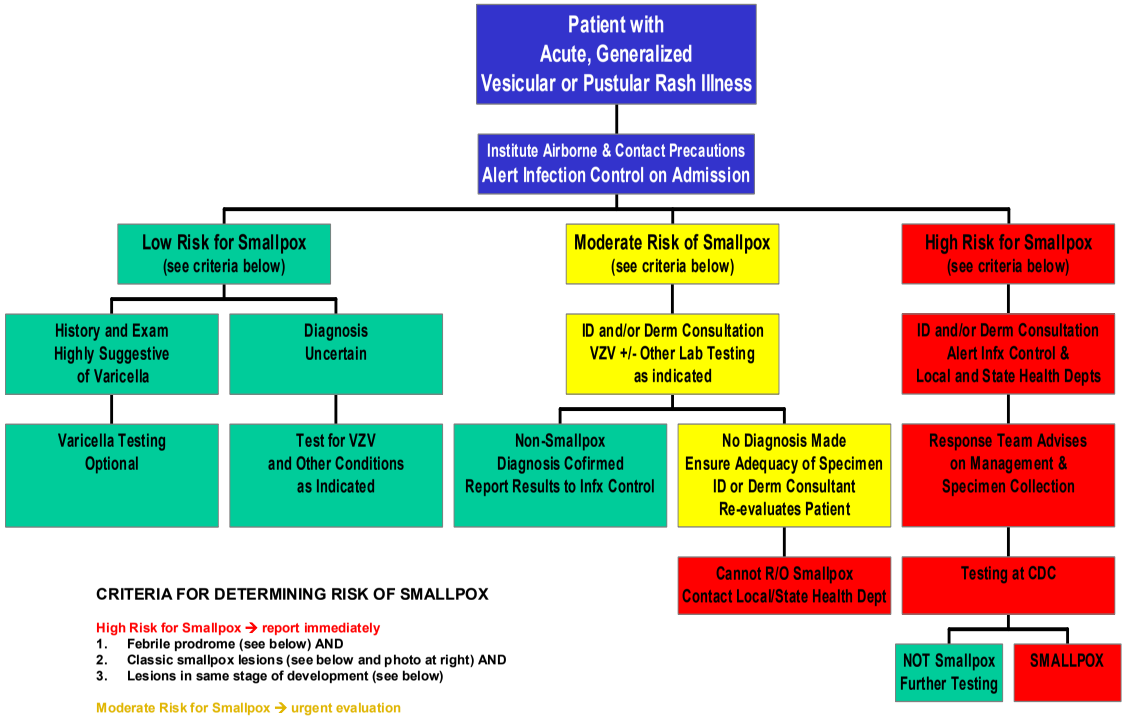
Contact No.	NAME	Age	Sex	ADDRESS	Vaccination History				Control Vaccination			Surveillance		Dates																				
					Date last vaccinated	Date last take	Scar Y/N		Date	Date major Reaction	Date Revacc -inated	Begin	End	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20

Instructions:

1. Fill in the number, name, age, sex, address, vaccination info., and dates of surveillance period of each contact.
2. In the block above the column labeled "18" write the date of the onset of smallpox patient's symptoms.
3. Working backwards from the date of onset of the smallpox patient's symptoms, fill in the appropriate dates above columns 1-17.
4. Fill in the appropriate dates above column 19 through the column which represents 18 days after the smallpox patient was isolated (e.g., if the smallpox patient was isolated on day 20 [2 days **after** the onset of symptoms], you would fill in the dates through column 38). Extend the form so that there are as many columns as necessary.
5. For each contact, shade in all the blocks prior to the date of last contact.
6. For each contact, shade in all the blocks following the date, which is 18 days after last contact.
7. Use the following codes to describe the status of each contact on each day during the surveillance period (unshaded blocks)

   Seen and Well – W
   Seen and Sick – S
   Not Seen – N

Generalized Vesicular or Pustular Rash Illness Protocol



A suspected case of smallpox is a public health and medical emergency.

Clinical case definition of smallpox: an illness with acute onset of fever ≥101°F followed by a rash characterized by vesicles or firm pustules in the same stage of evolution without other apparent cause.

Report ALL *suspected* cases (without waiting for lab results) to:
1. Hospital Infection Control ( ) ___-____ or ( ) ___-____ Pager
2. (Local) health department ( ) ___-____ or ( ) ___-____ Pager
3. (State) health department ( ) ___-____ or ( ) ___-____

Questions ? Centers for Disease Control and Prevention:
(404)639-3532 days; Nights/weekends/holidays: (770) 488-7100

CRITERIA FOR DETERMINING RISK OF SMALLPOX

High Risk for Smallpox → report immediately
1. **Febrile prodrome (see below) AND**
2. **Classic smallpox lesions (see below and photo at right) AND**
3. **Lesions in same stage of development (see below)**

Moderate Risk for Smallpox → urgent evaluation
1. **Febrile prodrome (see below) AND**
2. **One MAJOR smallpox criterion (see below)**

OR

1. **Febrile prodrome (see below) AND**
2. **≥4 MINOR smallpox criteria (see below)**

Low Risk for Smallpox → manage as clinically indicated
1. **No viral prodrome OR**
2. **Febrile prodrome and <4 MINOR smallpox criteria (no major criteria) (see below)**

Smallpox Criteria

MAJOR SMALLPOX CRITERIA

▪**FEBRILE PRODROME**: occurring 1-4 days before rash onset: fever >102°F **and** at least one of the following: prostration, headache, backache, chills, vomiting or severe abdominal pain. All smallpox patients have a febrile prodrome. The fever may drop with rash onset.

▪**CLASSIC SMALLPOX LESIONS**: deep, firm/hard, round, well-circumscribed; may be umbilicated or confluent

▪**LESIONS IN SAME STAGE OF DEVELOPMENT:** on any one part of the body (e.g., the face, or arm) all the lesions are in the same stage of development (i.e. all are vesicles, or all are pustules)

MINOR SMALLPOXCRITERIA

▪Centrifugal distribution: greatest concentration of lesions on face and distal extremities

▪First lesions on the oral mucosa/palate, face, forearms

▪Patient appears toxic or moribund

▪Slow evolution: lesions evolve from macules to papules→pustules over days

▪Lesions on the palms and soles (majority of cases)

CHICKENPOX (VARICELLA) IS THE MOST LIKELY CONDITION TO BE MISTAKEN FOR SMALLPOX.

How varicella (chickenpox) differs:

▪No or mild, brief (1 day) prodrome

▪Lesions are superficial vesicles: "dewdrop on a rose petal"

▪Lesions appear in crops; on any one part of the body there are lesions in different stages (papules, vesicles, crusts)

▪Centripetal distribution: greatest concentration of lesions on the trunk, fewest lesions on distal extremities. May involve the face/scalp. Occasionally entire body equally affected.

▪First lesions appear on the trunk, or occasionally on face

▪Patients rarely toxic or moribund

▪Rapid evolution: Lesions evolve from macules → papules→ vesicles →crusts quickly (<24 hours)

▪Palms and soles spared

▪Patient lacks reliable history of varicella or varicella vaccination

▪50-80% recall an exposure to chickenpox or shingles 10-21 days before rash onset

Conditions With Vesicular or Pustular Rashes

Condition	Clinical Clues
Varicella (primary infection with varicella-zoster virus)	Most common in children <10 years; children usually do not have a viral prodrome
Disseminated herpes zoster	Prior history of chickenpox; immunocompromised hosts
Impetigo (*Streptococcus pyogenes, Staphylococcus aureus*)	Honey-colored crusted plaques with bullae are classic but may begin as vesicles; regional not disseminated
Drug eruptions and contact dermatitis	Exposure to medications; contact with possible allergens
Erythema multiforme (incl. Stevens Johnson Sd)	Major form involves mucous membranes and conjunctivae
Enteroviruses incl. Hand, Foot and Mouth disease	Summer and fall; fever and mild pharyngitis at same time as rash; distribution of small vesicles on hands, feet and mouth or disseminated
Disseminated herpes simplex	Lesions indistinguishable from varicella; immunocompromised host
Scabies; insect bites (incl. fleas)	Pruritis; in scabies, look for burrows (vesicles and nodules also occur); flea bites are pruritic, patient usually unaware of flea exposure
Molluscum contagiosum	Healthy afebrile children; HIV+ individuals
Bullous Pemphigoid	Bullous lesions. Positive Nikolski sign.
Secondary syphilis	Rash can mimic many diseases; rash may involve palms and soles; 95% maculo-papular, may be pustular. Sexually active persons

Variant presentations of smallpox: approximately 3-5% of persons never vaccinated for smallpox will present with **hemorrhagic smallpox** (see photo-- can be mistaken for meningococcemia, hemorrhagic varicella, Rocky Mountain spotted fever, erlichiosis, acute leukemia) and 5-7% with **flat-type smallpox** (see photo). Both variants are highly infectious and carry a high mortality.

Laboratory Testing for Varicella: Collect *at least* 3 good specimens from each patient

- Direct fluorescent antibody (DFA)—rapid, depends on adequate specimen (see below)
- Indirect fluorescent antibody (IFA) —rapid, depends on adequate specimen (see below)
- Polymerase chain reaction (PCR)--available in research labs, some tertiary care centers
- Serologic testing: an IgG (collected at time of rash) provides evidence of prior varicella, and makes acute varicella infection unlikely but does not rule out herpes zoster in persons at risk of dissemination. IgM is not useful for diagnosis.
- VZV culture—results delayed, useful only if processed in-house
- EM (electron microscopy)—can identify herpes viruses

How to Collect a Specimen for DFA or IFA Testing

1. Unroof (open) vesicle or pustule with a sterile lancet
2. Swab base of vesicle vigorously with a sterile swab
3. Smear swab onto 3 areas (or wells) of a microscope slide
4. Allow slide to air dry
5. Transport to lab for immediate fixing and staining
6. VZV positive specimens are seen with varicella (chickenpox) and herpes zoster (shingles)

The hospital lab performs _____ test
For DFA/IFA , call _____ (specimen is tested at outside lab)

ANNEX B TO SMALLPOX RESPONSE PLAN 29 September 2002
VACCINATION GUIDELINES.

REFERENCES.

a. CDC Smallpox Response Plan, Guide B, Vaccination Guidelines for State & Local Health Agencies, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

b. CDC Smallpox Response Plan, Annex 2, Guidelines for Smallpox Vaccination Clinics, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

c. CDC Smallpox Response Plan, Annex 3, Vaccine Adverse Events Reporting, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

d. Army Regulation 40-562; Navy Bureau of Medicine & Surgery Instruction 6230.15; Air Force Joint Instruction 48-110; Coast Guard Commandant Instruction M6230.4E. Immunizations & Chemoprophylaxis. Washington, DC, 1 November 1995. http://www.e-publishing.af.mil/pubfiles/af/48/afji48-110/afji48-110.pdf.

e. US Army Medical Department. Managing Adverse Events After Vaccination, June 2002. http://www.anthrax.mil/media/pdf/cpguidelines.pdf and http://www.anthrax.mil/media/pdf/algorithm.pdf.

f. US Army Medical Command. “How To” Guide for Command Surgeons: Implementation Guidelines for Investigational New Drug (IND) Protocols. Falls Church, VA, May 2002.

g. US Army Medical Command. “How To” Guide for Unit Leaders and Unit Health Care Providers: Implementation Guidelines for Investigational New Drug (IND) Protocols. Falls Church, VA, May 2002.

h. US Army Medical Command. “How To” Guide for Investigational New Drug (IND) Protocols, Supplement: Smallpox Vaccination (IND # 10664). Falls Church, VA, publication pending.

i. National Vaccine Advisory Committee. Adult immunization programs in nontraditional settings: Quality standards and guidance for program evaluation. *MMWR* 2000;49(RR-1):1-13. ftp://ftp.cdc.gov/pub/Publications/mmwr/rr/rr4901.pdf.

j. Advisory Committee on Immunization Practices. Vaccinia (smallpox) vaccine. *MMWR* 2001;50(RR-10):1-25. http://www.cdc.gov/mmwr/PDF/rr/rr5010.pdf.

1. General. This DoD Annex augments CDC Guide B. Appendix B-1 summarizes CDC Guide B and this DoD Annex on one page.

a. Mission. Military treatment facilities (MTFs) will prepare to administer smallpox vaccinations to military personnel and healthcare beneficiaries, according to policies directed by the Secretary of Defense. On order and with vaccine provided from higher headquarters, MTFs will be capable of beginning emergency smallpox vaccinations within 24 to 48 hours of notification. The magnitude of local smallpox vaccination programs could range from a few dozen members of smallpox response teams to hundreds of thousands of people in a metropolitan area in a post-outbreak scenario. MTFs will thoroughly screen for bars (contraindications) to vaccination (Appendix B-11). If directed by higher headquarters, DoD personnel will be dispatched to assist with vaccination programs in civilian communities. In addition to quality vaccine delivery, MTFs will develop education programs to inform healthcare workers, military personnel, and beneficiaries about the benefits and risks of smallpox vaccination. MTFs will conduct quality programs to manage adverse events after vaccination, including detailed adverse-event reporting.

b. Background. Few U.S. service members have been vaccinated since 1990. Routine smallpox vaccinations of civilians in the United States ceased around 1972. Military personnel received routine periodic smallpox vaccination until 1984. Between 1984 and 1990, vaccination of military recruits was intermittent. In 1990, the Defense Department suspended routine vaccination of military recruits.

c. Assumptions.

(1) License Status. The smallpox vaccine (consisting of live vaccinia viruses) may be either (a) licensed by the Food & Drug Administration (FDA) at the time of vaccination or (b) unlicensed but permitted by FDA to be used under Investigational New Drug (IND) provisions of the Food Drug & Cosmetic Act. If smallpox vaccine is used as an IND medication, additional education, documentation, and consent requirements apply, compared to use of licensed vaccines (Appendix B-17). This document is written in a manner to take advantage of smallpox vaccine regardless of its IND status, recognizing the additional requirements of fulfilling IND regulations.

(2) No Presidential Waiver. This document assumes that the Department of Defense will not seek a Presidential waiver of consent to administration of IND smallpox vaccine, under provisions of 10 USC 1107, Executive Order 13139, 21 CFR 50.23(d), and DoD Directive 6200.2. Even if a waiver were granted, a Presidential waiver cannot diminish DoD's responsibility to educate Service Members about IND medications and to document IND administration in individual health records.

(3) Concentration. Smallpox vaccine will be administered in the standard full-strength concentration (as per original labeled reconstitution instructions), unless the CDC, FDA, or other responsible health authority issues explicit instructions to the contrary. Recent data demonstrate that 1:5 dilutions of *Dryvax* (Wyeth Laboratories)

produce an immune response comparable to full-strength Dryvax. Because these data are still being assembled as this document is being written, this document will await specific recommendations from CDC and FDA at the time vaccine is to be used.

(4) Bifurcated Needles. Sufficient sterile bifurcated needles will be available for single patient use before discarding. If not, refer to Guide B and CDC Annex 2 for resterilization considerations.

d. Planning Factors.

(1) Magnitude. A smallpox outbreak could be contained to a limited geographic area, in which case DoD resources (including vaccinated personnel) can go to that area to render assistance (e.g., smallpox vaccination, care of adverse events after vaccination). If a smallpox outbreak is dispersed widely, involving multiple MTFs, DoD experts will use telemedicine and other telecommunication tools to enhance the skills of local medical personnel.

(2) Contact Defined. Smallpox vaccination may be warranted for contacts of people infected with smallpox (Annex A). For this purpose, contact is defined as prolonged face-to-face contact with a suspected, probable, or confirmed case of smallpox. Risk of disease transmission increases with close contact ($\leq$ 6 feet), increasing time of exposure (e.g., > 3 hours), and presence of rash or cough. Consider smallpox cases potentially infectious from date of onset of fever > 101°F (38.3°C).

(3) VHC. The DoD Vaccine Healthcare Center (VHC) Network, developed in 2001, serves as a clinical resource for DoD healthcare providers and vaccine recipients regarding the value of vaccinations, reporting of adverse events after vaccination, and clinical management of adverse events after vaccination (Appendix B-19). The VHC Network is DoD's counterpart to the Clinical Immunization Safety Assessment (CISA) Centers being developed by CDC.

(4) Expected Adverse Events. The overall risk of serious complications following smallpox vaccination is low. Complications occur more frequently in people receiving their first dose of smallpox vaccine, and among children younger than 5 years of age. The first (primary) smallpox vaccination can produce swelling and tenderness of regional lymph nodes, beginning 3 to 10 days after vaccination, persisting for 2 to 4 weeks after the vaccination site heals. A fever is common after smallpox vaccination. About 70% of children experience 1 or more days with temperatures $\geq$ 100ºF for 4 to 14 days after primary vaccination, and 15% to 20% of children experience temperatures $\geq$ 102ºF. After revaccination, 35% of children experience temperatures $\geq$ 100ºF, and 5% experience temperatures $\geq$ 102ºF. Fever is less common among adults after vaccination or revaccination. Erythematous or urticarial rashes can occur ~ 10 days after primary vaccination and can be confused with generalized vaccinia. However, the vaccine recipient is usually afebrile with this reaction, and the rash resolves spontaneously within 2 to 4 days. Rarely, bullous erythema multiforme (i.e., Stevens-Johnson syndrome) occurs. The most frequent serious complications of smallpox vaccination are

described in detail in Appendix B-15. Common significant symptoms and signs after primary smallpox vaccination appear in Appendix B-15.

(5) Adequate Care. If a serious adverse event after smallpox vaccination occurs, encourage vaccine recipients to seek medical care promptly. Military health-care providers should contact infectious-disease, dermatology, or allergy-immunology specialists for consultation about managing adverse events. In appropriate cases (e.g., eczema vaccinatum, progressive vaccinia, ocular vaccinia, afebrile-pruritic-"toxic" generalized vaccinia), vaccinia immune globulin (VIG) treatment may be appropriate, for individual patient treatment under IND protocol (Annex H). Although its use is somewhat speculative, the antiviral agent cidofovir may be offered to treat vaccination reactions, if the supply of VIG dwindles or is exhausted (Annex H).

(6) Bars. Contraindications (bars to vaccination) and special handling of people at increased risk of vaccine complications are the subject of national discussion among subject-matter experts. DoD smallpox vaccination programs will take into account evolving guidelines and recommendations from the CDC, public-health advisors, and medical specialty associations.

(7) Auto-Inoculation. The most frequent complications of smallpox vaccination are inadvertent inoculation (transfer) of vaccinia viruses from the vaccination site to other sites of the body. This complication accounts for about half of all complications following primary vaccination (a person's first smallpox vaccination) and re-vaccination (booster doses of smallpox vaccine). Auto-inoculation (i.e., accidental infection) occurs at a rate of about 1 in 2,000 primary vaccinations, usually involving transfer by hand to places that itch, such as the face, eyelid, nose, mouth, genitalia, or rectum. Children may be more likely to need a covering over the vaccination site, if they are less able to adhere to instructions not to touch the site. Washing the hands after touching the vaccination site can prevent inadvertent inoculation. Using alcohol-based rinses also may be helpful for hand cleaning. Most of the resulting lesions heal without specific therapy, but vaccinia immune globulin (VIG) may be useful in treating some cases of ocular inoculation. VIG is a solution of human antibodies that neutralize vaccinia viruses, acting as a kind of antidote.

e. Coordinating Instructions.

(1) Civil Support. Installations and MTFs will give priority to the protection and well-being of military personnel and DoD healthcare beneficiaries. With concurrence of higher headquarters, an installation with excess capacity to administer vaccinations may provide support to health authorities in surrounding communities. Under normal circumstances, requests for military support services should be formally submitted to the Directorate of Military Support (DOMS, see also Appendix 2).

(2) VAERS. As with any medication, vaccinations can produce side effects or adverse reactions. Good clinical care is important to treat adverse events after any vaccination. Adverse events involving hospitalization, loss of 24 or more hours of duty

time, or symptoms suggesting contamination of a vaccine vial must be reported to the Vaccine Adverse Event Reporting System (VAERS) as described in reference d and detailed below. DOD encourages submission of VAERS reports for other adverse events by health care providers. Any patient who believes that he or she may have had a severe or unusual reaction to a vaccine is welcome to submit one, as well. Submitting VAERS reports adds to the safety database on each vaccine.

(3) VHC. The DoD Vaccine Healthcare Center (VHC) Network offers clinical consultation to healthcare providers regarding symptoms and conditions that may be related to any vaccination (Appendix B-18). The VHC will refer vaccine recipients who contact the VHC directly to the vaccine administration site (e.g., MTF, public-health facility) or primary-care treatment facility (e.g., military or Tricare) for individualized evaluation, management, and reporting of the adverse event. VHC staff will assist providers and vaccine recipients in case management, if specialty services are required and not locally available.

(4) IND Coordination. VIG investigators and cidofovir investigators will coordinate with the Walter Reed National Vaccine Healthcare Center (VHC, Appendix B-18) on status of individuals treated with VIG or cidofovir under IND protocol. Specialized treatment teams, investigators, and the VHC will assist in centralized tracking and case management and provide coordination with CDC's Clinical Immunization Safety Assessment (CISA) centers of excellence.

f. Legal Considerations. Any medications administered under Investigational New Drug provisions of U.S. law or regulation will be carefully documented and administered with appropriate education, as detailed in references f, g, and h.

2. Execution.

a. Concept of Operations. Depending on the magnitude of a smallpox outbreak, regional teams with medical, logistic and administrative expertise may be assigned to assist with post-outbreak vaccination programs. These teams should include infectious disease, dermatology, allergy-immunology, neurology, nursing and pharmacy representation, plus coordination with vaccine-safety expertise. If a smallpox outbreak becomes widely distributed, involving multiple MTFs, it may not be possible to dispatch augmenting teams to every location. In such cases, DoD experts will use telemedicine and other telecommunication tools to coach and consult local medical personnel. If the smallpox vaccine is to be administered as an investigational new drug (IND), the US Army will support with teams that help train local health-care providers in implementing IND protocols in contingency settings.

b. Tasks and Responsibilities.

(1) Site Planning. Before a smallpox outbreak, MTF commanders will identify controlled vaccination sites other than normal hospital or clinic locations at which mass vaccinations can be effectively delivered. Sites will take into consideration security;

appropriate ventilation, workflow, and other factors addressed in Appendix B-2, Appendix B-3, and Appendix B-6.

(2) IND Planning. Before a smallpox outbreak, MTF commanders will identify health-care providers willing to serve as local principal investigators (PIs), in case investigational new drugs (INDs) need to be administered in the course of implementing this document. MTFs will arrange training in Good Clinical Practices in advance for these likely PIs (see also Appendix B-17).

(3) Training. The military medical departments will develop standardized training programs with provision for competency assessment for healthcare staff. Considerations in impromptu staffing and training appear in Appendix B-4 and Appendix B-5. The Vaccine Healthcare Center Network and the Military Vaccine Office will coordinate this effort. The VHC Network and the Military Vaccine Office will also develop educational materials to help the public understand smallpox and smallpox vaccination.

(3) Implementation.

(a) Vaccination Coordinator. The MTF commander will designate one person to be responsible for vaccine administration during a smallpox outbreak. This person will work with Federal and other state emergency-management authorities to implement vaccine-administration strategies.

(b) IND Coordinator. The MTF commander will identify a health-care provider to serve as local principal investigator (PI) for any investigational new drug (IND) needed to implement this document. MTFs will arrange training in Good Clinical Practices in advance for these likely PIs (see also Appendix B-17).

(c) Thorough Screening. All MTFs will institute thorough prevaccination screening to identify possible contraindications to smallpox vaccination (e.g., skin disorders, immunodeficiencies). When large numbers of people need to be vaccinated quickly, self-screening tools will be important. An annotated guide to screening questions appears in Appendix B-11.

(d) Individual Education. Before vaccination, recipients or parent/guardian will receive information about vaccine benefits and risks, plus instructions on how to contact a DoD provider or the nearest military or Tricare treatment facility if the vaccine fails to take or if an adverse event develops (e.g., Military Medical Support Office, 888-647-6670). MTFs will use tools to help vaccine recipients recognize adverse events (e.g., colored diagrams showing expected site reactions, Appendix B-13), so they know when to report for additional care. Tools to help vaccine recipients avoid auto-inoculation will be emphasized. Efforts will be made to help people with low competency in English.

(e) Information Resources. The Military Vaccine Office will provide educational materials to help the public understand smallpox and smallpox vaccination (Appendix E-

2). Information about smallpox vaccine for the general public also will be available from other sources, including the CDC's National Immunization Hotline (800-232-2522, www.cdc.gov/nip) and others

(f) Documentation.

(i) Vaccination sites will employ the Services' immunization tracking systems to document administration of smallpox (vaccinia) vaccine (e.g., Medical Protection System (MedPROS), Air Force Complete Immunization Tracking Application (AFCITA), Shipboard Automated Medical System (SAMS)). Both contemporary and historical smallpox vaccinations should be entered into these tracking systems. These applications relay immunization data daily to the Defense Eligibility Enrollment Reporting System (DEERS), operated by the Defense Manpower Data Center (DMDC), Monterey, California. The Department of Defense standard is for vaccinations to be entered into the immunization-tracking system on the day of vaccination. If automated systems are temporarily unavailable, a manual system of documentation must be employed (e.g., SF 601, PHS Form 731). DD Form 2766C (Computer Generated)-AFCITA, Vaccine Administration Record, complies with article 80 of the WHO international health regulations and can be used in place of the PHS 731 when traveling outside the United States.

(ii) Appendix B-8 provides a list of recipient-specific documents required in a smallpox vaccination operation and a summary of the information to collect. One copy of each of the documents must be available (and in appropriate languages) for each vaccine recipient. CDC is developing a web-based application as part of an electronic smallpox data management system (SDMS). Guidance on use of this system will be provided at a later date. In the ideal scenario, all person-specific documents will be printed on-site for each vaccine recipient. However, paper copies of all documents must be available in sufficient quantities so that clinic operations can continue if the computer system fails. Whether during the clinic or later, electronic entry of critical data will be necessary.

(g) International Travel. Because smallpox vaccination may become an important factor in passage of international boundaries in the future, vaccination clinics will maintain the ability to issue Public Health Service (PHS) Form 731, International Certificate of Vaccination ("yellow shot records").

(h) Vaccination-Site Care.

(i) Background. National consensus has not yet fully formed on how to most appropriately prevent transfer of vaccinia virus from vaccination sites to other parts of the recipient's body or transfer to family members or other contacts. Options include occlusive, non-occlusive, or no bandaging. During the 1980s, during routine smallpox vaccination programs for recruits, military policy called for no routine covering with any bandages immediately after inoculation, with the vaccination site being allowed to air-dry instead. Sites were to be covered with a loose dressing only if an individual would

be in close contact with unvaccinated people (e.g., a recruit departing on emergency leave).

(ii) DoD Guidance. Appropriate care will be taken to prevent the spread of vaccinia virus from the vaccination site. The following standard precautions will be observed. In general, it is appropriate to leave most vaccination sites unbandaged, especially when alone. Airing will help speed healing of the vaccination site. Wearing long-sleeve clothing and/or using a loose bandage can reduce the opportunity for contact transfer (i.e., a touch-resistant barrier), until the scab falls off on its own. Bandaging may be appropriate in confined spaces (e.g., ships, aircraft) to help reduce contact spread and accidental infection (i.e., auto-inoculation). If bandages are used, dispose of contaminated bandages and the vaccination scab as biohazardous waste. If this is not feasible, dispose of these items in sealed plastic bags, double-bagged if possible.See Appendix B-14 for specific instructions on vaccination-site care.

(i) Isolation of Vaccine Recipients.

(i) Background. National consensus on the degree to which vaccinated people should be separated from people with contraindications (bars) to vaccination has not fully formed. Most recommendations call for voluntary efforts by vaccinated people to avoid contact with those for whom vaccinia virus could be a risk. In the case of household contacts of contacts contraindicated from vaccination, CDC recommends separate housing until the vaccination scab falls off. During the 1980s, during routine smallpox vaccination programs for recruits, only basic trainees remaining at the training site for at least 4 weeks would receive smallpox vaccine. This policy was intended to reduce the risk of transmission of vaccinia virus to unvaccinated civilian contacts. In the current era, about two-thirds of military personnel entered service since 1990 and thus have never been vaccinated against smallpox. Similarly, most of the civilian population is unvaccinated against smallpox.

(ii) DoD Guidance. MTF staff will provide verbal and written counseling to vaccine recipients to avoid contact with people for whom vaccinia virus could be a risk. This counseling will be reinforced with training to avoid auto-inoculation or otherwise touching the vaccination site. If somebody in the vaccine recipient’s household has eczema, an immune-suppressing condition, or another reason to avoid vaccinia virus, take reasonable precautions for physical separation until the scab falls off. This separation will include not allowing the vaccine recipient to share sleeping or close living space (e.g., bedroom, sleeping bay, tent) with susceptible people. Washing hands before changing a child’s diapers (or having someone else change the diapers) is prudent. Commanders will provide on-base housing to Service Members who wish to avoid exposing family members or other close contacts to vaccinia virus until the vaccination-site scab falls off. Scheduling vaccinations just before deployments or family separation is another option. Wearing long-sleeve clothing during the day and at night can further reduce the opportunity for contact transfer.

(iii) Health-care Workers. Recently vaccinated health-care workers should avoid contact with unvaccinated patients, particularly those with immunodeficiencies, until the scab falls off. However, if contact with unvaccinated patients is unavoidable, health-care workers can continue to have contact with patients, including those with immunodeficiencies, as long as the vaccination site is well-covered and thorough hand-hygiene is maintained. In this setting, a more occlusive dressing might be appropriate. However, exudates can accumulate beneath the dressing, and care must be taken to prevent viral contamination when the dressing is removed. To prevent accumulation of exudates, cover the vaccination site with dry gauze, then apply the dressing over the gauze. The dressing should also be changed at least once a day, such as at the beginning of each duty shift. Wearing long-sleeve clothing can further reduce the opportunity for contact transfer. The most critical measure in preventing inadvertent contact spread is thorough hand-hygiene after changing the bandage or after any other contact with the vaccination site. For high-risk-density assignments (e.g., intensive-care, transplant, oncology, burn units), medical commanders should consider staggering staff vaccinations to allow reassignment to other duties, taking into account local staffing, case mix, and workload.

(j) Clinical Care and Consultation. MTF commanders will provide for education of primary-care providers regarding recognition of adverse events after vaccination, and the need for prompt referral of patients for specialized care. Information on how to access VAERS will be prominently featured in this education, with instructions for submitting VAERS reports displayed at every immunization clinic.

(k) Vaccine Safety Surveillance. Depending on the extent of vaccine administration, a variety of surveillance activities may be conducted.

(i) Active surveillance for adverse events may be conducted when the number of vaccine doses administered is limited. Vaccine recipient would receive a diary report card to document their response to the vaccine (e.g., prototype shown in CDC Annex 3).

(ii) To identify serious adverse events, active surveillance will be conducted for people receiving vaccinia immune globulin (VIG) or cidofovir, pharmaceutical agents indicated for the treatment of certain severe vaccine complications (Annex H). Active surveillance for VIG and cidofovir use will not be limited based on the number of vaccine doses administered.

(iii) Stimulated passive surveillance (i.e., requests that people report if they recognize an adverse event) and follow-up of serious adverse events will be conducted whether limited or large numbers of vaccine doses are administered. The Vaccine Adverse Events Reporting System (VAERS) is considered a passive surveillance system because reports are not actively solicited. However, with enhancements to VAERS marketing, such as informing every vaccine recipient how to contact VAERS, options for web-based reporting, and follow-up of all smallpox reports, the passive system can be enhanced.

(iv) If widespread vaccination is conducted, DoD's Defense Medical Surveillance System and CDC's Vaccine Safety Datalink can be used to compare and contrast vaccinated and unvaccinated people.

(v) Other safety assessment programs according to the circumstances of vaccine use. The Military Vaccine Office and the VHC will coordinate with CDC, FDA, and other relevant parties to stay abreast of advances in understanding of the side-effect profile of smallpox vaccination in the current era.

(vi) The Military Vaccine Office will work with CDC and FDA personnel to obtain copies of VAERS reports (redacted of personal identifiers) involving smallpox vaccine and military personnel or DoD beneficiaries, to enable DoD-specific vaccine-safety surveillance.

(l) Security. The installation commander will provide sufficient personnel to maintain order and preserve the security of personnel, clients, property, supplies, and equipment, and enforcing any restriction of movement rules. The security plan will include designated entrances and exits for staff use, a list of authorized staff for each clinic site, staff check-in and check-out procedures, methods and locations to safeguard vaccine and other clinic supplies, and maintaining a system to vaccinate clients in their order of arrival.

(m) Workplace Safety. Healthcare workers will observe good infection prevention and control procedures (Annex C, Annex F). Vaccination clinic procedures will address disposal of used or contaminated supplies.

(n) Confirmation of Take. Successful smallpox vaccination results in a pustular lesion in previously unvaccinated people 6 to 8 days after vaccination (Appendix B-13). In previously vaccinated people, either a pustular lesion or an area of definite induration or congestion around a central lesion develops by 6 to 8 days after vaccination. Take will be individually confirmed for all contacts and contacts of contacts. Take will also be individually confirmed for members of smallpox response teams vaccinated pre-outbreak, with documentation in occupational-health records. Based on availability of labor, take can be individually confirmed in some or all of the following groups: healthcare workers, other occupational groups, other medically defined groups, and every vaccine recipient.

(o) Inadequate Take. Equivocal reaction, including accelerated, modified, vaccinoid, immediate, early, or immune reactions, are defined as all responses other than major reactions. If an equivocal reaction is observed, check vaccination procedures and repeat the vaccination by using vaccine from another vial or vaccine lot, if available. The reaction was blunted due to immunity, insufficiently potent vaccine, or vaccination technique failure. If the repeat vaccination by using vaccine from another vial or vaccine lot fails to elicit a major reaction, health-care providers should consult public-health authorities before attempting another vaccination.

(p) Blood Donation. People vaccinated against smallpox would likely be deferred from donating blood for 30 days after vaccination, according to evolving standards of the Armed Services Blood Program Office (www.tricare.osd.mil/asbpo/asb_immu.html).

(q) Vaccine-Vaccine Interactions. In general, administer live-virus vaccines either on the same day or separated by 30 days, to prevent inhibition of viral replication. Simultaneous administration of live poliovirus, measles, and yellow fever vaccines with smallpox vaccine is permissible, if 30-day intervals are not feasible.

c. Reporting.

(1) During a smallpox outbreak, DoD vaccination sites will report the number of smallpox vaccinations administered daily to higher headquarters and to the CDC reporting system.

(2) Report adverse events after smallpox vaccination through usual channels, with one exception. Usual channels involve service reportable-disease channels (reference d) and the Vaccine Adverse Events Reporting System (VAERS). There is no need to report adverse events to VAERS that involve smallpox vaccine treated with vaccinia immune globulin (VIG) or cidofovir under IND protocol. The FDA will review all clinical data for patients treated with VIG or cidofovir under IND protocol under separate report filings. Filing reports to the Vaccine Adverse Event Reporting System (VAERS) in cases involving VIG or cidofovir under IND protocol is inappropriate, because filing a VAERS report will lead to double-counting of the case.

3. Operational Constraints. Space and patient flow must be adequate to allow storage, screening, education, documentation, vaccination, infection control, and other essential functions.

4. Administration and Logistics.

a. Because the supply of smallpox vaccine is limited and the demand for vaccine may be extremely high, take care to protect the vaccine supply from theft and fraud.

b. Because each vaccine vial contains 100 to 500 doses, plan carefully to minimize vaccine wastage that may result from discarding partially used vials. Storage and handling considerations appear in Appendix B-10.

c. Because of these factors, each dose and vial must be accounted for before and after each clinic session.

d. If DoD’s or CDC’s electronic immunization tracking systems are used, and data is entered on-line in “real time” as vaccine recipients are being processed, the number of doses administered will automatically be counted. CDC’s system will automatically

record doses administered on a Daily Smallpox Vaccine Tracking Report. If CDC smallpox data management system (SDMS) is not used or not operational, manually tally the number of doses administered from the paper copies of the Clinic Vaccination Records of people receiving vaccine that day and enter the data on the Daily Vaccine Tracking Record.

e. Assure adequate quantities of consumable supplies (Appendix B-9).

f. Assure proper infection-control and prevention procedures (Annex C).

5. Special Situations.

a. Ships Underway. Ships that have been completely isolated for 18 days without development of a smallpox case, and which can maintain this isolation, will be provided smallpox vaccine for unvaccinated crewmembers with a lower priority than ships that have not been isolated in this manner. Vaccine supply, if needed acutely, will be conducted by replenishment while underway.

b. Air crews on missions away from home base. Aircrews will be vaccinated either at their current location or upon return to home base, depending on vaccine distribution.

c. Troops deployed outside CONUS in theater. Deployed troops will receive priority for vaccination, depending on distance from recognized smallpox cases, relative isolation from potentially infected groups, and the tactical situation in theater.

d. Troops deployed outside CONUS Returning to CONUS. Once a smallpox outbreak develops, troops will not return to CONUS until they have been vaccinated against smallpox. Returning troops with medical contraindications to vaccination will be exempted from smallpox vaccination, but may need to be isolated for an appropriate interval of time to assure they are not incubating a case of smallpox. Troops returning to CONUS unable to be vaccinated abroad may receive smallpox vaccine at port of entry and then be isolated until confirmation of vaccine take, according to instructions from preventive-medicine officials.

e. Child-care centers. MTF commanders will provide advice to installation child-care centers regarding prevention of contact transmission of vaccinia from vaccination sites.

APPENDIX B-1
Vaccination Guidelines – Summary.

1. Priority for Post-Outbreak Vaccination:
   a. People exposed to an initial release of smallpox virus, if known.
   b. People with prolonged face-to-face or household contact (≤ 2 m or 6 feet) with a confirmed/suspected smallpox patient after fever and before all scabs fell off.
   c. People selected for direct evaluation, care, or transport of confirmed/suspected cases (including selected laboratory, laundry, and waste-handling personnel).
   d. Household contacts of the contacts in group b above.
   e. People essential to support of response activities (e.g., selected law enforcement, emergency response, military personnel).
   f. Based on risk analysis and extent of exposure, vaccinate people present in a hospital when a smallpox case was present and not appropriately isolated.

2. Bars or Warnings Before Pre-Outbreak Vaccination. Note: For face-to-face contact with a smallpox case, bars are usually waived. Household members with these conditions should house themselves separately from vaccinated people until site heals.
   a. People ever diagnosed with eczema (see Appendix B-16).
   b. People with acute or chronic skin conditions (e.g., atopic dermatitis, burns, impetigo, varicella zoster (shingles)), psoriasis, or uncontrolled acne, until the condition resolves (Appendix B-16).
   c. Immunodeficiency diseases (e.g., AIDS, cancer, agammaglobulinemia).
   d. Life-threatening allergies to polymyxin B, streptomycin, tetracycline, neomycin.
   e. Women who are pregnant.

3. Vaccination Clinic Procedures.
   a. Leave most vaccination sites uncovered. Alternately, loosely cover site with porous bandage (e.g., gauze), until scab separates on its own. Wear long-sleeve clothing.
   b. Counsel vaccine recipients to avoid contact with people for whom vaccinia virus could be a risk. Offer separate on-base housing, to avoid exposing family members to vaccinia virus until the vaccination-site scab separates.
   c. Teach vaccinees to avoid touching the vaccination site, to prevent spreading vaccine virus to eyes, nose, mouth, genitals, or rectum. Reemphasize this point.
   d. Teach: Wash hands with soap and water if you touch vaccination site by accident.
   e. Double-bag bandages and scab and discard in the trash.
   f. During an outbreak, report vaccination counts daily to headquarters.

4. Reporting. Report adverse events after vaccination to allow for monitoring vaccine safety. Detailed instructions on adverse-event reporting appear in CDC Annex 2.

5. Care. If a serious adverse event after smallpox vaccination occurs, seek medical care promptly. Military health-care providers should contact infectious-disease, dermatology, or allergy-immunology specialists for consultation on managing adverse events. In appropriate cases (e.g., eczema vaccinatum, progressive vaccinia, ocular vaccinia,

generalized vaccinia), vaccinia immune globulin or cidofovir treatment may be appropriate, for individual patient treatment under IND protocol (Annex H).

APPENDIX B-2
Planning for Vaccine Delivery.

1. Understand vaccination strategy. The immediate response to confirmed or probable cases of smallpox would be vaccination of first responders on the scene (i.e., medical personnel who attend the infected people and vaccinate contacts of the cases). Local smallpox plans should include localized lists of job categories that must receive vaccine immediately if a case of smallpox occurs. In addition, all face-to-face contacts of the cases must be vaccinated. Because the rapidity with which this can be accomplished will determine the ultimate extent of the outbreak, organizing a separate vaccination operation (e.g., clinic site, staff, supplies) for each group is recommended.

2. Determine resource needs. Based on the vaccination strategy, calculate the number of clinics, duration of clinics, and number of staff required. The number of personnel needed for any one clinic will vary depending on the size and layout of clinic facilities, location of clinic, geographic area being served by the clinic, and estimated number of vaccine recipients at each clinic (Appendix B-4).

3. Identify potential clinic sites. The size and type of the facilities needed for smallpox immunization clinics will vary depending on the number of people to be served. Very small clinics, such as those to immunize first responders or primary contacts, can be conducted in almost any available space. Larger clinic sites could be industrial locations, office buildings or apartment complexes. Schools are the preferred location for any clinic larger than can be held in the local health department. Schools have parking lots, long corridors, large classrooms, cafeterias, private offices, and other immediately available resources such as tables and chairs, and offer an ideal physical structure that can meet most clinic needs. Elementary schools are preferable if staffing is adequate, because they are numerous and serve fairly well defined neighborhoods convenient to the public. Using the largest number of locations that staffing permits will minimize parking and crowding problems. Use of middle or high schools may also be considered. If smallpox cases expose many people in locations such as schools and office buildings, these locations may be sites where vaccine clinics can offer vaccine quickly and efficiently to many contacts. However, to avoid wasting reconstituted vaccine, clinics should be selected and organized to administer one vaccine vial –or multiples thereof – each day. In selecting clinic sites, allow for a smooth flow of clients, accessibility of the facility to major streets, restroom facilities, parking, refrigeration, heating/air conditioning, and protection from elements if lines will form outside. Before final selection, a visit should be made to the location to ensure that the facility meets the needs of the vaccination operation.

4. Obtain prescriber authorization or standing orders. If the vaccine is in IND status, identify the principal investigator (PI) who signed the FDA Form 1572 and is responsible for vaccine delivery. Before a clinic can begin vaccinating, obtain standing orders to vaccinate from the public-health authority (e.g., chief of preventive medicine) or the principal investigator. Standing orders are also needed for responding to medical

emergencies that occur during vaccination clinics (e.g., epinephrine). In addition to providing standing orders, the health officer or designee must approve the content of informational materials and serve as medical consultants for nursing staff.

5. Plan training for vaccination staff. All health-care workers involved in smallpox vaccination efforts should receive training in screening for contraindications and in proper administration of smallpox vaccine. Training should also include procedures for reporting suspected cases. Large numbers of clinic staff can be trained through a train-the-trainer approach through satellite-based courses, web pages, videocassettes, CD-ROM courses and written training materials. A supplemental chapter on smallpox is included in CDC's "Pink Book" (*Epidemiology & Prevention of Vaccine-Preventable Diseases*, 7th edition, http://www.cdc.gov/nip/publications/pink/#download). Educational materials should provide detailed medical information about smallpox and the smallpox vaccine, and should highlight potential vaccine side effects and their clinical management. Impromptu training elements appear in Appendix B-5.

6. Publicize the clinic. Public education materials should be presented in multiple languages, reproduced in appropriate quantities. After a smallpox vaccination clinic site and recipient populations are determined, release public announcements with information about the clinic as expediently as possible. The information disseminated must clearly describe the groups for whom the clinic is intended (and not intended). Specific zip codes or alphabetic letters may be designated for a specific date and timeframe. Certain language groups may be asked to come at a specific time when translator resources are available. Also state the clinic location and directions, dates and times of operation, length of time the vaccination process may take, type of clothing to wear, and culturally appropriate information in as many languages as needed. State that those who do not meet the defined criteria will not be accepted for vaccination. In addition to information about the specific clinic being publicized, a concerted effort should be made to provide information to the public that emphasizes (a) the rationale of the vaccination strategy, (2) disease-containment measures are effective, (3) multiple measures are being taken to prevent the further spread of the disease, and (4) cooperation with efforts to isolate cases and contacts will speed control of the outbreak.

APPENDIX B-3
Vaccination Clinic Process.

Step 1: Orientation and Paperwork. As vaccine recipients arrive, security personnel handle outside traffic flow and route people to the clinic entrance. Upon entering the building vaccine recipients are directed to a location where a greeter-educator briefs groups (up to 30 people) about what is going to take place during the clinic process, provides required paperwork (preferably in a packet form) and instructs the vaccine recipients how to complete the necessary paperwork. If the vaccine is in IND status, this will include informed-consent documents. Allow time for reading and filling in the required personal information (e.g., name, address). The number of people in the orientation briefings can vary to accommodate the rate at which people arrive. Multiple educator-greeters locations may be necessary, so that people arriving after an orientation has begun can be directed to another location where another orientation will soon begin. Orientation locations can also serve as holding locations if bottlenecks occur along the clinic line. This method will ensure a steady flow of vaccine recipients to the next step.

Step 2: Registration. After orientation and completion of the paperwork, the clinic-flow coordinators direct vaccine recipients to registration tables where staff members check each vaccine recipient's form for completeness and accuracy.

Step 3: Medical Assessment. After ensuring that paperwork is completed appropriately, vaccine recipients are directed by clinic-flow controllers to the medical assessment area. Here medical screening personnel discuss with each vaccine recipient individually the medical conditions that might would prevent receipt of the vaccine and determine if any such conditions are present. They also review the common reactions to the vaccine with each vaccine recipient. People with possible medical contraindications are directed to a separate station for more in-depth evaluation. Each vaccine recipient is asked to sign the consent form before proceeding further.

Step 4: Vaccination. After medical assessment, vaccine recipients with no medical contraindications are directed to the vaccination area. This area is a screened area that affords privacy to people who find it necessary to remove clothing to expose the vaccination site. A vaccination assistant helps vaccine recipients expose their upper arm and cleanses the vaccination site, if necessary. The vaccine recipient then proceeds to the vaccine administrator who administers the vaccine and completes the necessary documentation. Immediately thereafter, a vaccination assistant applies a bandage to the vaccination site and instructs the vaccine recipient on post-vaccination care of the vaccination site.

Step 5: Forms Collection and Exit. Before leaving the clinic, vaccine recipients move to a forms collector stationed near the exit. This individual collects all required paperwork, answers any remaining questions and informs vaccine recipients that they are finished with the process.

APPENDIX B-4
Vaccination Clinic Staffing.

1. The official responsible for over-all direction of the vaccination operation assigns a clinic manager, responsible for overall clinic operation. The clinic manager is the primary decision-maker for the site, and supervises all non-medical personnel. If the vaccine is in an IND status, the clinic manager must know who is the principal investigator responsible for vaccine administration. All staffing assignments should be documented on a clinic assignment sheet.

2. Management and Coordination Functions. To assist the manager with large clinic operations, coordinators should be identified for the various clinic functions as outlined below:

a. Nurse Coordinator: Oversees nursing staff assigned to the clinic; assists clinic manager in making clinic assignments for nursing staff; assists on-duty nurses as needed.

b. Supply Officer/Vaccine Manager: Ensures clinic supplies are on site and available in sufficient quantities during clinic operations; maintains an inventory of supplies; oversees distribution of supplies to appropriate locations in the clinic; ensures that sufficient vaccine is available, that the cold chain is maintained through proper handling and storage; ensures that vaccine is stored in a secure manner at the clinic site and that unused vaccine is returned and accounted for; and maintains adequate vaccine and other supplies at the vaccination station.

c. Security Coordinator: Oversees personnel assigned to security activities at the clinic site; assists the clinic manager in making duty assignments of security personnel; determines appropriate number of security staff necessary according to clinic size and location; maintains a list of authorized clinic staff and their phone numbers; assigns and coordinates use of cell phones and pagers; establishes staff check-in and check-out procedures; ensures that all staff wear identification badges; maintains communication with local law enforcement officials.

d. Volunteer Coordinator: Oversees volunteer activity at the clinic site. Assists the clinic manager in making duty assignments of volunteer staff; maintains roster of people available for volunteer duty; and maintains a schedule of times that volunteers will be available to work.

3. Staff Functions. Following is a summary of suggested responsibilities of the staffing roles as outlined in the operational concept above:

a. Greeter-Educators: Greet and conduct initial orientation of potential vaccine recipients upon their arrival; provide basic information (verbally or with a video presentation) about the vaccine and the vaccination process; distribute informational

material and clinic document; explain how to complete the documents and answers questions. Greeter-educators must be able to explain the purpose of receiving the vaccine, outline the vaccination clinic process, and distribute and explain the clinic documents to vaccine recipients individually and in groups.

b. Registration Staff: Review each vaccine recipient's documents for completeness and accuracy; assist clients with completing documents. The registration staff must be familiar with each form distributed. They must be able to follow instructions on how to respond to exceptional situations, such as non-English speaking patients or patients who are anxious, hostile, or disoriented. If the form has not been completed correctly or completely, registration staff must be able to address and correct these problems. They should be prepared to read the forms to illiterate or semi-literate people needing their assistance.

c. Medical Screeners: Assess clients for contraindications to vaccination; when necessary perform physical examination of patients who state that they have dermatological conditions that may constitute contraindications; and answer medical questions. This role should be filled by a physician, nurse or paraprofessional who has good interviewing skills and is well-versed in the technical information regarding exposure risks, medical contraindications to vaccination, risks of vaccination, and risk-benefit analysis. Medical screeners will review the list of normal or expected reactions to the vaccine with each vaccine recipient. If necessary, medical screening personnel will contact a designated physician consultant to assist in making a final decision about whether or not to vaccinate. If the vaccine is still in Investigational New Drug status, medical screening personnel ensure that the consent form has been read, understood, and signed by each potential vaccine recipient.

d. Vaccination Assistants: Assist the vaccine administrator with all aspects of pre- and post-vaccination activities; prepare vaccine with diluent, ensure that vaccination station maintains adequate supplies; instruct recipients on location of vaccination; assist vaccine recipients in preparing the vaccination site (e.g., roll up sleeve, remove arm from shirt/blouse); clean vaccination site with quick-drying acetone, if necessary; apply dressing to the vaccination site; instructs clients about care and changing of the dressing. Vaccination assistants must have a thorough understanding of the vaccination process and the necessary supplies, proper technique for reconstituting the vaccine with diluent, proper care and handling of vaccine in the clinic, how to disinfect contaminated surfaces and dispose of soiled materials, and where to access additional supplies. Vaccination assistants are also responsible for entering the vaccine and diluent lot numbers on the patient's consent form and clinic record and providing the vaccine recipient with a vaccination card that documents when and where the vaccine was administered.

e. Vaccine Administrators: Oversee the vaccination process; administer the vaccine; sign the clinic record; observe vaccine recipients for immediate reaction or complications. Vaccine administrators can be nurses, physicians, pharmacists, or designated paraprofessionals who have received technical training in administration of

smallpox vaccine. Vaccinators must have the ability to quickly develop a high level of skill in vaccinating with a bifurcated needle (Appendix B-12). They must have in-depth understanding of proper vaccination techniques, methods to prevent contamination of the vaccine, exposure risks, the medical conditions that constitute contraindications for vaccinations, the risks of vaccination, preparation of the vaccination site, normal and abnormal post vaccination responses, and proper follow-up care of the vaccination site. Vaccinators must also be prepared to respond to medical emergencies that may occur within the vaccination area. Vaccinators should not have any personal contraindications to smallpox vaccination.

f. Forms Collectors: Verify that forms are correctly completed; collect all necessary forms from recipients before departure. The forms collector is responsible for checking that the vaccination staff signs the clinic record and entered the lot numbers on the appropriate documents. As the last staff member to talk with vaccine recipients, the forms collector must have the ability to ensure a response by the appropriate staff to any remaining concerns that clients may have.

g. Clinic-Flow Controllers: Direct vaccine recipients through the clinic process and monitor clinic flow. Clinic-flow coordinators are responsible for continuously monitoring and directing client activity throughout the facility. They must be able to calmly manage and assist people who may be anxious or unable to follow directions. When congestion (backlog) arises, flow controllers determine if staff at other locations are less busy and request assist in the congested area. They are also responsible for feeding back information about the number and rate of “upstream” clients to the vaccination assistants, to enable them to maximize use of all vaccine doses in opened vaccine vials. Flow controllers may be in a position to provide early alert of situations that that may require additional security personnel.

h. Security Staff: Ensure an orderly flow of traffic and parking at the clinic site; assist in maintaining orderly movement of vaccine recipients through the clinic process; provide necessary control if people become unruly; assist supply officer in maintaining security of vaccines and other clinic supplies. Security staff can be off-duty law enforcement officers, professional security personnel, or volunteers experienced and trained in crowd control.

i. Emergency Medical Personnel: Respond to medical emergencies. Emergency personnel must be able to respond to medical emergencies, including reactions ranging from the minor to anaphylactic shock and serious medical emergencies that are incidental and unrelated to vaccination but can be expected to occur whenever large groups of people congregate. For large operations, a physician, physician assistant, nurse practitioner or emergency medical technician should be on-site at all times during clinic operations.

APPENDIX B-5
Vaccination Clinic Staff Training.

1. The staff operating a clinic site should receive a group orientation to the overall purpose, function, and flow of the vaccination clinic, as well as specific verbal and written directions for their individual roles.

2. During the orientation, a diagram with annotations should be provided to show traffic flow (see Appendix B-7), the functions of all clinic stations, and a list of staff assigned to each role and each station, if possible. The general responsibilities of each area of the vaccination clinic are reviewed with the entire staff. All staff need to know where they will work, where their supplies and resources are located, and who their consults are as well as how to summon them.

3. In small clinics, there are roles within the clinic that can be flexed to accommodate to the needs of the clinic and decrease congestion and waiting time (i.e., bottlenecks, lags) and to permit breaks for staff. In larger clinics, this can be accomplished by cross-training. Therefore, orienting staff in small, interchangeable units is suggested.

4. For training vaccine administrators and assistants, a demonstration video is available from CDC. Ideally, vaccinators should practice on each other and other staff before administering vaccine to the public. Copies of package inserts, Vaccine Information Statements (VISs), and other significant administration materials should be available during training and actual vaccine clinic. Technical references for health-care providers appear at the bottom of this appendix.

5. If time permits, a mock vaccination clinic or role-playing session should be conducted to train and evaluate the potential performance of staff. Vaccinating clinic staff as well as first responders and other health care providers is suggested as a way to provide critical training and experience for all staff, especially the vaccine administrators.

6. Emergency personnel should also attend the group orientation and be given information about smallpox and managing potential exposure to smallpox. They should be familiar with the layout of the clinic site and know where ill patients will be maintained before transport for further care.

7. Daily post-clinic debriefings should be held to assess staff performance and ascertain if additional training or clinic reconfiguration is needed.

8. References:

a. Advisory Committee on Immunization Practices. Vaccinia (smallpox) vaccine. *MMWR* 2001;50(RR-10):1-25. http://www.cdc.gov/mmwr/PDF/rr/rr5010.pdf.

b. Atkinson W, Wolfe C, Humiston S, Nelson R, ed. Chapter 18, Smallpox. In: *Epidemiology & Prevention of Vaccine-Preventable Diseases*, 7th ed. Atlanta: Centers for Disease Control & Prevention, Apr 2002. http://www.cdc.gov/nip/publications/pink/#download.

c. Breman JG, Henderson DA. Diagnosis and management of smallpox. *N Engl J Med* 2002; 346:1300-8. http://content.nejm.org/cgi/reprint/346/17/1300.pdf.

d. Henderson DA, Inglesby TV, Bartlett JG, Ascher MS, Eitzen E, Jahrling PB, Hauer J, Layton M, McDade J, Osterholm MT, O'Toole T, Parker G, Perl T, Russell PK, Tonat K, Working Group on Civilian Biodefense.Smallpox as a biological weapon: Medical and public health management. *JAMA* 1999;281:2127-37. http://jama.ama-assn.org/issues/v281n22/ffull/jst90000.html.

e. World Health Organization. Smallpox. *Weekly Epidemiologic Record* 2001;76:337-44. http://www.who.int/wer/pdf/2001/wer7644.pdf.

f. Canadian National Advisory Committee on Immunisation. Statement on smallpox vaccination. *Can Comm Dis Rep* 2002;28(ACS-1):1-12. http://www.hc-sc.gc.ca/pphb-dgspsp/publicat/ccdr-rmtc/02pdf/acs28-1.pdf.

APPENDIX B-6
Vaccination Clinic Flow.

1. Clinics should have clearly marked entrance and exit points, with adequate waiting space for queues of people seeking vaccination. Post security staff at both locations to maintain order. Control the traffic flow within the clinic so that it follows a logical path from entry to exit. A linear path of traffic flow from entry to exit on opposite sides of the facility is optimal. If time permits, provide easy-to-read signage to guide people through the clinic process. See Appendix B-7 for a sample clinic-flow diagram.

2. If the clinic is being held in response to a smallpox outbreak, some people may arrive at the clinic with a referral form indicating that they are a contact to a diagnosed case of smallpox. Give these people the highest priority and escorted them directly to a registrar who will orient them and expedite the paperwork, medical assessment, and vaccination process. Alert security personnel and greeter-educators to this possibility.

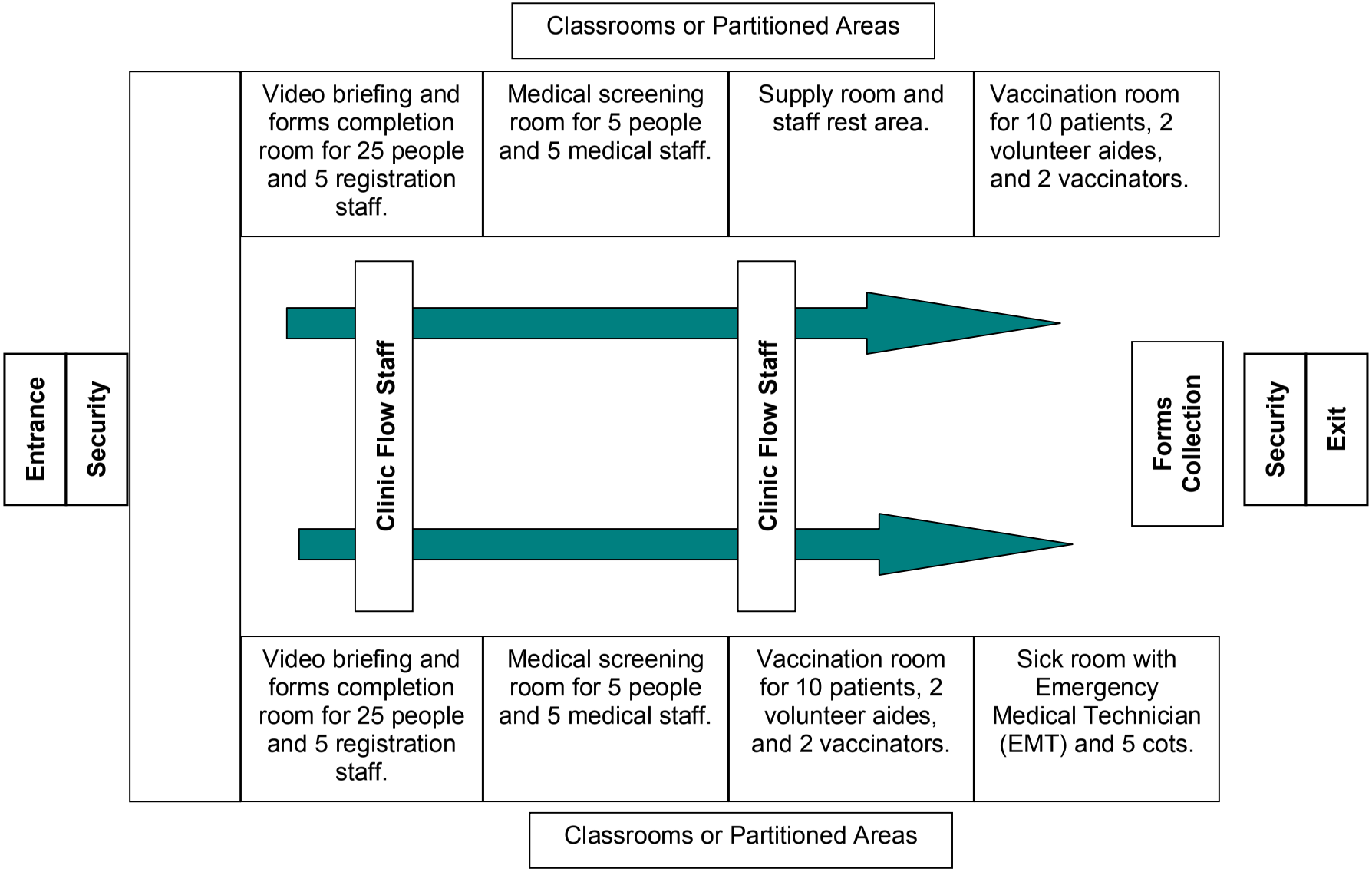
3. Ideally, locate greeter-educators and registration staff in a separate room from the vaccine administration station. This will help reduce the anxiety of people uncomfortable with viewing the vaccination process.

4. The registration and medical-screening processes probably will be the most time-consuming clinic activities. Assign sufficient staff to move people steadily through these areas, to keep a steady flow of people to the vaccination areas.

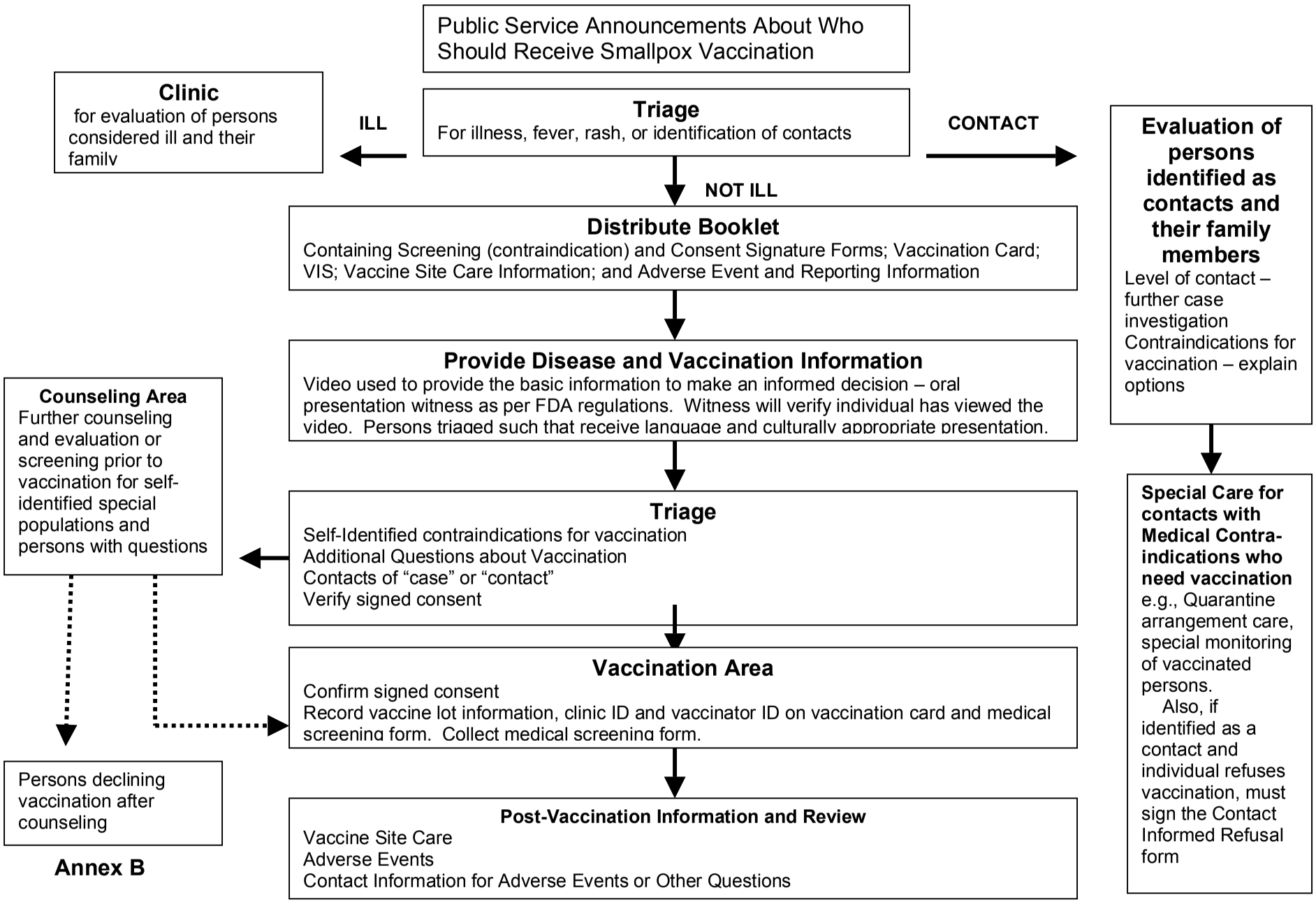
5. Keep traffic in the area where vaccine is being administered to minimum. Ideally, set up the vaccine administration tables so that staff members have their backs to the wall and patients are not congregating or walking behind them. The three steps of the actual vaccination process (i.e., site preparation, vaccination, dressing application) will all take place in a relatively small space (one or two tables) in the same area. Because some vaccine recipients may need to remove shirts or blouses to be vaccinated, use a separate, screened, private area, out of view of other people lined up for vaccination.

6. Locate the medical emergency area as close to the vaccine administration area as possible.

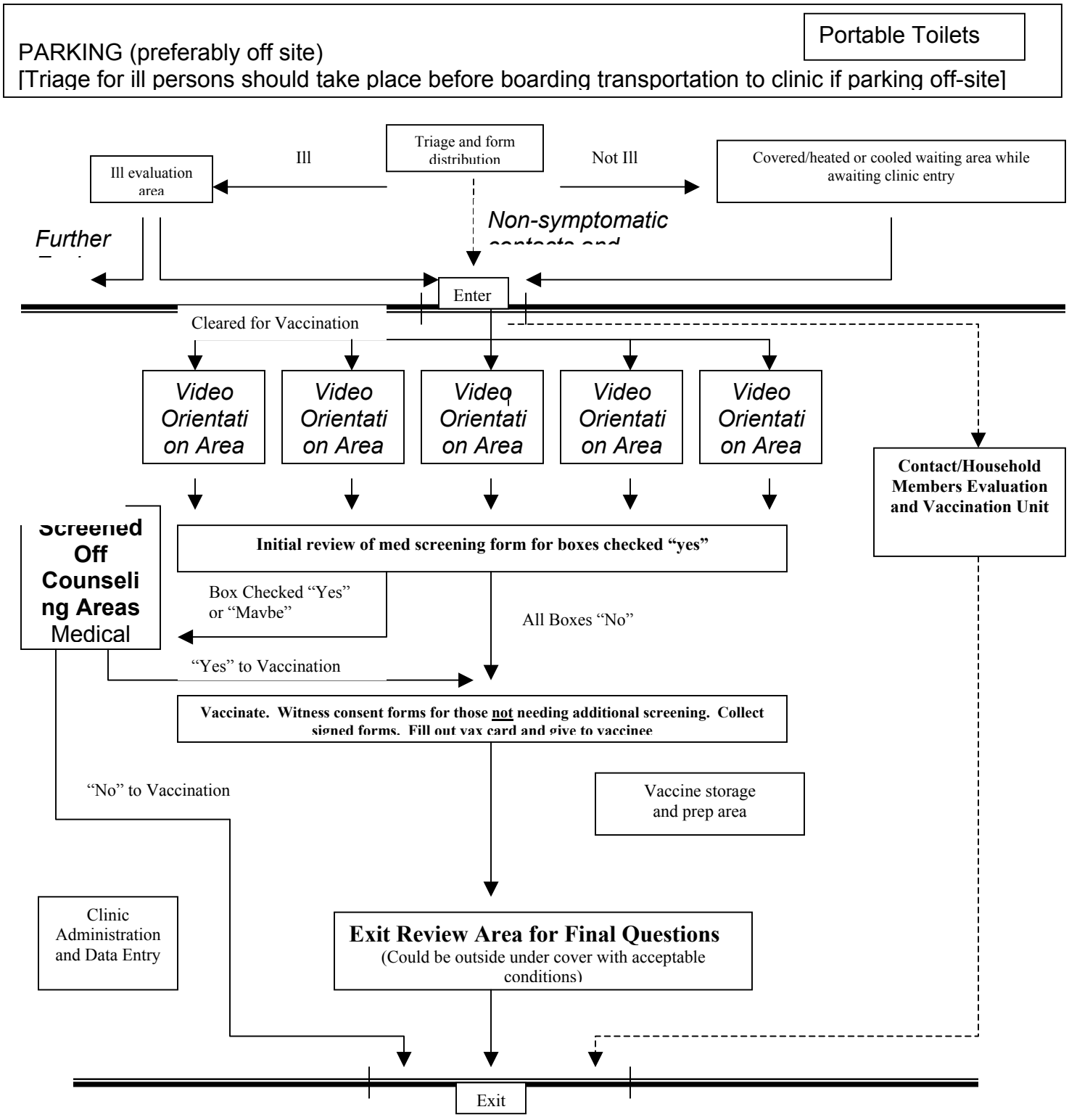
APPENDIX B-7
Vaccination Clinic Diagrams.



Informed Consent Process Flow for Use During Emergency Smallpox Vaccination



Annex B


PARKING (preferably off site)
[Triage for ill persons should take place before boarding transportation to clinic if parking off-site]
Portable Toilets
Triage and form distribution
Ill
Not Ill
Ill evaluation area
Covered/heated or cooled waiting area while awaiting clinic entry
Non-symptomatic
Further
Enter
Cleared for Vaccination
Video Orientation Area
Video Orientation Area
Video Orientation Area
Video Orientation Area
Video Orientation Area
Contact/Household Members Evaluation and Vaccination Unit
Screened Off Counseling Areas Medical
Initial review of med screening form for boxes checked "yes"
Box Checked "Yes" or "Mavbe"
All Boxes "No"
"Yes" to Vaccination
Vaccinate. Witness consent forms for those not needing additional screening. Collect signed forms. Fill out vax card and give to vaccinee
"No" to Vaccination
Vaccine storage and prep area
Clinic Administration and Data Entry
Exit Review Area for Final Questions
(Could be outside under cover with acceptable conditions)
Exit

APPENDIX B-8
Vaccination Documents.

Document	Information Collected	How Used
Medical/Epidemiologic Risk Screening Sheet	Medical contraindications, epidemiological risk status	Preliminary screening tool; people with potential risk routed for in-depth medical screening or priority vaccination.
Informed Consent Document for Investigational New Drug (IND)	Name, address, age or date of birth, gender, lot number, date, signature verifying consent	Vaccine recipient reads and signs in presence of staff.
Vaccine Recipient Diary	Name, address, age or date of birth, gender, lot number, date, list of contraindications, list of symptoms	Vaccine recipients take home and check off any symptoms they may have each day for 4 weeks.
CDC Vaccine Information Statement (VIS)	Verbal Yes/No: Have you read? Do you have any questions?	Given to vaccine recipients to take home.
Instructions on Care of the Vaccination Site	How to care for vaccination site; what vaccination site should look like; who/where to call if reaction occurs	Given to vaccine recipients to take home.
Clinic Vaccination Record	Name, address, age or date of birth, gender, Social Security number, lot number, date	Official clinic medical record
Vaccination Card	Name, address, age or date of birth, gender, lot number, date, signature/stamp	Vaccine recipient receives and keeps card to verify vaccination status.
Vaccination Referral	Name, physical description, gender, signature of referring case worker, case referral number, date, risk category	Presented by people referred for priority vaccination because of their epidemiological risk status (e.g., contact to a case of smallpox).
Expanded Vaccine Adverse Events Report	Name, address, gender, date, lot number	Documentation of adverse events for IND and the Vaccine Adverse Events Reporting System (VAERS).

APPENDIX B-9
Vaccination Clinic Supplies & Equipment.

General Supplies & Equipment	Vaccination Supplies	Emergency Supplies
Tables Chairs Water and cups Paper Pens, pencils Envelopes Rubber bands Tape Stapler, staples Scissors Post-it® notes Clipboards File boxes Telephone Fax machine Photocopy machine Paper towel Kleenex® tissue Table pads and clean paper to cover table for work site Garbage containers and trash bags Regulated medical waste red bags Identification badges for staff List of emergency phone numbers 5 or more large-screen video setups with VCRs or DVD players to show orientation video 7 orientation video tapes Cleaning supplies (e.g., mop, bucket)	Smallpox vaccine cooler or refrigerator Vaccine diluent Sterilized bifurcated needles Puncture-resistant (“sharps”) containers for each vaccination station Latex gloves Latex-free gloves Antibacterial hand-washing solutions Acetone pads Rectangular Band-Aids® Gauze Adhesive tape Spray bottle of bleach solution Paper gowns for patients wearing clothes that do not give ready access to the arm Screens, for changing, counseling, vaccination, as needed	Standing orders for emergencies Epinephrine 1:1000 syringes, auto-injectors, or ampoules, subcutaneous Diphenhydramine 50-mg syringes or vials, intramuscular 3-ml syringes with 1-inch, 25-gauge needles 1.5-inch needles Tuberculin syringes with 5/8" needles (for epinephrine) Alcohol wipes Tongue depressors Adult and pediatric pocket masks with one-way valves Adult and pediatric airways Oxygen tank with tubing IV solutions and tubing Sphygmomanometers (various sizes) Defibrillator and pads Tourniquet Gurney Stethoscope Flashlight Cots Blankets Pillows ER report form Bronchodilator inhaler Thermometer Emesis basin Aspirin, acetaminophen, insulin, D50
	Crowd Management & Triage Supplies Signs for clinic stations and between stations and at triage area Queue partitions (to keep people in lines)	Computer Equipment and Supplies Computers Printers Paper Internet access

Additional Supply Considerations.

Additional Clinic Supplies and Personnel Support for Each Vaccination Clinic (VC).

- Duplication – 1 or more rapid copy machines for duplicating IND paperwork as needed; crate of duplicating paper at each VC; extra machine toner cartridges.
- Computers – 12 desktops and/or laptops for data entry (all need internet connection if Web-based database used) with appropriate software (need to standardize software, if possible).
- Centralized supplies warehouse(s) – Estimate quantity of clinic supplies needed for 1 week of operation (paper, pens, staplers, etc.) and package accordingly for single unit delivery to each VC, weekly deliveries for continued.
- Shipping – Dedicated trucks/vehicles, staff, and drivers and preplanned routes to support vaccine and supplies delivery to 20 VCs.

Communications Equipment.

- Telephones – 5 telephones/separate lines for each VC + 1 fax machine at each VC.
- Cell phones should be considered for nondata/fax needs and/or if easy access to phone lines might be difficult within the vaccination area (e.g., gymnasiums, auditoriums).
- Hand-held radio system to communicate on site without having to send a runner.

Emergency Management.

- Each VC should have clear, written procedures established to deal with emergencies caused by both vaccine adverse reactions and other reactions that could be triggered by the stress of the event (e.g., heart attacks, anaphylactic shock, asthma).

Provision of Food and Beverages for Clinic Personnel.

- Consider using resources, such as Red Cross.
- Local businesses may be willing to donate food and beverages.

Information Materials.

- Obtain 2-day supply of forms (e.g., VIS, IND forms, contraindications, vaccine take, adverse event diary, and vaccination cards) directly from national stockpile (120,000 sets to support 20 VCs for first day) or pre-print forms locally as part of planning.
- Arrange to duplicate adequate numbers of all forms for day 2, day 3, etc. (120,000/day).
- Arrange for dedicated trucks, staff, and drivers and preplanned route to support delivery to 20 VCs.
- Provide information on local clinics and laboratories that can provide HIV testing to individuals who elect to have testing done before getting vaccinated.

APPENDIX B-10
Smallpox Vaccine Handling & Storage Instructions.

Note: Several types of smallpox vaccine might be distributed in a post-outbreak emergency. This sheet refers to Dryvax-brand smallpox vaccine. If another type of smallpox vaccine is provided, refer to information provided with that vaccine.

1. Store smallpox vaccine in the MTF pharmacy. Vaccinia virus vaccine (Dryvax®, Wyeth Laboratories) is a live-virus vaccine that must be reconstituted with diluent. It is prepared from calf lymph.

2. Diluent. Pre-filled syringes of glycerin in water with transfer needle. Manufactured by Baxter.

3. Condition on Arrival.

a. Vaccine should be between 2° to 8°C (35° to 46°F). Refrigerate upon arrival.

b. Diluent should be between 2° to 8°C (35° to 46°F). Refrigerate upon arrival.

4. Storage requirements.

a. Powdered (unreconstituted) vaccine. Long-term storage: vaccine can be preserved indefinitely at -20°C. Short-term storage: store in the refrigerator between 2° to 8°C (35° to 46°F). Local transportation and day use. Storage in Styrofoam containers and cool packs is adequate.

b. Accompanying diluent. Store in refrigerator between 2° to 8°C (35° to 46°F).

5. Reconstitution.

a. Diluent is required for the reconstitution of the smallpox vaccine before administration. The originally licensed diluent for use with smallpox vaccine contained 50% glycerin, 0.25% phenol in Sterile Water for Injection, USP, and 0.005% brilliant green. Reconstitution of a single vial of smallpox vaccine with 0.25 mL of diluent would yield approximately 100 doses. However, this pre-packaged diluent is no longer available. The diluent that will be utilized in this protocol is similar in formulation to the licensed diluent except that it lacks the 0.005% brilliant green. This change in formulation does not affect the ability of the vaccine to produce immunity to smallpox

b. Directions. Remove vaccine vial from refrigerated storage. Allow vial to come to room temperature. Lift up tab of aluminum seal on vaccine vial just enough to expose the top of the stopper. Do not break off or tear down tab. Wipe off vial stopper with an alcohol pad and allow to dry. Place vaccine vial upright on a hard, flat surface. Remove cap from the pre-filled syringe. Take a 1 ml syringe (e.g., tuberculin syringe) and withdraw 0.25 mL

from the opening in the pre-filled diluent syringe. Inject the 0.25 mL of diluent into the vaccine vial to reconstitute the vaccine. Withdraw needle and syringe and discard in the appropriate biohazard sharps container. Allow the vaccine vial to stand undisturbed for 3 to 5 minutes. Then, if necessary, swirl vial gently to effect complete reconstitution. In the space provided on the vaccine vial label, record the date and time that the diluent vial was entered for the purpose of vaccine reconstitution. The vaccine is now ready for use.

6. Storage of Reconstituted Vaccine. Store reconstituted Dryvax in the refrigerator between 2° to 8°C (35° to 46°F). Reconstituted Dryvax may be used for 3 months if stored below 4°C (39°F), or preferably below 0°C (32°F) when not in use.

7. Vaccine Labeling and Packaging.

a. Labels. Wyeth Laboratories manufactured the existing inventory of Dryvax-brand smallpox vaccine. The vaccine vials have commercial labels reading "Smallpox Vaccine, Dried, Calf Lymph Type, DRYVAX®." However, this product is currently considered an investigational new drug (IND) product, because it is packaged with a diluent not yet approved by the Food & Drug Administration for standard use. These commercially labeled vials have lot numbers 7 digits long.

b. Packaging. Fifty vials of Dryvax vaccine are packaged in each carton (i.e., the secondary package). Up to twelve (12) cartons will fill VaxiCool® insulated shipping containers (about the size of a large Coleman®-style cooler), without further tertiary packaging or overwrap. Diluent need not be refrigerated and may be shipped outside of the VaxiCool containers.

APPENDIX B-11
Screening for Bars (Contraindications) to Smallpox Vaccination.

(Annotated Version)

1. How are you today? Do you have a fever, diarrhea, or vomiting today?
_____

2. Have you ever had a serious reaction to any vaccine? YES NO
If so, please describe it: _____

3. Do you have any drug allergies? YES NO
If so, please list them: _____

Note: People who have had serious allergic reactions to the antibiotics polymyxin B, streptomycin, tetracycline, or neomycin should talk with a physician before vaccination.

4. Have you ever received smallpox vaccination before? YES NO DON'T KNOW
Marked in records. Where? _____
Have a smallpox scar. Where? _____
Born in 19____. Where? _____
Entered US military service in 19_____

5. Are you being treated by a doctor for a disease? YES NO
If so, please describe it: _____

Note: People treated for arthritis or Crohn's disease may be taking medications that affect their immune system (e.g., etanercept/*Enbrel*, infliximab/*Remicade*). Other people in similar situations may include those treated with interferon alfa (e.g., *Intron-A, Roferon-A*; for hepatitis B or hepatitis C infection), interferon beta (e.g., *Avonex, Betaseron, Rebif*; for multiple sclerosis), or interferon gamma (e.g., *Actimmune* for chronic granulomatous disease).

6. Do you or anyone in your household have any form of cancer, leukemia, or immune system problem? For example:

a. People taking anticancer drugs, x-ray treatments, cortisone, prednisone, or other steroids (other than inhalers). YES NO

b. People with leukemia, lymphoma, or generalized cancers (malignancy). YES NO

c. People who had an organ or bone-marrow transplant. YES NO

d. People with any other problem with the immune system, such as agammaglobulinemia, acquired immune deficiency syndrome (AIDS) or infected with the human immunodeficiency virus (HIV). YES NO

Note: People with certain medical conditions can have a higher risk of developing severe complications after they receive smallpox vaccination themselves. There is also a risk if someone in their household gets smallpox vaccine and then viruses at the vaccination site spread by touch to a member of the household.

7. Have you ever been told by a doctor that you have eczema or atopic dermatitis? YES NO

Eczema and atopic dermatitis usually involve an itchy, red, scaly rash that lasts more than 2 weeks. It often comes and goes. You should not receive smallpox vaccine at this time unless you and a healthcare provider are sure that this rash is not atopic dermatitis or eczema.

8. Has anyone in your household ever been told by a doctor that he or she has eczema or atopic dermatitis? YES NO

Note: If the answer is yes, do not give smallpox vaccine because of the risk that the recipient or the household contact might develop eczema vaccinatum.

9. Do you have any other current skin conditions, such as burns, impetigo, varicella zoster (chickenpox or shingles), psoriasis, or severe or uncontrolled acne?

10. Have you received a transfusion of blood or plasma or any medicine containing antibodies (immune or gamma globulin) in the past 12 months?

If so, you may be slightly less likely to benefit from smallpox vaccination. Watch the vaccination site carefully and get revaccinated if no blister appears by day 6 to 8 after vaccination.

11. For women: Was your last menstrual period normal and on time? YES NO

Could you be pregnant? Or have you had unprotected sex since your last normal period?

Note: As with most vaccines, vaccination of pregnant women should be deferred unless it is clearly needed. Live-viral vaccines are usually barred (contraindicated) during pregnancy. But if you have been exposed to smallpox, you would probably be vaccinated against it. Smallpox vaccine is not known to cause birth defects. On very rare occasions, vaccinia infection of the fetus has been reported after vaccinating the mother. This fetal vaccinia infection may result in stillbirth or death of the infant soon after delivery. About 50 of these fetal cases have been recorded after vaccinating billions of women around the globe. Smallpox infection among pregnant women has been reported to result in a more severe infection than among nonpregnant women.

APPENDIX B-11 (continued)
Screening for Bars (Contraindications) to Smallpox Vaccination.

Screening Before Smallpox Vaccination.

1. How are you today? Do you have a fever, diarrhea, or vomiting today?			
2. Have you ever had a serious reaction to any vaccine? If so, please describe it:	YES	NO	
3. Do you have any drug allergies? If so, please list them:	YES	NO	
4. Have you ever received smallpox vaccination before? When?	YES	NO	DON'T KNOW
a. Marked in records. Where?			
b. Have a smallpox scar. Where?			
c. Born in 19 . In United States?			
d. Entered US military service in 19 .			
5. Are you being treated by a doctor for a disease? If so, please describe it:	YES	NO	
6. Do you or anyone in your household have any form of cancer, leukemia, or immune system problem? For example:			
a. People taking anticancer drugs, x-ray treatments, cortisone, prednisone, or other steroids (other than inhalers).	YES	NO	
b. People with leukemia, lymphoma, or generalized cancers (malignancy).	YES	NO	
c. People who had an organ or bone-marrow transplant.	YES	NO	
d. People with any other problem with the immune system, such as agammaglobulinemia, acquired immune deficiency syndrome (AIDS), or infected with the human immunodeficiency virus (HIV).	YES	NO	
7. Have you ever been told by a doctor that you have eczema or atopic dermatitis?	YES	NO	
Eczema and atopic dermatitis usually involve an itchy, red, scaly rash that lasts more than 2 weeks. It often comes and goes. You should not receive smallpox vaccine at this time unless you and a healthcare provider are sure that this rash is not atopic dermatitis or eczema.			
8. Has anyone in your household ever been told by a doctor that he or she has eczema or atopic dermatitis?	YES	NO	
9. Do you have other current skin conditions, such as burns, impetigo, varicella zoster (chickenpox or shingles), psoriasis, or severe or uncontrolled acne?	YES	NO	
10. Have you received a transfusion of blood or plasma or any medicine containing antibodies (immune or gamma globulin) in the past 12 months?	YES	NO	
11. For women: Was your last menstrual period normal and on time?	YES	NO	
Could you be pregnant? Have you had unprotected sex since your last normal period?	YES	NO	DON'T KNOW

APPENDIX B-12
How to Use a Bifurcated Needle.

Use skin over the insertion of the deltoid muscle (preferred) or the posterior aspect of the arm over the triceps muscle for smallpox vaccination. Do not use alcohol to prepare the skin, because it dries to slowly and can inactivate the vaccinia virus. If the area is grossly contaminated, use warm water. Alternately, if acetone is used, the skin must be allowed to dry thoroughly (for several minutes) to prevent inactivation of the vaccine virus.

The multiple-puncture technique uses a sterilized bifurcated needle inserted vertically into the vaccine vial, causing a droplet of vaccine to adhere between the needle prongs. The droplet contains the recommended dosage of vaccine. Confirm the presence of the droplet between the prongs visually. Holding the bifurcated needle perpendicular to the skin, make 15 punctures rapidly with strokes vigorous enough to allow a trace of blood to appear after 15 to 20 seconds. Wipe off any remaining vaccine with dry sterile gauze, then dispose of the gauze in a biohazard waste container.

Leave the site uncovered, if the individual is thoroughly counseled about the hazards of touching the vaccination site. Alternately, cover the site with a loose bandage to deter touching the site and perhaps transferring virus to other parts of the body.

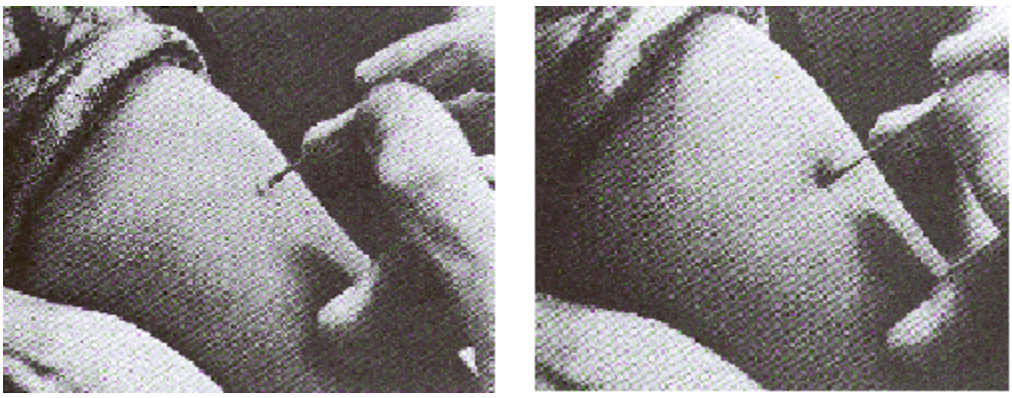
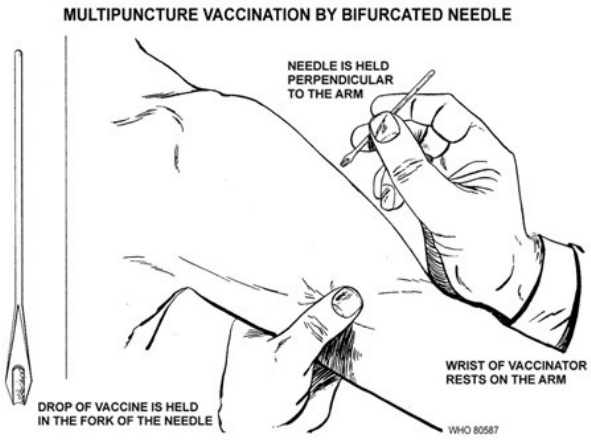


Figure – Needle held at a 90° angle to skin then rapid, up-and-down perpendicular strokes are used to administer the vaccine. [Fenner F, Henderson DA, et al. *Smallpox and its Eradication.* WHO. 1988, Reprinted with permission of WHO]



APPENDIX B-13
Response to Smallpox Vaccination.

Day After Vaccination	Major (Primary) Reaction	Major Reaction, for revaccinated people *	Equivocal: Delayed Hypersensitivity Reaction	Equivocal: All Other Reactions
Day 1			Erythema	
2			Erythema **	
3	Papule (bump, pimple)	Papule	No further rxn.	
4				
5	Vesicle (blister)	Vesicle		
6		Pustule, induration or congestion around	Requires revaccination	Requires revaccination
7	Pustule -- pus-filled blister (center collapses) (if previously vaccinated, may show 'induration' (hard swelling) only)			
8				
9		scab or ulcer		
10				
11				
12				
13				
14	Scab (dark, then flesh-colored)			
15				
16				
17				
18		* greatest erythema occurs after 3d day after revaccntn; implies viral propagation.	** vesicles infrequently	
19				
20	Scab falls off (day 14 to 21)			
21				

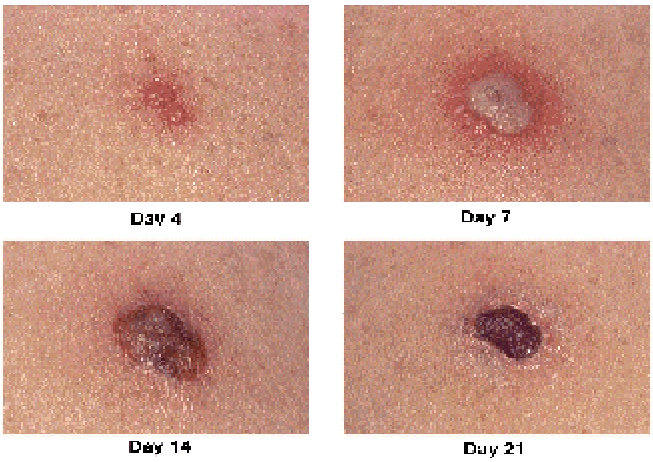


Figure. Major (primary) reaction. Expected local reaction after primary smallpox vaccination or revaccination after a prolonged period since primary vaccination.

APPENDIX B-14
Care of the Vaccination Site.

Three Key Points:

(a) Don't touch the vaccination site.
(b) If you touch it by accident, wash your hands right away with soap and water.
(c) Do not let others contact your vaccination site or materials that covered it.

Smallpox vaccine contains live vaccinia viruses, which grow at the vaccination site, mainly when a bump appears 3 to 5 days after vaccination. The bump becomes a vesicle (blister), then a pustule (fills with pus). It gets bigger until the 8th to 10th day after vaccination. The viruses persist until the scab falls off, 14 to 21 days later.

Spreading vaccinia virus to some other part of the body is called auto-inoculation or accidental infection. Auto-inoculation is the most common among the serious side effects of smallpox vaccination, affecting about 600 out of 1,000,000 people getting smallpox vaccine for the first time. The most common sites involved are places that itch: eyelids, nose, mouth, genitalia, and rectum.

Vaccinia virus can also be spread to a contact of the vaccinated person, especially if that other person has an immune deficiency or eczema. During the 1960s, the risk of spreading vaccinia virus to a contact (usually a household member) was about 8 to 27 per 1,000,000 vaccinations overall, mainly children 5 years or younger. Today, more people in the community are living with problems to their immune systems. Follow instructions about caring for your vaccination site, to minimize the chance of spreading vaccinia virus to a contact.

After vaccination, you can either leave the site uncovered or cover it with a loose, breathable dressing (e.g., standard Band-Aid®, gauze), until the scab falls off on its own. Airing will help speed healing of the vaccination site. Using a touch-resistant barrier can reduce for contact transfer. Do not use an occlusive bandage (one that doesn't breathe), because fluid could collect under the bandage, soak the skin, and damage the skin. Wearing long-sleeve clothing during the day and at night is another good idea. Minimize close contact with infants less than one year of age. Wash your hands before changing a child's diapers (or having someone else change the diapers).

If you cover the vaccination site, change bandages daily or every few days to prevent fluid buildup. Use paper (or hypoallergenic) tape, if appropriate. Dispose of contaminated bandages and the scab as biohazardous waste in a hospital. If this is not possible, dispose of bandages in sealed or double plastic bags, to keep others away from the virus. Consider adding a small amount of full-strength chlorine bleach to the bandages.

Keep the site dry. Frequent airing will speed healing. Do not use creams or ointments, to avoid softening it and prolonging healing. Long-sleeve clothing worn during the day and at night can protect the site from dirt. Rolling up sleeves in clean locations helps the site

heal. Decontaminate clothing and linens that touch the site with routine laundering in hot water with soap or bleach.

Normal bathing can continue. Dry the area carefully, so that the towel does not rub or spread virus elsewhere. Do not allow others to use that towel until after laundering. Use a waterproof adhesive bandage (e.g., Band-Aid) if you exercise enough to cause sweat to drip. Swimming can make the site soft and gooey.

Arrange clothing and load-bearing equipment to avoid excessive pressure or rubbing at the vaccination site. Avoid contact sports (e.g., wrestling). Be careful not to get sunburn, because the viruses can spread to damaged skin.

Wash your hands if you touch the vaccination site by accident. Use soap and water. Alcohol-based rinses are useful as well. Do not let others touch your vaccination site, bandages, or linen. Have them wash their hands too. It may be a good idea to wash your hands before using the bathroom.

People who live with others who have a bar (caution) against smallpox vaccination should house themselves separately, until the vaccination site heals. This will reduce the risk of spreading virus from the vaccination site to the other person.

Extra Steps for Healthcare Workers.

Recently vaccinated healthcare workers should minimize contact with unvaccinated patients, particularly those with immunodeficiencies, until the scab falls off. Even patients vaccinated in the past may be at increased risk due to current immunodeficiency. If contact with unvaccinated patients is essential and unavoidable, healthcare workers can continue to have contact with patients, including those with immunodeficiencies, as long as the vaccination site is well-covered and thorough hand-hygiene is maintained. In this setting, a more occlusive dressing might be appropriate.

Semi-permeable polyurethane dressings (e.g., Opsite®, Tegaderm®) are effective barriers to vaccinia and recombinant vaccinia viruses. However, exudate may accumulate beneath the dressing, and care must be taken to prevent viral contamination when the dressing is removed. In addition, accumulation of fluid beneath the dressing may increase the maceration of the vaccination site. To prevent accumulation of exudates, cover the vaccination site with dry gauze, and then apply the dressing over the gauze. The dressing should also be changed daily or every few days (according to type of bandaging and amount of exudate), such as at the start or end of a duty shift.

Military treatment facilities will develop plans for site-care stations, to monitor workers' vaccination sites, promote effective bandaging, and encourage scrupulous hand hygiene. Wearing long-sleeve clothing can further reduce the risk for contact transfer. The most critical measure in preventing inadvertent contact spread is thorough hand-hygiene after changing the bandage or after any other contact with the vaccination site.

APPENDIX B-15

Complication Rates After Vaccination with New York City Board of Health Strain of Smallpox Vaccine.

Key Points:

1. Deaths due to smallpox vaccination are of greatest concern among infants younger than 1 year old and adults receiving their first smallpox vaccination.
2. Serious complications after smallpox vaccination are relatively more common among people getting their first smallpox vaccination (primary vaccination), compared to those getting a repeat or booster smallpox vaccination, although rare for both groups.
3. An exception is that progressive vaccinia is relatively more common among adult vaccine recipients than younger vaccine recipients, although rare for both groups. The elevated rate may be due to unrecognized immunosuppression due to cancer not yet diagnosed at time of vaccination.
4. The most frequent serious complication after smallpox vaccination is accidental infection (auto-inoculation). This complication can be avoided by frequent hand washing.

Vaccinia Complications per 1,000,000 **Primary** (First) Vaccinations	< 1 Year	1-4 Years	5-19 Years	20+ Years	Overall
Death (all causes)	5 to 14	0.5	1.5	1 to 5 *	1.1 to 1.5
Post-vaccinial encephalitis or other neurologic conditions (e.g., enceph-alomyelitis, transverse myelitis)	6 to 42	2 to 10	3 to 9	4	3 to 12
Progressive vaccinia (vaccinia necrosum)	1	0.4 to 3	1	7	1 to 1.5
Eczema vaccinatum	8 to 14	11 to 44	7 to 35	24 to 30	10 to 39
Generalized vaccinia	70 to 394	17 to 233	13 to 140	45 to 212	23 to 242
Accidental (inadvertent) inoculation (e.g., auto-inoculation)	11 to 507	33 to 577	18 to 371	14 to 606	25 to 529
Total (including complications not specifically mentioned)	1,549	1,262	856	1,515	1,254

Vaccinia Complications per 1,000,000 **Repeat** (Re-) Vaccinations **	< 1 Year	1-4 Years	5-19 Years	20+ Years	Overall
Death (all causes)			0.23	0.26	0.23
Post-vaccinial encephalitis or other neurologic conditions (e.g., enceph-alomyelitis, transverse myelitis)				4.5	2
Progressive vaccinia (vaccinia necrosum)			0.5	1 to 7	1 to 3
Eczema vaccinatum		2	2	4.5	1 to 3
Generalized vaccinia			1 to 10	2 to 9	1 to 9
Accidental (inadvertent) inoculation (e.g., auto-inoculation)		109	1 to 48	1 to 25	1 to 42
Total(including complications not specifically mentioned)		200	86	114	108

* The number of deaths among 288,000 adults receiving primary vaccination in the 1960s was zero, but CDC extrapolates the expected rate as “5?” (the question mark originates with the CDC).

** The applicability of these revaccination data to modern circumstances is limited, because the setting of the 1960s involved a higher average number of doses per person, with shorter average intervals between vaccinations.

Rare adverse events reported after smallpox vaccination (causality consistent with other vaccines): Immediate hypersensitivity, anaphylaxis, urticaria, edema.
Rare adverse events reported after smallpox vaccination (causality undetermined): vaccinia osteomyelitis, skin cancer at site of vaccination scar, keratitis, and ocular neuritis.

Sources:
Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968: national surveillance in the United States. *N Engl J Med* 1969;281:1201--8.
Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968: results of ten statewide surveys. *J Infect Dis* 1970;122:303--9.
Lane JM, Millar JD, Neff JM. Smallpox and smallpox vaccination policy. *Annu Rev Med* 1971;22:251--72.
ACIP. Vaccinia (smallpox) vaccine. *MMWR* 2001;50(RR-10):1-25.
Centers for Disease Control & Prevention. Smallpox Response Plan, 23 Sep 02.

Population	Age (yrs)	Number vaccinated (millions)		Outcomes - Rate in Cases per Million Vaccinations or (# Cases), [# deaths]															
				Deaths (all causes)		Post-vaccinial encephalitis		Progressive Vaccinia (V. Necrosum)		Eczema Vaccinatum		Generalized Vaccinia		(Accidental) Inadvertent Inoculation		Other[1]		TOTAL[2]	
U.S. general surveys (1968)		Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]	Nat'l[3]	Ten State[4]
Primary vaccinations	<1	0.614	0.071	4.9[3]	14[1]	6.5[3]	42[1]	…	...	8.1	14	70	394	11	507	16	155	112	1549
	1-4	2.733	0.317	[0]	…	2.2	9.5	0.4	3.2	11	44	17	233	33	577	15	237	79	1262
	5-19	1.959	0.229	1.5[3]	…	2.6[1]	8.7	1.0[2]	...	7.1	35	13	140	18	371	5	214	46	856
	20+	0.288	0.033	[0]	…	3.5	...	6.9	...	24	30	45	212	14	606	17	636	111	1515
Total		**5.594**	**0.65**	**1.1[6]**	**1.5[1]**	**2.9[4]**	**12[1]**	**0.9[2]**	**1.5**	**10**	**39**	23	**242**	**25**	**529**	**12**	**266**	**75**	**1254**
Re-vaccinations	1-4	0.478	0.055	[0]	…	…	…	…	…	2.1	…	…	…	…	109	2.1	18	4.2	200
	5-19	4.3	0.503	0.23[1]	…	…	…	0.5[1]	…	1.6	2.0	0.23	9.9	0.7	48	0.5	24	3.5	86
	20+	3.796	0.44	0.26[1]	…	…	4.5	1.1[1]	6.8	…	4.5	2.4	9.1	0.8	25	1.6	55	5.8	114
Total		**8.574**	**0.998**	**0.23[2]**	**0**	**…**	**2.0**	**0.7[2]**	**3.0**	**0.9**	**3.0**	1.2	**9**	**0.8**	**42**	**1**	**39**	**4.7**	**108**
Contacts[5]	<1	…	...	[0]	[0]	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(9)	(1)	(1)	(1)	(14)	(2)
	1-4	…	...	[1]	[0]	(0)	(0)	(0)	(0)	(38)[1]	(4)	(1)	(1)	(16)	(12)	(6)	(0)	(61)	(18)
	5-19	…	...	[0]	[0]	(0)	(0)	(0)	(0)	(9)	(6)	(0)	(0)	(10)	(5)	(0)	(0)	(19)	(11)
	20+	…	...	[0]	[0]	(0)	(0)	(0)	(0)	(9)	(3)	(1)	(0)	(9)	(11)	(0)	(0)	(19)	(14)
Total				**0.07[1]**	**[0]**	**(0)**	**(0)**	**(0)**	**(0)**	**4.2[1]**	**7.9**	**0.14**	**0.6**	**3.1**	**18**	**0.5**	**0.6**	**8**	**27**
Grand Totals		**14.17**	**1.648**	**0.6[9]**	**0.6[1]**	**1.1[4]**	**6.1[1]**	**0.8[4]**	**2.4**	**8.9[1]**	**25**	**10**	**101**	**14**	**252**	**5.9**	**129**	**40**	**587**
Military																			
Israeli Recruits (1991-1996)[6]			> 0.300		(0)		(0)		(0)		15		9		6		6		**40**
U.S. Forces WWII (1942-1945)[7]			~16.4		0.18[3]		0.48(8)[3]		…		…		…		…		…		**NA**
U.S. Recruits (1971-1975)[8]			~1.97		(0)		(0)		…		…		4		…		16 to 35		**54**
AD (1977-1981)[8]			(?)		(0)		(0)		…		…		…				…		…
Recruits (1981)[8]			~0.322		(0)		(0)		…		…		37(12)		…		149(48)		**186(60)**

1 - "Other" includes secondary infections, miscellaneous complications, and erythema multiforme in Nat'l[3] study (with 9 cases of Stevens-Johnson syndrome). Erythema multiforme was a separate category in Ten State[4] (rate 165/M primary, 10/M re-vaccination; 1 contact case) and Israeli Recruit[6] studies (rate 3/M)).

2 - Total rates include cases with either unknown age (N=63) or vaccination status (N=31 Nat'l[3], N=65 Ten State[4]) and 118 cases of e. multiforme (Ten State[4]).

3 - Lane et al. *NEJM*;281(22), 1969. National surveillance of smallpox complications from seven sources (83% of reports from Red Cross VIG usage records).

4 - Lane et al. *J Inf Dis*;122(4), 1970. Ten state direct survey of U.S. physicians regarding complications (more complete reporting, especially for minor events).

5 - Overall rate of contact complications estimated by dividing total events in category by total vaccinations (denominators for each age group unavailable).

6 - Haim et al. *Mil Med* 165(4), 2000; Note: denominator was not supplied in article but minimum estimate calculated from rates.

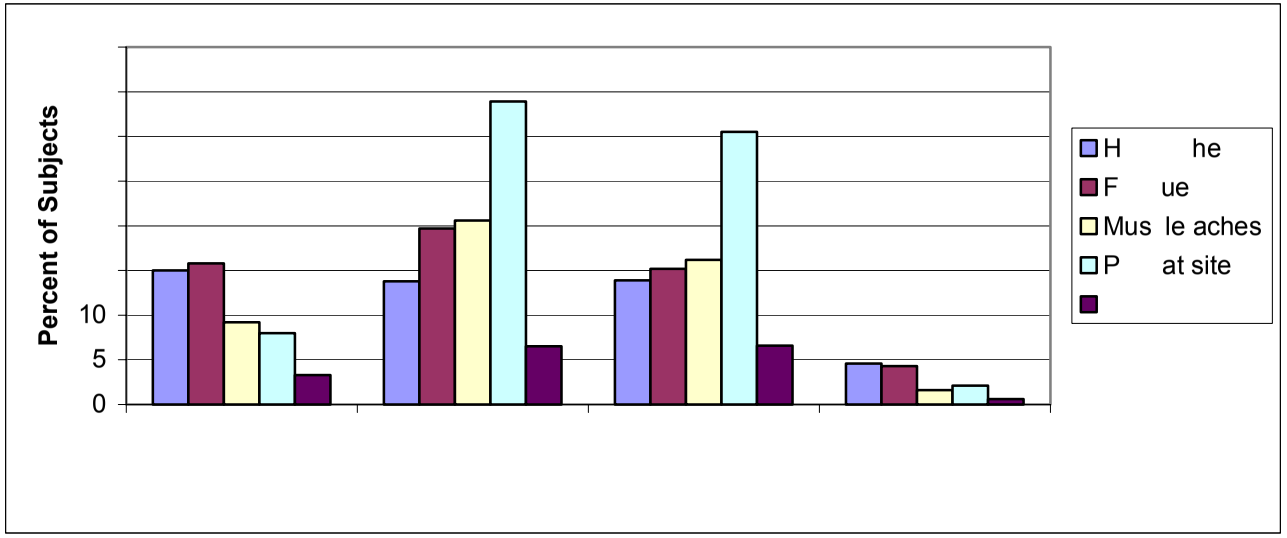
7 - Cases of PVE and deaths from Coates & Hoff. *Preventive Medicine in WWII*, Vol. III, 1955:280-7. Denominator estimate = total troops mobilized in WWII (*World Almanac*, 1998).

8 - Armed Forces Epidemiology Board Transcripts, 1977 (rates) and 1984 (cases). Recruit denominators obtained from Defense Manpower Data Center.

Frequency of Moderate to Severe Symptoms After Primary Smallpox Vaccination (n=655)

Moderate or severe symptom frequencies listed, if total frequency of reporting > 5%.
Moderate = bothersome, but did not preclude activity. Severe = precluded performance of routine activities.
Source: Frey et al. Clinical responses to undiluted and diluted smallpox vaccine. *N Engl J Med* 2002;346(17):1265-1274.

Sy Sign	Severity	Day 0-6	Day 7-9	Day 10-12	Day 13-14
	Moderate	12.9	11.7	11.3	3.8
	Severe	2.1	2.1	2.6	0.8
Headache	**Total**	**15**	**13.8**	**13.9**	**4.6**
		13.4	17.1	12.6	3.
		2.4	2.6	2.6	1.
Fatigue	**T l**	**15.8**	**19.7**	**15.2**	**4.3**
	Moderate	8.3	18	14.1	1.1
	Severe	0.9	2.6	2.1	0.5
Muscle aches	**Total**	**9.2**	**20.6**	**16.2**	**1.6**
	Mod ate	7	31.9	27.2	2.1
		0	2	3.3	0
	Total	**8**	**33.9**	**30.5**	**2.1**
	Moderate	2.4	4.7	5.1	0.3
	Severe	0.9	1.8	1.5	0.3
Chills	**Total**	**3.3**	**6.5**	**6.6**	**0.6**



APPENDIX B-16
Skin Diseases Affecting Smallpox Vaccination.

Adapted from the recommendations of the Ad Hoc Task Force on Bioterrorism of the American Academy of Dermatology, 2002

1. Several skin diseases place affected people at risk for developing eczema vaccinatum after smallpox vaccination. Eczema vaccinatum is a localized or disseminated cutaneous vaccinial eruption. In some cases, the condition can be severe and life-threatening. The severe form, although uncommon, usually occurs in people who have true atopic dermatitis (see 2a). In contrast, if eczema vaccinatum develops in patients with non-atopic skin diseases (see 2b, 2c, 2d), it is usually confined to the areas of disturbed skin. This form of eczema vaccinatum is usually mild and self-limited. Many of these patients may be vaccinated once their underlying skin disease is under control.

2. Cutaneous disorders that place a person at risk are reviewed below.

a. Atopic dermatitis or a history of atopic dermatitis (often called childhood eczema). People with atopic dermatitis or a history of atopic dermatitis are at increased risk for developing adverse reactions. The risk of an adverse reaction, specifically eczema vaccinatum, is highest in people with active atopic dermatitis. The presence of active disease, treated or resolved diseases, or even a past history of atopic dermatitis, is a contraindication to vaccination. Every effort should be made to identify patients with a history of cutaneous atopic disease, and any patient with active or inactive disease should not be vaccinated. Positive responses to two or more of the following five questions should be considered consistent with the diagnosis of atopic dermatitis:

(1) Has a doctor ever diagnosed eczema in the patient?
(2) Has the patient had itchy rashes that lasted more than two weeks?
(3) Has the patient ever had itchy rashes in the folds of the arms or legs?
(4) Did the patient have eczema or food allergies during infancy and childhood?
(5) Has a doctor ever diagnosed asthma or hay fever in the patient?

b. People with eczema or dermatitis that is not atopic dermatitis. [Note that childhood eczema is another name for atopic dermatitis and is addressed in 2a above.] Eczema, also called dermatitis, is a general term used to describe several skin conditions that exhibit eczematous skin changes (skin that is itchy, red, and scaling or oozing; vesiculating; crusting). In addition to atopic dermatitis (childhood eczema), these disorders include seborrheic dermatitis, contact dermatitis, nummular eczema, dyshidrotic eczema, and others. Although eczema is frequently used to denote atopic dermatitis, the term eczema is not synonymous with atopic dermatitis, but rather encompasses the above-mentioned disorders. Patients with non-atopic forms of eczema or dermatitis may receive smallpox vaccine when their skin condition is under good control. Such patients may occasionally auto-inoculate remaining areas of compromised skin, but this is usually mild and uncomplicated. They will also have the other usual risks for vaccine-related adverse events.

c. Other chronic exfoliative, erosive, pustular, or blistering skin disorders that disrupt the epidermis. Examples include moderate or extensive psoriasis, epidermolysis bullosa, severe acne (on face or torso), and pemphigus vulgaris. Patients with these disorders (e.g., focal psoriasis on elbows and knees only) may receive the vaccine when their skin condition is under good control. Such patients may occasionally auto-inoculate remaining areas of compromised skin, but this is usually mild and uncomplicated. They will also have the other usual risks for vaccine-related adverse events.

d. Acute, self-limited and non-relapsing skin disorders that disrupt the epidermis: Examples include (but are not limited to) impetigo, varicella, pityriasis rosea, acute contact dermatitis, or acute burns. These patients may receive the vaccine when their condition has resolved and the skin is fully re-epithelialized.

e. Some medications alter the immunity of the skin or the physical integrity of the epidermis and may theoretically increase the risks associated with smallpox vaccine. These medicines include topical immunomodulators (e.g., tacrolimus/Protopic®, pimecrolimus/Elidel®). Retinoids (both topical and oral) may dry the skin and cause numerous epidermal microfissures, possibly increasing the risk of eczema vaccinatum or focal auto-inoculation. If the medications are temporarily discontinued before vaccination, and if the epidermal barrier is restored, the patient may receive smallpox vaccination, and then resume medications once the scab or crust has separated (approximately 18 to 21 days later).

f. Smallpox vaccination involves replication of live vaccinia virus at the site of inoculation. Therefore recent vaccination sites are contagious and can potentially transmit vaccinia to bystanders until the crusts at the vaccination site have fully separated (roughly 18 to 21 days after vaccination). Patients with skin conditions described in 2a through 2e above are at particular risk. The risk for transmission to household contacts may be 27 infections per 1,000,000 vaccinations overall. The risk is higher among young children ($\leq$ 5 years of age), accounting for nearly half of cases reported. Contact transmission rarely results in postvaccinal encephalitis or progressive vaccinia. Approximately 30% of the cases of eczema vaccinatum reported resulted from contact transmission. Eczema vaccinatum may be more severe among contacts than those vaccinated, perhaps because multiple inoculations occur.

g. For these reasons, vaccination is not recommended for people who have a household member or regular close contact with an acute or active chronic skin disorder that disrupts the epidermis. Postpone vaccination until the contact's skin disorder is under control. Furthermore, if a household member or regular close contact has active atopic dermatitis or a history of atopic dermatitis, withhold the vaccination. Alternatively, if vaccination is required in such circumstances, the vaccinee should not have close household contact with at-risk individuals until the crusts at the vaccination site have fully separated, roughly 18 to 21 days after vaccination.

APPENDIX B-17
Investigational New Drugs (INDs) for Force Health Protection.

1. References. 10 USC 980, 10 USC 1107, Executive Order 13139, FDA's 21 CFR 50.23(d), FDA's 21 CFR 312, DoD Directive 6200.2.

2. Purpose. This appendix describes in general terms the tasks that need to be accomplished to administer medications (including vaccines) under the federal rules that apply to **investigational new drugs** (INDs). Documents that describe in detail how the IND medication will be administered are known as **IND protocols**. More detailed information on use of INDs is furnished in the references cited above and in "How To Guides" (references e, f, and g of this annex) developed by the US Army Medical Command. One of the core differences between IND and licensed medications involves the federal requirements for documentation, described below. If a licensed smallpox vaccine is administered, rather than IND smallpox vaccine, it will be administered with the standard record-keeping requirements applied to other licensed vaccines.

3. INDs. An IND medication is a medication that the Food and Drug Administration (FDA) allows (on a limited, voluntary basis) to be used in humans, after people receive information about benefits and risks. But an IND medication has not yet been fully accepted by the FDA as safe and effective for its intended use. The FDA requires animal data on safety and effectiveness to be collected before use in humans is allowed.

4. Standards. The FDA has very rigorous standards for licensing or approving a medication. The FDA generally requires evidence that a new drug (or vaccine) is both safe and effective in humans before they will license it. The DoD administers unlicensed medications only under the FDA's IND rules. With products such as smallpox vaccine, DoD has a vaccine nearing full FDA approval, but we must be ready to use it under IND rules, if required, before the licensing process is complete. With other products of military interest, such as nerve-agent pretreatments or antidotes, it is not ethical to expose people to a harmful substance (e.g., nerve agent) to show that the medication works in humans. So the only way DoD can use them is as INDs.

5. Informed Consent. Consent is permission to receive an IND medication, given by an individual or someone legally responsible for that individual. Consent is only considered informed if the person receives information about the potential benefits and side effects of a medication and has the opportunity to have questions answered.

6. Education. The unit commander is responsible for ensuring each service member and health-care provider in the unit receives proper education regarding the use of an IND medication, the reason why the medication is to be given, the possible side effects and risks, as well as benefits of using the medication. Unit commanders are also responsible for other tasks described below.

7. Documentation. Medical records must accurately document receipt when an IND medication or medication unapproved for its applied use is given. Medical records must also include a copy of the written notice or consent form used.

8. Responsibilities of Unit Leaders Regarding INDs. Ensure health-care providers and service members receive the appropriate education required for them to make informed decisions about whether to accept or decline an IND medication. Assign an ombudsman to assist with the informed-consent process. Assist people in finding answers to their questions about INDs. Foster an environment where people can freely choose whether or not to receive the IND medication. Foster an environment where health-care providers administer the IND medication in accordance with the approved IND protocol. Provide support for documentation of IND medication administration in health records. Ensure preservation of medical records and IND records. Refrain from discriminating, when assigning missions, against Service Members who decline to consent to participate in an IND protocol. Assist people in getting any additional necessary doses of IND product. Assist people, with health-care provider support, in reporting adverse events after IND administration, so that a complete and accurate understanding of IND product safety or side effects can be determined. Assist people in getting needed medical care.

9. Responsibilities of the Services. Services educate personnel about IND responsibilities in general, provide training to Principal Investigators, implement the requirements of DoD D 62002, provide storage, distribution, disposition, and accountability of IND products, and provide quality control/quality assurance of IND protocol documentation.

10. Responsibilities of the Combatant Commands: The Combatant Command designates an officer (or officers) to be the responsible Principal Investigator(s) within the Command. The Combatant Commanders request authority to administer IND medications for force health protection through the Chairman of the Joint Chiefs of Staff to the Secretary of Defense. If necessary, the Command may request waiver of consent (see below). The Combatant Commander is responsible for fully and carefully implementing any IND protocol.

11. Responsibilities of the Principal Investigator (PI). PIs will receive training in the rules for conducting an IND protocol, known as Good Clinical Practices (GCP). These practices emphasize detailed record keeping, informed consent, implementing the protocol as written, product accountability, and other topics. PIs must sign a FDA Form 1572, accepting responsibility for faithfully conducting the protocol according to the protocol and FDA-accepted procedures. Deviations from the protocol must be recorded and reported. Unexpected and serious adverse experiences must be noted and reported.

12. Responsibilities of Clinical Project Manager (CPM). Also trained in GCP, the Clinical Project Manager will store protocol documentation, submit safety reports to the US Army Medical Materiel Development Activity (USAMMDA), DOD's representative to the

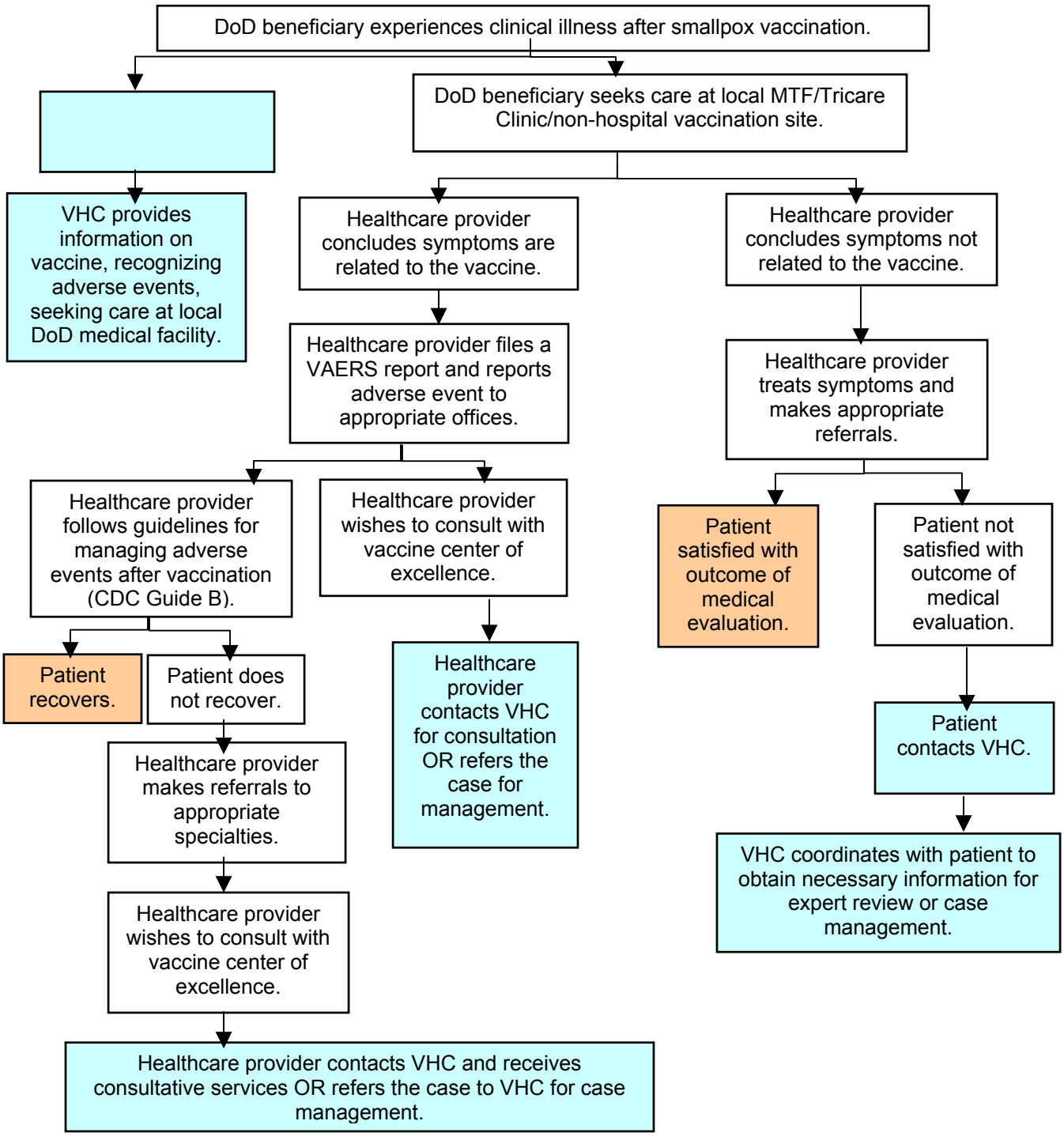
US Food and Drug Administration. The CPM will provide an annual report, track data entered into the service immunization tracking records, and retain sufficient data for subject follow up. The CPM will prepare a final report for the IND protocol.

13. Responsibilities of the Medical Monitor: The Medical Monitor will investigate all serious and unexpected adverse experiences reported to the FDA. The Medical Monitor will authorize suspension or withdrawal of volunteers from the protocol if medically appropriate.

14. Presidential Waiver. Under very limited circumstances, the President may waive requirement for consent to administration of IND medications to Service Members. To qualify for waiver, various agencies of the federal government must comply with 18 requirements specified in 21 CFR 50.23(d). If the President waives consent, use of the IND medication changes from being voluntary to being mandatory. In effect, the President issues an order directly the Service Member to receive the medication. But the President may not waive federal requirements for education or documentation in health records of IND medication administration. Federal law requires education and documentation regardless of whether consent is waived or not. In other words, the President can waive the “consent” requirement, but not the requirement for Service Members to be informed or the requirement for documentation in health records. And the Service Member must be informed of the reason for the President’s waiving of consent.

APPENDIX B-18
Vaccine Healthcare Center (VHC) Services.

Vaccine Healthcare Center, c/o Walter Reed Army Medical Center, PO Box 59605, Washington, DC 20012-0605, 202-782-0411 (DSN: 662); fax: 202-782-4658; Email: askVHC@na.amedd.army.mil; www.vhcinfo.org (pending). After duty hours, ask for the Allergist-Immunologist on call: 202-782-1000 (DSN: 662) or 202-782-7309 (DSN: 662).



APPENDIX B-19
Vaccine Adverse Event Reporting System (VAERS) Forms.

Available from:

www.vaers.org/

800-822-7967

Submit reports online at: https://secure.vaers.org/VaersDataEntryintro.htm

A blank VAERS Form-1 appears on the next page.

VACCINE ADVERSE EVENT REPORTING SYSTEM

VAERS

24 Hour Toll Free Information 1-800-822-7967
P.O. Box 1100, Rockville, MD 20849-1100
PATIENT IDENTITY KEPT CONFIDENTIAL

For CDC/FDA Use Only

VAERS Number _____

Date Received _____

Patient Name:

Last First M.I.

Address

City State Zip

Telephone no. (____) _____

Vaccine administered by (Name):

Responsible Physician _____

Facility Name/Address

City State Zip

Telephone no. (____) _____

Form completed by (Name):

Relation to Patient ☐ Vaccine Provider ☐ Patient/Parent ☐ Manufacturer ☐ Other

Address *(if different from patient or provider)*

City State Zip

Telephone no. (____) _____

1. State

2. County where administered

3. Date of birth mm / dd / yy

4. Patient age

5. Sex ☐ M ☐ F

6. Date form completed mm / dd / yy

7. Describe adverse events(s) (symptoms, signs, time course) and treatment, if any

8. Check all appropriate:
- ☐ Patient died (date mm / dd / yy)
- ☐ Life threatening illness
- ☐ Required emergency room/doctor visit
- ☐ Required hospitalization (_____days)
- ☐ Resulted in prolongation of hospitalization
- ☐ Resulted in permanent disability
- ☐ None of the above

9. Patient recovered ☐ YES ☐ NO ☐ UNKNOWN

10. Date of vaccination mm / dd / yy
Time _____ AM PM

11. Adverse event onset mm / dd / yy
Time _____ AM PM

12. Relevant diagnostic tests/laboratory data

13. Enter all vaccines given on date listed in no. 10

	Vaccine (type)	Manufacturer	Lot number	Route/Site	No. Previous Doses
a.					
b.					
c.					
d.					

14. Any other vaccinations within 4 weeks prior to the date listed in no. 10

	Vaccine (type)	Manufacturer	Lot number	Route/Site	No. Previous doses	Date given
a.						
b.						

15. Vaccinated at:
- ☐ Private doctor's office/hospital
- ☐ Public health clinic/hospital
- ☐ Military clinic/hospital
- ☐ Other/unknown

16. Vaccine purchased with:
- ☐ Private funds
- ☐ Public funds
- ☐ Military funds
- ☐ Other/unknown

17. Other medications

18. Illness at time of vaccination (specify)

19. Pre-existing physician-diagnosed allergies, birth defects, medial conditions(specify)

20. Have you reported this adverse event previously?
- ☐ No
- ☐ To doctor
- ☐ To health department
- ☐ To manufacturer

Only for children 5 and under

22. Birth weight _____ lb. _____ oz.

23. No. of brother and sisters

21. Adverse event following prior vaccination (check all applicable, specify)

	Adverse Event	Onset Age	Type Vaccine	Dose no. in series
☐ In patient				
☐ In brother or sister				

Only for reports submitted by manufacturer/Immunization project

24. Mfr./imm. proj. report no.

25. Date received by mfr./imm.proj.

26. 15 day report? ☐ Yes ☐ No

27. Report type ☐ Initial ☐ Follow-Up

Health care providers and manufacturers are required by law (42 USC 300aa-25) to report reactions to vaccines listed in the Table of Reportable Events Following Immunization Reports for reactions to other vaccines are voluntary except when required as a condition of immunization grant awards.

Form VAERS-1(FDA)

"**Fold in thirds, tape & mail - DO NOT STAPLE FORM"**

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES
OR APO/FPO

BUSINESS REPLY MAIL

FIRST-CLASS MAIL PERMIT NO. 1895 ROCKVILLE, MD

POSTAGE WILL BE PAID BY ADDRESSEE

VAERS
P.O. Box 1100
Rockville MD 20849-1100

DIRECTIONS FOR COMPLETING FORM

(Additional pages may be attached if more space is needed)

GENERAL

Use a separate form for each patient. Complete the form to the best of your abilities. Items 3, 4, 7, 8, 10, 11, and 13 are considered essential and should be completed whenever possible. Parents/Guardians may need to consult the facility where the vaccine was administered for some of the information (such as manufacturer, lot number or laboratory data.)

Refer to the Reportable Events Table (RET) for events mandated for reporting by law. Reporting for other serious events felt to be related but not on the RET is encouraged.

Health care providers other than the vaccine administrator (VA) treating a patient for a suspected adverse event should notify the VA and provide the information about the adverse event to allow the VA to complete the form to meet the VA's legal responsibility.

These data will be used to increase understanding of adverse events following vaccination and will become part of CDC Privacy Act System 09-20-0136, "Epidemiologic Studies and Surveillance of Disease Problems". Information identifying the person who received the vaccine orthat person's legal representativewill not be made available tothe public, but may be available to the vaccinee or legal representative.

Postage will be paid by addressee. Forms may be photocopied (must be front & back on same sheet).

SPECIFIC INSTRUCTIONS

Form Completed By: To be used by parents/guardians, vaccine manufacturers/distributors, vaccine administrators, and/or the person completing the form on behalf of the patient or the health professional who administered the vaccine.

Item 7: Describe the suspected adverse event. Such things as temperature, local and general signs and symptoms, time course, duration of symptoms diagnosis, treatment and recovery should be noted.

Item 9: Check "YES" if the patient's health condition is the same as it was prior to the vaccine, "NO" if the patient has not returned to the pre-vaccination state of health, or "UNKNOWN" if the patient's condition is not known.

Item 10: Give dates and times as specifically as you can remember. If you do not know the exact time, please

Item 11: indicate "AM" or "PM" when possible if this information is known. If more than one adverse event, give the onset date and time for the most serious event.

Item 12: Include "negative" or "normal" results of any relevant tests performed as well as abnormal findings.

Item 13: List ONLY those vaccines given on the day listed in Item 10.

Item 14: List any other vaccines that the patient received within 4 weeks prior to the date listed in Item 10.

Item 16: This section refers to how the person who gave the vaccine purchased it, not to the patient's insurance.

Item 17: List any prescription or non-prescription medications the patient was taking when the vaccine(s) was given.

Item 18: List any short term illnesses the patient had on the date the vaccine(s) was given (i.e., cold, flu, ear infection).

Item 19: List any pre-existing physician-diagnosed allergies, birth defects, medical conditions (including developmental and/or neurologic disorders) for the patient.

Item 21: List any suspected adverse events the patient, or the patient's brothers or sisters, may have had to previous vaccinations. If more than one brother or sister, or if the patient has reacted to more than one priorvaccine, use additional pages to explain completely. For the onset age of a patient, provide the age in months if less than two years old.

Item 26: This space is for manufacturers' use only.

APPENDIX B-20
Mass Vaccination: Clinic Organization & Personnel Estimates.

Reference: CDC Smallpox Response Plan, Annex 3, Smallpox Vaccination Clinic Guide, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

1. This section describes a model of a vaccination program involving administration of smallpox vaccine under an investigational new drug (IND) protocol, as well as an example of personnel estimates for clinic staffing. The output goal of this example clinic model would be the administration of vaccine to 1 million people over 10 days. The model can be expanded or contracted, as needed, to address changes in vaccination administration goals for different population areas.

a. These staffing estimates were derived by CDC from: 1) review of previous large-scale-clinic models and publications, 2) considerations of requirements for administering an IND vaccine, and 3) computer modeling for clinic flow and output estimates with different example staff numbers. Parameters of low and high completion times for specific activities within the clinic were estimated. The time requirement for these activities may differ depending on the demands placed on the vaccine clinic system and could require adjustment of staffing. Local planners should evaluate these activity-time estimates and consider what staffing or flow adaptations may be needed to accommodate increases or decreases in activity-time requirements. The computer modeling of the example clinic to determine staffing needs utilized the following parameters:

- 97% of people presenting to clinic will be processed through the normal clinic flow.
    - 1% will have some illness that will require evaluation before processing through the clinic.
    - 2% will be identified as a contact or possible contact to smallpox and will be processed through the separate “contact evaluation” unit.
- 20% of people coming through the clinic will require medical counseling in addition to the orientation video.
    - Medical counseling/questions will require 5 to 15 minutes (recognizing that some individuals will require > 15 minutes and others will require < 5 minutes).
    - Physicians will be available to handle more difficult medical screening to keep clinic flowing.
- 50% of persons getting additional medical counseling (i.e., the 20% above) will be vaccinated, and 50% will defer vaccination because of contraindications or other reasons.
- Distributing IND packets and providing initial instructions would take between 30 seconds and 2 minutes.
- Video orientations will be done approximately every 30 minutes in 5 orientation rooms that hold 75 people per room.

- Individuals will take 2 to 3 minutes to fill out the medical history screening forms.
- Vaccination and completing vaccination cards would require between 0.5 and 2 minutes.

b. The numbers shown in the table below are estimates of the human resources needed with the above clinic assumptions and configuration. Changing the assumptions can be explored to determine ways to further maximize clinic output and human-resource utilization. Although staff numbers may vary depending upon the assumptions and clinic output requirements, the general tasks that must be addressed within the clinic (e.g., patient education, medical history screening, medical counseling, vaccination) would not change.

c. CDC plans to make available to public-health officials a software program ("Maxi-Vac") that will allow officials to further refine human-resource needs (e.g., physicians, nurses, other staff) to maximize patient flow-through. Conversely, this software program may also be used to determine maximum vaccination output that may be achieved with different human-resource estimates.

d. The model assumes that clinics can be operating at near full efficiency to meet vaccination goals once the decision to offer voluntary vaccination is made.

2. Clinic Estimates

Vaccination Clinics (VC)	20 clinic sites	More sites could be added to accommodate larger population bases.
Vaccination Stations (VS)	▪ 8 VS per shift ▪ 1 vaccinator per station ▪ 0.5 to 1 witness/helper per station (who can also alternate vaccinating) ▪ 16 vaccinators/witnesses per shift	
Hours of Operation	At a minimum 16 hours per day	Consider expanding hours for higher daily output or to address overflow.
Vaccination Delivery	▪ 30 to 60 vaccinations per VS per hour ▪ ~ 370 vaccinated per VC per hour ▪ ~ 5,900 vaccinated per VC per day ▪ ~ 118,000 per day total with 20 VC ▪ 1 million vaccinated in ~ 9 days	30 to 60 vaccinations per VS per hour allows for variations caused by vaccinator rotation, resupply requirements, completing vaccination card, and other considerations.

3. Breakdown of Clinic Personnel per Vaccination Clinic.

Position	Number per 8-hour Shift	Number per 16-hour Day	Experience
Forms Distribution +	9	18	Nonmedical volunteers

Triage for Ill or Contact	2	4	Nurse or EMT
Run Orientation Video	8	16	Nonmedical (five running rooms and three floating between rooms to assist)
Referral Personnel	16	32	Nonmedical volunteers
Medical Screeners	7	14	Medical training required nurse or MD
Physician Evaluators	2	4	Physicians to evaluate ill or more difficult medical history screening
Vaccinators, Witnesses, Surge Staff	16	32	Cross-trained to alternate vaccination, fill out vaccine card, and sign as witness
Vaccine Preparation, Supply to VS	2	4	Pharmacist, pharmacy technician, nurse familiar with medication reconstitution
Exit Review	2	4	Medical or public-health personnel for final questions and instructions
Medical Records/Data Entry	10	20	Nonmedical, data entry for information collected on vaccinees
Clinic Manager	2	4	Existing Vaccine Program Personnel
Supply Manager	2	4	Nonmedical
Clinic Flow, QA Review, Form Helpers	8	16	Nonmedical volunteers to assist with forms completion, collection, and clinic flow
Security	20	40	Non-public health resource
Traffic Flow	2	4	Nonmedical, assist with loading/unloading buses at site, if offsite parking utilized
Translator (not counted in total clinic staffing estimates)	$\geq$ 1 per major language per shift	Unknown	Language fluency with training
Float Staff	3	6	Nonmedical volunteers
Contact Evaluation	4	8	Public health
EMT	1	1	Medical
Information Technology (IT) Support	1	2	Nonmedical
Total Personnel	**117**	**234**	

- FORMS/INFO PACKET DISTRIBUTION – 9 x 2 shifts = 18 total – Personnel to assemble patient forms/information packets and hand out packets with information sheets/registration forms/informed consent/other IND forms (1 minute/person), clipboards, and pencils. People will begin filling in demographic information on forms while in line awaiting initial clinic entry for video briefing.

- TRIAGE [nurse or EMT] – 2 x 2 shifts = 4 total – Triage personnel to direct ill patients to other evaluation facilities and direct identified contacts, persons with contact with a case of rash illness in last 3 weeks, and their household family members to high-priority evaluation location within clinic (1 minute/person). Triage should also utilize signs explaining where people should go if they are ill or are identified contacts. [Note: Ill persons should be triaged out and evaluated at designated offsite parking sites before boarding bus for transportation to clinic if offsite parking with busing is used for clinics.]
- VIDEO ORIENTATION – 8 people x 2 shifts = 16 total – Personnel to run video orientation regarding clinic procedures, paperwork, IND consent information, reasons for vaccination, contraindications to vaccination; 5 rooms running concurrently that hold 75 people/session with 2 staff/room (~20 minutes per session, allowing for 5 to 10 minutes for moving people into and out of orientation room) or a total of approximately 2 sessions/hour (~750 people oriented/hour).
- REFERRAL PERSONNEL– 16 people x 2 shifts = 32 total – Can be trained volunteers with no medical background; to look at medical screening/vaccination consent forms and send persons without “yes” checked boxes who have signed form on to vaccination station and redirect people with contact checked boxes or other “yes” or “maybe” checked boxes on to contact or medical screeners. Float staff personnel can relieve as needed to allow all stations to continue running during staffing breaks.
- MEDICAL SCREENERS FOR CONTRAINDICATIONS, EVALUATION/INFORMED CONSENT QUESTIONS COUNSELING (should be medically trained personnel, such as physicians, nurses, physician assistants, or nurse practitioners) — 7 per shift x 2 shifts = 14 total – Medical screeners to review patient history for those with contraindications and answer questions for informed consent (~ 5 to 10 minutes/person); numbers may need to be increased if too many people require further screening and lines start to back up at this part of clinic.
- PHYSICIAN EVALUATORS – 2 x 2 shifts = 4 total – Physicians to evaluate/examine triaged ill persons and provide backup counseling if needed to contacts and noncontacts identified with possible contraindications by medical screeners (~ 10 minutes/person), and evaluate any immediate problems following vaccination (e.g., fainting or anaphylaxis).
- VACCINATORS/ASSISTANTS – 16 x 2 shifts = 32 total – Eight vaccination stations with 1.5 to 2 vaccinators per vaccination station/shift to trade off vaccination, fill out vaccination card, and witness/collect signed vaccination consent/med screening form (each of the eight stations vaccinating 35 to 45 people/hour for total of 360 people vaccinated/hour). Vaccinators should consist of those allowed to administer vaccine under state law.
- VACCINE PREPARATION FOR VS – 2 x 2 shifts = 4 total – For preparation of vaccine vials to supply VS as needed. Should be pharmacist, pharmacy technician, or other personnel trained in preparation of medications or reconstitution of vaccines and as allowed by state law.
- EXIT REVIEW PERSONNEL – (should be medical or public health personnel) 2 x 2 shifts = 4 total – Personnel to answer any final questions about site care, adverse

event symptoms or non-take reporting procedures/follow-up, and other issues following vaccination.

- MEDICAL RECORDS/DATA ENTRY PERSONNEL – 10 x 2 shifts = 20 total – Collect retained records and enter registration/vaccination information (e.g., name, Social Security number, passport number and country, and contact information) into database (estimated 1 minute/record entry if database already set up) – important to have onsite, if possible, to maintain "real-time" record of number of vaccinations and database for later use for adverse events or non-takes requiring revaccination; Web-based entry with centralized database of all clinics preferable.
- CLINIC MANAGERS – 2 x 2 = 4 total – Oversees all clinic functions/problem solving.
- SUPPLY MANAGERS – 2 x 2 = 4 total – Oversees all supply needs; tracks vaccine supply/lot numbers, distribution, and wastage; re-supplies vaccination stations.
- CLINIC FLOW/QA/FORMS HELPER PERSONNEL [volunteers] – 8 x 2 = 16 total – Help maintain clinic flow, assist with forms, quality assurance, retrieve clipboards and forms from VS and takes forms to medical record entry personnel and clipboards back to form distribution, rotate through waiting areas to answer questions, and talk with people to assure them, as needed.
- SECURITY PERSONNEL – 20 x 2 = 40 total – Maintain crowd control outside and security within clinic; assist with clinic and traffic control, and other security matters. Non-public health resource; however, arrangements must be made with appropriate agencies or organizations to provide security as part of coordinated planning.
- TRAFFIC FLOW PERSONNEL – 2 x 2 = 4 total – Maintain traffic flow and order in parking area if parking onsite; if busing from offsite parking is used, these personnel may not be needed.
- TRANSLATORS – One for each major language spoken in community per shift; more may be needed depending upon major language of clinic population. Translators proficient in sign language should also be identified to assist with deaf individuals. Local and state authorities should identify language translations needed based on makeup of the community. Consider identifying specific clinics for referral of populations who need translators.
- FLOAT STAFF PERSONNEL [volunteers] – 3 x 2= 6 total – Float staff personnel to answer telephones, assist clinic personnel as needed, collect forms, assist with handicapped and elderly, and similar functions.
- CONTACT EVALUATION UNIT PERSONNEL – 4 x 2 = 8 total – For separate medical screening, education, and registering of identified contacts and their household contacts. Contacts will also be registered for surveillance for smallpox symptoms and given instructions on any travel restrictions and reporting requirements. Must be educated on contact surveillance process, smallpox signs/symptoms, and contact evaluation issues.
- EMT – 1 x 2 = 2 total – To assist with medical emergencies, fainting, and similar situations.
- IT PERSONNEL – 1 per shift x 2 = 2 total – To support computer, programming, electronic equipment maintenance needs, and other information technology requirements.

Although not formally included in the above staffing estimates, the addition of mental

health staff at each clinic site should be considered.

4. Other Volunteers As Needed For Float Staff, Forms Assistance, Referral Personnel, And Related Clinic Activities.

a. VC Staff needed per single vaccination clinic (VC) to cover two 8-hour shifts – approximately 234 (117 per shift) + translators. Note: 40 people are security people from outside public-health resources.

b. Nonmedical volunteers can be used for: forms distribution, orientation video, referral personnel, data entry, supply manager, clinic flow/QA/forms assistance, security, traffic flow, translators, float staff, and IT support.

c. Total Staff needed for 20 Vaccination Clinics – 234 per VC x 20 VC = 4,680 personnel. Planners should consider increasing staffing by approximately 20% with cross-trained personnel to allow for absences, breaks, surge needs, and other contingencies. Note: ~ 17%, or 800, of these personnel should come from outside public-health resources to provide security.

5. Considerations for Assessing Vaccine Non-Takes and Adverse Events. Medical authorities should establish telephone lines for the following purposes:

a. Reporting and Handling of Vaccination Non-Takes.

(1) Noncontacts: Vaccinated individuals who are not otherwise identified as contacts to a smallpox case will be given vaccination cards and vaccination-take recognition cards at the time of their vaccination and instructed to call a designated number, if their vaccination site does not resemble the picture on the card at day 7. If they apparently have a vaccine non-take, they will be counseled through the hotline to return to a vaccination clinic (VC) with their vaccination card for revaccination. Individuals presenting back to VC for revaccination would not require repeat medical screening as long as they present their vaccination card from the previous VC visit, but may be required to review the informed consent material (video) and sign an additional consent form. Following this signing, they can be triaged directly to the vaccination area for revaccination.

(2) Contacts: Vaccinated contacts under surveillance and their household members will also receive vaccination-take recognition cards and vaccination cards. If possible, they will be followed up with visual confirmation of vaccine take as a part of the contact surveillance process. If visual confirmation is not possible because of a large number of contacts requiring surveillance by limited personnel, contacts and their household members will be instructed to report possible vaccine non-takes to a designated contact symptom surveillance telephone number at the local or state health department. Revaccination will be done for contacts and their household members who do not have a vaccine take at day 7. This revaccination may be done through referral back to the contact evaluation unit of a VC, referral to another specified location, or through direct

administration of vaccine by health department personnel at the time of visual evaluation.

b. Reporting, Evaluation, and Treatment of Suspected Adverse Events. Evaluation and treatment for vaccine adverse events should occur at a designated site or sites separate from VCs. Medical authorities should identify and staff a local telephone number for reporting of suspected adverse events. This number should be included with the Smallpox Vaccine Information Statement (VIS) handed out to vaccine recipients. Staff should be instructed on where to refer callers for further medical evaluation. As a part of smallpox bioterrorism (BT) planning, health authorities should designate the facilities where suspected vaccine adverse events will be referred, evaluated, and treated. For the DoD reporting and consultation mechanism for healthcare providers to report potential VIG-requiring adverse events, see Annex H.

6. Additional Considerations.

a. Mobile Facilities. Consider mobile facilities (for nontransportable populations) if needed for fixed population vaccination:

(1) Retirement communities, nursing homes, hospitals, prisons, or other residential facilities

(2) Defined high-density areas/facilities, such as apartment and housing complexes

b. People with Disabilities. Vaccination clinics must have accessibility for people with disabilities for clinics and transportation vehicles to clinics. Consider acquiring wheelchairs to assist the elderly who cannot ambulate from station to station.

c. Referral Testing. Strategies for the referral of persons who request HIV or pregnancy testing to local laboratories or medical clinics that perform confidential testing should be considered and communicated as a part of the overall clinic planning. Planners should maintain a list of local laboratories that offer this testing. In addition, consideration should be given to the potential use of rapid HIV tests within these clinics if an FDA-approved test is available.

d. Waste Disposal. Two to three disposal trucks and staff will be needed to collect medical and other waste from 20 VCs at least daily.

e. Rest Area. An area is needed for staff to rest or sleep if working more than 8 hours or if there is inclement weather and staff are unable to return to their homes after their shift.

f. Transportation for Staff. Depending on the location, arrangements may be needed to transport staff to the VC.

7. Public Announcements. Use television and radio networks to present uniform messages. Planners should consider how these messages could be quickly developed, locally, to accommodate sudden changes in sites and/or recommendations. Establish a list of non-English speaking media outlets that can be utilized to deliver messages to immigrants/refugees and other non-English speaking communities. Messages should state that a plan is being put into operation, conveying:

- urgency and patience, but not panic
- the number of VCs
- timing to prevent smallpox (i.e., vaccination 4 days after exposure is effective)
- vaccine supply
- trained personnel
- listing of collection areas where people will be picked up by buses
- materials to bring to clinic(identification to prove eligibility, loose clothing to allow easier vaccination)
- listing of normal activities being suspended
- hotline numbers
- review of vaccine recommendations.
- frequently updated “wait-times” for vaccination clinics to help determine clinic utilization.

8. Logistics for IND Administration of Smallpox Vaccine.

a. Triage for Illness: The first triage point for the vaccination clinic is triage for illness and/or contacts of confirmed cases of smallpox. This checkpoint is to screen out those individuals that may be ill or contacts from the rest of the individuals at the clinic so as not to expose the clinic population.

(1) Ill (e.g., fever or rash): These individuals will be taken out of the mainstream flow prior to entering the clinic and will be attended to as required by their symptoms/illness (e.g., monitoring, referral, supportive care).

(2) Contacts: These individuals will be taken out of the mainstream flow to be counseled on follow-up procedures and registered for monitoring for symptoms of smallpox. They will also be vaccinated.

(3) Not Ill (mainstream progression through the clinic): Those individuals that will progress to the next station within the clinic who have not presented as ill or a contact.

b. Distribution of Information Packet: All individuals (contacts and mainstream) will receive the “mainstream” information packet that will include the following information:

(1) Video script

(2) Screening form

(3) Vaccine Information Statement (VIS)

(4) Vaccination Site Care Card

(5) Proof of Vaccination Card

c. After receiving this information, “mainstream” individuals will proceed to the video screening area, while “contacts” will proceed to the contact evaluation area.

(1) Video Screening Areas: Individuals will view the video that contains the essential elements of informed consent as promulgated in 21 CFR 50.25. This video viewing will be witnessed to comply with FDA regulations for the oral presentation of consent information. The script of the video is included in the “mainstream” packet and will include, at a minimum, English presentations and Spanish language translations. Additional language translations may be needed at the local level to address special populations.

(2) After the video, the individuals will be instructed to complete the screening form that will move them through the remainder of the vaccination clinic.

(3) Post-video Triage: Individuals will proceed to this triage point with their completed screening forms. The screening forms are for self-identified contraindications for the individual or family members with contraindications (e.g., contact history, altered immune status, autoimmune diseases, concomitant medications that alter immune status, skin conditions, pregnancy, reactions to previous smallpox vaccinations, allergies to vaccine components, children less than 1 year old) and/or questions relating to the decision to be vaccinated.

(4) If individuals check “yes” or “maybe” to any of the boxes on the screening form, they will proceed to the counseling stations where they will receive additional information based on the contraindication that they checked.

(5) If individuals have no self-identified contraindications or questions, they will proceed to the vaccination area.

(6) If individuals decide to decline vaccination and are not a contact, they will be escorted to the exit.

d. Vaccination Area:

(1) At the vaccination station individuals who did not require additional counseling will sign the consent form located on the back of their Medical History Screening Form that states that they have viewed the video and had all questions answered. They will also have the chance here to ask any remaining questions; if they do have remaining questions, they may be referred back to the counseling area. Once signed by the vaccinee, these forms will be signed by the vaccinating assistant as a “witness to consent” and then collected.

(2) Individuals who were referred to the vaccination stations after receiving additional counseling will have had their consent forms witnessed by the medical counselor and will proceed with vaccination.

(3) Following vaccination, the “Proof of Vaccination” form will be stamped by the vaccinating assistant and returned to the vaccinee.

(4) Any noncontact who refuses vaccination will be allowed to exit the clinic. Contacts who decline vaccination will be instructed on appropriate quarantine measures, the symptoms to monitor for, and appropriate contact information within the “Contact Evaluation Unit” area.

e. Post-Vaccination Information and Review: This is the final station in the clinic for any remaining questions. This station should also ensure that individuals exit with *all* their information sheets and instructions. (A supply of extra information sheets should be kept here to distribute, as needed.)

APPENDIX B-21
Mass Vaccination: Clinic Preparation Checklists.

Reference: CDC Smallpox Response Plan, Annex 3, Smallpox Vaccination Clinic Guide, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

1. Overall Planning and Management Checklist.

- ❑ Installation or Command Headquarters Identified
- ❑ Location
- ❑ Staffing for General Operations
- ❑ Staffing for Problem-Solving
- ❑ Memoranda of Understanding (as required)
- ❑ Communications Protocol
- ❑ Central Vaccine Storage Site Identification
- ❑ Central Facility with Security and Backup Generator
- ❑ Central Supplies Warehouse
- ❑ Shipping Company Selection
- ❑ Printing Company Selection (for mass form production)
- ❑ All Supply Resources Identified (see Supply and Equipment Checklist)
- ❑ Vaccination Clinic Site Identification (x20)
- ❑ Procedure for Designating Vaccination Site/Time (i.e., zip code? SSN?)
- ❑ Procedure for Identification
- ❑ Computer Networking Identified for Exchange of Data
- ❑ Standing Orders for Emergencies
- ❑ Agreement(s) with local media for public service announcement coverage/production

2. Smallpox Post-Outbreak Clinic Site Checklist.

Clinic Site: Number of

☐ Facility Resources

- ☐ Large, open space to accommodate clinic flow
- ☐ Weather protection for those in line
- ☐ Portable toilets to accommodate waiting lines
- ☐ Ability to be made secure
- ☐ Backup generator
- ☐ Accessible for people with disabilities
- ☐ Ease of access for community
- ☐ Communication resources available
- ☐ Equipment resources available (See Supply and Equipment Checklist)
- ☐ Tables available
- ☐ Screening rooms available
- ☐ Waste disposal
- ☐ Rest area for staff
- ☐ Transportation/parking for staff

☐ Transportation Procedures

- ☐ Parking identified
- ☐ Bus service company selection
- ☐ Routes for bus service

☐ Vaccination Clinic Personnel Identified (See Personnel Checklist)

- ☐ Vaccinators
- ☐ Physician evaluators
- ☐ Support functions

☐ HIV Testing and/or Referral Plan

☐ Equipment Resources Identified (See Supply and Equipment Checklist)

3. Supply and Equipment Checklist.

Clinic Site: Number of

Equipment Needs

- ☐ Copier
- ☐ Fax machine
- ☐ 12 computers or laptops
- ☐ 5 DVD or VCR players
- ☐ 5 Large-screen televisions
- ☐ Cell phones
- ☐ Handheld radios

General Supplies

- ☐ Tables
- ☐ Chairs
- ☐ Water and Cups
- ☐ Paper
- ☐ Pens, Pencils
- ☐ Envelopes
- ☐ Rubber Band
- ☐ Tape
- ☐ Stapler/Staples
- ☐ Paper Clips
- ☐ Scissors
- ☐ Post-It Notes
- ☐ File Boxes
- ☐ Telephone
- ☐ Paper Towel
- ☐ Tissues
- ☐ Table pads, clean paper
- ☐ Garbage containers
- ☐ Trash bags
- ☐ ID Badges for staff
- ☐ 7 Copies of Video
- ☐ Food and drink for staff
- ☐ List of emergency phone #s
- ☐ Cleaning supplies

Crowd Management and Triage Supplies

- ☐ Queue Partitions
- ☐ Signs for Site Designation
- ☐ Signs for Clinic Flow

Vaccine Administration Supplies

- ☐ Smallpox Vaxicools/Refrigerator
- ☐ Vaccine Diluent
- ☐ Sterilized Bifurcated Needles
- ☐ Sharps Containers
- ☐ Latex Gloves
- ☐ Latex-Free Gloves
- ☐ Anti-bacterial hand washing solutions
- ☐ Acetone
- ☐ Rectangle Band-Aids
- ☐ Gauze
- ☐ Adhesive Tape
- ☐ Spray Bottle of Bleach Solution
- ☐ Paper Gowns
- ☐ Vaccination Screens

Emergency Supplies

- ☐ Standing Orders for Emergencies
- ☐ “Code” kit with defibrillator
- ☐ Ampules of Epinephrine 1:1000 SC, or
- ☐ Epi-Pen Adult and Epi-Pen Pediatric
- ☐ Ampules of diphenhydramine (50 mg IM)
- ☐ 3 ml syringes with 1”, 25-guage needles
- ☐ 1.5” needles
- ☐ Tuberculin syringes with 5/8” needles
- ☐ Alcohol Wipes
- ☐ Blood Pressure Cuffs (Various Sizes)
- ☐ Oxygen Tank
- ☐ Oxygen Tank Tubing
- ☐ IV Solution
- ☐ IV Solution Tubing
- ☐ Thermometer
- ☐ Aspirin, Tylenol, Regular insulin, D50
- ☐ Asthma Inhaler
- ☐ Tongue Depressors
- ☐ Emesis basis
- ☐ Adult pocket masks with one-way valve
- ☐ Pediatric pocket masks with one-way valve
- ☐ Adult and pediatric airways
- ☐ Tourniquet
- ☐ Gurney
- ☐ Stethoscope
- ☐ Flashlight
- ☐ Cots, Blankets, and Pillows
- ☐ ER Report Form

4. Personnel Checklist.

Clinic Site: Number of

☐ Forms Distribution

AM Shift

1. 6.
2. 7.
3. 8.
4. 9.
5.

PM Shift

1. 6.
2. 7.
3. 8.
4. 9.
5.

☐ Triage for Ill People or Contacts of Smallpox Cases

AM Shift

1. 2.

PM Shift

1. 2.

☐ Run Orientation Video

AM Shift

1. 5.
2. 6.
3. 7.
4. 8.

PM Shift

1. 5.
2. 6.
3. 7.
4. 8.

☐ Referral Personnel

AM Shift

1.
2.
3.
4.
5.
6.
7.
8.
9.
10.
11.
12.
13.
14.
15.
16.

PM Shift

1.
2.
3.
4.
5.
6.
7.
8.
9.
10.
11.
12.
13.
14.
15.
16.

☐ Medical Screeners

AM Shift

1.
2.
3.
4.
5.
6.
7.

PM Shift

1.
2.
3.
4.
5.
6.
7.

☐ Physician Evaluators

AM Shift

1.
2.

PM Shift

1.
2.

☐ Vaccinators

AM Shift

1.	9.
2.	10.
3.	11.
4.	12.
5.	13.
6.	14.
7.	15.
8.	16.

PM Shift

1.	9.
2.	10.
3.	11.
4.	12.
5.	13.
6.	14.
7.	15.
8.	16.

☐ Vaccine Preparation/Supply

AM Shift

1.	2.

PM Shift

1.	2.

☐ Exit Review

AM Shift

1.	2.

PM Shift

1.	2.

☐ Medical Records/Data Entry

AM Shift

1. 6.
2. 7.
3. 8.
4. 9.
5. 10.

PM Shift

1. 6.
2. 7.
3. 8.
4. 9.
5. 10.

☐ Clinic Manager

AM Shift

1. 2.

PM Shift

1. 2.

☐ Supply Manager

AM Shift

1. 2.

PM Shift

1. 2.

☐ Clinic Flow/Quality-Assurance Reviewer/Forms Helpers

AM Shift

1. 5.
2. 6.
3. 7.
4. 8.

PM Shift

1. 5.
2. 6.
3. 7.
4. 8.

☐ Security

AM Shift

1. 16.
2. 17.
3. 18.
4. 19.
5. 20.
6. 21.
7. 22.
8. 23.
9. 24.
10. 25.
11. 26.
12. 27.
13. 28.
14. 29.
15. 30.

PM Shift

1. 16.
2. 17.
3. 18.
4. 19.
5. 20.
6. 21.
7. 22.
8. 23.
9. 24.
10. 25.
11. 26.
12. 27.
13. 28.
14. 29.
15. 30.

☐ Traffic Flow

AM Shift

1. 2.

PM Shift

1. 2.

☐ Translators

AM Shift
1. Language:
2. Language:

PM Shift
1. Language:
2. Language:

☐ Float Staff

AM Shift
1. 3.
2. 4.

PM Shift
1. 3.
2. 4.

☐ IT Support

AM Shift
1.

PM Shift
1.

☐ Contact Evaluation

AM Shift
1. 3.
2. 4.

PM Shift
1. 3.
2. 4.

APPENDIX B-22
Alternate Housing Arrangements..

Situation:

A person is eligible for smallpox vaccination due to duty assignment and medical history. However, that person has a household contact (e.g., spouse, child) who has a medical contraindication (e.g., eczema, immune-suppression, pregnancy) related to the vaccinia virus within smallpox vaccine. By DoD policy, exempt individuals should be physically separated and exempt from duties that pose the likelihood of contact with potentially infectious materials (e.g., clothing, towels, linen) from recently vaccinated people. This separation will include not having the vaccine recipient share or alternate use of common sleeping space (e.g., cot, bunk, berth) with people with contraindications to vaccination.

The risk to be avoided is the spread of vaccinia virus from the vaccination site to another person by inadvertent contact, either directly, or by means of clothing, towels, sheets, or other common-access items that could transfer the virus. Historically, the rate of spread of vaccinia virus to contacts was quite rare, about 27 cases per million vaccinations. DoD's goal is to reduce the risk as much as possible.

Unacceptable:

Permitting a vaccinated Service Member to reside in a house, trailer, apartment, or similar close arrangements (e.g., "hot-bunking") with a medically-barred contact is unacceptable, until the scab falls off on its own.

Acceptable:

Having the vaccinated Service Member use alternate lodging (e.g., barracks, dormitory room, tents) on a military installation, vessel, or aircraft, or in contracted space, is acceptable.

Having the vaccinated Service Member voluntarily arrange for alternate lodging in privately-owned or managed space is acceptable, if the commander has a reasonable expectation that the Service Member will comply with the requirement to not share living and toileting space with a medically-barred household contact.

Berthing barges, familiar to naval forces whose berthing spaces were refitted during a shipyard period, can be used at naval installations near the water.

The vaccinated Service Member can continue to have reasonable access to a medically-barred household contact, so long as the access includes careful hand-washing and does not involve extensive physical contact or contact involving clothing, sheets, towels, or other items likely to transfer vaccinia virus.

ANNEX C TO SMALLPOX RESPONSE PLAN 29 September 2002
ISOLATION AND QUARANTINE GUIDELINES.

REFERENCES.

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1. General. DoD will augment CDC Guide C with current science-based data published by USAMRIID, the Association for Professionals in Infection Control and Epidemiology (APIC), Society of Healthcare Epidemiologists of America (SHEA), Infectious Diseases Society of America (IDSA), American Hospital Association (AHA), American Institute of Architects (AIA), and American Society for Healthcare Engineering (ASHE), in responding to a smallpox outbreak. Appendix C-1 summarizes CDC Guide C and this DoD Annex on one page. Appendix C-2 and Appendix C-3 summarize infection-control principles for acute-care and home-care settings, respectively.

2. Mission. Health-care workers and the public will isolate suspected and confirmed cases of smallpox. Infection-control officers in each military treatment facility (MTF) will provide subject-matter expertise on specific procedures. Infectious-disease physicians, preventive-medicine personnel, and public-health personnel will provide additional support and guidance as indicated.

3. Plan.

a. Definitions.

(1) Isolation. Isolation is defined as the separation of a person or group of persons from other people to prevent the spread of infection.

(2) Quarantine. Quarantine is defined as the restriction of activities or limitation of freedom of movement of those presumed exposed to a communicable disease, to prevent contact with people not exposed. Although quarantine measures may be instituted and enforced for either individuals or populations, the term is used more frequently to discuss measures taken at a population level.

b. Assumptions.

(1) Infection-Control Risk Assessment. Infection-control professionals (ICPs) include facility-specific assessment of bioterrorism response, readiness, and containment in Infection Control Risk Assessments (ICRAs). Each ICRA addresses ventilation-system design to accommodate several patients requiring airborne precautions (Appendix C-8), as in smallpox. The ICRA is integrated into each facility's assessment.

(2) Facility Design and Renovation. The first person to recognize a case of smallpox is likely to be a healthcare provider in a triage setting. This creates the need for new construction to have negative-airflow triage and emergency room waiting areas. These areas should be under negative pressure and have direct exhaust ventilation to the outside. If air cannot be exhausted outside, it may be recirculated to other areas of the facility, provided that the air is first passed through a HEPA filtration system. The American Institute of Architects (AIA) guidelines require that new emergency room suites include an Airborne Infectious Isolation Room (AIIR). The AIA also requires the use of ICRAs for long-term design planning, including replacement ventilation systems or hospital renovation or design.

(3) Alternate Facilities. MTFs possess only a limited number of operational negative airflow rooms. Each isolation room may only hold one to four people. Therefore, MTFs will examine existing large spaces adaptable for use as triage and treatment areas, remote from other patient care areas to permit ventilation disruption and use of portable HEPA filter units. This document will detail and supplement each facility's existing individual and regional Emergency Preparedness Plans, including hospitals, medical clinics, hospital ships, and other ships.

(4) Dedication of Resources. In an outbreak scenario, patient care areas (e.g., wards, units, barracks) may be dedicated for smallpox patients.

c. Planning Factors.

(1) Immediate recognition of a case of smallpox is integral to timely response. Smallpox education and training must take place before any outbreak occurs.

(2) Effective response includes appropriate transmission-based isolation measures. MTF leaders will keep track of the number of functional negative airflow rooms available in their facility, as well as in the surrounding region.

(3) Installation and MTF commanders will identify Airborne Infectious Isolation Rooms (AIIRs) and areas in their local plans. Airborne-isolation contingency plans must be developed. Plans must be sufficient to deal with caseloads ranging from one index case to multiple index and secondary cases. If the size of a smallpox outbreak exceeds available areas for triage, treatment and care of smallpox patients in appropriate AIIRS,

then housing in cohorts known as Type C, X, and R facilities is an acceptable means of infection prevention and control (Appendix C-4).

(4) MTF commanders should consult with industrial hygiene and facilities management personnel regarding the specific heat-ventilation-air-conditioning (HVAC) characteristics of each hospital, clinic, and other building to be used in the execution of this document. HVAC systems should not be turned off without understanding the effects of such a change on airflow within a building. For example, turning off an HVAC system could compromise airflow in sensitive areas (e.g., operating rooms, negative airflow rooms).

(5) Routine resources may be quickly overwhelmed in a large outbreak, so local plans will identify courses of action to access alternate sources of supply.

d. Coordinating Instructions. The first section within an MTF to recognize the admission or arrival of a potential smallpox case will notify the following individuals immediately. Then the MTF activates its disaster plan, contacting the following internal experts:

(1) Preventive-medicine / public-health officer.

(2) Infection-control service and epidemiology staff.

(3) Community health nurses.

Specific policies for reporting smallpox cases outside the MTF are described in Annex A. In brief, (a) submit a report immediately through established Service disease-reporting systems, beginning with the local preventive-medicine/public-health service, (b) submit a Serious Incident Report (SIR) to higher military headquarters, (c) notify CDC Emergency Preparedness & Response Branch (770-488-7100), (d) notify state health department, then (e) notify other appropriate authorities (e.g., local health department).

e. Duty to Care.

(1) Most states require by law that emergency care be rendered by hospitals whenever requested. Rendering care must also be done to avoid sanctions and civil liability under the antidumping provisions of the Social Security Act. Under Section 504 of the Federal Rehabilitation Act of 1973, federal government agencies must provide nondiscriminatory treatment.

(2) Therefore, discrimination against contagious patients is unethical and may be illegal under federal and state laws prohibiting discrimination (e.g., denial of hospitalization or treatment) against handicapped persons.

(3) Once the MTF admits a smallpox patient, the MTF is obligated to provide appropriate care or risk potential liability for abandonment. If an MTF staff member refuses to care for a patient with a contagious disease, the MTF has a responsibility to see that care is rendered, even if this means transferring the patient to another facility where appropriate care will be provided.

(4) Healthcare personnel will not be excused from providing care to patients with infectious diseases. MTF personnel policies should specifically address employee insubordination or unreasonable refusals to treat patients.

(a) MTFs will provide their staff specific information to assuage fears of occupational exposure. Content will include the provision of smallpox vaccine as well as appropriate personal protective equipment (PPE, e.g., gowns, gloves, respirators, goggles) to protect against the transmission of infectious diseases.

(b) If an employee, after individual education and counseling, refuses to perform his or her duties in caring for infected patients, the MTF may either attempt to accommodate the employee by job reassignment or institute disciplinary action for insubordination. In doing this, the hospital will have to act within any relevant limitations imposed by the National Labor Relations Act or collective bargaining agreement.

f. Quarantine. Appendix C-9, Appendix C-11, and Appendix C-12 discuss various laws, regulations, and factors affecting quarantine.

4. Execution.

a. Concept of Operations.

(1) Recognition of a single patient with smallpox will constitute an international public-health emergency. The control of disease is primarily a public-health strategy, with rapid identification of cases and immediate isolation of cases. Patients should be hospitalized if adequate facilities permit. Appropriate infection-control procedures will be paramount and must include contact and airborne isolation. Cohorting is recommended. In other words, place patients with the same illness but no other transmission-based infections in rooms together, considering other relevant factors (e.g., age, sex, room size, staffing patterns) (Appendix C-7). Render medical care appropriate for the acuity of illness. Minimal-care or out-of hospital care of smallpox cases is possible and may be desirable.

(2) If a smallpox case is recognized within an MTF, secure the entrances and exits of the affected unit, until a roster of names, addresses, and telephone numbers can be created of people who had face-to-face contact ($\leq$ 6 feet) with the suspected smallpox case. After this roster is completed, these people may be released, with instructions that they will be contacted by preventive-medicine/public-health personnel about the possible need for smallpox vaccination within the next few days. Advise these people not to travel more than 20 miles from their city of residence. There is no need to close

installation gates, unless this effort would be useful to find named face-to-face contact(s) (≤ 6 feet) of a suspected smallpox case. The MTF should then prepare to isolate the case (Appendix C-4) and initiate contact tracing (Appendix A-3).

b. Tasks and Responsibilities. These tasks/issues will need to be coordinated:

(1) Respiratory Protection Program. Each MTF will develop or enhance a Respiratory Protection Program that includes medical clearance of personnel likely to called on to wear a NIOSH-approved N95 particulate respirator, fit testing of that respirator, and appropriate occupational record-keeping. These programs will comply with Occupational Safety & Health Administration standard 1910.134.

(2) Vaccination. Smallpox vaccination is indicated for all care providers and exposed patients. Decisions regarding pre- versus post-outbreak vaccination will reflect current DoD policy. MTFs will develop procedures for identifying healthcare workers who cannot be immunized due to medical contraindications (e.g., pregnancy, immune compromise, eczema, history of eczema) or who decline vaccination. People declining vaccination should sign a statement acknowledging that they have been advised of the risks of disease and the benefits and risks of vaccination. Vaccination programs will include appropriate follow-up services (e.g., adverse event surveillance and management, documentation). See Annex B for details.

(3) Personal Protective Equipment (PPE). MTFs will develop plans for providing PPE to their staff, in various sizes and at no cost to the workers.

(4) Safety and Security. MTFs will coordinate with installation provost marshals or other military police units for the physical security of MTF property and personnel.

(5) Air-Handling Issues. MTFs will develop plans for appropriate emergency changes in air-handling within the facility. MTFs will post appropriate air-handling procedures in emergency department offices and other appropriate locations (e.g., which controls to turn to which position, before or after seeking engineering advice).

(6) Patient Placement. Do not admit smallpox patients once hospitals reach maximum capacity. Preferably, hospitals will divert smallpox patients to Type C facilities before this stage is reached. Implement hospital disaster plan before maximum capacity is reached. Close hospital to non-critical admissions. Provide notification of significant incoming casualties to affected personnel and facilities. Establish and operate a Medical Command Center within the facility. Relocate non-infected patients to another facility. Establish and operate Acute Care Centers (ACCs), to provide definitive and supportive care to acute patients. Establish methods for tracking patient movements in the system. See also Appendix C-6 and Appendix C-7.

(7) Disaster Medical Assistance Teams (DMATs). Provide DMATs and individual public-health and medical personnel to assist in providing care. DMATs can provide triage, medical or surgical stabilization, and continued monitoring until patients can be

evacuated to other locations for definitive care. In addition to DMATs, active-duty and reserve component units can be deployed for casualty clearing or staging, and also for other missions.

5. Operational Constraints.

a. Training and Education.

(1) MTFs will know how to readily access educational materials (e.g., CDC and DoD websites), including fact sheets specific for healthcare workers (HCW), ancillary staff, families, worried well, and patients. Have paper or CD-ROM versions of fact sheets available, in case access to the Internet is lost.

(2) MTFs will provide education for people with special needs (e.g., those with low English literacy), using culturally appropriate and culturally competent providers.

(3) MTF policies and procedures will be readily available to staff using appropriate technology (e.g., intranet, CD-ROM, paper).

b. Signage. MTFs will prepare a supply of standard precaution and transmission-based precaution instructional signs (e.g., airborne-isolation signs, contact-isolation signs).

c. Staff Safety. MTFs are responsible for vaccination of healthcare providers, as well as fit-testing of NIOSH-approved N-95 particulate respirators.

6. Administration and Logistics.

a. Supplies and Equipment.

(1) Linen. Transmission of smallpox virus via contaminated bedding occurred only rarely in the past. Nonetheless, due attention to infection prevention is appropriate for occupational safety. MTFs will develop plans for handling linens in a smallpox outbreak. Linen will be handled with care to avoid contamination of the environment. MTFs will provide laundry workers with appropriate PPE, including a fit-tested NIOSH-approved N95 particulate respirator, gown, and disposable gloves. Workers will receive vaccination and wear PPE appropriately when in contact with soiled linen. Linen will be sanitized using appropriate hot wash temperatures, detergent according to manufacturers' recommendations, and adequate amounts of bleach (reference g).

(2) Regulated Medical Waste (RMW). MTFs will develop plans for handling regulated medical waste (RMW) in a smallpox outbreak. Abide by whichever regulations are most stringent in your area: federal, state, or local. All bodily fluids are safely disposed of via the sanitary sewer. All waste generated by smallpox cases will be treated as RMW.

(3) Ordering and Storage. MTFs will identify Prime Vendor (PV) capabilities for increased deliveries of all medical supplies and equipment. MTFs will develop contingency plans for requisitioning medical supplies, in case standard channels are inadequate. Just-in-time delivery by prime vendors may not be sufficient to meet needs during outbreaks, based on the large volume of supplies that may be needed throughout a region. MTFs will monitor Inventory levels closely for the following key supplies:

(a) PPE supplies: NIOSH-approved N-95 particulate respirators, gloves, fluid-resistant gowns (e.g., cloth, paper-disposable), face shields/goggles (if splashing or splattering of body fluids is anticipated).

(b) Medical supplies: Alcohol-based hand-hygiene agents, antimicrobial soap, RMW bags, EPA-approved hospital-grade disinfectants, and household bleach.

(4) Cleaning, Disinfection, and Sterilization of Equipment and Environment. A component of contact precautions (Appendix C-8) is careful management of potentially contaminated equipment and environmental surfaces.

(a) When possible, noncritical patient-care equipment should be dedicated to a single patient (or cohort of patients with the same illness).

(b) If use of common items is unavoidable, do not use potentially contaminated, reusable equipment for the care of another patient until it has been appropriately cleaned and reprocessed. MTFs will establish policies and monitor for compliance.

(c) EPA-approved hospital-grade germicides (“hospital-approved disinfectants,” HAD) easily kill both smallpox (variola) virus and vaccinia virus (the active ingredient in smallpox vaccine).

b. Major Equipment.

(1) Negative airflow rooms. MTF leaders will keep track of the number of functional negative airflow rooms available in their facility, as well as in the surrounding region. Hospitalized smallpox patients require placement in rooms that meet ventilation and engineering requirements for airborne precautions (Appendix C-7 and Appendix C-8). These requirements include:

(a) Monitored negative air pressure relative to the corridor and surrounding areas.

(b) 6 to 12 air exchanges per hour.

(c) Appropriate discharge of air to the outdoors, or use of monitored high-efficiency particulate air (HEPA) filtration before circulation to other areas in the facility.

(d) A door that is kept closed.

Knowledge of facility heat, ventilation and air conditioning (HVAC) system is critical to determining airflow within a facility. Therefore, proper functioning and maintenance of HVAC systems and HEPA filters is essential to prevent disease transmission. Circumstances that alter the balance of supply and exhausted air will disrupt continuous negative airflow. Examples of altered airflow and balance include activation of fire-alarm systems, elevator shaft work, changes in ventilation dampers, changing of large bag filters and shutting down portions of a ventilation system. These factors must be integral to local facility plans. Other discussion of facility specifications appears in CDC Annex C.

(2) Ventilators and related respiratory support.

c. Transportation. Personnel in transport vehicles (e.g., ground and air ambulances, ships and smaller vessels) carrying patients with smallpox will follow airborne and contact precautions, by placing all crew members in a fit-tested NIOSH-approved N95 particulate respirator, gown, and gloves, by placing a surgical mask on the patient (if feasible), and disinfecting the transport vehicle according to Annex F before transport of patients without smallpox.

7. Special Situations.

a. Recall of troops from community onto a military installation after outbreak detected.

(1) If smallpox cases have been detected in a community with no apparent connection to the military installation, troops returning to that installation will be vaccinated against smallpox (except as provided in Annex B). The installation will start active surveillance for generalized vesicular or pustular rash illness with or without fever (GVPRI, GFVPRI). See Annex A.

(2) If smallpox cases have been detected in a community near or with apparent connections to the military installation, troops returning to that installation will be isolated on the installation, vaccinated against smallpox (except as provided in Annex B), observed for an appropriate interval of time (i.e., 18 days from last contact with a possible smallpox patient or 14 days after verification of vaccine take, to rule out the possibility of disease despite vaccination), and then returned to their normal military routine. The troops do not need to be quarantined away from other base occupants (except for contacts of smallpox cases or contacts of contacts during periods of possible contagiousness). Observation may take the form of twice-a-day verbal questions about fever ≥ 101º F (38ºC) and appearance of rash. This observation could occur at unit formations or assemblies. If urgent military contingencies disperse the personnel, inform them to report fever at sick call and maintain surveillance for generalized febrile Vesicular or Pustular Rash Illness (see Annex A).

(3) For family members and government civilians seeking entry onto a military installation, the provisions of subparagraph (1) above will also apply.

(4) Family members and government civilians leaving a military installation may be advised, if applicable, that they may be going into an area of possible smallpox exposure. These individuals may be advised, if applicable, that they may be subject to isolation or public-health surveillance upon return to the military installation.

b. Ships underway. Depending on specific shipboard airflow patterns, the crew will isolate potential cases of smallpox until ship's company has been vaccinated. Hospital ships will implement their infection-control procedures relevant to airborne and contact precautions.

c. Air crews on missions away from their home base. After a suspected smallpox outbreak is identified, aircrews at that location will be permitted to depart only after medical coordination with installation and aviation commanders for active questioning about fever and rash, recognizing the risk of spreading infection to the crews' destination(s).

d. Troops deployed outside CONUS. Field medical units will implement isolation procedures to limit disease transmission.

e. Troops deployed outside CONUS intending to return to CONUS. Troops outside CONUS during a smallpox outbreak will be vaccinated before returning to CONUS or promptly upon returning to CONUS. These vaccinated troops will be observed for an appropriate period of time, to rule out disease despite vaccination.

f. Patient movement. Limit the movement and transport of patients with suspected or confirmed smallpox to essential medical transport only. When transport is necessary, minimize the dispersal of respiratory droplets by placing a simple surgical mask on the patient, if possible. The patient will wear clean gown/pajamas when exiting negative airflow room. If the patient is shedding scabs, all the lesions must be securely covered. Tuck pant legs into socks and tuck shirttails into pants. Limit patient movement within an MTF to medically essential testing. If possible, have the patient wash their hands or use an alcohol-based hand-hygiene agent.

g. Discharge management. In general, patients with smallpox will not be discharged from a healthcare facility until they are no longer infectious. However, the number of patients may overwhelm the medical system. Either other facilities may be designated to house these patients or those not needing specialized medical care will be sent home for care. Adapt discharge instructions according to the situation.

h. Post-mortem care. Use standard, airborne, and contact precautions (Appendix C-8) for post-mortem care. Cremation is preferable to burial for the remains of smallpox patients.

APPENDIX C-1
Isolation and Quarantine Guidelines – Summary.

1. Spread. Smallpox is usually spread by exhaled droplets at close range, usually face-to-face (≤ 6 feet) or household contact. Fine-particle aerosols from exhaled droplets of smallpox virus can travel further distances, which warrant airborne precautions.

2. Isolation. Contagious people (those with a rash or scabs) need to be isolated, to prevent contact with nonvaccinated or susceptible people, during their period of infectiousness (from onset of rash until all scabs have fallen off), to limit disease spread. Smallpox patients generally are infectious from first appearance of rash, but the early stages of the rash may be difficult to recognize. Before the rash appears, the patient will run a high fever for 2 to 3 days. Isolation of a possible case from onset of fever will provide enough time to put isolation measures in place before the main infectious period occurs. This isolation strategy, in addition to vaccination of all close contacts to the case, will help sharply limit the spread of smallpox. See Appendix C-10.

3. Quarantine of people exposed to a smallpox case. Use only after obtaining legal counsel. If you restrict movement, you may be responsible for sustaining those restricted. See also Appendix C-9, Appendix C-11, and Appendix C-12.

4. Restriction of Movement: To limit the spread of smallpox, encourage people to be vaccinated and to limit unnecessary public activities. Overly tight restrictions may cause more harm than good, if it keeps people from food or shelter or leads to civil disorder. Exposure to infected people 2 weeks ago may lead to smallpox cases diagnosed tomorrow. In other words, restrictions imposed today will have little value until 2 or more weeks in the future. Restrictions rarely can be implemented tightly enough to be fully protective.

5. Alternative Infection Control. Communities can work together to reduce disease spread.

a. Postpone large public gatherings, until other outbreak control measures in place (e.g., surveillance, vaccination, isolation of cases).

b. Encourage people to make fewer trips to common destinations (e.g., markets).

6. Military installations will develop local plans that identify Airborne Infectious Isolation Rooms (AIIRs). Installations will also identify facilities suitable for Types C and X treatment facilities, in case AIIRs are overwhelmed. Local plans also will address laundry and food service for and disposal of medical waste from non-medical facilities. See Appendix C-4. Early in an outbreak, admission of confirmed or suspected smallpox patients into a hospital facility not designated for the sole purpose of isolating smallpox patients may be unavoidable.

APPENDIX C-2
Acute-Care Guidelines for Isolation & Infection Control.

ACUTE-CARE GUIDELINES FOR ISOLATION & INFECTION CONTROL **Negative Air-Pressure Room – Location(s): _____** **IMPORTANT PHONE NUMBERS:** **Infection Control: _____ ER: _____** **Safety Officer: _____ Infectious Disease: _____**
Patient Room Placement/Requirements (see also Appendix C-7)
Negative pressure (per Military Handbook 1191) – at least 30 feet from exhaust outlets. Exhaust air direct to outdoors. Recirculation permitted in existing facilities if exhaust system equipped for HEPA filtration. CDC: No buildings within 100 feet of exhaust.
Private room
Door closed at all times.
Proper Airborne Infection Isolation Room (AIIR) – Conduct and record daily airflow testing to ensure negative flow unless maximum capacity of negative airflow rooms has been exceeded and patients are cohorted in non-negative pressure areas.
Cohort 'like' patients when private room unavailable.
Isolation Requirements – Strict Adherence is Mandatory
Standard Precautions for all aspects of patient care – Strictly enforced.
Contact Precautions – Place sign on the door. - Fluid-resistant gown and disposable gloves to enter the room. - Disposable gowns – treat as regulated medical waste (RMW). - Cloth gowns will be laundered per facility guidelines for isolation linen. - Respirator/eye shield/face shield for procedures prone to splashing, spraying.
Airborne Precautions – Must be in negative airflow room – Place sign on the door.
Use of NIOSH-approved **N95** particulate respirator by **all** individuals entering the room. - Personnel must be in Respiratory Protection Program.
Alcohol-based hand-hygiene agents before entering room and on exit. Or wash hands with antimicrobial soap.
Monitor staff entrance and exit.
Serve food and sanitize dishes per routine protocols. Ensure dietary staff are trained to wear gloves when handling all soiled dishes from isolation rooms and ensure compliance with water temperatures and detergents.
Cleaning & Disinfection of Equipment
Thorough terminal cleaning of room with hospital-approved disinfectant (HAD).*
Alternative is to also disinfect surfaces with 1 part bleach and 9 parts water (10% solution). Store bleach in an opaque bottle. Label accurately.
Dedicated equipment discarded when the patient is discharged.
Thermometers – Prefer use of glass thermometers or strip type.
Stethoscope and blood-pressure cuff – Dedicated and disposable.
Place linen hamper in the room. See linen management below.
Treat non-regulated medical waste the same as RMW.
RMW handled per MTF policy.

Regulated Medical Waste (RMW) Management
Discard non-sharp RMW in rigid containers lined with red 3-ml leak-proof bags.**
Discard sharps in rigid, puncture-resistant containers.
Dispose of pathological waste into RMW containers lined with RMW bags.
Discard bulk blood, blood products and body fluids in accordance with this plan.
Discard full, partially full or empty vials of smallpox vaccine in sharps containers.
Use carts made of readily cleanable material to transport RMW within the facility.
Clean carts used to transport RMW with EPA-registered hospital disinfectant.
Place RMW bags in leak-proof rigid container marked with Universal Biohazard symbol.
Containers used to transport RMW must comply with 49 CFR and state requirements.
** your state may have a more stringent requirement for RMW bags.
Housekeeping
Trash container emptied and disinfected.
Low dusting and cleaning all exposed surfaces with HAD.*
Patient's bed cleaned and free of soiling & foreign matter.
Fixtures, walls, lights, doorknobs, bedrails, and overbed tables cleaned and free of fingerprints/hand marks with HAD.*
Floor damp-mopped using two-bucket method using HAD.*
Vents, grills, windowsills and blinds damp wiped with HAD.*
Sink and toilet bowl disinfected.
Cotton mop changed after each room and placed into plastic bag for laundering.
Mopping water changed after each room.
Must wear PPE -- NIOSH-appr. N-95 particulate respirator, fluid-resistant gown, gloves.
Linen Management – Additional Detail in Decontamination Guideline
Use leak-proof bags. Label "biohazardous" before moving to linen service area.
Ensure staff are vaccinated and trained appropriately to the risk.
Staff must wear NIOSH-approved N-95 particulate respirator and fluid-resistant gowns and gloves when handling or sorting soiled linens.
Ensure appropriate hot water and dryer temperatures, detergents, bleach used.
Use quality-assurance tool/evaluator to validate linen process.
Patient Transport
Place surgical mask on patient to reduce dispersal of respiratory droplets.
Limit movement to essential medical purposes only.
Thoroughly clean wheelchairs and stretchers with HAD.*
Visitors
Only people who have been vaccinated or are immune by history of smallpox infection may visit.
NIOSH-approved N-95 particulate respirator required.
Adherence to all other aspects of isolation mandatory.
Discharge Management
Home-care providers need to be taught principles of standard precautions.
Not discharged from hospital until determined no longer infectious.

Post-Mortem Care
Follow principles of standard precautions.
Airborne precautions.
- Use of NIOSH-approved **N95** particulate respirator by **everyone** entering the room.
- Negative pressure. Direct exhaust to the outside.
Contact precautions.
Thorough terminal cleaning of room with HAD following autopsy or a fresh solution of 1 part bleach and 9 parts water (10% solution).
Burial / Storage Issues
Cremation is preferred to burial.

*** HAD**: Hospital-approved disinfectant - Tuberculocidal - must be EPA registered. HAD is mixed, used, and labeled per manufacturer's instructions.

Hemorrhagic smallpox has been described as "more contagious" than typical smallpox, perhaps as a result of the additional care provided the acutely ill patient, leading to closer contact with caregivers and increasing exposure risk. In the 21st century, basic hygienic measures and awareness of the mechanisms of disease transmission are much improved. PPE requirements remain the same - regardless of the severity of illness.

APPENDIX C-3
Home Care Guidelines for Isolation.

HOME-CARE GUIDELINES FOR ISOLATION & INFECTION CONTROL IMPORTANT PHONE NUMBERS: Health Department: _____ Physician: _____
Patient Room Requirements
Use private room, if possible. Keep door closed. Avoid close or intimate contact with other family members.
Keep household members in the same state of disease in the same room together ("Cohorting"), if necessary.
Keep infected person home until scabs fall off and no longer contagious.
Isolation Requirements – Strict Adherence is Important
Wash hands with an antibacterial soap if they are visibly soiled. And use an alcohol-based hand rinse frequently, before entering patient's room and on exit.
Wear disposable gloves if you expect to touch blood, body fluids, or pox drainage or scabs from the patient.
Cleaning & Disinfecting Equipment
Thermometers – may use glass thermometers (soak in alcohol after each use) or strip type (use once and throw away).
Housekeeping
Bag trash and use routine disposal for your community.
Empty and disinfect the trash container when visibly soiled. Cover with a lid.
Sanitize dishes with detergent in a dishwasher, if available. If washing by hand, add one capful of household bleach to dish water.
If you use paper plates and plastic utensils, discard them into the household trash.
Clean surfaces, furniture, fixtures, lights, doorknobs, bedrails, tables, and walls thoroughly with household disinfectant (e.g., Lysol), following manufacturer's directions.
An alternative is to disinfect surfaces with solution of 1 part bleach and 9 parts water (10% solution) Store bleach in an opaque bottle. Label accurately.
Clean the sink, tub, and toilet bowl with household disinfectant (e.g., Lysol) daily.
Use a cotton mop to clean the floors in the sick rooms and then launder the mop heads.
Clean carpets and upholstery using an EPA-approved germicidal detergent per manufacturer's recommendations.
Linen Management
Launder bedding, linens, clothing, curtains, or other material that came in contact with smallpox patient in hot water (71ºC or 160ºF, or hottest setting) for an adequate time (e.g., 25 minutes), adding 1 cup of bleach per load. Dry laundry in hot dryer if possible.
Place linen hamper in the patient's room.
Patient Leaving the House. Limit movement to essential medical purposes only.
Place clean pajamas and a surgical mask on patient before leaving the house, to reduce dispersal of droplets.
Thoroughly clean wheelchairs and stretchers with disinfectant.
Visitors
Only people who have been vaccinated may visit.

APPENDIX C-4
Criteria for Type C, X, and R Facilities.

If a large number of smallpox cases overwhelms an MTF's ability to provide triage, treatment, and care of smallpox patients in appropriate Airborne Infection Isolation Rooms (AIIRs), then housing these patients in facilities known as Type C, X, and R facilities is an acceptable means of infection prevention and control. In such cases, follow these criteria:

1. Known or presumed infectious individuals. Isolate members of these groups in a Type C Facility (dedicated isolation facility):

a. People with a compatible illness and laboratory confirmation of smallpox (confirmed case).

b. People with a compatible illness following suspected/known exposure with pending laboratory confirmation (probable case).

c. People referred by an expert as suspected cases of smallpox but who do not have a typical clinical presentation.

Type C (Contagious) Facility: Structure with non-shared ventilation system. Controlled access (e.g., fence, monitored entries). Adequate utilities. Adequate 2-way communication system (e.g., telephone, intercom, Internet). Ability to provide medical care (e.g., IV fluids, medications, skin care, oxygen monitoring, vital signs, CPR, respiratory support, basic laboratory, portable radiology). Patients may be released from a Type C facility only with approval of the designated medical officer.

2. Febrile contacts without rash. Isolate members of these groups in a Type C or preferably a Type X facility: Vaccinated contacts under surveillance who develop oral temperatures ≥ 101º F (38ºC) on two successive readings (but do not have a rash). If rash does not develop within 5 days and the fever is diagnosed as being a result of vaccination or some other non-smallpox-related cause, the contact may be released to complete fever surveillance at home by the designated medical officer.

Type X (Uncertain) Facility: Same isolation and general supply requirements as Type C Facility, but only basic medical services needed (e.g., monitoring vital signs).

3. Asymptomatic Contacts of Smallpox Patients. Isolate members of these groups in Type R = Residential Facilities for 18 days after last exposure or until 14 days following successful vaccination (whichever comes first), by permission of the designated medical officer.

a. Afebrile vaccinated contacts.

b. Afebrile vaccinated individuals who were with a smallpox patient 10 to 18 days before the onset of the patient's rash (possible common exposure).

c. Contacts who refuse smallpox vaccination.

Type R (Residential) Facility: A person's own home. Continue routine daily activities, remaining within ~ 20 miles of their city of residence. Twice-daily temperature readings. Daily telephone contact with health department. If contacts without symptoms cannot be housed in their own residences due to logistical difficulties or other reasons, establish Type R facilities in designated barracks, recreation centers, guest houses, or similar facilities with sleeping accommodations and utilities.

Implementation details appear in Appendix C-5.

APPENDIX C-5
Isolation Procedures.

1. Situation. Patient presents to the urgent care center, clinic, or emergency department.

INFECTION CONTROL PRACTICES

2. For characteristic rashes of smallpox on the face or upper extremities, healthcare personnel will ask the patient to promptly put on a simple surgical mask that they hand to the patient. Immediately notify a nurse or physician, who will place the patient in the airborne isolation holding room number _____located at _____.

3. If an airborne isolation holding room is not immediately available in the clinic, the patient will be given a simple surgical mask and placed in an empty patient exam room with the door closed.

4. Do not allow patient to wait in the common area with other patients. Move the patient to an airborne isolation room for examination. See Patient Placement & Transport and Appendix C-7.

5. Start CONTACT and AIRBORNE PRECAUTIONS immediately (Appendix C-8). ALL staff members will don NIOSH-approved N95 respirator, gown, and gloves. Use eye protection if there is a risk of body fluids splashing or spraying.

6. Remove gowns and gloves before leaving the patient room.

7. HANDWASHING AFTER ENTERING ROOM WITH ANTIMICROBIAL SOAP IS MANDATORY. Waterless hand-hygiene agents may be used as a supplement to washing with soap and water.

8. Use disposable equipment or clean durable equipment using the hospital-approved disinfectant. Or use dedicated-patient equipment as much as possible. Also follow this procedure with diagnostic equipment (e.g., stethoscopes, reflex hammers) used in the patient room.

9. Handle linen according to MTF policies for isolation-room linen.

10. People who handle soiled linen will be vaccinated and wear fit-tested NIOSH-approved N95 particulate respirators, as part of their PPE.

CLINICAL EVALUATION & TREATMENT

11. Clinical Condition.

a. Patient History. 1 to 2 days of influenza-like symptoms (e.g., high fever, headache, severe backache, malaise, myalgia, nausea, vomiting).

b. Synchronous rash (lesions all at same state of development) on face, forearms, hands (including palms) that may have spread to legs (including soles of feet) and/or trunk. Rash may have progressed to the vesiculo-papular (blistery, bumpy) stage.

12. Release clinical specimens only to the FBI or to Health Department officials with a documented established chain-of-custody. See Annex D. Send samples only to a facility designated by the CDC. Laboratory/Pathology Service will provide appropriate containers and packaging for transport of specimens that meet packaging requirements for Infectious Substance Packaging will be kept in the location _____.

13. If physician suspects smallpox, initiate an emergency telephonic infectious-disease and/or dermatology consult. The patient will remain in the airborne isolation room. Staff will come to the room to evaluate the patient. If the patient needs a chest radiograph (CXR), bring portable x-ray equipment to the patient, if possible.

14. Consult infectious-disease or other medical services, as appropriate. Consider treatment with cidofovir as an investigational new drug (IND) (Annex G).

NOTIFICATION

15. **Internal Notification**. The attending physician or charge nurse will notify
Chief, Infectious Diseases Section, Dr. _____ @ xxx-xxxx or
ID Consult Attending (Operator)/ID fellow _____@ xxx-xxxx
AND the Infection Control Officer _____ @ xxx-xxxx
for any suspected smallpox case. Use the emergency call roster during any off-duty tour or if unable to reach the initial contact person.

16. The Infection Control Officer will notify the MTF leadership promptly:
MTF commander _____
MTF chief of staff (deputy commander for administration) _____,
MTF deputy commander for clinical services _____,
and the MTF Nursing Administrator _____

17. **External Notification**. Specific policies for reporting smallpox cases outside the MTF are described in Annex A. In brief, (a) submit a report immediately through established Service disease-reporting systems, beginning with the local preventive-medicine/public-health service, (b) submit a Serious Incident Report (SIR) to higher military headquarters, (c) notify CDC Emergency Preparedness & Response Branch (770-488-7100), (d) notify state health department, then (e) notify other appropriate authorities (e.g., local health department).

PATIENT PLACEMENT & TRANSPORT (see also Appendix C-7).

18. Place suspect or confirmed smallpox patients in an airborne isolation room in designated location_____.

19. Place critically-ill suspected/confirmed patient in designated location_____.

20. Hospitalized patients who may be exposed should be grouped together (cohorted). Optimally, staff members caring for suspected smallpox patients or hospitalized exposed patients should care for only this designated group of patients.

21. Limit transport of patient within the facility to only initial placement and movement most essential to patient care. This includes appropriate bathing, clean clothing, and placement of simple surgical mask on the patient before transport.

22. Remove unnecessary items from ambulances to avoid contamination and facilitate decontamination. Vaccinate patient transport personnel before transport or within 24 hours. Equip ambulance with appropriate supplies (e.g., NIOSH-approved N95 respirators (if fit-tested), disposable gloves, gowns, biohazard bags). Decontaminate ambulance before reuse to transport patients not infected with smallpox.

23. Cover patients in transport in a sheet, gloves and simple surgical mask. Transport personnel will also wear gown, gloves and NIOSH-approved N95 particulate respirator. Secure transport elevators using the key system. Transport the patient as the sole occupant of the elevator. Use the route with the least contact with other people.

24. Transport of patients to a designated location outside of the facility will be determined by joint decision of MTF leadership and the receiving facility.

25. If a large number of smallpox cases overwhelms an MTF's ability to provide triage, treatment, and care of smallpox patients in appropriate Airborne Infection Isolation Rooms (AIIRs), then housing these patients in facilities known as Type C, X, and R facilities is an acceptable means of infection prevention and control. Type C facilities and Type X facilities will establish lists of vaccinated people who may enter the facility. This should be the smallest number of people required for patient care, investigation, and facility maintenance. The nurse on duty or other personnel responsible for monitoring access to and egress from the facility should keep the list. All personnel who enter should have been recently vaccinated (within 3 to 10 years). All personnel should monitor themselves for fever every 12 hours, until confirmation of successful vaccination. At the beginning of each shift, all staff members will present to the person responsible for coordinating employee illness surveillance to report any temperatures or other illness. On days they are not at the facility, staff members are required to call in by telephone each morning to report their temperatures. Once successful vaccination has been confirmed, personnel are not required to routinely check their temperatures, however, they are still required to report any illness to people coordinating employee illness surveillance.

26. Arrange to have food prepared on the premises or brought into the facility in disposable containers, if possible. Otherwise, all serving ware, plates, cups, and utensils can be safely sanitized in a standard dishwasher.

EMPLOYEE AND PATIENT EXPOSURES.

27. Infection control service will establish patient and employee exposure cohorts in consultation with the chief of the Infectious disease section. Employee cohorts and vaccination will be managed and tracked by the employee health service. All personnel caring for and transporting smallpox patients will be vaccinated, as well as affected laundry workers, and waste-disposal personnel.

28. Patient exposures within the facility cohorts will be managed by infection control service, with assistance from department of nursing and preventive-medicine/public-health personnel.

29. Individuals are considered infectious from the onset of their eruptive exanthem (rash) until separation of all scabs.

APPENDIX C-6
Exposure Definitions.

1. Face-to-face close contacts (≤ 6 feet), or household contacts to smallpox patients after the onset of the smallpox patient's fever. Note A.

2. People exposed to the initial release of the virus, if the release was discovered during the first generation of cases and vaccination may still provide benefit.

3. Household members (without contraindications to vaccination) of contacts to smallpox patients. This will help protect household contacts should smallpox case contacts develop disease while under fever surveillance at home. Note B.

4. People involved in the direct medical care, public-health evaluation, or transportation of confirmed or suspected smallpox patients. Note C.

5. Laboratory personnel involved in the collection and/or processing of clinical specimens from suspected or confirmed smallpox patients.

6. Other people who have a high likelihood of exposure to infectious materials (e.g., hospital waste disposal, laundry services, housekeeping, contact tracing, vaccination, isolation or enforcement, law-enforcement interviews of suspected smallpox patients). Note C.

7. People permitted to enter any facilities designated for the evaluation, treatment, or isolation of confirmed or suspected smallpox patients (only essential personnel should be allowed to enter such facilities). Note D.

8. People present in a facility or conveyance with a smallpox case, if fine-particle aerosol transmission was likely during the time the case was present (e.g., hemorrhagic smallpox case, case with active coughing). Note E.

Note A. Although people with smallpox are not infectious until the onset of rash, vaccinating contacts from onset of fever helps provide a buffer and assures that contacts who may have been exposed at the early onset of rash, when the rash may have been faint and unrecognized, have been vaccinated.

Note B. Household members of contacts who have contraindications to vaccination should be housed separately from the other vaccinated household members until the vaccination-site scab separates (~ 2 weeks), to prevent inadvertent transmission of vaccinia virus. Household members of contacts also should be housed separately from the contact until the incubation period for smallpox has passed and the designated medical officer releases the contact from surveillance.

Note C. Includes personnel whose public-health activities involve direct patient contact such as case interviewing.

Note D. Choose only personnel without contraindications to vaccination for activities that would require vaccination for their protection. Personnel with contraindications should not perform duties that would place them at risk for smallpox exposure and should otherwise only be vaccinated if an exposure has already occurred.

Note E. Evaluation of the potential risk for aerosol transmission and initiation of vaccination for non-direct contacts will be done by federal, state, and local public-health personnel. The decision to offer vaccination to non-direct contacts of smallpox cases will be made jointly by federal and state health officials.

APPENDIX C-7
Patient Placement Considerations.

1. Patient placement depends upon clinical presentation and physical-plant capabilities of the facility. Each of the following groups of patients has specific isolation considerations.

- People known or presumed to be infectious.
- People with a compatible illness and laboratory confirmation of smallpox (confirmed case).
- People with a compatible illness after suspected or known exposure, with pending laboratory confirmation (probable case).
- People referred by an expert as suspected cases of smallpox, but who do not have a typical clinical presentation.
- Vaccinated Contacts with Fever but without Rash: Vaccinated contacts under surveillance who become febrile with oral temperatures ≥101º F (38ºC) on two successive readings, but do not have a rash.
- Asymptomatic Contacts.
    - Afebrile vaccinated contacts.
    - Afebrile vaccinated individuals who were with a smallpox patient 10 to 18 days before the onset of the patient's rash (possible common exposure).
    - Contacts who refuse vaccination.

2. Healthcare facilities without patient rooms appropriate for airborne precautions (Appendix C-8) will have a plan for transfer of suspected or confirmed smallpox patients to other facilities with appropriate airborne isolation environments. Existing facilities could substantially benefit from dedicating resources to ensuring appropriate air handling and ventilation systems for existing clinics, emergency departments, and isolation rooms. This would provide the added benefit of controlling more likely exposures to infectious droplet nuclei (e.g., tuberculosis, disseminated varicella zoster, chicken pox, measles), in addition to minimizing or eliminating the likelihood of intra-facility transmission of smallpox.

3. Patient placement in a private room is preferred. However, in the event of a large outbreak, patients who have active infections with the same disease (i.e., smallpox) may be cohorted in rooms that meet appropriate ventilation and airflow requirements for airborne precautions (Appendix C-8).

APPENDIX C-8
Infection-Control Precaution Categories.

Category	Negative-Pressure Room	Respirator (NIOSH-approved N95)	Gown, Face Mask, Eye Shield	Gloves	Applicable Diseases
Standard *	No	No	If splashing likely.	Before touching blood or body fluids or non-intact skin.	All
Airborne	Yes	Yes	If splashing likely.	Before touching blood or body fluids or non-intact skin.	Tuberculosis, varicella zoster, measles, smallpox @
Contact	No	Only for other isolation needs	Yes #	Yes #	Enteric diseases, lice, smallpox, viral hemorrhagic diseases. Patients colonized or infected with antibiotic-resistant organisms.
Droplet	No	Yes, if coming within 3 feet of patient. Simple surgical mask is sufficient.	If splashing likely. %	Before touching blood or body fluids or non-intact skin. %	*Neisseria meningitidis*, diphtheria, pneumonic plague

* To protect your mucous membranes or nonintact skin from anticipated contact with any blood or any body fluids from all patients at all times.

@ Gown and gloves may be needed to protect you from drainage from weeping smallpox lesions or scabs, so you do not accidentally take germs to the next patient.

Gown and gloves protect you from drainage from weeping smallpox lesions, drainage from wounds, and lice, lessening the chance that personnel will accidentally convey infectious materials from one patient to another.

% Gown and gloves may be needed to protect you from secretions from coughing or sneezing patients or where there is gross environmental contamination.

Adapted from Hospital Infection Control Practices Advisory Committee:
http://www.cdc.gov/ncidod/hip/isolat/isopart2.htm

APPENDIX C-9
Issues in Quarantine.

1. Introduction. Limited experience with the application and success of various quarantine measures precludes inclusion of standardized guidelines for the implementation of such measures during a bioterrorism event. State quarantine laws are dated and varied. The division of legal authority between the state and Federal governments requires rapid and efficient coordination of actions to provide a public-health response. Such coordination is an essential part of planning. Both state and federal public-health officials need to develop plans for the implementation and logistics of both individual and population level quarantine measures under their current authorities.

2. Potential Quarantine Actions.

a. State Quarantine Laws. The major source of legal authority for public-health interventions is the police power, the inherent authority of all sovereign governments to enact laws and promote regulations that safeguard the health, welfare, and morals of its citizens. The 10th Amendment to the U.S. Constitution reserves to the States all powers not expressly granted to the Federal government nor otherwise prohibited by the Constitution, including the police power. The courts have repeatedly held that state quarantine laws are a proper exercise of their police power. Such laws, for example, may be used to detain individuals within a circumscribed area and to exclude healthy persons from entering the area. Assuming that legal authorities are sufficient to allow public health officers to use personal control measures, many practical questions remain: (1) who enforces a quarantine, (2) who detains an infected or exposed person, (3) how due process is accommodated, and (4) what actions government may take if a person disobeys a quarantine order.

b. CDC Guide C lists public-health powers needed for adequate response to a bioterrorism event. That list appears below, with an annotation of its applicability on military installations. Military commanders' actions regarding isolation or quarantine on a military installation of infected or possibly infected DoD and non-DoD personnel will be determined by the nature of the outbreak and the laws, regulations and policies concerning those specific types of situations. Commanders must obtain legal advice on individual situations from their legal advisors.

(1) Collection of Records and Data.

(a) CDC Guide C discusses: Reporting of diseases, unusual clusters, and suspicious events. Access to hospital and provider records. Data sharing with law-enforcement agencies. Veterinary reporting. Reporting of work-place absenteeism. Reporting from pharmacies.

(b) DoD Application. Service regulations mandate disease reporting within the Military Health System. Commanders are generally responsible for the health of Service Members in their commands. Commanders are also responsible for worksite safety. Commanders are authorized to use government-owned medical (including pharmacy) records for official purposes to preserve public health and safety.

(2) Control of Property.

(a) CDC Guide C discusses: Right of access to suspicious premises. Emergency closure of facilities. Temporary use of hospitals and ability to transfer patients. Temporary use of hotel rooms and drive-through facilities. Procurement or confiscation of medicines and vaccines. Seizure of cell phones and other “walkie-talkie” type equipment. Decontamination of buildings. Seizure and destruction of contaminated articles.

(b) DoD Application. Military installations, buildings, and equipment are federal property. Penalties for violating orders for the protection or security of installations provided at 50 USC 797 (Internal Security Act of 1950). Seizure of personal property requires legal consultation before action.

(3) Management of Persons.

(a) CDC Guide C discusses: Identification of exposed persons. Mandatory medical examinations. Mandatory vaccination of civilians. Collect lab specimens and perform tests. Rationing of medicines. Tracking and follow-up of persons. Isolation and quarantine. Logistical authority for patient management. Enforcement authority through police or National Guard. Suspension of licensing authority for medical personnel from outside jurisdictions. Authorization of other doctors to perform functions of medical examiner.

(b) DoD Application. Military commanders are responsible to protect personnel and property, maintain good order and discipline, and ensure successful performance of military missions. Military commanders may remove or exclude a person from an installation or take other actions relating to ingress or egress for the protection or security of the installation (18 USC 1382; 50 USC 797), subject to judicial review. Under the Posse Comitatus Act (18 USC 1385), military personnel generally may not assist local law-enforcement officials in enforcing civilian laws, except where authorized by the Constitution or Act of Congress. Thus, military police often detain civilians until civilian police can be called, rather than arresting them outright. By analogy, it may be preferable to avoid involuntarily locating any civilian in a DoD-managed isolation facility, but rather detaining that person until local civilian public-health authorities arrange for similar surveillance in civilian-managed facilities. Seek local legal advice on specific circumstances.

(4) Access to Communications and Public Relations.

(a) CDC Guide C discusses: Identification of public health officers (e.g., badges). Dissemination of accurate information. Establishment of a command center. Access to elected officials. Access to experts in human relations and post-traumatic stress syndrome. Diversity in training, cultural differences, dissemination of information in multiple languages.

(b) DoD Application. Consistent will military missions.

(5) Legal Advice to Commanders. Commanders should seek legal counsel from staff judge advocates before exercising any nonstandard authority.

3. Federal Assistance in Enforcement of State Quarantine. Federal assistance may be provided by and through CDC to state and local authorities in enforcing their quarantine and other health regulations pursuant to section 311 of the Public Health Service Act. (42 USC 243(a)). In addition, while intrastate control of communicable diseases generally may be the purview of state and local officials, CDC's domestic quarantine regulations authorize Federal intervention "in the event of inadequate local control." See 42 CFR 70.2 and 21 CFR 1240.30.

4. Federal Intervention When State Response is Inadequate. While the Constitution reserves the police power to the States, the Federal government has extensive authority over public health under the Commerce Clause of the U.S. Constitution, which grants the Federal government the exclusive power to regulate interstate and foreign commerce. Under 42 U.S.C. § 264, the Secretary of Health and Human Services may issue regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the United States and from one state or possession into another. The statute defines interstate movement to include authority over individuals who might expose other persons engaged in travel to other States. The current implementing regulations, found at 42 CFR Part 70, authorize:

a. Imposition of permit requirements by the Surgeon General of the Public Health Service for interstate travel, or travel on conveyances engaged in interstate traffic, applicable to any person in the communicable period of smallpox, or who, having been exposed to smallpox, is in the incubation period (42 CFR 70.5(a)).

b. Federal enforcement of State-required travel permits (42 CFR 70.3).

c. Imposition of disease mitigation requirements and reporting for interstate carriers transporting infected individuals or those suspected of infection (42 CFR 70.5(b) and 70.4)).

d. These regulations, through section 70.2, authorize action by the Centers for Disease Control and Prevention in the event that measures taken by local and State health authorities are insufficient to prevent the spread of smallpox to other States. The Director of the CDC is empowered to "take such measures to prevent such spread of the diseases as he/she deems reasonably necessary, including inspection, fumigation,

disinfection, sanitation, pest extermination, and destruction of animals or articles believed to be sources of infection." This section, in conjunction with other sections of the interstate quarantine regulations, authorizes the apprehension and examination of "any individual reasonably believed to be infected with a communicable disease in a communicable stage," so long as the individual either is "moving or about the move from a State to another State," or is "a probable source of infection to individuals who, while infected with such diseases in a communicable stage, will be moving from a State to another State."

5. Imposing Quarantine. The successful implementation of individual and population-level quarantine measures hinge on numerous factors, including (a) prior identification of legal authority empowered to invoke and enforce such authorities, (b) public trust and compliance with government directives, and (c) assured vaccination and other protection of personnel required to implement and enforce quarantine measures.

a. Factors Affecting Policy (Appendix C-11). The determinants that contribute to reaching the public-health threshold for initiating population-wide quarantine measures include (a) the number of cases and exposed people, (b) the projected morbidity and mortality, (c) the expected ease and rapidity of spread of disease, (d) current patterns of movement in and out of the community, (e) available resources for implementing measures of treatment and control, (f) perceived or actual need for urgent public health action, (g) and the risk for public panic.

b. Cordon Sanitaire. The first approach would be to apply concentric levels of quarantine to restrict movement of individuals and conveyances between communities ("cordon sanitaire") in an effort to control the spread of smallpox. In addition to enforcement activities, other considerations and strategies that should be taken into account when implementing quarantine measures include:

(1) Communication strategies (e.g., issuing travel alerts and press releases and notification of interagency partners)

(2) Movement of essential personnel (e.g., rescue workers and first responders), and requirements for their validation of movement, into and out of the quarantined area.

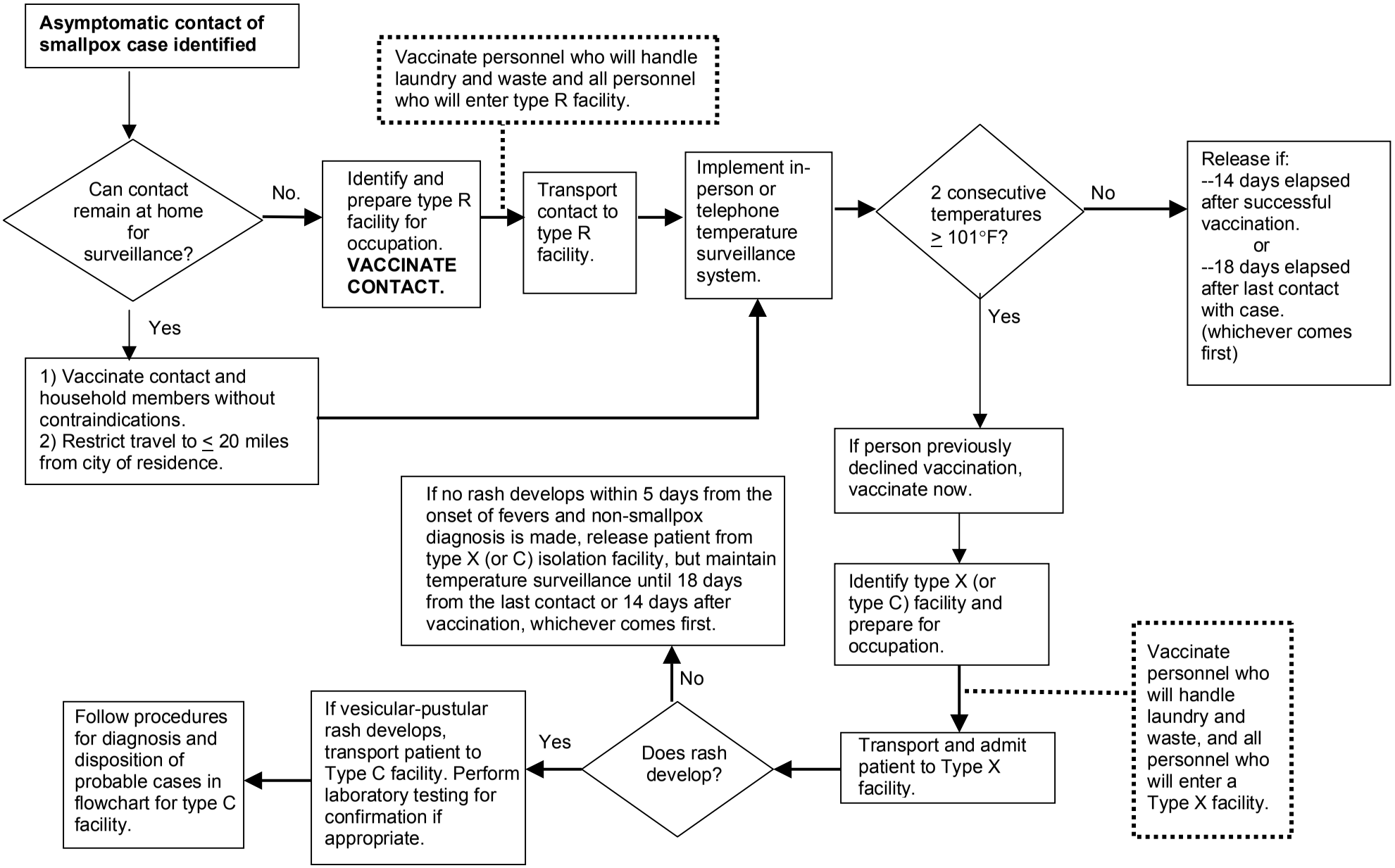
(3) Movement of materials (e.g., food, medical supplies, and garbage) into and out of the quarantined area, and provision of essential services (e.g. utilities, water).

(4) Movement of individuals out of the quarantined area for legitimate health and safety reasons (e.g. need for specialized and unavailable medical care or facility).

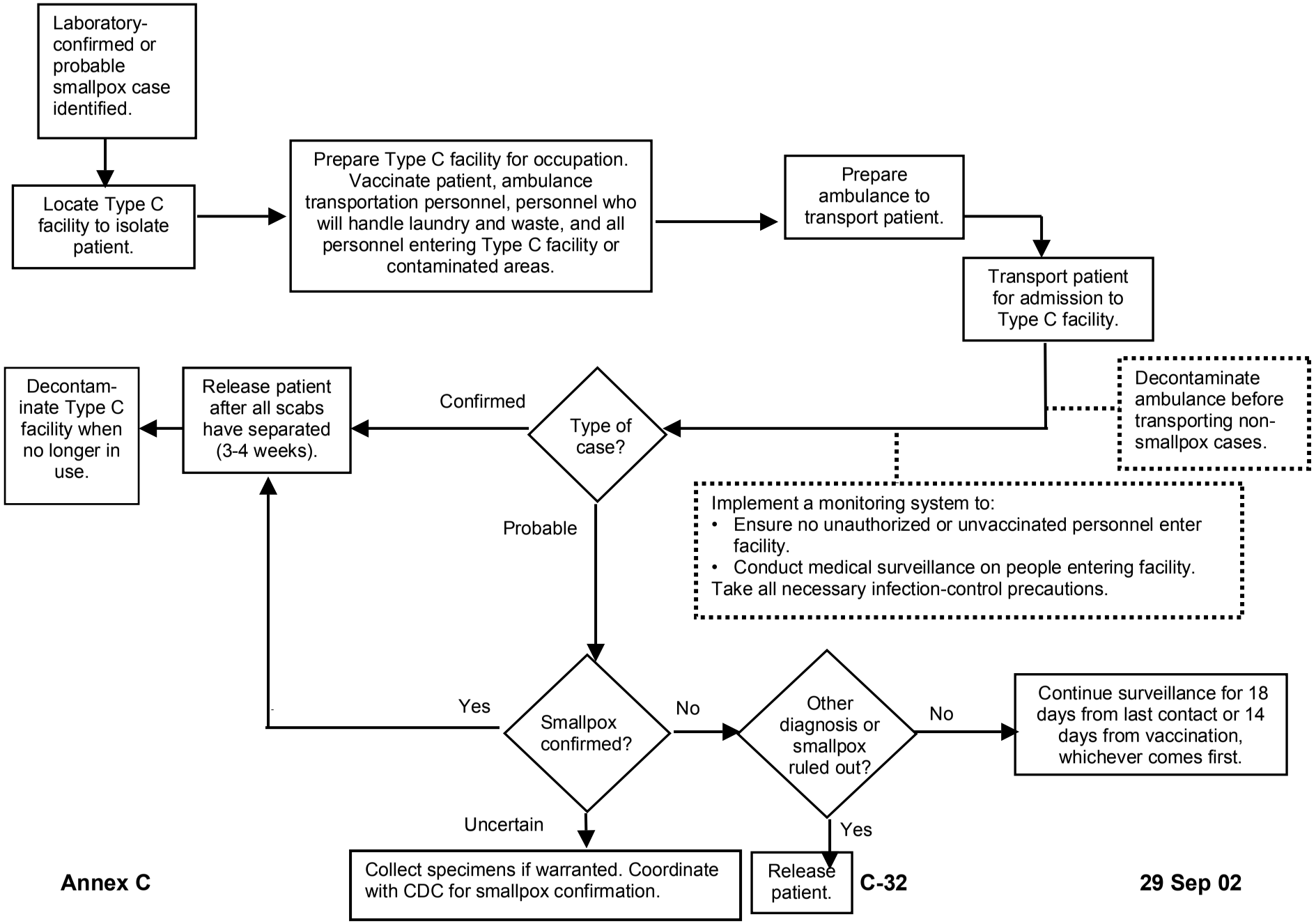
(5) Community-wide intervention strategies (e.g., mass vaccination).

c. When implementing the quarantine of an individual or a community or other population, consider the requirements necessary to terminate quarantine measures. For individuals, ongoing monitoring for disease manifestations or lack of such developments

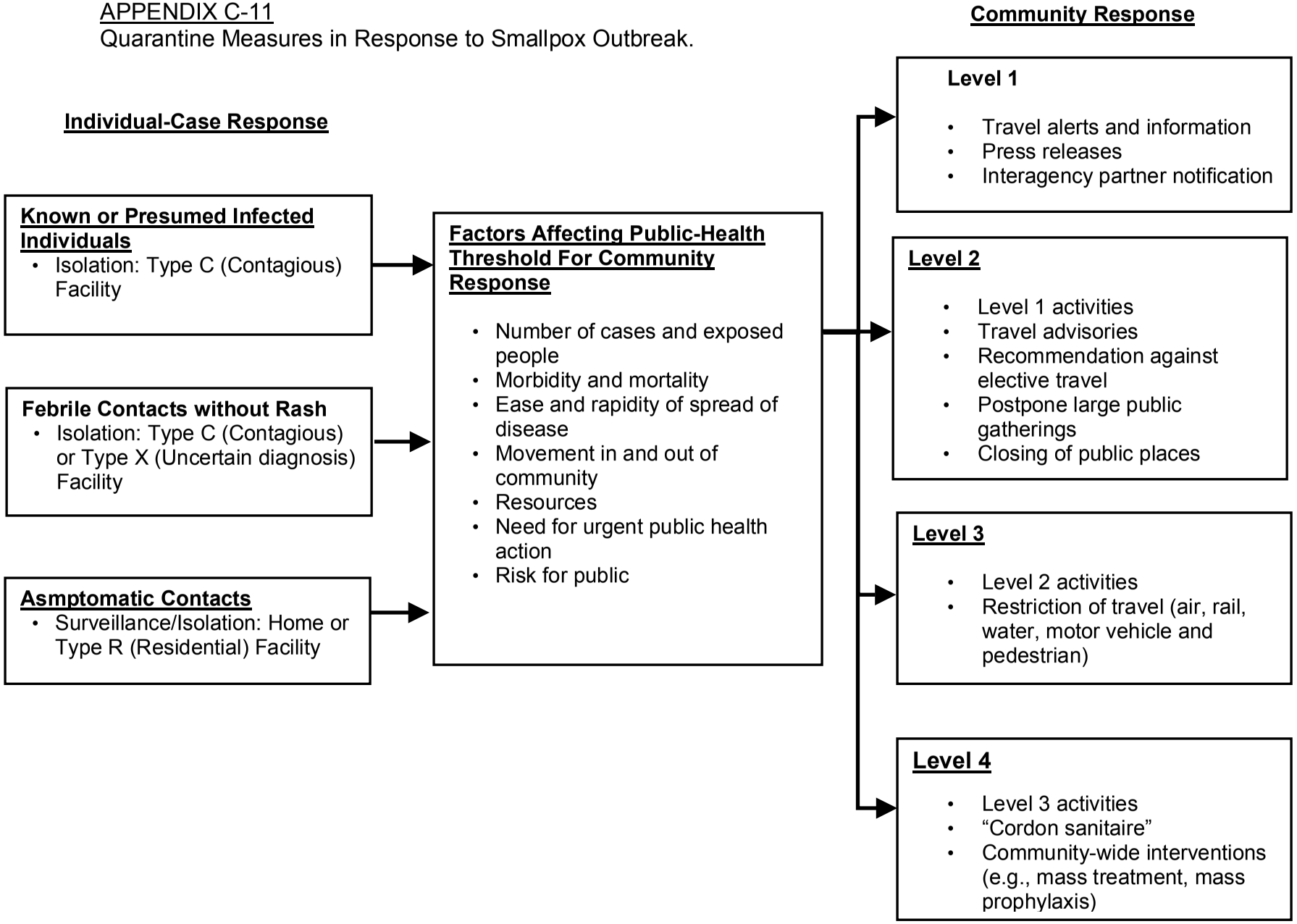
during the longest usual communicable or incubation or communicable period for smallpox will determine the effectiveness of quarantine activities. At the population level, continued surveillance for lack of new cases in the quarantined area, and no demonstrated spread to contiguous areas will be important measures of containment and control activities.


Asymptomatic contact of smallpox case identified
Can contact remain at home for surveillance?
No.
Yes
Identify and prepare type R facility for occupation. VACCINATE CONTACT.
Vaccinate personnel who will handle laundry and waste and all personnel who will enter type R facility.
Transport contact to type R facility.
Implement in-person or telephone temperature surveillance system.
2 consecutive temperatures ≥ 101°F?
No
Release if:
--14 days elapsed after successful vaccination.
or
--18 days elapsed after last contact with case.
(whichever comes first)
Yes
1) Vaccinate contact and household members without contraindications.
2) Restrict travel to ≤ 20 miles from city of residence.
If person previously declined vaccination, vaccinate now.
Identify type X (or type C) facility and prepare for occupation.
Vaccinate personnel who will handle laundry and waste, and all personnel who will enter a Type X facility.
Transport and admit patient to Type X facility.
Does rash develop?
Yes
No
If vesicular-pustular rash develops, transport patient to Type C facility. Perform laboratory testing for confirmation if appropriate.
If no rash develops within 5 days from the onset of fevers and non-smallpox diagnosis is made, release patient from type X (or C) isolation facility, but maintain temperature surveillance until 18 days from the last contact or 14 days after vaccination, whichever comes first.
Follow procedures for diagnosis and disposition of probable cases in flowchart for type C facility.

Isolation Flow Chart, part 2.



APPENDIX C-11
Quarantine Measures in Response to Smallpox Outbreak.



APPENDIX C-12
Quarantine Regulations of the Armed Forces Pertaining to Ships, Aircraft, and Other Conveyances.

Selected Passages from: Army Regulation 40-12, SECNAVINST 6210.2A, Air Force Regulation 161-4. Quarantine Regulations of the Armed Forces. 24 January 1992. http://www.usapa.army.mil/pdffiles/r40_12.pdf.

1. PURPOSE AND SCOPE. These regulations conform to regulations of the United States Departments of Health and Human Services; Agriculture; Treasury; Interior; and Commerce. The regulations are intended to prevent the introduction and dissemination, domestically or elsewhere, of diseases of humans, plants and animals, prohibited or illegally taken wildlife, arthropod vectors, and pests of health and agricultural importance. Introduction and dissemination may occur by movements of vessels, aircraft, or other transport of the Armed Forces arriving at or leaving Armed Forces installations in the United States and foreign countries or ports or other facilities under the jurisdiction of the above Federal agencies in the United States and its territories, commonwealths, and possessions.

…

3. COOPERATION WITH OTHER AGENCIES. To fully comply with the quarantine regulations of the executive departments referred to above, full cooperation will be given at all times to officials of these agencies. Inspectors of the above services are authorized to board ships, aircraft, and any other means of conveyance of the Armed Forces and to inspect ports and other facilities. Commanders will provide full support for inspections. Cooperation will be given to foreign officials following applicable host country agreements. All examinations will be subject to all restrictions necessary to preserve the security of classified material.

…

5. QUARANTINE REQUIREMENTS. Ships, aircraft, or other conveyances of the Armed Forces proceeding to a foreign port will meet the quarantine requirements published by proper authority for such port. The U.S. Government asserts the full panoply of rights of sovereign immunity with respect to U.S. warships and military aircraft, USNS vessels, and afloat prepositioning force ships. They will not be subject to inspections or searches by officials for any purpose. Commanding officers, masters, and aircraft commanders may certify compliance with quarantine regulations and restrictions to foreign health officials. If requested by host authorities, certification may include a general description of measures taken by U.S. officials in compliance with local requirements. At the discretion of the commanding officer, master, or aircraft commander, foreign health officials may be received on board for the purpose of receiving certification of compliance. Such officials may not, however, inspect the ship or aircraft, or act as

observers while U.S. personnel conduct such inspections. Actions by foreign officials inconsistent with this guidance must be reported immediately to the chain of command and U.S. embassy.

…

Public Health Service Requirements – Surface Transportation.

7. PREDEPARTURE REQUIREMENTS.

a. The commanding officer of a ship will comply with sanitary measures prescribed by the health authorities in the port of departure to prevent the embarking of persons infected with a quarantinable disease or the introduction on board the ship of possible agents of infection or vectors of a quarantinable disease. The quarantinable diseases are cholera, plague, and yellow fever.

Note. The U.S. Public Health Service, under the authority of an Executive Order signed by the President of the United States (E.) 12452 of December 22, 1983) and CFR Part 71 has the authority to detain, isolate, or place under surveillance individuals believed to be infected with 4 diseases in addition to those listed above. The 4 diseases are: diphtheria, infectious tuberculosis, suspected smallpox, and suspected viral hemorrhagic fevers (Lassa, Marburg, Ebola, Congo-Crimean, and others not yet isolated or named).

b. Those measures outlined in sections IV and V for domestic quarantines will be applied to ship predeparture and arrival requirements, as applicable.

8. PROCEDURES APPLICABLE TO ARRIVAL AT U.S. PORTS.

a. Public health quarantine procedures are required for ships which, in the last 15 days prior to arrival in the U.S. or since departure from the last U.S. port (whichever period is shorter) have or have had any passengers or crew on board with the following conditions or illness:

(1) Has a temperature of 100°F (38°C) or greater accompanied by a rash, glandular swelling, or jaundice, or which has persisted for more than 48 hours.

(2) Has diarrhea, defined as the occurrence in a 24-hour period of three or more loose stools or of a greater than normal (for the person) amount of loose stool.

(3) Death due to illness other than battle causalities or physical injuries.

b. When one or more of the above conditions exist, the commanding officer of a ship, or senior officer of a group of ships will, between 12 and 72 hours prior to arrival, forward a radio report or message of conditions to the senior naval officer in command at the port of arrival. For ships of the other Armed Forces, the report will be sent to such

authority as appropriate and to the local port authority. Send information copies to the military quarantine inspector and to the responsible local preventive-medicine/public-health service in the port area. A reply confirming receipt of the radio message or report will be made if circumstances indicate and will contain applicable quarantine instructions. Unless otherwise indicated in the reply, a ship may proceed directly to berth and begin normal business activity. This quarantine procedure does not exempt a ship from control measures or public health inspection subsequently deemed necessary, or from the requirements of other Government agencies. When illness is reported or if the ship has been in a plague-infected country, appropriate inspections may be required.

…

11. QUARANTINE PROCEDURES FOR AIRCRAFT ARRIVING IN FOREIGN COUNTRIES.

a. When flights are contemplated to foreign countries or landing is to be made at any airport not under Armed Forces jurisdiction, the aircraft commander will abide by the medical and agricultural quarantine regulations published for landing at the airport concerned. (See USAF Foreign Clearance Guide, AFR 8-5, and OPNAVINST 3710.2E for individual country requirements.)

b. Commanders of Armed Forces installations located in foreign countries will publish local directives to assure that agricultural and public health quarantine requirements and procedures of the host country are observed by arriving aircraft. Overseas commanders will recommend changes to AFR 8-5 if indicated. Suggested changes to AFR 8-5 must be sent to HQUSAF/XOXXG, Washington, DC 20330.

12. QUARANTINE RESPONSIBILITIES OF AIRCRAFT COMMANDERS.

a. AR 40-562/NAVMEDCOMINST 6230.3/AFR 161-13/CGCOMDTINST M6230.4D, paragraph 2, task port commanders with the responsibility for ensuring that travelers meet the immunization requirements for the areas to which they are traveling.

b. On each flight to the United States, its territories, commonwealth, or possessions, when illness has occurred characterized by the signs and symptoms in paragraph 8a(1) and (2), the aircraft commander will send a radio message requesting an inspection by the military or public health quarantine inspectors. The request should be made at the earliest feasible time at which contact can be made with the airport of arrival. Upon landing, all persons must be placed in a suitable isolation area by the aircraft commander until released by designated Armed Forces quarantine personnel. SECTION-III IMPORTANCE OF PLANTS, PLANT PRODUCTS, SOIL, PLANT PESTS, BIRDS, ANIMALS, ANIMAL PRODUCTS, GARBAGE, AND INFECTIOUS AGENTS

…

17. GENERAL. The entry into the United States, its territories, commonwealths, and possessions of certain items specified in paragraphs 21 and 22 and their means of conveyance is prohibited or restricted by regulations and instructions administered by the USDA; Customs Service of the U.S. Treasury Department, the U.S. Public Health Service (USPHS), the Food and Drug Administration, U.S. Department of Health and Human Services (USDHHS); and the U.S. Department of Interior. (The movement of such materials and their means of conveyance from Hawaii, Puerto Rico, the United States Virgin Islands, Guam, or other U.S. territories and commonwealths to other parts of the United States is prohibited or restricted in various ways by regulations administered by the USDA (sec. IV).) These regulations and instructions are designed to prevent the introduction and dissemination of human, plant, and animal diseases, and vectors and pests of medical or agricultural importance, and the introduction of prohibited or illegally taken wildlife.

…

Section V. INTERSTATE MOVEMENT OF ETIOLOGIC AGENTS.

27. GENERAL. The interstate movement within the United States of etiologic agents is regulated by section 72.3, part 72, title 42, Code of Federal Regulations of the United States Public Health Service (USPHS) Regulations. These regulations are designed to prevent the spread of disease from one State to another. The USPHS enforces these regulations and the State health departments cooperate in this activity. Military commanders will establish and maintain liaison as needed with the USPHS and the following regional offices: ….

28. ETIOLOGIC AGENTS.

a. For the purpose of this section, an etiologic agent is defined as a viable microorganism or its toxin which causes or may cause human disease. These include bacterial, fungal, viral, rickettsial, and chlamydial agents. A complete listing of the etiologic agents is contained in section 72.3 of part 72, title 42, Code of Federal Regulations.

b. Packaging, labeling, and shipment requirements applicable to the transportation of etiologic agents in interstate commerce are also contained in section 72.3 of part 72, title 42, Code of Federal Regulations. An etiologic agent/biomedical material label, issued by the Centers for Disease Control, will be attached to each package or container of a shipment made within the United States. This label is stocked by the Defense Personnel Support Center, Medical Material Directorate, 2800 South 20th Street, Philadelphia, PA 19101, as a medical stock item NSN 7690-00-082-9705. The packaging procedures outlined for importing etiologic agents in paragraph 19a(3) apply to interstate shipments.

c. Additional instructions and regulations may be obtained by communicating directly with the appropriate Surgeon General; the Director, Centers for Disease Control,

Attention: Office of Biosafety, Atlanta, GA 30333; or with the nearest Public Health Service regional office.

d. Each service of the Armed Forces will implement policy on the preparation and forwarding of annual reports from respective activities under the permit to Director, Centers for Disease Control, Attention: Office of Biosafety, Atlanta, GA 30333.

APPENDIX C-13
Glossary of Infection-Control Terms.

Airborne Infectious Isolation Room (AIIR): Rooms designed with special air-handling and ventilation to reduce the risk of airborne transmission of infectious agents.

Cohorting: Placing of patients with the same illness but no other transmission-based infections in rooms together, considering other relevant factors (e.g., age, sex, room size, staffing patterns).

Cordon Sanitaire (sanitary barrier). Concentric levels of quarantine to restrict movement of individuals and conveyances between communities, to control the spread of disease.

Disaster Medical Assistance Team (DMAT). Personnel designated to assist in providing triage, patient care, medical or surgical stabilization, and continued monitoring until patients can be evacuated to other locations for definitive care.

Etiologic Agent. A viable micro-organism or its toxin that causes or may cause human disease. These include bacterial, fungal, viral, rickettsial, and chlamydial agents (see 42 CFR 72.3 for complete list of etiologic agents).

Heating-Ventilation-Air-Conditioning (HVAC). Air handler or air handling unit.

High Efficiency Particulate Air (HEPA) Filter Unit. Air-filtering unit that is 95% to 99.97% efficient in removing particles with a diameter of 0.3 microns or more.

Infection-Control Risk Assessment (ICRA). The facility-specific assessment of bioterrorism response, readiness and containment.

Isolation. The separation of an infected person or group of infected people from other uninfected people to prevent the spread of infection.

Negative Airflow Rooms. A “containment space” or “negative isolation room” used for activities that produce vapors, odors or microorganisms that must not be allowed to escape into adjacent areas. To accomplish this, the space is maintained under negative pressure, causing air to flow continuously *into* the space from adjacent areas.

Personal Protective Equipment (PPE). Equipment designed to protect employees from serious workplace illness or injury resulting from contact with chemical, biological, radiological, physical, or other workplace hazards. PPE includes a variety of devices and garments, such as goggles, coveralls, gloves, vests, and respirators.

Positive Airflow Rooms. A “clean-room” or “positive isolation room” used for activities requiring absence of dust particles and other airborne contaminants. To prevent particulate matter or infectious organisms from entering the space, the room must be

positively pressurized, forcing air to flow continuously *out* of spaces around doors and windows and other small openings in the walls and ceiling of the room.

Quarantine. The restriction of activities or limitation of freedom of movement of those presumed or potentially exposed to a communicable disease, to prevent contact with people not exposed. Although quarantine measures may be instituted and enforced for either individuals or populations, the term is used more frequently to discuss measures taken at the population level.

Regulated Medical Waste (RMW). Any of the following waste generated in the diagnosis, treatment, or immunization of human beings or animals, in research pertaining thereto, or in production and testing of biologicals, provided however, that RMW shall not include hazardous waste identified or listed pursuant to Section 27-0903 of the Environmental Conservation Law, or any household waste promulgated under this section. Six subcategories exist within the general definitions of regulated medical waste. The last subcategory provides for the Commissioner of Health to designate specific items that previously have not been considered as regulated medical waste. As no items have yet to be added to this subcategory, the remaining five are considered to be part of the current working definitions of regulated medical waste. They are:

- Cultures and Stocks. "This waste shall include cultures and stocks of agents infectious to humans, and associated biologicals, cultures from medical or pathological laboratories, cultures and stocks of infectious agents from research and industrial laboratories, wastes from the production of biologicals, discarded live or attenuated vaccines, or culture dishes and devices used to transfer, inoculate or mix cultures."

- Human Pathological Wastes. "This waste shall include tissue, organs, and body parts (except teeth and the contiguous structures of bone and gum), body fluids that are removed during surgery, autopsy, or other medical procedures, or specimens of body fluids and their containers, and discarded material saturated with such body fluids other than urine, provided that the Commissioner, by duly promulgated regulation, may exclude such discarded material saturated with body fluids from this definitions if the Commissioner finds that it does not pose a significant risk to public health. This waste shall not include urine or fecal materials submitted for other than diagnosis of infectious diseases."

- Human Blood and Blood Products. "This waste shall include: (I) discarded waste human blood, discarded blood components (e.g. serum and plasma), containers with free flowing blood or blood components or discarded saturated material containing free flowing blood or blood components; and (II) materials saturated with blood or blood products provided that the commissioner, by duly promulgated regulation, may exclude such material saturated with blood or blood products from this definitions if the commissioner finds that it does not pose a significant risk to public health."

- Sharps. "This waste shall include but not be limited to discarded unused sharps and sharps used in animal or human patient care, medical research, or clinical or pharmaceutical laboratories, hypodermic, intravenous, or other medical needles, hypodermic or intravenous syringes to which a needle or other sharp is still attached, Pasteur pipettes, scalpel blades, or blood vials. This waste shall include, but not be limited to, other types of broken or unbroken glass (including slides and cover slips) in contact with infectious agents. This waste shall not include those parts of syringes from which sharps are specifically designed to be easily removed and from which sharps have actually been removed, and which are intended for recycling or other disposal, so long as such syringes have not come in contact with infectious agents."

- Animal Waste. "This waste shall mean discarded materials including carcasses, body parts, body fluids, blood, or bedding originating from animals known to be contaminated with infectious agents (i.e. zoonotic organisms) or from animals inoculated during research, production of biologicals, or pharmaceutical testing with infectious agents."

Respiratory Protection Program. Program that includes medical clearance of personnel likely to be called on to wear a NIOSH-approved fit-tested N95 particulate respirator and appropriate occupational record-keeping. These programs will comply with OSHA standard 1910.134.

Synchronous Rash. Lesions all at same state of development on face, forearms, hands (including palms) that may have spread to legs (including soles of feet) and/or trunk.

Type C (Contagious) Facility. A structure with non-shared ventilation system, controlled access, adequate utilities, two-way communication system, and the ability to provide medical care.

Type X (Uncertain) Facility. The same isolation and general supply requirements as Type C facilities, but only basic medical services provided.

Type R (Residential) Facility. A person’s own home. If contacts without symptoms cannot be housed in their own residence due to logistical or other reasons, establish alternate Type R facilities in designated barracks, recreation centers, guest houses, or similar facilities with sleeping accommodations and utilities.

ANNEX D TO SMALLPOX RESPONSE PLAN 29 September 2002
SPECIMEN-COLLECTION & TRANSPORT GUIDELINES.

REFERENCES.

a. CDC Smallpox Response Plan, Guide D, Specimen Collection and Transport Guidelines, 23 Sep 02.
http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideD/Guide-D.doc.

b. CDC Laboratory Response Network (LRN). Protocol for Interim Guidelines for Collection and Shipment of Specimens from Suspected Smallpox Patients, 15 Apr 02.

1. General. This DoD Annex augments CDC Guide D. Appendix D-1 summarizes CDC Guide D and this DoD Annex on one page.

a. Mission. Military medical treatment facility (MTF) clinical laboratories participate in the Laboratory Response Network (LRN), a collaborative effort of the Centers for Disease Control & Prevention (CDC) and the Association of Public Health Laboratories (www.bt.cdc.gov/LabIssues/index.asp). These laboratories maintain personnel trained to process clinical-microbiology specimens and detect suspicious microbes that might indicate use of bioterrorism agents. Accordingly, they will follow CDC guidance for collecting and processing specimens. MTFs will be prepared to collect and ship clinical specimens for further laboratory evaluation, as specified in this annex.

b. Assumptions. Not applicable.

c. Planning Factors.

(1) MTF clinical laboratories are designated as Level A and Level B laboratories within the LRN (see also Appendix D-2).

(2) Recommended procedures at various biosafety levels are described in Appendix D-3.

d. Coordinating Instructions. With a suspected case of smallpox, inform command channels as soon as possible. MTF headquarters will promptly submit a Serious Incident Report to their higher headquarters and report to other public-health authorities, as specified in Annex A. After consultation with the CDC, the MTF will arrange the collection of appropriate samples for testing by CDC, the US Army Medical Research Institute of Infectious Diseases (USAMRIID), or another member of the LRN designated by the CDC. If the case is considered high risk for smallpox, no additional clinical specimens will be collected from that person for testing within the hospital or clinic laboratory. CDC or the local MTF will notify the Federal Bureau of Investigation (FBI), so

the FBI can arrange for transport of the specimen(s) to the LRN laboratory designated by the CDC.

e. Legal Considerations. Early in a smallpox outbreak, maintain a chain-of-custody record for critical specimens, to allow for their use as forensic evidence of the use of a bioweapon.

(1) Environmental or clinical specimens submitted to LRN laboratories by law-enforcement agents will be delivered with a chain-of-custody record. The receiving laboratory will sign the record, and the form will stay with the materials and culture until the specimen is signed over to a referral laboratory or back to authorized law-enforcement personnel. If neither of these events occurs, the laboratory will keep the chain-of-custody record on file.

(2) If a Level A laboratory isolates a suspicious culture and refers it to a Level B laboratory for confirmation, the Level A laboratory will initiate a chain-of-custody form to accompany the referred culture to the Level B laboratory. The Level A laboratory will sign over the referred culture either to the laboratory shipping section for packaging and shipment or to a law-enforcement agent charged with delivering the specimen to the next laboratory.

2. Execution.

a. Concept of Operations. Training providers in identification of smallpox cases is a key requirement to ensure MTFs can identify, collect specimens, and confirm cases. In a case where smallpox is considered possible, notify local infectious-disease, dermatology, or other medical experts as soon as possible to determine if the case warrants a smallpox laboratory work-up. Once CDC is notified, their Rapid Response and Advanced Technology Laboratory may send a team to assist. If CDC decides not to send a team, but further laboratory confirmation is warranted, then a specimen-collection team identified by the MTF commander and trained in smallpox collection techniques should collect these specimens. At no time should a health-care provider request the MTF laboratory undertake isolation or identification of variola virus (smallpox). Smallpox virus is a biosafety level 4 (BSL-4) agent (Appendix D-3). Avoid any possibility of viral spread to the general population. In the future, CDC will recognize specific BSL-3 laboratories with the capability to identify smallpox virus. It is not appropriate to perform laboratory tests outside strict containment conditions to rule out any other virus in a suspected smallpox case. Instead, the CDC will receive the specimens and perform the testing. The CDC is the primary site for all smallpox testing. The US Army Medical Research Institute of Infectious Diseases (USAMRIID) is a backup facility in case of surge demand for smallpox testing. CDC will coordinate with USAMRIID if it needs assistance.

b. Tasks and Responsibilities.

(1) MTF Commander:

(a) The MTF commander is responsible for training health-care providers on the symptoms for smallpox and notification procedures for a suspected smallpox case.

(b) The MTF commander is responsible for providing a smallpox specimen-collection team with necessary supplies (Appendix D-4). As smallpox vaccinations resume, these collection teams will be provided smallpox vaccination. Team members will use proper personal protective equipment in the course of their duties.

(c) The MTF Commander is responsible for ensuring that the clinical laboratory is trained and qualified to provide proper shipping of smallpox specimens, and that the pathology department is able to safely remove cadavers with suspected or known smallpox infection.

(2) The initial health-care provider: Any provider who suspects a diagnosis of smallpox in a patient will notify the MTF commander immediately (Annex A). The MTF will implement infection-control measures consistent with Annex C.

(3) Specimen-Collection Team. Each MTF will appoint and train a smallpox specimen-collection team. Appendix D-5 below specifies in detail the procedures for the collection and shipment of specimens from suspected smallpox patients. These teams will document training in procedures identified in Appendix D-5.

(a) Only personnel successfully vaccinated against smallpox within the previous 3 to 10 years and wearing appropriate barrier protection (e.g., gloves, gown, shoe covers, protective eyewear) will be involved in specimen collection for suspected cases of smallpox. Masks and eyewear or face shields should be used if splashing is anticipated.

(b) If unvaccinated personnel must collect specimens, use only those without contraindications to vaccination, as they would require prompt vaccination if the diagnosis of smallpox is confirmed. Fit-tested N95 masks should be worn by unvaccinated individuals caring for suspected patients.

(c) These teams will document training in specimen-collection procedures. MTFs will document periodic competency assessment (e.g., quarterly) and confirmation of adequate smallpox specimen-collection supplies and protective equipment.

(4) The Laboratory Medical Director, Department of Pathology, will ensure that laboratory personnel responsible for shipping specimens are trained on shipping procedures and maintain inventories of proper shipping supplies (Appendix D-6, Appendix D-7). The laboratory must have a person trained and certified in shipment of hazardous substances including infectious-disease shipping. This person must be recertified every 2 years. The US Army Center for Health Promotion and Preventive Medicine (USACHPPM) provides such training (“Transport of Biomedical Materials"), as may other Services or Agencies. Information on this training is provided on the CHPPM

web page at http:/chppm-www.apgea.army.mil/TrainCon/datePage.aspx. The Medical Director is also responsible for following guidelines in Appendix D-5 for collecting and disposing of autopsy specimens, as well as transporting an autopsy cadaver.

c. Reporting**.** Will be performed as indicated in Annex A, as well as via Serious Incident Reports through command channels.

3. Administration and Logistics.

a. Supply and Storage. The MTF will maintain a smallpox specimen-collection kit at all times, inspected at least every six months to ensure no items have outdated. Materials required for specimen collection from each patient are listed in Appendix D-4.

b. Equipment. The MTF will provide fit-tested NIOSH-approved N-95 masks or higher or HEPA-filtered respirators to personnel designated as part of the smallpox specimen-collection teams. See also Annex C.

c. Air Transportation. MTFs will support transportation of smallpox specimens (biological agents), coordinated with the FBI, according to International Air Transport Association (IATA) guidelines. A copy of the Dangerous Goods Regulations (DGR) can be obtained by calling 1-800-716-6326 or through the Internet at www.iata.org or www.who.int. Biological agents are considered hazardous materials and their transportation is subject to regulatory control. Appendix D-5 directs the detailed procedures for packaging possible smallpox samples. A designated person in the MTF laboratory must be certified in infectious-disease shipping. Prior coordination is required with personnel at the local Transportation Office or the Air Transportation Operations Center (ATOC) to ensure shipping requirements are followed for movement by military air or ground transportation. See also Appendix D-6 for additional regulations.

d. Maritime Transportation. Maritime shipping of hazardous agents is covered by the International Maritime Dangerous Goods Code (incorporating Amendment 30-00). This document is published by the International Maritime Organization (www.imo.org/home.asp).

4. Command, Control, & Communications. Communication about a suspected smallpox case cannot be delayed. Notification of higher headquarters is required. If at anytime an MTF Level A laboratory has difficulty in communicating to a civilian laboratory, they should notify their regional Level B laboratory for assistance.

5. Special Situations.

a. Specimen collection in U.S. European Command (EUCOM). Landstuhl Regional Medical Center (LRMC) has a BSL-3 laboratory. A microbiologist there is trained on CDC LRN procedures and guidelines. This person can assist with specimen collection, transportation, and notification of the Department of State and the FBI, for further shipment to an LRN laboratory designated by the CDC. Additionally the Technical

Escort Unit (TEU) may be available for sample transport. Coordination with the TEU flows from the MTF commander to the Unified Command Surgeon's Office.

b. Specimen collection in U.S. Pacific Command (PACOM). Tripler Army Medical Center currently has a BSL-2 laboratory, with BSL-3 capabilities planned for FY03. A microbiologist there is trained on CDC LRN procedures and guidelines. This person can assist with specimen collection, transportation, and notification of the Department of State and the FBI, for further shipment to an LRN laboratory designated by the CDC. Additional, the Navy Environmental & Preventive Medicine Unit—6 (NEPMU-6) at Pearl Harbor has a BSL-2 laboratory and can also support processing suspicious samples/substances.

c. Troops deployed outside CONUS in a theater in conflict. Field Medical Facilities should inform their command of any suspected smallpox case. Isolate this patient from unvaccinated people. If the theater is near to a fixed MTF with an LRN laboratory, that MTF will provide assistance. If this is not feasible, the Command Surgeon for that theater should develop an appropriate detailed concept of operations for biological threat agents in the medical annex. A designated Army Special Medical Augmentation Response Teams (SMART), Air Force Infectious Disease Team (ID Team), or other Service equivalent teams may be able to provide collection and shipping capabilities. Deployable assets such as the Theater Army Medical Laboratory (TAML), the Navy Forward Deployed Laboratory, or the Air Force Biological Augmentation Team (BAT), and special theater or regional fixed-site laboratories such as those supporting bio-identification for biosensor systems are options for theater operations.

APPENDIX D-1
Specimen Collection -- Summary

1. Laboratories at military treatment facilities (MTFs) belong to either level A or level B of the Laboratory Response Network (LRN), coordinated by the Centers for Disease Control & Prevention (CDC) (Appendix D-2). Levels refer to the level of technical capability at that laboratory.

2. Each MTF will periodically train its laboratory staff in the collection, handling, and shipping of possible smallpox-infected specimens at least once a year (Appendix D-5, Appendix D-6, Appendix D-7).

3. MTFs will maintain a supply of shipping materials suitable for shipping smallpox-infected specimens (Appendix D-4).

4. All specimens will be shipped to a member of the LRN designated by CDC. The Federal Bureau of Investigation (FBI) oversees shipments of possibly smallpox-infected specimens.

5. Early in a smallpox outbreak, collect specimens with preservation of forensic evidence in mind. Maintain a chain-of-custody record for critical specimens.

6. Overseas laboratories (e.g., Landstuhl, Tripler, NEPMU-6) can provide support.

APPENDIX D-2
Levels in the Laboratory Response Network (LRN).

1. Level A Laboratories – Standard clinical laboratories. Bio-Safety Level 2 (BSL-2). Typical roles: detect early (presumptive cases) of disease, minimal identification of agents. Rule-out or Refer. Role vis-à-vis smallpox—None.

2. Level B Laboratories – Reference laboratories (e.g., state health departments, larger military medical centers). Bio-Safety Level 2 or 3 (BSL-2 or -3). Typical roles: perform identification, confirmation, and susceptibility testing. Isolate. Rule-in and Refer. Role vis-à-vis smallpox—None.

3. Level C Laboratories – Reference laboratories (e.g., CDC, Armed Forces Institute of Pathology, large facilities laboratories with advanced capacity for testing, some molecular technologies). Bio-Safety Level 3 (BSL-3). Typical roles: rapid identification. Rule-in and Refer. Role vis-à-vis smallpox—In future, at BSL-3.

4. Level D Laboratories – Bio-Safety Level-4 Laboratories (i.e., CDC, USAMRIID). Typical roles: high-level characterization, special surge capacity and advanced molecular typing techniques. Probe for universe of agents. Role vis-à-vis smallpox—definitive diagnosis.

Source: Centers for Disease Control & Prevention, www.bt.cdc.gov/LabIssues/index.asp.

APPENDIX D-3
Recommended Biosafety Levels for Infectious Agents

BSL	Agents	Practices	Safety Equipment (Primary Barriers)	Facilities (Secondary Barriers)
1	Not known to consistently cause disease in healthy adults	Standard Microbiological Practices	None required	Open bench top sink required
2	Associated with human disease, hazard = percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers = Class I or II Biological Safety Cabinets (BSCs) or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials; personal protective equipment (PPE): laboratory coats; gloves; face protection as needed	BSL-1 plus: Autoclave available
3	Indigenous or exotic agents with potential for aerosol transmission; disease may have serious or lethal consequences	BSL-2 practice plus: • Controlled access • Decontamination of all waste • Decontamination of lab clothing before laundering • Baseline serum	Primary barriers = Class I or II BSCs or other physical containment devices used for all open manipulations of agents; PPEs: protective lab clothing; gloves; respiratory protection as needed	BSL-2 plus: • Physical separation from access corridors • Self-closing, double-door access • Exhausted air not recirculated • Negative airflow into laboratory
4	Dangerous/exotic agents which pose high risk of life-threatening disease, aerosol-transmitted lab infections; or related agents with unknown risk of transmission	BSL-3 practices plus: • Clothing change before entering • Shower on exit • All material decontaminated on exit from facility	Primary barriers = All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure personnel suit	BSL-3 plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum, and decontamination systems • Other requirements outlined in the text

Source: Department of Health & Human Services. Biosafety in Microbiological and Biomedical Laboratories, 4th ed, May 1999. http://bmbl.od.nih.gov/

APPENDIX D-4
Supplies Needed for Specimen Collection.

Some or all of the following materials will be required for specimen collection from each patient.

- Disposable protective latex or vinyl gloves (sterile gloves not required)
- Disposable protective gowns
- NIOSH-approved N-95 masks or higher properly fitted HEPA-filtered respirators (see below)
- Protective eyewear
- Shoe covers
- Biohazard plastic disposable bags
- Rigid ("sharps") container(s)
- Disposable scalpel with No. 10 blade
- Several sterile 26-gauge needles
- 3.5 or 4 mm punch biopsy kit
- Needle driver
- Suture
- Suture removal kit
- 4 to 8 sterile dry polyester or cotton swabs
- 4 clean plastic or glass microscope slides
- 4 plastic single-slide holders
- 2 or more electron microscopy grids
- Electron microscopy quality forceps
- Electron microscopy grid box
- Eight 1.5 to 2.0 ml sterile screw-capped plastic vials (Sarstedt with o-ring)
- 5 or 10 ml syringe with 18- or 20-gauge needle
- 1 Vacutainer holder
- 2 Vacutainer needles (20 gauge, 1½ inch)
- One 10 ml marble-topped Vacutainer tubes, **or** one 10 ml yellow-topped serum-separator tube for serum collection (plastic tube preferable)
- One 5 ml purple-topped tubes for whole blood buffy-coat collection for viral isolation (plastic tube preferable)
- Parafilm

APPENDIX D-5
Specimen Collection Procedures.

1. General Considerations.

a. Because of the risk of breakage, avoid glass containers whenever possible. Use plastic vials, bottles, or slide holders as the primary container for all specimens.

b. Each patient's lesion specimens must be packaged separately from other patient specimens to avoid cross-contamination.

c. All procedures involving handling potentially infectious material should be performed in laboratories utilizing Biosafety Level 2 or 3 practices. Any activity that brings hands or fingers in contact with mucosal surfaces, such as eating, drinking, smoking, or applying make-up should be avoided. Thorough hand-washing using soap or soap containing Lysol or soaps such as *Hibiclens* should be done before leaving the laboratory. Areas of the skin known to have come in contact with virulent variola or monkeypox virus should be washed with soap and decontaminated with 0.5% sodium hypochlorite with at least a 1 minute contact time. Administration of smallpox vaccination, and possibly VIG, should be determined in coordination with CDC.

d. In the event of a large outbreak of confirmed smallpox, other laboratories with smallpox diagnostic capabilities may used to meet diagnostic surge demand. CDC will designate these laboratories. Instructions for sending specimens to these laboratories will be given at the time of their designation.

2. Specimen-Collection Procedure for Patients with Vesicles or Pustules. Blood samples from people with severe, dense smallpox rash may be difficult to draw, as the skin may slough off. A central line may be needed for access, in cases where a peripheral blood draw is difficult.

a. Put on protective equipment described above

b. Use scalpel (or a sterile 26-gauge needle) to open, and remove, the top of the vesicle or pustule and place the skin of the vesicle top into a 1.5-2 mL screw-capped plastic tube. Allow the material to dry. Label the tube as outlined below**.**

c. Scrape the base of the vesicle or pustule with the blunt edge of the scalpel, or with the wooden end of an applicator stick or swab and do the following:

(a) Apply a microscope slide to the vesicular fluid multiple times, with progressive movement of the slide, to make a touch prep.

(b) Allow the fluid to air-dry for 10 minutes, without smearing.

(c) Label the slide as outlined below.

(d) Store the dried slide in a plastic slide container

(e) Store slides in plastic slide holders for shipping. Parafilm may be used to wrap the slide holder to prevent accidental opening. Store slides from different patients in separate plastic slide holders to prevent cross contamination.

(f) If a slide is not available, swab the base of the lesion with a polyester or cotton swab, place in a screw-capped plastic vial, break off applicator handle, and screw on lid. Do not add transport medium to the vial. Label the container as outlined below.

d. If available, lightly touch an electron microscope grid to the unroofed base of the lesion and allow to air dry. Repeat this procedure two more times, varying the pressure applied to the unroofed lesion (lighter or firmer pressure). Place in grid box and record which slot is used for each patient specimen.

e. Biopsy two vesicles with 3.5 or 4 mm punch biopsy kit.

(1) Place one biopsy specimen in formalin.

(2) Place one biopsy specimen in a 1.5-2 mL screw-capped container. Do not add any fluid.

(3) Label the containers as outlined below.

f. Draw 10 ml of blood into a plastic marble-topped tube, or a plastic yellow-topped serum-separator tube. Label the tube as outlined below and place in collection bag. If plastic tubes are not available:

(1) Draw blood into a glass marble-topped or yellow-topped serum-separator

(2) Label glass tube as outlined below and place glass tube into a Styrofoam protector for packaging and shipping.

g. Test in Validation: Swab or brush posterior tonsillar tissue, then break off end of applicator into a 1.5-2 mL screw-capped tube. Do not add transport medium. Label the tube as outlined below.

h. Test in Validation: Draw 5 ml of blood into plastic purple-topped tube. Gently shake the tube containing the blood to mix the tube contents and prevent clotting of blood. Label the tube as outlined below and place in collection bag. If plastic tubes are not available:

(1) Draw blood into a glass purple-topped tube.

(2) Gently shake tube to mix the contents

(3) Label tube as outlined below and place in Styrofoam protector for packaging and shipping.

i. Label all samples as follows:

(1) Patient name.

(2) Date of collection.

(3) Source of specimen (vesicle, pustule, or scab).

(4) Social Security number or date of birth of patient (for cross-referencing specimens).

(5) Name or initials of person collecting specimen.

(6) If patient is hospitalized, include hospital identification number (e.g., surgical pathology number).

j. Place specimens from a single patient into a biohazard bag with an outside label that includes:

(1) Patient name.

(2) Date of collection.

(3) Social Security number or date of birth of patient.

k. Package specimens from a single patient (<u>except biopsies</u>):

(1) On gel packs at 4°C.

(2) In appropriate shipping containers in a manner to withstand shocks, pressure changes, or other conditions incident to ordinary handling in transportation.

(3) In a manner to avoid leakage of contents.

l. Package non-formalin lesion biopsy for shipping on dry ice, leave formalin-fixed biopsy at room temperature. DO NOT FREEZE formalin-fixed biopsy sample.

m. Specimens may be stored in conditions outlined above, if shipped within 24 hours of collection. If this is not possible, store samples on dry ice or at –20°C to -70°C until, and through, shipment. A key exception applies to electron microscope grids and

serum, which should remain at 4°C. If there will be a delay in shipping, spin serum to separate from clot, store at 4°C, and ship at 4°C.

n. Final instructions regarding transportation will be given at the time of consultation and may involve a personal escort carrier to ensure sample tracking and integrity.

o. After specimen collection is completed, all protective materials worn by the specimen collector (e.g., gloves, mask, gown) and all used sample collection materials (e.g., Vacutainer holders, swabs) must be placed in red biohazard bags and autoclaved or incinerated prior to disposal. Dispose of needles in an appropriate sharps container.

3. Specimen-Collection Procedure for Patients with Scab Lesions.

a. Put on protective equipment as outlined above and use a 26-gauge needle to pick or pry off between 4 and 10 scabs.

b. Place two scabs in each of two screw-capped plastic 1.5 to 2 mL vials.

c. Biopsy two lesions with 3.5 or 4 mm punch biopsy kit.

(1) Place one biopsy specimen in formalin

(2) Place one biopsy specimen in a 1.5 to 2 mL screw-capped container.

(3) Label the containers as outlined below.

d. Draw 10 ml of blood into a plastic marble-topped tube, or a plastic yellow-topped serum-separator tube. Label the tube as outlined below and place in collection bag. If plastic tubes are not available:

(1) Draw blood into a glass marble-topped or yellow-topped serum-separator tube.

(2) Label glass tube as outlined below and place glass tube into a Styrofoam protector for packaging and shipping.

e. Test in Validation: Swab or brush posterior tonsillar tissue, then break off end of applicator into a 1.5 2 mL screw-capped tube. Do not add transport medium. Label the tube as outlined below.

f. Test in Validation: Draw 5 ml of blood into plastic purple-topped tube. Gently shake the tube containing the blood to mix the tube contents and prevent clotting of blood. Label the tube as outlined below and place in collection bag. If plastic tubes are not available:

(1) Draw blood into a glass purple-topped tube.

(2) Gently shake tube to mix the contents.

(3) Label tube as outlined below and place in Styrofoam protector for packaging and shipping.

g. Label all samples as follows:

(1) Patient name.

(2) Date of collection.

(3) Source of specimen (vesicle, pustule, or scabs).

(4) Social Security number or date of birth of patient (for cross-referencing specimens).

(5) Name or initials of person collecting specimen.

(6) If patient is hospitalized, include hospital identification numbers (e.g., surgical pathology number).

h. Place specimens from a single patient into a biohazard bag with an outside label that includes:

(1) Patient name.

(2) Date of collection

(3) Social Security number or date of birth of patient.

i. Package specimens from a single patient (except for biopsies):

(1) On gel packs at 4°C.

(2) In appropriate shipping containers in a manner to withstand shocks, pressure changes, or other conditions incident to ordinary handling in transportation.

(3) In a manner to avoid leakage of contents.

j. Package non-formalin lesion biopsy specimens for shipping on dry ice. Package formalin-fixed biopsy specimens at room temperature. DO NOT FREEZE formalin-fixed biopsy samples.

k. Specimens may be stored in conditions outlined above, if shipped within 24 hours of collection. If this is not possible, store samples on dry ice or at –20°C to –70°C

(except for serum and formalin-fixed biopsy specimens). If there will be a delay in shipping, spin serum to separate from clot, store at 4°C, and ship at 4°C.

l. Final instructions regarding transportation will be given at the time of consultation and may involve a personal escort carrier to ensure sample tracking and integrity.

m. After specimen collection is completed, all protective materials worn by the specimen collector (e.g., gloves, mask, gown) and all used sample collection materials (e.g., Vacutainer holders, swabs) must be secured in red biohazard bags and autoclaved or incinerated prior to disposal. Needles should be disposed of in an appropriate sharps container.

4. Autopsy Specimens.

a. Freeze autopsy specimens for virus isolation, including portions of skin containing lesions, liver, spleen, lung, lymph nodes, and/or kidney. Ship these specimens on dry ice.

b. Formalin-fixed tissue is suitable for histopathology, immunohistochemistry and PCR, but should not be frozen and must be packaged separately from autopsy specimens for virus isolation (which must be frozen). All major organs (e.g., liver, spleen, skin, lung, lymph nodes, kidney) should be adequately sampled and submitted for evaluation.

c. Specimens should be labeled and packaged for transport as outlined above.

d. After specimen collection, all non-reusable specimen collection and barrier protection materials should be placed in red biohazard bags and autoclaved prior to disposal. All re-usable autopsy equipment must be autoclaved or disinfected according to standard laboratory procedures before re-use.

e. Extreme precautions are necessary to prevent dissemination of smallpox virus during an autopsy. Standard precautions should be observed for all contact with the body. Contact the CDC (NCID Division of Healthcare Quality Control at 404-498-1250 or Pathology Activity 404-639-3133) before an autopsy, to review the containment features of individual autopsy suites, procedures for autopsy, and disinfection after an autopsy. To transport the body to the autopsy suite, wrap the body in a large, impervious plastic bag, or a disaster pouch, sealed airtight with tape. The body should be sealed in a second large, impervious plastic bag before transportation to the autopsy suite. Ideally, the autopsy would be performed in a room with negative air pressure with respect to the surrounding facilities. All doors and windows of the autopsy rooms should be closed during the autopsy, and the air exhausted must not be recirculated. Only necessary personnel with up-to-date vaccination (within 3 to 10 years) should participate in the autopsy. Vaccinated personnel should wear disposable clothing, gowns, gloves, caps, booties, and masks and face shields or protective eyewear to prevent splashing of the mucus membranes. No personal clothing should be worn. All

clothing articles from the autopsy room should be placed in biohazard bags and autoclaved or incinerated. After autopsy, the body should be double-bagged in another set of large, impervious plastic bags. If vaccination before autopsy is not possible, unvaccinated personnel should perform the autopsy wearing, in addition to the protective garments above, respiratory protection (e.g., HEPA-filtered breathing apparatus or a self-contained breathing apparatus).

APPENDIX D-6
Specimen Shipping.

1. Guidelines for Packaging and Transporting Biological Agents.

a. Biological agents include infectious agents of humans, plants, and animals, as well as the toxins that may be produced by microbes and by genetic material potentially hazardous by itself or when introduced into a suitable vector. Etiologic agents and infectious substances are closely related terms that are found in the transfer and transportation regulations. Biological agents may exist as purified and concentrated cultures, but may also be present in a variety of materials such as body fluids, tissues, and soil samples. Biological agents and the materials known or suspected to contain them are recognized by federal and state governments as hazardous materials and their transportation and transfer is subject to regulatory control.

b. Transportation refers to the packaging and shipping of these materials by air, land, or sea, generally by a commercial conveyance. Transfer refers to the process of exchanging these materials between facilities.

2. Transportation. Regulations on the transportation of biological agents are aimed at ensuring that the public and the workers in the transportation chain are protected from exposure to any agent that might be in the package. Protection is achieved through:

a. the requirements for rigorous packaging that will withstand rough handling and contain all liquid material within the package without leakage to the outside,

b. appropriate labeling of the package with the biohazard symbol and other labels to alert the workers in the transportation chain to the hazardous contents of the package,

c. documentation of the hazardous contents of the package should such information be necessary in an emergency situation, and

d. training of workers in the transportation chain to familiarize them with the hazardous contents so as to be able to respond to emergency situations.

3. Regulations.

a. U.S. Public Health Service. 42 CFR Part 72. Interstate Transportation of Etiologic Agents. This regulation is in revision to harmonize it with the other U.S. and international regulations. http://www.cdc.gov/od/ohs/biosfty/shipregs.htm

b. U.S. Department of Transportation. 49 CFR Parts 171-178. Hazardous Materials Regulations. Applies to the shipment of both biological agents and clinical specimens. http://hazmat.dot.gov/rules.htm.

c. U.S. Postal Service. 39 CFR Part 111. Mailability of Etiologic Agents. Codified in the Domestic Mail Manual 124.38: Etiologic Agent Preparations. http://www.access.gpo.gov or www.usps.gov.

d. Occupational Health and Safety Administration (OSHA). 29 CFR Part 1910.1030. Occupational Exposure to Bloodborne Pathogens. Provides minimal packaging and labeling requirements for transport of blood and body fluids within the laboratory and outside of it. http://www.osha.gov/comp-links.html.

e. Dangerous Goods Regulations (DGR). International Air Transport Association (IATA). These regulations provide packaging and labeling requirements for infectious substances and materials, as well as clinical specimens that have a low probability of containing an infectious substance. These are the regulations followed by the airlines. These regulations are derived from the Committee of Experts on the Transport of Dangerous Goods, United Nations Secretariat, and the Technical Instructions for the Transport of Dangerous Goods by air that is provided by the International Civil Aviation Organization (ICAO). http://www1.iata.org/NR/ContentConnector/CS2000/SiteInterface/pdf/cargo/dg/43rev8April22.pdf.

f. Importation of Etiologic Agents of Human Disease. 42 CFR Part 71 Foreign Quarantine. Part 71.54 Etiologic Agents, Hosts and Vectors. This regulation requires an import permit from the Centers for Disease Control and Prevention for importing etiologic agents of human disease and any materials, including live animals or insects, that may contain them. An application and information on importation permits may be obtained by calling 1-888-CDC-FAXX and enter document number 101000 or via http://www.cdc.gov/od/ohs/biosfty/imprtper.html. See also http://www.unm.edu/~sheaweb/sheamanual/biosfty/biosaf_i.htm.

g. Importation of Etiologic Agents of Livestock, Poultry and Other Animal Diseases. 9 CFR Parts 92, 94, 95 96, 122 and 130. These regulations requires an import permit from the United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Veterinary Services to import or domestically transfer etiologic agents of livestock, poultry, other animals, and any materials that might contain these etiologic agents. Information may be obtained at (301) 734-3277, or from the Internet at: http://aphisweb.aphis.usda.gov/ncie.

h. Transfer of Select Biological Agents of Human Disease. Regulations on the transfer of biological agents are aimed at ensuring that the change in possession of biological materials is within the best interests of the public and the nation. These regulations require documentation of the personnel, facilities, and justification of need for the biological agent in the transfer process and subsequent approval of the transfer process by a federal authority. The following regulations fit in this category: 42 CFR Part 72.6 Additional Requirements for Facilities Transferring or Receiving Select Agents. Facilities transferring or receiving select agents must be registered with the CDC and

each transfer of a select agent must be documented. Information may be obtained on the Internet at: http://www.cdc.gov/od/ohs/lrsat.

i. Export of Etiologic Agents of Humans, Animals, Plants and Related Materials. Department of Commerce. 15 CFR Parts 730 to 799. This regulation requires that exporters of a wide variety of etiologic agents of human, plant and animal diseases, including genetic material, and products which might be used for culture of large amounts of agents, will require an export license. Information may be obtained by calling the DoC Bureau of Export Administration at 202-482-4811 or through the Internet at: http://bxa.fedworld.gov, or http://www.bxa.doc.gov.

APPENDIX D-7
Specimen Packaging.

1. General Packaging Requirements for Transport of Biological Agents and Clinical Specimens. Figures 1 and 2 illustrate the packaging and labeling of infectious substances and clinical specimens in volumes of less than 50 ml, in accordance with the provisions of subparagraph 72.3(a) of the regulation on Interstate Shipment of Etiologic Agents (42 CFR, Part 72). A revision is pending that may result in additional package labeling requirements, but this has not been issued in final form as of the publication of this fourth edition of *Biosafety in Microbiological and Biomedical Laboratories* (BMBL).

a. Figure 1 below shows the generalized "triple" packaging (i.e., primary receptacle, water tight secondary packaging, durable outer packaging) required for a biological agent of human disease or materials known or suspected of containing them. This packaging requires the "Infectious Substance" label shown in Figure 2 on the outside of the package. This packaging must be certified to meet rigorous performance tests as outlined in the DOT, USPS, PHS, and IATA regulations.

b. Clinical specimens with a low probability of containing an infectious agent are also required to be "triple" packaged, but performance tests require only that the package shall not leak after a 4-foot drop test. DOT, PHS, and IATA require a "clinical specimen" label on the outside of the package.

c. The shipper's name, address and telephone number must be on the outer and inner containers.

d. For additional information about proper use of dry ice, see 49 CFR parts 100-185 and the IATA Dangerous Goods Regulations.

e. For additional information about shipping paper requirements, see 49 CFR 172.200 and in Section 8 of the IATA Dangerous Goods Regulations.

2. Shipping suspected biological threat agents to the CDC.

a. Use the following address: Centers for Disease Control and Prevention, 1600 Clifton Road NE, ATTN: DASH (forward to RRAT Lab), Atlanta, GA 30333.

b. For shipping questions relating to sending specimens to the CDC, call (404) 639-3235.

Figure 1. Packing and Labeling of Infectious Substances

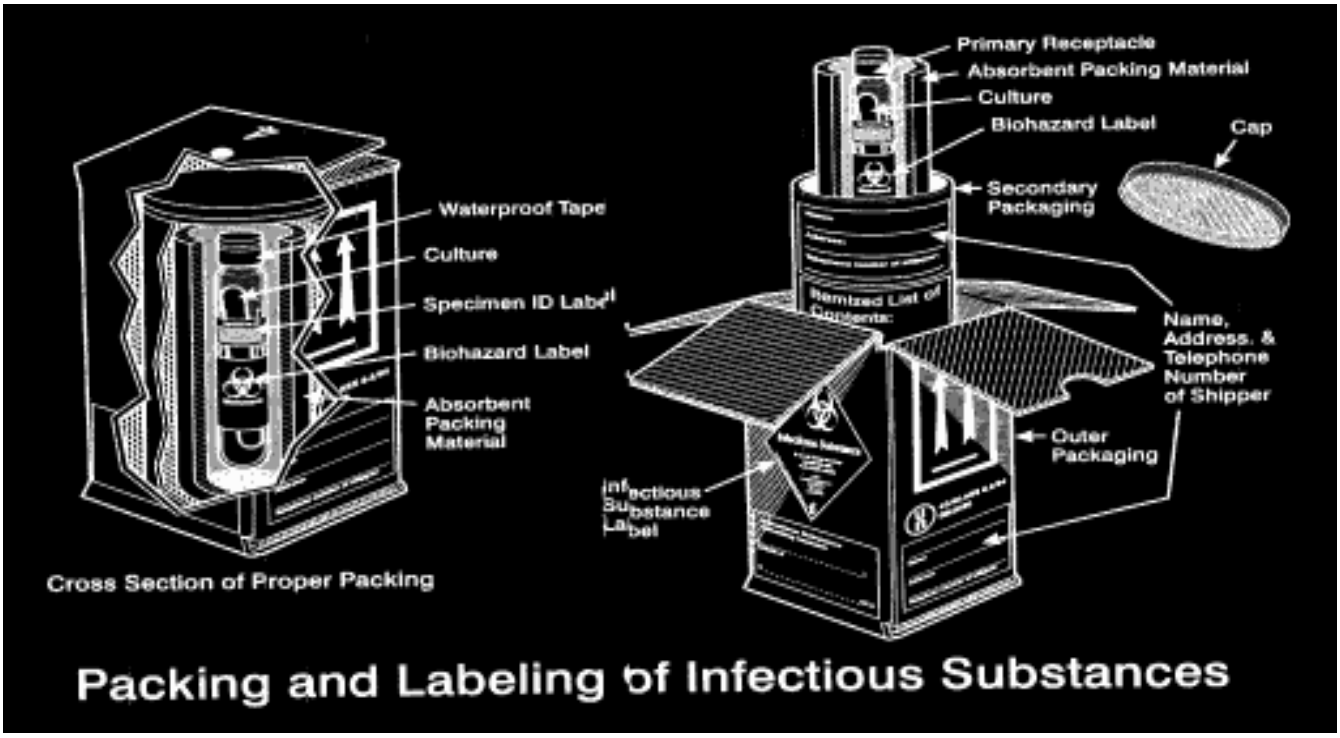
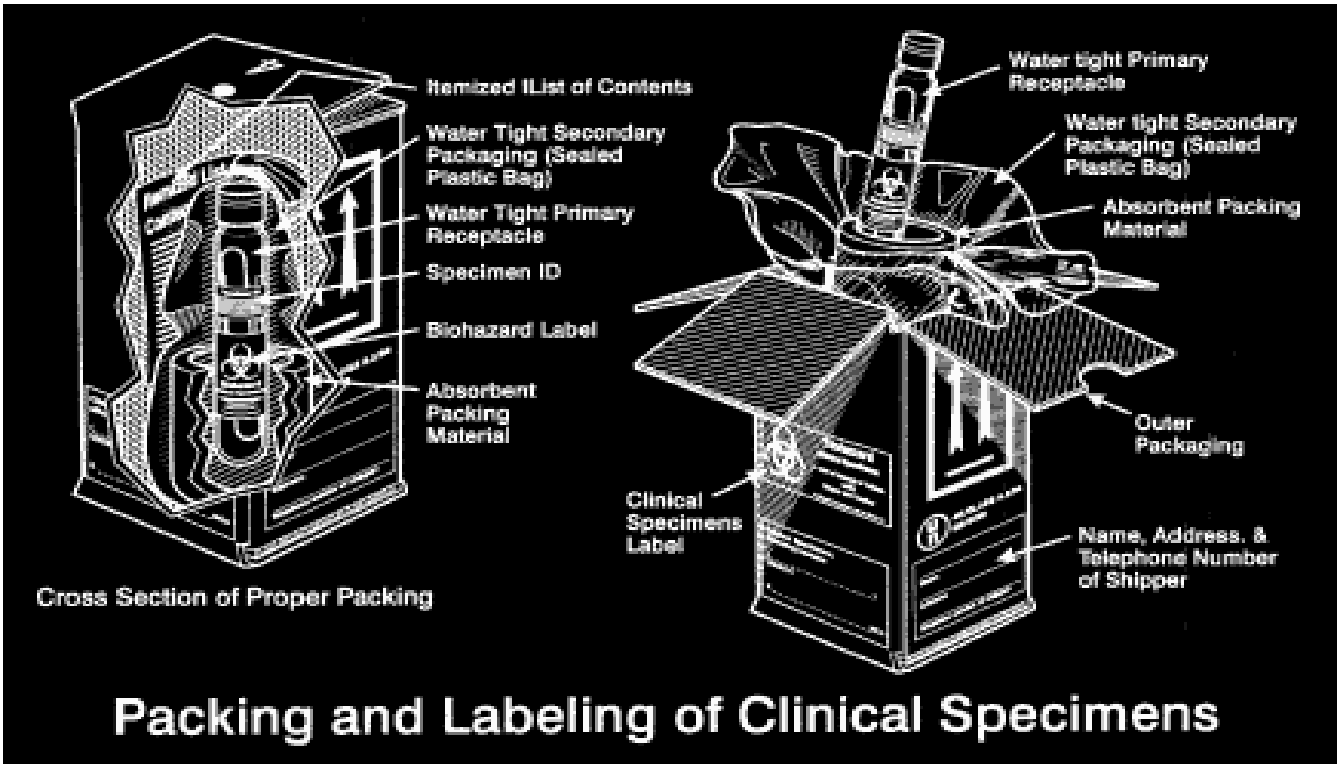


Figure 2. Packing and Labeling of Clinical Specimens



ANNEX E TO SMALLPOX RESPONSE PLAN 29 September 2002
COMMUNICATIONS PLANS AND ACTIVITIES.

REFERENCES.

a. CDC Smallpox Response Plan, Guide E, Communications Plans and Activities, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideE/Guide-E.doc.

b. United States Army. Army Crisis Communications Preparation Guide. Washington, DC: January 1999. http://www.dtic.mil/armylink/apac/Documents/crisiscommguide.pdf.

1. General. This DoD Annex implements reference a. Appendix E-1 summarizes CDC Guide E and this DoD Annex on one page.

a. Mission: Public affairs officers (PAOs) throughout DoD will use risk-communication principles as they inform and educate relevant audiences about smallpox infection, its symptoms, and consequences. PAOs will also educate relevant audiences about important health strategies to prevent and control smallpox (e.g., vaccination, contact tracing, isolation). Further, PAOs will support and augment the Centers for Disease Control & Prevention's Joint Information Center (JIC), to respond to media queries relating to military support to civilian authorities.

b. Assumption: The first suspected or confirmed case of smallpox will generate intensive local, regional, state, national, and international media interest. Dealing with a smallpox outbreak will require extensive communications activities among numerous government agencies.

c. Background: Reference a outlines CDC plans and activities before and after a smallpox outbreak. This document reflects CDC goal of synchronizing messages from federal agencies ("speaking with one voice"). Reference b provides suggestions for developing installation communications plans and stakeholder-involvement plans for dealing with emergency situations.

d. Coordination. PAOs will coordinate with representatives of the Lead Federal Agency during a smallpox outbreak.

2. Communications Objectives.

a. To instill and maintain public confidence in the DoD leadership's credibility, its healthcare system, and its ability to work in coordination with civilian authorities to respond to, and manage, a smallpox outbreak. Public messages from DoD will provide accurate, rapid, and complete information to educate, calm fears, and maintain public order.

b. To minimize, as much a possible, public panic and fear related to smallpox.

c. To rapidly provide the public, healthcare providers, policymakers, and the media access to accurate, consistent, and comprehensive information about smallpox, smallpox vaccine, and the management of the situation.

d. To address, as quickly as possible, rumors, inaccuracies, and misperceptions.

e. To provide accurate, consistent, and highly accessible information and materials through the coordination of communication efforts with other federal, state, and local partners.

3. Strategies.

a. Support timely and aggressive education for military members, DoD civilians, retirees, and their families about smallpox.

b. Ensure the public and media perceive that the military and public health systems are prepared for such contingencies and are working to treat those affected and to contain the disease. This would be demonstrated by establishing stakeholder-involvement plans before an outbreak.

c. Ensure all services have credible and trained spokespersons to answer media, Congressional, and public queries related to the military's support of the CDC's efforts.

d. Encourage media and other interested parties with questions to use DoD and CDC websites (e.g., www.bt.cdc.org).

e. Leverage all DoD communications tools and products to support the CDC's efforts and to educate the various publics.

f. Decentralize information to the lowest level, empowering local commands to provide answers to media and other public inquiries about the military's support of CDC's efforts as well as the military's handling of any cases that occur on military installations.

4. Communication Challenges and Threats. To address these challenges, specific communication tools have been and will be developed (Appendix E-2). The Military Vaccine Office will develop message maps to guide future communications.

a. Identifying source of outbreak.

b. The subtle differences between quarantine, isolation, and restriction of movement.

c. The purpose of contact tracing and surveillance.

d. Prioritization for immunization priorities.

e. Counteracting misinformation, controlling rumors and minimizing alarm.

5. Primary Audiences and Stakeholders.

a. U.S. military personnel, including active duty, reserve components, civilians and contractors.

b. Family members and other healthcare beneficiaries.

c. DoD leadership.

d. Congress and the Executive Branch.

e. Government civilian agencies that respond to terrorist events.

f. American public via public media.

6. Responsibilities:

a. Office of the Assistant Secretary of Defense (Public Affairs).

(1) Provide Public Affairs Guidance (PAG), including expected questions and answers.

(2) Respond to incoming media inquiries on DoD-wide policy issues.

(3) Coordinate media interviews with DoD personnel and subject matter experts.

b. Office of the Assistant Secretary of Defense (Health Affairs).

(1) Engage internal and external (third-party) experts to explain the science underlying DoD smallpox policies.

(2) Take action necessary to maintain public confidence in the DoD healthcare system, and its ability to work in coordination with civilian authorities to respond to and manage a smallpox outbreak.

(3) Address as quickly as possible, rumors, inaccuracies, and misperceptions by providing accurate, consistent, and highly accessible information and materials.

(4) Conduct education programs with targeted information products for Active and Reserve Components, DoD civilians, retirees and their families about smallpox and the smallpox vaccine

(5) Inform key executive and legislative branch leaders of DoD's operations, plans, and policies.

c. Services' Chief of Public Affairs Office.

(1) Prepare and distribute press releases, in coordination with DoD, if an outbreak develops and as it progresses. Additional involvement needed for outbreaks directly affecting military installations.

(2) Create and maintain an on-going crisis communications plan.

(3) Create and distribute PAG and other informational products as needed to Services' major commands and other subordinate units.

(4) Prepare advisories and respond to media queries.

(5) Train senior leadership to respond to smallpox interview questions.

(6) Post appropriate messages/articles about smallpox on the Service websites.

(7) Support smallpox education efforts in Service command information products and ensure all products include the CDC's website: www.bt.cdc.org.

d. Public Affairs Offices Supporting the Service Surgeons General.

(1) Provide PAG and all other products to Service Medical Department family PAOs, to assist in answering media queries.

(2) Encourage each Military Treatment Facility (MTF) commander to act as a media spokesperson and/or to identify a subject matter expert for local media queries.

(3) Coordinate with DoD agencies and CDC subject matter experts to respond to requests for interviews.

(4) Design or modify websites with smallpox information, updates, fact sheets, frequently asked questions and answers, and healthcare provider resources, including patient and public education materials. DoD's Military Vaccine Office is coordinating this work now, in advance of any outbreak.

(5) Monitor public media for articles and inform leadership of stories that have high impact on the medical department(s).

(6) Provide public-affairs advice to all agencies that request assistance.

e. Installation Public Affairs Offices.

(1) Identify PAO representatives to augment the CDC's Joint Information Center once established.

(2) Respond quickly and accurately to requests for information about the military's support of CDC.

(3) Use all available command information tools to educate the public on smallpox.

(4) Establish contact with the CDC's Field Communications Media Liaison, who will serve as the principal CDC media advisor in the field, and assist the CDC smallpox response team leader in serving, as appropriate, as a media spokesperson.

(5) Design or modify websites with smallpox information, updates, fact sheets, frequently asked questions and answers, and healthcare provider resources, including patient and public education materials. Support for this effort will come from DoD's Military Vaccine Office.

(6) Monitor public media for articles and inform leadership of stories that have high impact on the medical command.

(7) Provide public affairs advice to all agencies that request assistance.

f. Healthcare Providers: Augment their own knowledge of smallpox disease and smallpox vaccination, to ensure their ability to answer soldiers' questions and relieve anxiety.

APPENDIX E-1
Communications Plans and Activities – Summary.

1. The Office of the Assistant Secretary of Defense (Public Affairs) will:

   a. Provide Public Affairs Guidance (PAG), including questions and answers.
   b. Respond to incoming media inquiries on DoD-wide policy issues.
   c. Coordinate media interviews with DoD personnel and subject matter experts.
   d. Coordinate with Lead Federal Agency.

2. The Office of the Assistant Secretary of Defense (Health Affairs) will:

   a. Engage medical experts to explain the science underlying DoD smallpox policies.
   b. Address inaccuracies and misperceptions with accurate, consistent information.
   c. Conduct education programs with targeted information products.
   d. Inform key executive and legislative branch leaders of DoD's plans and policies.

3. Service Public Affairs Offices will:

   a. Prepare and distribute press releases.
   b. Create and maintain an on-going crisis communications plan.
   c. Create and distribute PAG and informational products commands and units.
   d. Prepare advisories and respond to media queries.
   e. Train senior leadership to respond to smallpox interview questions.
   f. Post appropriate messages or articles about smallpox on Service websites.
   g. Support smallpox education efforts in Service command information products.

4. Public Affairs Offices Supporting the Service Surgeons General will:

   a. Provide PAG and other products to Service Medical Department family PAOs.
   b. Encourage commanders to identify subject matter expert for media queries.
   c. Coordinate with DoD agencies and CDC experts to respond to requests.
   d. Design or modify websites to provide smallpox information.
   e. Monitor public media for articles and inform leadership of relevant stories.
   f. Provide public-affairs advice to all agencies that request assistance.

5. Installation Public Affairs Offices will:

   a. Identify PAO representatives to augment the CDC's Joint Information Center.
   b. Respond accurately to requests for information about the military's role.
   c. Use command information tools to educate the public on smallpox.
   d. Establish contact with the CDC's Field Communications Media Liaison.
   e. Design or modify websites to provide smallpox information.
   f. Monitor public media for articles and inform leadership of relevant stories.
   g. Provide public affairs advice to all agencies that request assistance.

APPENDIX E-2
Common Questions & Answers.

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2. For Health-Care Providers.

a. Smallpox Vaccine Safety - Health-care Providers (HCP).

b. How To Administer Smallpox Vaccine - HCP.

c. Treating Complications Of Smallpox Vaccination - HCP.

d. Evidence Of Immunity And Vaccination-Response Interpretation - HCP.

e. Vaccination Site Care - HCP.

f. Infection-Control Measures.

g. Decontamination.

3. Other Sources of Information for the Public.

a. World Health Organization.
www.who.int/emc/diseases/smallpox/factsheet.hml

b. Centers for Disease Control & Prevention.
www.bt.cdc.gov/DocumentsApp/FAQSmallpox.asp?link=2&page=bio

c. Infectious Disease Society of America.
http://immunizationinfo.org/search/results2.cfm?id=26

1. a. Smallpox - The Disease.

What is smallpox?

Smallpox is a very serious disease. Smallpox is caused by a virus called variola, which spreads from person to person through prolonged face-to-face contact. Indirect spread is less common.

Smallpox can cause:

- A severe rash covering the whole body that can leave permanent scars.
- High fever.
- Severe headache or backache.
- Death (in about 30% of infected people).
- Blindness in some survivors.

Natural cases of smallpox have been eradicated from the planet. The last natural case of smallpox was in Somalia in 1977.

The incubation period for smallpox is about 12 to 14 days (range: 7 to 17 days) after exposure. Initial symptoms include high fever, fatigue, headache, and severe back pain.

A characteristic rash, notably on the face, arms, and legs, follows 2 to 3 days after the initial symptoms. The rash starts with flat red lesions that progress at the same rate. These lesions fill with pus and begin to crust early in the second week. Scabs develop, then separate, and fall off after about 3 to 4 weeks.

Is smallpox fatal?

Most patients infected with smallpox recover. Smallpox kills about 3 out of 10 people infected. Many smallpox survivors have permanent scars over large areas of their body, especially their face. People who survive smallpox have lifelong immunity against getting smallpox a second time.

Is smallpox contagious? How does smallpox spread?

People are most infectious during the first week of the rash, because that is when the largest amount of virus is present in saliva. However, some risk of transmission lasts until all scabs fall off.

The most common way to transmit smallpox would be from person-to-person. People infected with smallpox exhale little droplets that carry the virus to the nose or mouth of bystanders. The greatest risk comes from prolonged face-to-face contact (6 feet or less, most often after 1 or more hours), with an infected person, especially one who is

coughing. Indirect contact is less efficient at spreading the virus, but it still occurred via fine-particle aerosols or inanimate objects carrying the virus.

Contaminated clothing or bed linen could spread the virus. Special precautions need to be taken to thoroughly clean all bedding and clothing of smallpox patients with bleach and hot water. Disinfectants such as household bleach or hospital-grade quaternary ammonia disinfectants can be used for cleaning contaminated surfaces.

Smallpox is not spread by animals or insects. Smallpox is not spread by food or water.

1. b. Smallpox - Vaccine Overview.

What is smallpox vaccine?

The smallpox vaccine does not contain smallpox virus, so the name of the vaccine is a bit confusing. Smallpox vaccine contains a live virus called vaccinia. It is more technically correct to call smallpox vaccine by the name “vaccinia vaccine,” but "smallpox vaccine" is more commonly used. Vaccinia is sometimes called “cowpox.”

Vaccinia virus is similar to the smallpox (variola) virus. Edward Jenner reported in 1796 that people given vaccinia (smallpox) vaccine become protected from smallpox. Smallpox vaccine was the very first vaccine and has been used successfully for over 205 years.

Getting smallpox vaccine *before* exposure will protect most people from smallpox. Getting the vaccine *within 4 days after exposure* may prevent the disease or make it less severe. Getting the vaccine *within a week after exposure* may still make the disease less severe. Immunity after vaccination generally lasts 3 to 10 years. National recommendations for revaccination have varied over time, ranging from every 3 years to every 10 years. People who received several doses of smallpox vaccine may be protected for longer periods of time.

Why get vaccinated?

Smallpox vaccination is the best way to avoid being infected with smallpox. Until the late 1970s, many billions of people around the globe received smallpox vaccine. Smallpox vaccine is still used routinely to protect a small number of people who work with vaccinia virus or similar viruses.

Authorities are concerned that terrorists or governments hostile to the United States may have some of the variola virus that causes smallpox disease. If so, they could use it as a biological weapon in bombs or sprays or by other methods. People exposed to variola virus, or those at risk of being exposed, can be protected by vaccinia (smallpox) vaccine.

There is no proven treatment for the smallpox disease, but research to evaluate new antiviral medications is ongoing. Patients with smallpox can benefit from supportive therapy (e.g., intravenous fluids, medicine to control fever or pain) and antibiotics for any secondary bacterial infections that occur from all the skin problems smallpox causes.

Who should get smallpox vaccine and when?

Who: Routine non-emergency users include laboratory workers who handle cultures or animals infected with vaccinia or other orthopox viruses (e.g., monkeypox, cowpox, variola). Other health-care workers who handle materials (e.g., dressings) that may be contaminated with vaccinia virus should also be vaccinated.

When: These at-risk workers should get one dose of smallpox vaccine before the risk of exposure begins. In general, they should get revaccinated every 10 years.

Who: Bioterrorism could result in people being exposed to the variola virus. These people would go on to develop smallpox disease, further exposing their close contacts, those involved in their medical care or transportation, and lab personnel who collect or process specimens from smallpox patients. Vaccination of other selected groups (e.g., medical, law enforcement, emergency response, military) may be recommended by public-health authorities.

When. One dose of smallpox vaccine, before imminent release of virus for those at high risk of exposure, or one dose as soon as possible after release of virus for those exposed to or at risk of contact with patients or virus.

How long has smallpox vaccine been around?

Smallpox vaccination was the very first vaccination. Edward Jenner first developed it in 1796.

1.c. Smallpox - Vaccine Effectiveness.

If I get vaccinated against smallpox, how protected will I be?

The effectiveness of the vaccine has never been measured precisely in controlled trials. But smallpox vaccination was so successful that it eradicated the natural form of the disease from planet Earth. Scientists estimate that about 95% of vaccine recipients are protected from smallpox.

If people got smallpox vaccination in the past, when it was used routinely, will they still be immune?

Immunity decreases with the passage of years. In the United States, routine vaccination against smallpox ended around 1972 in most places. Military smallpox vaccination programs continued longer. In 1984, routine military vaccinations were limited to recruits entering basic training. Between 1984 and 1989, some service members were immunized but not others. In 1990, the Department of Defense discontinued routine vaccination of recruits.

The level of immunity persisting among people vaccinated more than 10 years ago is uncertain. Therefore, these people are assumed to be susceptible, needing revaccination. The more doses of smallpox vaccine a person received in a lifetime, the longer immunity is likely to persist. Even if people vaccinated long ago are not completely immune from infection nowadays, these people would be less likely to spread smallpox than completely unvaccinated people. Previously vaccinated people would be less infectious because they would shed fewer viruses.

One way to measure how long immunity lasts is to look at the chance of dying from smallpox if one is infected with smallpox. This was calculated in Europe several decades ago.

Risk of dying:
- 58% in unvaccinated adults (28 out of 48 unvaccinated adults infected in this small sample; 30% is the overall average mortality rate).
- 11% in people vaccinated 21 or more years earlier.
- 7% in people vaccinated 11 to 20 years earlier.
- 1.4% in people vaccinated 1 to 10 years earlier.

(Mack TM. Smallpox in Europe, 1950-1971. *Journal of Infectious Diseases* 1972;125:161-9.)

Who received smallpox vaccination in the past?

Most Americans received smallpox vaccine as children up until about 1972, 30 years old. Most Americans younger than 30 years old have never been vaccinated against smallpox.

Most American civilians born before 1972 have gone 30 or more years since their last smallpox vaccination. Those born since 1972 who never served in the US military probably never got smallpox vaccination.

How often should somebody get smallpox vaccination?

Most estimates suggest immunity from smallpox vaccination is almost complete for 3 to 10 years. Immunity can be boosted effectively with a single revaccination at an interval based on level of risk.

1. d. Smallpox Vaccine - Safety.

Is smallpox vaccine safe?

Most people who get smallpox vaccine have no complications. But smallpox vaccine is not completely safe. Rarely, smallpox vaccination can lead to serious complications. About 1 out of 1,000,000 smallpox vaccine recipients will die as a result of this vaccination. Like all vaccines, smallpox vaccine can cause headache and fatigue.

Smallpox vaccine does not contain variola virus, so it cannot cause smallpox. Smallpox vaccine contains live vaccinia viruses, which cross-protect against variola viruses.

Why should I take this vaccine?

People in many countries are concerned about the potential use of smallpox as a bioterrorism agent. The likelihood that smallpox would be used as a bioweapon is unknown. About 30 percent of people who contract smallpox die; about 70% survive.

Vaccination prevents almost all cases of smallpox. If symptoms of smallpox do appear, they are generally milder than in unvaccinated people.

What are the temporary side effects after smallpox vaccination?

As with all vaccines, side effects can result from smallpox vaccination. Mild to moderate problems include a possible blister, which may later form a scar, at the vaccination site. This is an expected reaction. Swelling and tenderness of lymph nodes can last 2 to 4 weeks after the blister heals. About 70% of vaccinated children can get a fever of over 100°F, and 15% to 20% of children can get a fever of over 102°F. About five per 10,000 people may have blisters away from the vaccination site. Some individuals may have rashes that last 2 to 4 days. These side effects are usually temporary and self-limiting, meaning they go away on their own or with minimal medical treatment (e.g., aspirin, rest).

What are the serious side effects after smallpox vaccination?

Moderate to severe reactions are also possible. About 2 to 3 per 10,000 people may have vaccinia rashes on their bodies. These rashes may be more common among toddlers, children 1 to 4 years of age. About four per 10,000 can have severe eczema (a kind of skin inflammation).

Encephalitis or neurologic problems can occur in about one per 100,000 people. Severe infection beginning at the vaccination site can occur in 1 to 2 per million people.

Death can occur in about 1 per 1,000,000 people vaccinated against smallpox. The greatest risk of death occurs with people with suppressed immune systems.

Can someone vaccinated against smallpox infect someone else?

Adverse reactions, sometimes severe, can also occur in people who come in contact with a vaccinated person. These problems result from touching the vaccination site and transferring vaccinia viruses to another person. More information on this appears below.

Are there any medical conditions that would bar me from taking the smallpox vaccine?

If you have one of the following medical conditions, you should not receive smallpox vaccine, unless you have been exposed to someone who is actually infected with smallpox. These medical conditions include atopic dermatitis, a past history of atopic dermatitis, a suppressed immune system (e.g., AIDS, cancer), or taking a medication that suppresses the immune system. Also, if you have certain skin conditions (e.g., allergic rash, burns, impetigo, or chickenpox) or are moderately ill, you discuss your options with a physician. If possible, wait until your condition clears up before getting the smallpox vaccine. Again, these bars to vaccination may not apply in an emergency. Consult your physician.

What if I am pregnant or breast-feeding?

As with most vaccines, vaccination of pregnant women should be deferred unless it is clearly needed. Live-viral vaccines are usually barred (contraindicated) during pregnancy. But if you have been exposed to smallpox, you would probably be vaccinated against it. Smallpox vaccine is not known to cause birth defects. On very rare occasions, vaccinia infection of the fetus has been reported after vaccinating the mother. This fetal vaccinia infection may result in stillbirth or death of the infant soon after delivery. About 50 of these fetal cases have been recorded after vaccinating literally billions of women around the globe.

Smallpox infection among pregnant women has been reported to result in a more severe infection than among nonpregnant women. Therefore, the risks to the mother and fetus from smallpox infection clearly outweigh any potential risks resulting from vaccination. In addition, vaccinia virus has not been found to cause birth defects, and the incidence of fetal vaccinia is low. When the level of exposure risk is undetermined, the decision to vaccinate should be made after discussion by the clinician and patient of the potential risks versus the benefits of smallpox vaccination.

Breast-feeding is not a bar (contraindication) to any vaccination. Vaccination has no effect on the breast-feeding mother, nor the breast-fed child.

What other medical conditions should I inform the medical staff about?

If you have had a life-threatening reaction to polymyxin B, streptomycin, chlortetracycline, neomycin or a previous dose of smallpox vaccine, it may not appropriate to get vaccinated. Talk with your physician.

1. e. Smallpox In The Environment.

Do tests exist to show if smallpox is in the environment, like tests for anthrax?

Various agencies are currently developing tests designed to test for the smallpox virus in the environment. Like all tests of their kind, these tests can generate both false-positive results (test says positive, but it's really negative) and false-negative tests (test says negative, but it's really positive). These tests must be interpreted carefully by experienced laboratory professionals.

If smallpox is discovered or released in a building, or if a person develops symptoms in a building, how can that area be decontaminated?

The smallpox virus is very fragile. If smallpox virus is released into the air, all viruses will be naturally inactivated or dissipated within 1 to 2 days. Buildings exposed to the initial aerosol release of the virus do not need to be decontaminated. By the time the first cases are identified, typically 2 weeks after the release, the virus in the building will be gone. Infected patients, however, will be capable of spreading the virus and possibly contaminating surfaces while they are sick. Scabs can transmit smallpox virus, but this is unusual.

Standard hospital-grade disinfectants such as quaternary-ammonia compounds are effective in killing the virus. They should be used on surfaces to disinfect hospitalized patients' rooms or other contaminated surfaces. Although less desirable because it can damage equipment and furniture, hypochlorite (bleach) is an acceptable alternative. In the hospital setting, patients' linens should be autoclaved or washed in hot water with bleach added. Infectious waste should be placed in biohazard bags and autoclaved before incineration.

What should people do if they suspect a person has smallpox or suspect that smallpox has been released in their area?

On military installations, report suspected cases of smallpox or suspected intentional release of smallpox to your local hospital or clinic. In civilian communities, report suspected cases of smallpox or suspected intentional release of smallpox to your local health department. The hospital, clinic, or local health department will evaluate the situation and make needed reports to higher headquarters, the CDC, and the state health department.

How can we stop the spread of smallpox after someone comes down with it?

The most important steps to stop a smallpox epidemic are case isolation and contact tracing and vaccination.

Patients showing signs of smallpox are capable of spreading the virus. Patients should be placed in medical isolation so that they will not continue to spread the virus. In addition, people who have come into close contact with smallpox patients should be vaccinated immediately and closely watched for symptoms of smallpox. Vaccination and isolation are the key strategies for stopping the spread of smallpox.

2. For Health-Care Providers.

2. a. Smallpox Vaccine Safety - Health-Care Providers (HCP).

Besides the normal side effects covered already, is there more information I need to know as a health-care provider?

Inadvertent inoculation at other sites is the most frequent complication of vaccinia vaccination. It accounts for about half of all complications of primary (first) vaccination and revaccination. Inadvertent inoculation usually results from auto-inoculation of vaccinia virus, transferred from the site of vaccination. The most common sites involved are places that itch: the face, eyelids, nose, mouth, genitalia, and rectum.

Most auto-inoculation lesions heal without specific therapy, but vaccinia immune globulin (VIG) can help treat cases of ocular implantation. However, if vaccinial keratitis is present, VIG is barred (contraindicated) because it might increase corneal scarring.

Erythematous or urticarial rashes can occur about 10 days after primary (first) vaccination and can be confused with generalized vaccinia. However, the vaccinee is usually afebrile with this reaction, and the rash resolves spontaneously within 2 to 4 days. Rarely, bullous erythema multiforme (i.e., Stevens-Johnson syndrome) occurs.

What about moderate to severe adverse reactions?

Moderate and severe complications of vaccinia vaccination include eczema vaccinatum, generalized vaccinia, progressive vaccinia, and postvaccinial encephalitis. These complications are rare, but occur at least 10 times more often among primary vaccinees than among revaccinees. These serious skin complications also are more frequent among infants than among older children and adults. A study of Israeli military recruits aged 18 years or older, who were vaccinated during 1991 and 1996, reported rates of progressive vaccinia (0 out of 10,000 vaccinees) and postvaccinial encephalitis (0 out of 10,000 vaccinees) similar to those reported in previous studies.

What is eczema vaccinatum?

Eczema vaccinatum is a localized or systemic dissemination of vaccinia virus among people who have atopic dermatitis or a history of atopic dermatitis or other exfoliative skin conditions (e.g., atopic dermatitis). Usually, this illness is mild and self-limited, but can be severe or fatal. The most serious cases among vaccine recipients occur among primary vaccinees, even among people who do not have active skin disease. Severe cases have been observed after recently vaccinated people had contact with people with atopic dermatitis or a history of atopic dermatitis.

What is generalized vaccinia?

Generalized vaccinia involves a vesicular rash of varying extent that can occur among people without underlying illnesses. The rash is generally self-limited and requires minor or no therapy, except among patients whose conditions might be “toxic” (as it refers to children) or who have serious underlying immunosuppressive illnesses (e.g., acquired immunodeficiency syndrome [AIDS]).

What is progressive vaccinia?

Progressive vaccinia (also called vaccinia necrosum or vaccinium gangrenosa) is a severe, potentially fatal illness. It appears as progressive necrosis reaching out from the vaccination site, often with metastatic lesions. It occurred almost exclusively among people with cellular immunodeficiency.

What is postvaccinial encephalitis?

The most serious complication is postvaccinial encephalitis. Two main forms were noted. The first affected children younger than 1 year old receiving their first (primary) smallpox vaccination, involving convulsions. These children may have residual paralysis after recovery.

The second form affected children 2 years or older, adolescents, and adults receiving a their first (primary) smallpox vaccination. These patients developed abrupt onset of fever, vomiting, headache, and malaise, followed by loss of consciousness, amnesia, confusion, convulsions, and coma. About 1 in 3 of these patients died.

How often this complication occurred varies with the strain of vaccinia virus and was higher in Europe than in the United States. The principal strain of vaccinia virus used in the United States, the New York City Board of Health (NYCBOH) strain, was associated with the lowest incidence of postvaccinial encephalitis. About 15% to 25% of affected vaccinees with this complication die, and 25% have permanent neurological sequelae. Fatal complications caused by vaccinia vaccination are rare, with approximately 1 death per 1,000,000 primary vaccinations and 1 death per 4,000,000 revaccinations. Death most often results from postvaccinial encephalitis or progressive vaccinia.

What should we ask about before people get smallpox vaccine?

Before smallpox vaccination, ask people if they have any problems with their immune system (e.g., due to cancer treatment, transplantation, AIDS, other conditions), if they are infected with HIV, if they have atopic dermatitis or other chronic skin conditions, or if they had atopic dermatitis as a child.

Who is barred (contraindicated) from smallpox vaccine?

No absolute bars (contraindications) exist for vaccination of a person with a high-risk exposure to smallpox. People at greatest risk for experiencing serious vaccination complications are also at greatest risk for death if exposed to smallpox.

If a relative contraindication to vaccination exists, the risk for experiencing serious vaccination complications must be weighed against the risk for experiencing a potentially fatal smallpox infection. When the level of exposure risk cannot be determined, the decision to vaccinate should be made after discussion by the clinician and the patient of the potential risks versus the benefits of smallpox vaccination.

2. b. How To Administer Smallpox Vaccine - HCP.

Vaccination has been successfully and safely administered to people of all ages, from birth onward. As with all vaccinations, the smallpox vaccination process should begin with careful individualized assessment of vaccine indications and contraindications.

The skin over the insertion of the deltoid muscle or the posterior aspect of the arm over the triceps muscle are the preferred sites for smallpox vaccination. Alcohol or other chemical agents are not required for skin preparation for vaccination, unless the area is grossly contaminated. If alcohol is used, the skin must be allowed to dry thoroughly (requiring several minutes) to prevent inactivation of the vaccine by the alcohol. Acetone dries more quickly.

The multiple-puncture technique uses a presterilized bifurcated needle inserted vertically into the vaccine vial, causing a droplet of vaccine to adhere between the prongs of the needle. The droplet contains the recommended dosage of vaccine. Confirm the presence of the droplet between the prongs of the bifurcated needle visually. Holding the bifurcated needle perpendicular to the skin, make 15 punctures rapidly, with strokes vigorous enough to allow a trace of blood to appear after 15 to 20 seconds. Wipe off any remaining vaccine with dry sterile gauze, then dispose of the gauze in a biohazard waste container.

Cover the site with a loose, nonocclusive bandage to deter the individual from touching the site and perhaps transferring virus to other parts of the body. Alternately, the site can be left uncovered, if the individual is thoroughly counseled about the hazards of touching the vaccination site.

After about 3 days, a red papule appears at the vaccination site and becomes vesicular on about the fifth day. By the seventh day, it becomes the typical Jennerian pustule -- whitish, umbilicated (sunken center), multilocular, containing turbid lymph and surrounded by an erythematous (reddened) areola (circle) that may continue to expand for 3 more days. Swollen lymph nodes nearby and fever are not uncommon. As many as 70% of children have 1 or more days of temperature higher than 39°C (100°F)

between days 4 and 14. The pustule (pus-filled blister) gradually dries, leaving a dark crust, which normally falls off after about 3 weeks.

A successful vaccination for those with some preexisting immunity may manifest a range of responses. These can include what appears to be a primary take (described above) or an accelerated reaction. In an accelerated reaction, there may be little more than a papule (bump) surrounded by erythema (redness) that reaches a peak between 3 and 7 days. A response that reaches a peak in erythema within 48 hours represents a hypersensitivity reaction and does not reflect that growth of the vaccinia virus occurred. People exhibiting a hypersensitivity reaction should be revaccinated.

2. c. Treating Complications of Smallpox Vaccination - HCP.

What treatment can be given to patients who had a reaction to smallpox vaccine?

The only product that was FDA-licensed for treatment of complications of vaccinia vaccination is vaccinia immune globulin (VIG). VIG is an isotonic solution of immunoglobulin G harvested from the plasma of people who received smallpox (vaccinia) vaccine. VIG is effective in treating eczema vaccinatum and some cases of progressive vaccinia.

VIG might be useful also in the treatment of ocular vaccinia resulting from inadvertent implantation. However, VIG is barred (contraindicated) for the treatment of vaccinial keratitis.

VIG is recommended for severe generalized vaccinia, if the patient is extremely ill or has a serious underlying disease. VIG provides no benefit in the treatment of postvaccinial encephalitis and has no role in the treatment of smallpox.

Current supplies of VIG are limited. VIG is currently reserved for treatment of vaccine complications with serious clinical manifestations (e.g., eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, severe ocular implantation).

What is the treatment regimen for using VIG?

The recommended dosage of the currently available VIG for treatment of complications is 0.6 ml/kg of body weight. The original form of VIG must be administered intramuscularly, as early as possible after onset of symptoms. Because therapeutic doses of VIG might be substantial (e.g., 42 ml for a person weighing 70 kg), the product can be administered in divided doses over a 24- to 36-hour period. Doses can be repeated, usually at intervals of 2 to 3 days, until recovery begins (e.g., no new lesions appear).

Newer formulations of VIG will require intravenous administration. Health-care providers should refer to the manufacturer's product labeling for proper dosages and other therapeutic details.

Military healthcare providers may obtain VIG via the US Army Medical Materiel Agency (see Annex H and Annex I), after appropriate consultation with infectious-disease, dermatology, or allergy-immunology specialists. CDC is currently the only source of VIG for civilians.

What about VIG during a smallpox outbreak?

If vaccination of people with bars (contraindications) is required because of exposure to smallpox virus, current stores of VIG are insufficient to allow its prophylactic use along with vaccination. Because of the limited stores of VIG, its use in such a scenario should be reserved for severe, life-threatening complications (e.g., progressive vaccinia, eczema vaccinatum, or severe, “toxic” generalized vaccinia).

If additional VIG becomes available in sufficient quantities to allow its prophylactic use, VIG should be administered at a dose of 0.3 mg/kg along with smallpox (vaccinia) vaccine to people with bars (contraindications) who require vaccination.

Are there other treatment options for those that have vaccinia vaccine complications?

The Food and Drug Administration has not approved the use of any antiviral compound for the treatment of vaccinia virus infections or other Orthopoxvirus infections, including smallpox (variola infection). Certain antiviral compounds are active against vaccinia virus or other Orthopoxviruses in vitro and among test animals. However, the safety and effectiveness of these compounds for treating vaccinia vaccination complications or other Orthopoxvirus infections among humans is unknown. Questions also remain regarding the effective dose and the timing and length of administration of these antiviral compounds.

Additional information could become available. Health-care providers should consult infectious-disease experts for updated information regarding treatment options for smallpox vaccination complications.

2. d. Evidence of Immunity and Vaccination-Response Interpretation.

After vaccination, what evidence suggests an individual developed immunity against smallpox?

Smallpox vaccination with live vaccinia virus causes the body to produce neutralizing IgG antibodies, as well as vaccinia-specific cell-mediated immunity. In a person with

normal immune function, neutralizing antibodies appear about 10 days after primary vaccination and 7 days after revaccination. Clinically, people are considered fully protected after a successful response is demonstrated at the site of vaccination, about 7 days after vaccination.

The vaccination site should be inspected 6 to 8 days after vaccination and the response interpreted at that time. The World Health Organization (WHO) Expert Committee on Smallpox defines two types of responses. The responses include:

(a) a major reaction, which indicates that virus replication has taken place and vaccination was successful; or

(b) an equivocal reaction, which either indicates (1) a possible consequence of immunity adequate to suppress viral multiplication or (2) allergic reactions to an inactive vaccine without production of immunity.

What is a "major reaction"?

Major (i.e., primary) reaction is defined as a vesicular (blister) or pustular lesion or an area of definite palpable induration (hardness) or congestion surrounding a central lesion that might be a crust or an ulcer. The usual progression of the vaccination site after primary vaccination is as follows:

a. The inoculation site becomes reddened and itchy 3 to 4 days after vaccination.

b. A vesicle (blister) surrounded by a red areola then forms, which becomes umbilicated (sunken center) and then pustular (pus-filled) by days 7 to 11 after vaccination.

c. The pustule begins to dry, the redness subsides, and the lesion becomes crusted between the second and third week.

d. By the end of about the third week, the scab falls off, leaving a permanent scar that at first is pink in color, but eventually becomes flesh-colored.

Skin reactions after revaccination might be less pronounced with more rapid progression and healing than those after primary vaccinations. Revaccination is considered successful if a pustular lesion is present or an area of definite induration or congestion surrounding a central lesion (i.e., scab or ulcer) is visible upon examination 6 to 8 days after revaccination.

What is an "equivocal reaction"?

Equivocal reactions consolidate a variety of previous terms, including accelerated, modified, vaccinoid, immediate, early, or immune reactions. Equivocal reactions are defined as all responses other than major reactions.

If an equivocal reaction is observed, check vaccination procedures and repeat the vaccination by using vaccine from another vial or vaccine lot, if available. It is often difficult to determine if the reaction was blunted by immunity, insufficiently potent vaccine, or vaccination technique failure. If the repeat vaccination using different vaccine fails to elicit a major reaction, health-care providers should consult CDC or their state or local health department before attempting another vaccination.

2. e. Vaccination Site Care - Health-Care Providers

Is it true that the virus can be transmitted from recently vaccinated people?

Transmission of vaccinia virus can occur when a recently vaccinated person has contact with a susceptible person. In a 1968 10-state survey of complications of vaccinia vaccination, the risk for transmission of vaccine virus to contacts was 27 infections out of 1,000,000 vaccinations; 44% of those contact cases occurred among children aged 5 years or younger.

Before the U.S. military discontinued routine smallpox vaccination in 1990, occurrences of contact transmission of vaccinia virus from recently vaccinated military recruits had been reported, including six cases resulting from transmission from one vaccine recipient.

Are there precautions I can take as a health-care provider to help my patients avoid spreading vaccinia to others?

Vaccinia virus can be found at the site of primary vaccination beginning at the time of development of a papule (i.e., 2 to 5 days after vaccination) until the scab separates from the skin lesion (i.e., 14 to 21 days after vaccination). During that time, care must be taken to prevent spread of the virus to another area of the body or to another person by inadvertent contact.

Perform thorough hand-hygiene with soap and water or disinfecting agents after direct contact with the site, as well as materials that came into contact with the site. This will help remove virus from the hands and prevent accidental inoculation to other areas of the body. In addition, take care to prevent unvaccinated people from having contact with the site or contaminated materials from the site.

The vaccination site can be left uncovered, or it can be loosely covered with a porous bandage (e.g., gauze) until the scab separates on its own, to provide additional barrier protection against inadvertent inoculation. An occlusive bandage should not be routinely used because maceration (prolonged soaking that can lead to break down) of the site might occur. Change bandages used to cover the vaccination site frequently (i.e., every 1 to 2 days), to prevent maceration of the site from fluid buildup. Use hypoallergenic tape for people who experience tape hypersensitivity.

Keep the vaccination site dry, although normal bathing can continue. No salves or ointments should be placed on the vaccination site. Place contaminated bandages and, if possible, the vaccination site scab, after it has fallen off, in sealed plastic bags. Dispose of this waste in the trash to further decrease the potential for inadvertent transmission of the live virus contained in the materials. Clothing or other cloth materials that have had contact with the site can be decontaminated with routine laundering in hot water with bleach.

If I must continue care of patients, what I can do to protect them from the viruses at my recent vaccination site?

Recently vaccinated health-care workers should avoid contact with unvaccinated patients, particularly those with immunodeficiencies, until the scab separates from the skin at the vaccination site. However, if continued contact with unvaccinated patients is unavoidable, health-care workers can continue to have contact with patients, including those with immune deficiencies, as long as the vaccination site is well-covered and thorough hand-hygiene is maintained.

In this setting, a more occlusive dressing might be required. Semipermeable polyurethane dressings (e.g., Opsite®) are effective barriers to vaccinia and recombinant vaccinia viruses. However, exudates can accumulate beneath the dressing, and care must be taken to prevent viral contamination when the dressing is removed. In addition, accumulation of fluid beneath the dressing can increase the maceration of the vaccination site. Accumulation of exudates can be decreased by first covering the vaccination site with dry gauze, then applying the dressing over the gauze. The dressing should also be changed at least once a day. To date, experience with this type of containment dressing has been limited to research protocols.

The most critical measure in preventing inadvertent implantation and contact transmission from vaccinia vaccination is thorough hand-hygiene after changing the bandage or after any other contact with the vaccination site.

2.f. Infection-Control Measures.

Should smallpox patients be isolated? What precautions should be taken by the hospital or clinic?

Isolation of confirmed or suspected smallpox patients will be necessary to limit the potential exposure of unvaccinated and, therefore, nonimmune people. Although droplet spread is the major mode of person-to-person smallpox transmission, airborne transmission through fine-particle aerosol can occur. Therefore, initiate airborne precautions using correct ventilation (e.g., negative air-pressure rooms with high-efficiency particulate air filtration) for hospitalized confirmed or suspected smallpox

patients, unless the entire facility has been restricted to smallpox patients and recently vaccinated people.

Recently vaccinated people who demonstrated an immune response should be fully protected against infection with variola virus. Nonetheless, continue to observe standard and contact precautions (i.e., using protective clothing and shoe covers) when in contact with smallpox patients or contaminated materials, to prevent inadvertent spread of variola virus to susceptible people and potential self-contact with other infectious agents.

Personnel should remove and correctly dispose of all protective clothing before contact with unvaccinated people. Reuseable bedding and clothing can be autoclaved or laundered in hot water with bleach to inactivate the virus. Laundry handlers should be vaccinated before handling contaminated materials.

What about other facilities (i.e., individual homes)?

Nonhospital isolation of confirmed or suspected smallpox patients should be of a sufficient degree to prevent the spread of disease to nonimmune people during the time the patient is considered potentially infectious (i.e., from onset of fever until all scabs separate). Private residences or other nonhospital facilities used to isolate confirmed or suspected smallpox patients should have nonshared ventilation, heating, and air-conditioning systems. Limit access to those facilities to recently vaccinated people with a demonstrated immune response. If suspected smallpox patients are placed in the same isolation facility, vaccinate them to guard against accidental exposure caused by misclassification as someone with smallpox.

In addition to isolation of infectious smallpox patients, start fever surveillance of contacts during their potential incubation period. Transmission of smallpox virus rarely occurs before the appearance of the rash that develops 2 to 4 days after the prodromal fever. If a vaccinated or unvaccinated contact experiences a fever of 101°F (38°C) or higher during the 17-day period after his or her last exposure to a smallpox patient, the contact should be isolated immediately to prevent contact with unvaccinated or nonimmune people until smallpox can be ruled out by clinical or laboratory examination.

What other procedures and considerations should medical communities be aware of?

As soon as the diagnosis of smallpox is made, immediately isolate all individuals in whom smallpox is suspected. Vaccinate all household and other prolonged face-to-face contacts and place them under fever surveillance. Because the widespread dissemination of smallpox virus by aerosol poses a serious threat in hospitals, isolate patients in the home or other nonhospital facility whenever possible. Home care for most patients is a reasonable approach, given the fact that little can be done for a patient other than to offer supportive therapy.

In the event of an aerosol release of smallpox and a subsequent outbreak, the rationale for vaccinating patients suspected to have smallpox at this time is to ensure that some with a mistaken diagnosis are not placed at risk of acquiring smallpox. Vaccination administered within the first few days after exposure may prevent or significantly reduce subsequent illness. An emergency vaccination program is also indicated for health-care workers at clinics or hospitals that might receive patients, essential disaster-response personnel, and mortuary staff. Personnel for whom vaccination is not barred (contraindicated) should be vaccinated immediately regardless of prior vaccination status.

Vaccination administered within 4 days of first exposure offers some protection against acquiring infection and significant protection against a fatal outcome. Those who have been vaccinated at some time in the past will normally exhibit an accelerated immune response. Thus, it would be prudent, when possible, to assign those who had been previously vaccinated to duties involving close patient contact.

Use discretion used in identifying contacts of patients to focus vaccination and fever surveillance measures on those at greatest risk. People do not transmit smallpox until after the fever gives way to rash.

Contacts, even if infected, are not contagious until onset of rash. So, a practical approach is to have contacts check their temperatures at least once each day, preferably in the evening. Any increase in temperature higher than 38°C (101°F) during the 17-day period after last exposure to the case suggests possible development of smallpox. In such a case, isolate the patient immediately, preferably at home, until it could be determined clinically and/or by laboratory examination whether the contact has smallpox. All close contacts of the patients should be promptly vaccinated.

2. g. Decontamination.

Vaccinia virus, if released as an aerosol and not exposed to ultraviolet (UV) light, may persist for as long as 24 hours or somewhat longer under favorable conditions. Variola virus is believed to exhibit similar properties.

By the time patients become ill with smallpox (12 to 14 days after exposure), there would be no viable smallpox virus remaining in the environment. Vaccinia virus, if released as an aerosol, is almost completely destroyed within 6 hours in an atmosphere of high temperature (31° to 33°C) and humidity (80%). In cooler temperatures (10° to 11°C) and lower humidity (20%), about two-thirds of a vaccinia aerosol survives up to 24 hours. Variola would probably behave similarly.

The occurrence of smallpox infection among personnel who handled laundry from infected patients is well documented, but rare. Variola viruses in such material remain viable for extended periods. Thus, special precautions need to be taken to ensure that

all bedding and clothing of smallpox patients is autoclaved or laundered in hot water to which bleach has been added. Disinfectants that are used for standard hospital infection control, such as hypochlorite and quaternary ammonia, are effective for cleaning surfaces possibly contaminated with virus.

Virus in scabs is more durable. At a temperature of 35°C and 65% relative humidity, the virus can persist for 3 weeks. At cooler temperatures (26°C), the virus can survive for 8 weeks at high relative humidity and 12 weeks at a relative humidity less than 10%. Variola virus can be found in scabs sitting on a shelf for 13 years. It is unlikely, however, that the smallpox virus, bound in the fibrin matrix of a scab, is infectious in humans. This is borne out by studies conducted during the eradication program and by surveillance for cases in newly smallpox-free areas. If the virus were able to persist in nature and infect humans, natural cases would have occurred for a prolonged period after person-to-person disease transmission stopped. But cases of this type were not observed.

ANNEX F TO SMALLPOX RESPONSE PLAN 29 September 2002
DECONTAMINATION GUIDELINES.

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o. Title 29 Code of Federal Regulations, Section 1910.1200. Hazard Communication.

1. General. This annex augments and modifies CDC Guide F (reference a), based on current national infection-control and prevention guidelines (references b, c, d, e, f, and g). Appendix F-1 summarizes this annex on one page. Appendix F-2 (Decontamination Quick Reference Guide) summarizes the clinical, safety and occupational health requirements and guidelines for personnel conducting decontamination activities discussed in this protocol. Appendix F-3 provides a reference guide for patients housed in homes or temporary facilities. Appendix F-4 summarizes guidance on disinfecting environmental surfaces in healthcare facilities. Appendix F-5 provides definitions of technical terms used in this annex.

a. Mission. Health-care workers and the public will clean and disinfect areas potentially contaminated with smallpox virus or vaccinia virus, as well as properly dispose of hazardous and regulated medical waste (RMW) according to local, state, and federal regulations.

b. Definitions. Additional definitions appear in Appendix F-5.

(1) Decontamination. A procedure that removes pathogenic microorganisms from objects so they are safe to handle.

(2) Disinfection. Disinfection is the use of chemical reactions to eliminate virtually all recognized pathogenic microorganisms, but not necessarily all microbial forms (e.g., bacterial endospores) on inanimate objects. There are three levels of disinfection: high, intermediate, and low. High-level disinfection kills all organisms, except high levels of bacterial spores, by means of a chemical germicide cleared for marketing as a sterilant by the Food and Drug Administration (FDA). Intermediate-level disinfection kills mycobacteria, most viruses, and bacteria with a chemical germicide registered as a "tuberculocide" by the Environmental Protection Agency (EPA). Low-level disinfection kills some viruses and bacteria with a chemical germicide registered as a hospital disinfectant by the EPA.

(3) Cleaning. The removal, usually with detergent and water or enzymatic detergent and water, of adherent visible soil, blood, protein substances, and other debris from the surfaces, crevices, serrations, joints, and lumens of instruments,

devices, and equipment by a manual or mechanical process that prepares the items for safe handling and/or further decontamination.

c. Assumptions.

(1) Preparation. Personnel responsible for decontamination have been vaccinated against smallpox, trained in these procedures, and provided with appropriate safety measures and supplies, including personal protective equipment (PPE) (e.g., gowns, gloves, respirators, goggles).

(2) Ecology. Variola virus, if protected from ultraviolet light, may persist for as long as 24 hours, or somewhat longer under favorable conditions.

(3) Disinfection. Variola virus is easily killed by hospital-approved disinfectants (HAD) labeled as tuberculocidal. These disinfectants will be used in accordance with manufacturer's labeled instructions, including appropriate wet contact time.

d. Planning Factors.

(1) General Planning. Prompt recognition of a case of smallpox is integral to timely response, including decontamination. Education and training in the control of smallpox must occur before any smallpox outbreak occurs. Each facility must know its inventory of PPE for personnel involved in decontamination.

(2) Reusable Devices. Reusable devices and items that touch mucous membranes should, at a minimum, receive high-level disinfection between patients. These devices include reusable flexible endoscopes, endotracheal tubes, anesthesia breathing circuits, and respiratory therapy equipment. Sterilization is not required, except for critical items that will penetrate sterile body sites. In general, reusable medical devices or patient-care equipment that enter normally sterile tissue or the vascular system or through which blood flows should be sterilized before each use. Sterilization means the use of a physical or chemical procedure to destroy all microbial life, including highly resistant bacterial endospores. The major sterilizing agents used in hospitals are:

(a) Moist heat by steam autoclaving. Follow manufacturers' standard protocols for autoclave decontamination.

(b) Ethylene oxide. Place equipment to be decontaminated using this method in plastic bags permeable to gaseous ethylene oxide. Humidify the material to be sterilized by injecting water into the plastic-bagged material, to produce a relative humidity of 50% to 70%. Place the bags into an ethylene oxide sterilizer and allow an exposure of at least 24 hours at a concentration of at least 800 mg per liter ethylene oxide. Allow the equipment to fully aerate after ethylene oxide decontamination.

(c) Dry heat. Dry-heat sterilization relies solely on temperature without steam to achieve sterilization. Therefore, it usually requires higher temperatures (320-338°F or

160-170°C) and longer exposure times (2 to 4 hours). Dry heat is also less effective than wet heat for sterilizing biohazardous materials. A *Bacillus*-species biological indicator can verify dry heat sterilization.

e. Coordinating Instructions. Military Treatment Facility (MTF) infection-control officer(s) coordinate and oversee infection prevention and control measures with healthcare providers, nursing staff, housekeeping, logistics, central material supply, and other MTF sections. The infection control officer may be required to brief the MTF command group and others on proper infection prevention and control measures within the MTF.

2. Execution.

a. Concept of Operations. Recognition of a single patient with smallpox constitutes an international public-health emergency. The control of disease is primarily a public-health strategy of rapid identification and immediate isolation of cases, with immediate vaccination of all significant contacts and healthcare providers. Patients should be hospitalized, if adequate Airborne Infectious Isolation Room (AIIR) facilities permit. Adequate infection-control procedures will be paramount to preventing further spread.

b. Key Personnel.

(1) Team leader – senior military medical officer.

(2) Infection-Control Professional/Officer – Preventive medicine, public health, epidemiologist, infection-control officer.

(3) Public health officer, environmental health officer, or bioenvironmental engineer.

(4) Surgical-supply and central-supply officer.

(5) Nursing personnel – corresponding to acuity of care needed.

(6) Public-health officer – senior community health nurse or epidemiologist.

(7) Housekeeping staff – proportionate to need.

(8) Industrial hygiene officer

c. Tasks and Responsibilities.

(1) Vaccination. Healthcare personnel and ancillary personnel subject to this document need smallpox vaccination. Vaccinations will be provided as described in Annex B. Medical follow-up to vaccine recipients will be provided by the occupational-health service, with support from infectious-disease, dermatology, and/or allergy-

immunology services for complications after vaccination. Active-duty military will report to sick call for any adverse events. Civilians and contractors experiencing an adverse event will report to the emergency department, occupational-health clinic, or other designated location.

(2) Respiratory Protection. Direct-care providers and ancillary staff will be entered in the respiratory protection program and wear a fit-tested NIOSH-approved N95 particulate respirator, eye protection if there is potential for splashing, gown, and gloves whenever patients having known or suspected smallpox are treated or housed within the MTF:

(3) Occupational Safety. Safety manager/facility manager, industrial-hygiene staff, and infection-control officer will assist supervisors in:

(a) Verifying applicable engineering controls (e.g., ventilation systems for Airborne Infection Isolation Rooms) are operational.

(b) Repairing nonfunctional engineering controls through facilities management.

(c) Ensuring personnel have adequate supplies of appropriate PPE.

(d) Verifying effectiveness of safe-work practices.

(e) Verifying that healthcare providers and staff required to wear respiratory protection participate in the MTF's respiratory protection program.

(f) Investigating engineering controls, administrative controls, work practices, PPE, when notified of known or suspected cases of smallpox.

(g) Providing safety education and training on infection-control procedures for smallpox.

(h) Establishing and implementing procedures for safe handling of contaminated clothing and linen, including outside work with contractors, if applicable.

(i) Identifying additional rooms in the MTF that can be used as isolation areas, if the number of patients to be isolated exceeds the capacity of existing Airborne Infection Isolation Rooms. Consider floors or wings of MTFs where patients can be isolated, or separate facilities (e.g., gymnasiums).

(4) Nursing staff will:

(a) Monitor and document proper negative airflow in Airborne Infection Isolation Rooms in use daily.

(b) Participate in the MTF's respiratory protection program.

(c) Adhere to standard precautions: Wash hands after patient contact with antimicrobial soap. Alcohol-based hand-hygiene agents may also be used. Wear gloves when touching blood, body fluids, secretions, excretions, or splashes of blood, body fluids, secretions or excretions. Handle used patient-care equipment and linen in a manner that prevents the transfer of microbes to people or equipment. Refer to MTF infection control manual. Use care when handling sharp objects and use a one-way valve mouthpiece or other ventilation device as an alternative to mouth-to-mouth resuscitation, when practical.

(d) In addition to standard precautions, adhere to airborne precautions: Place the patient in a private room with monitored negative air pressure, a minimum of six air changes per hour, and appropriate filtration of air before it exits the room. Cohorting (grouping like patients together) may be necessary if the number of patients exceeds available isolation rooms, and will need to be considered in the facilities' plans. (APIC's *Bioterrorism Readiness Plan: A Template for Healthcare Facilities* discusses this issue). Wear a fit-tested NIOSH-approved N95 particulate respirator when entering the room. Limit movement and transport of the patient to medically essential tests. Place surgical masks on smallpox patients, if they need to be moved.

(e) In addition to standard precautions, adhere to contact precautions: Place the patient in a private room, or cohort multiple patients with the same infection, if possible. Wear gloves when entering the room. Change gloves after contact with infective material. Wear a gown and fluid-resistant gown when entering the room. The smallpox lesions, drainage, and scabs are infective. Thorough hand washing and/or hand disinfection is required before entering and when exiting the room. Limit the movement or transport of the patient from the room. Ensure that patient-care items, bedside equipment, and frequently touched surfaces receive daily cleaning. Dedicate use of non-critical patient-care equipment (e.g., stethoscopes) to a single patient or cohort of patients with the same pathogen. If not feasible, adequately disinfect the equipment between patients.

(f) Limit access to the least number of people required for patient care or room maintenance.

(g) Report accidents, injuries, and other possible sources of exposures to supervisor and safety and/or occupational health services.

(5) Occupational-health / public-health staff will:

(a) Develop protocols for handling work-related infections and monitor staff health and report cases of known or suspected smallpox to safety/infection-control/public-health staff, as appropriate.

(b) Maintain employee medical records, as appropriate.

(c) Work in concert with immunization personnel to formulate written protocol for providing immunizations, according to Annex B.

(d) Respond to adverse events reported after vaccination.

(e) Ensure appropriate referrals to infectious-disease staff.

(f) Complete documentation.

(g) Assist with the respiratory protection program, including medical evaluations for clearance, and record-keeping.

(6) The MTF will provide training on workplace hazards and the emergency preparedness plan and ensure employee attendance. Training will meet the CDC and HICPAC Guidelines for Infection Control in Healthcare Personnel, including the availability and use of PPE.

(a) Educational materials need to be readily available, including fact sheets specific for health care workers, families, worried well, and patients.

(b) Provide educational materials and training for people with special needs, such as people with low English literacy. Ensure employee, patient, family education sheets are available in the primary languages of the given population.

(c) Make policies and procedures available electronically and on paper.

(d) MTFs will ensure adequate supplies of standard precaution and transmission-based precaution instructional signs (e.g., airborne-isolation signs, contact-isolation signs).

3. Administration and Logistics.

a. Linen & Waste Management. MTFs will develop plans for handling linens and regulated medical waste (RMW), as well as ensuring adequate medical supplies. All waste generated by smallpox patients will be treated as RMW. Linen may be handled through normal in-house or contract mechanisms as long as provisions have been made for the appropriate protection of the personnel who will be handling the linen (i.e. vaccination and appropriate personal protective equipment).

b. Sources of Supply. MTFs will identify Prime Vendor (PV) capabilities for increased deliveries of all medical supplies and equipment. MTFs will develop contingency plans for requisitioning medical supplies, in case standard channels are inadequate. Just-in-time delivery by prime vendors may not be sufficient to meet needs during outbreaks, based on the large volume of supplies that may be needed throughout a region. Establish delivery protocols for delivery of key supplies and equipment.

c. Transport of Regulated Medical Waste. Logistics or housekeeping division will be responsible for collecting, packaging, and disposing of RMW according to local, state, and federal regulations, as well as maintaining required documentation (manifests). The environmental science officer or preventive-medicine staff provides guidance as needed. Facilities that perform regulated medical waste handling on site will ensure appropriate coordination with local and state officials.

4. Cleaning, Disinfecting, and Sterilization of Equipment and Environment.

a. A component of contact precautions is careful management of potentially contaminated equipment and environmental surfaces.

b. When possible, dedicate non-critical patient-care equipment to a single patient (or cohort of patients with the same illness), or use disposable items and discard them after each use.

c. If sharing non-critical patient care equipment is unavoidable, do not use potentially contaminated equipment for the care of another patient, until it has been appropriately cleaned and disinfected. Monitor actual practices for policy compliance.

d. HAD disinfectants easily kill variola and vaccinia viruses.

e. Each MTF will develop and implement written schedules and methods for cleaning and decontaminating environmental surfaces, work surfaces, equipment, and instruments to meet the needs of the area. If contract housekeeping services are used, review these instructions for accuracy in the cleaning of isolation rooms. Considerations include:

(1) Location within the facility (e.g., surgical operatory, patient room, biomedical maintenance equipment repair).

(2) Type of surface to be cleaned (e.g., hard-surfaced flooring, carpeting).

(3) Type of soil or spilled infectious material present (e.g., gross contamination. versus spattering, blood versus urine).

(4) Tasks or procedures being performed in the area (e.g., laboratory analyses, normal patient care)

(5) Base MTF policies and procedures for housekeeping on the recommendations found in Appendix F-4.

f. Patient-Transport Vehicles (e.g., ambulances). Remove unnecessary items from ambulances to avoid contamination and facilitate decontamination. Vaccinate patient transport personnel before transport or within 24 hours. Equip ambulance with appropriate supplies (e.g., N95 respirators (if fit-tested), disposable gloves, gowns, shoe

covers, biohazard bags). Decontaminate ambulance before reuse to transport patients not infected with smallpox, focusing on the passenger compartment and all door handles.

(1) All items that can be incinerated or autoclaved should be bagged and processed by one of these methods.

(2) Sterilize heat-sensitive, reusable items using ethylene oxide as outlined above.

(3) Decontaminate large items (e.g., stretcher) at the same time as the ambulance.

(4) Spray the entire interior of the ambulance heavily (until the solution runs off) with HAD. Personnel performing this step should wear respiratory protection.

(5) Allow the solution to stand on all surfaces per manufacturer's recommendations (e.g., 20 minutes).

(6) Wet vacuum or wet clean with clean cloths, disposable wipes, or mops with disposable mop heads, all surfaces inside the ambulance and all outside door handles

(7) Vacuum cleaner contents, cloths or disposable wipes, mop heads, and protective clothing worn by the decontamination personnel should be bagged and incinerated, autoclaved, or laundered as outlined above.

(8) Disinfect the vacuum cleaner with HAD after use.

g. Private Vehicles. The procedures above may not be possible for private vehicles used to transport smallpox patients. At a minimum, perform the following decontamination procedures:

(1) Bag and incinerate all disposable items in the vehicle.

(2) Thoroughly wipe down all surfaces in the vehicle with HAD. Allow the solution to remain on the surfaces for at least 20 minutes before being removed.

(3) Clean carpets and upholstery using HAD. Allow the solution to remain on the carpets and upholstery for at least 20 minutes before being wiped off. Allow cloth upholstery to completely dry before use.

(4) Thoroughly clean all outside door handles using HAD. Allow the solution to remain on the door handles for at least 20 minutes before being wiped off.

(5) Launder cloth material used to wipe down the inside of the vehicle using hot water (71ºC) and bleach or bagged and incinerated (see above).

h. Buildings. Historically, decontamination of whole buildings or parts of buildings has been advocated, using formaldehyde or amphyl fogger methods. These procedures are controversial due to the toxicity and carcinogenicity of the chemicals used. DoD does not advocate these methods, because variola virus is easily killed by hospital-approved disinfectants and because vaccinia virus (as a surrogate for variola) is inactivated by ultraviolet light. Variola can persist for longer times within a scab matrix than in air. Following procedures recommended in this annex (e.g., terminal cleaning of rooms with HAD; cleaning, decontamination, and disinfection of environmental surfaces, equipment, laundry, vehicles), will thoroughly decontaminate a facility.

5. Special Situations. The Joint Service Sensitive Equipment Decontamination (JSSED) system(s) will eventually provide the ability to decontaminate chemical and biological agents from sensitive equipment (e.g., avionics, electronics, electrical, and environmental systems and equipment), aircraft/vehicle interiors (during flight/ground/shipboard operations), and associated cargo. These systems are still in development.

6. General Guidelines.

a. Environmental Surfaces.

(1) Disinfectants/detergents. Use EPA-registered disinfectants/detergents for routine decontamination. Disinfectants used for standard hospital infection control, such as hypochlorite, phenolics, and quaternary ammonia, are effective for cleaning surfaces possibly contaminated with smallpox. The product selected by the institution is referred to in this document as the hospital-approved disinfectant (HAD).

(2) Scheduled tasks for a minimum cleaning schedule for isolation rooms include.

(a) Daily high dusting (i.e., above eye level; e.g., light fixtures) with chemically treated dust cloth or mop designed to prevent dust dispersal.

(b) Daily spot cleaning of walls, windows, doors, and door handles, as needed.

(c) Daily wiping of horizontal surfaces with a clean cloth dampened with HAD.

(d) Daily, disinfect cleaning equipment (e.g., water, bucket, cleaning cloths, mop heads) before use on another room.

(e) Upon Discharge. Thorough cleaning of walls, windows, doors, and door handles, plus patient equipment (e.g., monitors, IV pumps & poles, sphygmomanometer).

(3) Formaldehyde and Amphyl fogger decontamination methods are no longer recommended.

b. Patient-Care Equipment and Instruments.

(1) Critical devices (those that enter sterile tissue or the vascular system) require sterilization with FDA-registered sterilant or disinfectant. Follow the normal facility disinfection process.

(2) Semi-critical devices that touch mucous membranes, depending on type of device, require minimally high-level disinfection with an HAD disinfectant. Follow the normal facility disinfection process.

(3) Non-critical devices that touch intact skin require low-level disinfection with HAD. Follow the normal facility disinfection process.

c. Soiled Linen. Transmission of smallpox virus via contaminated bedding is documented in historical literature. Modern methods of linen management and infection control are sufficient to minimize the risk of infection transmission. The use of linen chutes is not recommended. An on–site laundry service is preferred.

(1) Linen service staff must:

(a)-Receive smallpox vaccine within previous 3 to 10 years and be trained appropriately to their risk and educational level of understanding.

(b) Wear fit-tested NIOSH-approved N95 particulate respirator and fluid-resistant gowns and gloves when handling or sorting soiled linens.

(c) Use quality-assurance monitoring tool and evaluator to validate linen process.

(2) Place covered linen hampers lined with impervious laundry bags just inside the door of an isolation room.

(a) Place only cloth items (not yellow paper gowns) in the hampers.

(b) Wrap linen soiled with blood or other body fluids in sheets or placed in a pillowcase to prevent dripping prior to placing in the linen hamper.

(c) Do not fill laundry bags more than two-thirds full and remove at least every 24 hours. Bag with minimum agitation at site of use. Follow MTF guidelines for identification of isolation linen.

(3) Laundering Procedures.

(a) Do not sort contaminated linens before washing, to minimize the exposure to personnel and to decrease the aerosolization of contaminated particles.

(b) Wash items with a detergent in hot water (71ºC, 160ºF) for at least 25 minutes.

(c) Bleach cycle achieves 50 to 150 parts per million (ppm).

(d) Add mild acid to neutralize any alkalinity in the water, soap, or detergent.

(e) Check dryer temperature. Clothes must be dried completely in a commercial dryer (not line dried).

d. Regulated Medical Waste. NOTE: Abide by whichever regulations are most stringent in your area: federal, state, or local.

(1) Dispose of all bodily fluids safely via the sanitary sewer, following routine protocols.

(2) Discharge Management. In general, patients with smallpox will not be discharged from a healthcare facility until no longer infectious or sent to another designated facility. Therefore, no special discharge instructions are required. However, patients who do not need specialized care may be discharged to their homes (but not barracks or dormitories) while infectious, because of lack of space in the MTF. MTFs will provide instructions for infection control to be observed by patients in their home (e.g., Appendix F-3).

e. Post-Mortem Care. Use airborne and contact precautions for post-mortem care. Cremation is preferable to burial for the remains of smallpox victims. The National Association of Medical Examiners (NAME) determined that embalming cadavers presents an infectious risk to the embalmer. Double-bag the bodies and decontaminate the outside of the outermost bag with a 1:10 bleach solution. Transfer bodies in hermetically sealed containers. As provided in Joint Publication 4-06: Remains suspected of biological contamination must be placed in two human-remains pouches and marked "BIOLOGICAL [BIO]" before to evacuation to a Mortuary Affairs Decontamination Collection Point (MADCP). These remains must be kept separate from other remains during the processing and while awaiting transportation. Mark the top of all case file forms "BIO."

APPENDIX F-1
Decontamination Guidelines – Summary.

1. Variola and vaccinia viruses, if protected from ultraviolet light, may persist for as long as 24 hours, or somewhat longer under favorable conditions. Variola and vaccinia viruses are easily killed by hospital-approved disinfectants (HAD) labeled tuberculocidal.

2. Decontamination removes foreign material, preceding disinfection or sterilization. People responsible for decontamination need several layers of personal protection: vaccination against smallpox, training, and personal protective equipment (PPE).

3. Disinfection uses chemical reactions to eliminate recognized pathogenic microbes, but not necessarily all microbial forms (e.g., bacterial spores) on inanimate objects. There are three levels of disinfection: high, intermediate, and low. High-level disinfection kills all organisms, except high levels of bacterial spores, by means of a chemical germicide recognized as a sterilant by the FDA. Intermediate-level disinfection kills mycobacteria, most viruses, and bacteria with a chemical germicide registered as a "tuberculocide" by the EPA. Use these disinfectants according to labeled instructions, including appropriate wet contact time.

4. Reusable devices and items that touch mucous membranes should receive at least high-level disinfection between patients. Sterilization is not required, except for critical items that will penetrate sterile body sites. Sterilization is a physical or chemical procedure to destroy all microbial life, including highly resistant bacterial endospores.

5. MTFs will develop plans for handling regulated medical waste (RMW). All waste generated by smallpox patients will be treated as RMW. Dispose of all bodily fluids safely via the sanitary sewer.

6. Bag soiled linen with minimum agitation at point of use. Do not sort linen prior to the completion of the wash and dry cycles. Explain procedures to contract laundry services.

7. When possible, dedicate non-critical equipment to a single patient (or cohort of patients with the same illness). If use of common items is unavoidable, do not use potentially contaminated, reusable equipment for the care of another patient, until it has been appropriately cleaned and reprocessed.

8. Post-mortem care. Use standard, airborne, and contact precautions for post-mortem care. Cremation is preferable to burial. The National Association of Medical Examiners (NAME) determined that embalming cadavers presents too great an infectious risk to the embalmer. Generally, double-bag bodies with superficial decontamination of the outside of the bag. Transfer bodies in hermetically sealed containers.

9. Appendix F-2 summarizes decontamination and infection-control procedures. Appendix F-3 summarizes home care and vehicle procedures.

APPENDIX F-2
Decontamination & Infection Control Reference Guide.

Isolation Requirements - Strict Adherence is Mandatory
Standard Precautions for all aspects of patient care - Strictly enforced.
Contact Precautions - Place sign on the door. - Fluid-resistant gown and gloves to enter the room. - Disposable gowns - treat as regulated medical waste (RMW). - Cloth gowns placed in leak-proof laundry bags. - Respirator/eye shield/face shield during procedures prone to splashing, spraying.
Airborne Precautions - Must be in negative airflow room - Place sign on the door.
Fit-tested, NIOSH-approved, **N95** particulate respirator by **anyone** entering room. - Must be in Respiratory Protection Program.
Alcohol-based hand-hygiene agent before entering room and on exit.
Wash hands with antimicrobial soap.
Monitor staff entrance and exit.
Serve food in disposable service ware - If large scale outbreak, ensure dietary staff are trained to wear gloves when handling dishes from isolation room and ensure compliance with water temperatures and detergents.
Cleaning & Disinfection of Equipment
Thorough terminal cleaning of room with hospital-approved disinfectant (HAD). *
Alternative is to also disinfect surfaces with solution containing 1 part bleach and 9 parts of water (10% solution) Store bleach in an opaque bottle. Label accurately.
Dedicated equipment - disinfect if reusable or discard as RMW if single-patient use, when patient discharged.
Thermometers - may use glass thermometers or strip type.
Stethoscope, BP cuff and sphygmomanometers - Dedicated or disposable.
Place linen hamper in the room. See linen management below.
Treat non-regulated medical waste the same as RMW.
RMW handled per MTF policy.
Housekeeping
Trash container emptied and disinfected.
Low dusting and cleaning all exposed surfaces with HAD. *
Patient's bed cleaned and free of soiling & foreign matter.
Fixtures, walls, lights, doorknobs, bedrails, and overbed tables cleaned and free of fingerprints/hand marks with HAD. *
Floor damp-mopped using two bucket method using HAD. *
Vents, grills, windowsills and blinds damp wiped with HAD. *
Sink and toilet bowl disinfected.
Cotton mop changed after each room and placed into plastic bag for laundering.
Mopping water changed after each room.
Must wear PPE – fit-tested NIOSH-approved N-95 particulate respirator, fluid-resistant gown and gloves.

Linen Management
An on–site laundry service is preferred.
Linen service staff must be vaccinated against smallpox (within previous 3 to 10 years) and trained appropriately to their risk and educational level of understanding.
The use of linen chutes is not recommended.
Staff must wear fit-tested NIOSH-approved N95 particulate respirator and fluid-resistant gowns and gloves when handling or sorting soiled linens.
Use quality-assurance monitoring tool.
Reusable cloth protective clothing and soiled linens may be transported to the laundry following MTF guidelines for identifying isolation linen.
Place linens in leak-proof bags, following MTF guidelines for identifying isolation linen.
Contaminated clothing and linens should be not sorted prior to washing to minimize the exposure to personnel and to decrease the aerosolization of contaminated particles.
Hot water washing: Wash items with a detergent in hot water (71ºC, 160ºF) for at least 25 minutes. Bleach cycle achieves 50 to 150 ppm. Add mild acid to neutralize any alkalinity in the water, soap, or detergent. Check dryer temperature.
Clothes must be dried completely in a commercial dryer (not line dried).
Transportation of Linens and RMW Off site
All personnel involved in handling, transportation, and disposal of medical waste from facilities where confirmed or potential smallpox patients are housed must have **recent** vaccination against smallpox (within 3 to 10 years).
Contaminated linen and RMW must be transported in accordance with local, state, and federal regulations.
Reusable Medical Equipment
Decontaminate reusable medical equipment using soap and water or the appropriate instrument detergent or enzymatic cleaner, in accordance with manufacturer's instruction.
Critical instruments that require sterilization – Manufacturers' standard protocols for autoclave use – steam sterilization, gas/plasma; paracetic acid and ethylene oxide.
Semi-critical items – High-level disinfection practices per the institution's policies.
Non-critical – After cleaning, these items may be wiped down with HAD.
Quality-assurance monitoring of disinfection and sterilization processes per routine procedures.
Post-Mortem Care
Follow principles of standard precautions.
Airborne precautions.
- Fit-tested NIOSH-approved **N95** particulate respirator used by **anyone** entering room.
- Negative-pressure rooms.
Contact precautions.
Thorough terminal cleaning of room with HAD* following autopsy or a fresh solution of 1 part bleach and 9 parts water (10% solution).
Burial / Storage Issues
Cremation is preferred over burial.
HAD: **Hospital-approved disinfectant (HAD) -Tuberculocidal - must be EPA registered. HAD is mixed, used, and labeled per manufacturer instructions.**

APPENDIX F-3
Home Care Guidelines for Infection Control.

1. If smallpox patients are housed in their own homes, at a minimum, perform the following decontamination procedures:

a. Bag and dispose of trash according to routine waste disposal methods for your community.

b. Launder bedding, linens, clothing, curtains, or other cloth material that came into contact with the smallpox patient in hot water, adding one cup of bleach per load. Dry laundry in a hot dryer, if possible.

c. Clean surfaces, furniture, fixtures, and walls thoroughly with a household disinfectant (e.g., Lysol), following manufacturer's recommendations.

d. Clean carpets and upholstery using an EPA-approved germicidal detergent, following manufacturer's recommendations.

2. Private Vehicles, if used to move the patient while infectious. Decontaminate using an EPA-approved germicidal detergent or HAD per manufacturer's recommendations

a. Bag and incinerate all disposable items in the vehicle.

b. Wipe down all surfaces in the vehicle thoroughly with a detergent per manufacturer's recommendations. Allow the solution to remain on the surfaces for at least 20 minutes before being removed.

c. Clean carpets and upholstery using detergent per manufacturer's recommendations. Allow the solution to remain on the carpets and upholstery for at least 20 minutes before being wiped off. Allow cloth upholstery to completely dry before use.

d. Clean all outside door handles thoroughly using a detergent per manufacturer's recommendations. Allow the solution to remain on the door handles for at least 20 minutes before being wiped off.

e. Launder cloth material used to wipe down the inside of the vehicle using hot water (71ºC) and bleach, or bagged and incinerated (see above).

APPENDIX F-4
Disinfecting Environmental Surfaces in Healthcare Facilities.

1. Healthcare Infection Control Practices Advisory Committee (HICPAC) Guideline for Disinfection and Sterilization in Healthcare Facilities, 2002, provides recommendations with the ultimate goal of reducing rates of healthcare-associated infections through the appropriate use of disinfectants and sterilization processes. Each recommendation is categorized on the basis of existing scientific data, theoretical rationale, and applicability. The CDC system for categorizing recommendations is as follows.

2. Rankings.

a. Category IA. Strongly recommended for implementation and strongly supported by well-designed experimental, clinical, or epidemiologic studies.

b. Category IB. Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale.

c. Category IC. Required by state or federal regulations. Because of state differences, readers should not assume that the absence of an IC recommendation implies absence of state regulations.

d. Category II. Suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.

e. No recommendation. Unresolved issue. Practices for which insufficient evidence or no consensus regarding efficacy exists.

3. Category IB.

a. Use a one-step process and an Environmental Protection Agency (EPA)-registered hospital-grade disinfectant or detergent (“hospital-approved disinfectant,” HAD) designed for housekeeping purposes.

b. Clean housekeeping surfaces (e.g., floors, wall, tabletops) on a regular basis, as spills occur, and when visibly soiled.

c. The frequency for environmental surface disinfection should comply with hospital policies and should minimally be done when visibly soiled and on a regular basis (e.g., daily, three times per week).

d. Follow manufacturers’ instructions for proper use of disinfecting products, especially the recommended concentration.

e. Prepare disinfecting solutions as needed and replace with fresh solution frequently (e.g., floor mopping solution every three patient rooms or changed no longer than 60-minute intervals) according to the facility's policy.

f. Wet-dust horizontal surfaces regularly (e.g., daily, three times per week) using clean cloths moistened with a HAD. Prepare the disinfectant as recommended by the manufacturer.

g. Decontaminate mop heads and cleaning cloths regularly to prevent contamination (e.g., launder at least daily and heat dry).

h. Phenolic disinfectants (i.e., those containing phenol-based compounds) should not be used to clean infant bassinets and incubators during the stay of an infant. If phenolics are used to terminally clean infant bassinets and incubators, the surfaces should be rinsed thoroughly with water and dried before the infant bassinets and incubators are reused.

i. If chlorine solution is not prepared fresh daily, chlorine may be stored for up to 30 days in a capped plastic bottle with a 50% reduction in chlorine concentration over 30 days (e.g., 1000 ppm chlorine at day 0 decreases to 500 ppm chlorine by day 30).

j. For site decontamination of spills of blood or other potentially infectious materials (OPIM), use protective gloves and other personal protective equipment (PPE) appropriate for this task. If sodium hypochlorite solutions are selected use a 1:100 dilution (i.e., 500 ppm available chlorine) to decontaminate nonporous surfaces after cleaning a small spill of either blood or OPIM. If a spill involves large amounts (e.g., > 10 ml) of blood or OPIM, use a 1:10 dilution for the first application of HAD disinfectant before cleaning.

4. Category IC.

a. Promptly clean and decontaminate spills of blood or other potentially infectious materials.

b. Occupational Safety and Health Administration (OSHA) requires that blood spills be disinfected using a HAD or a solution of 6% sodium hypochlorite (household bleach) diluted between 1:10 and 1:100 with water. A HAD that is labeled effective against human immunodeficiency virus (HIV) and hepatitis B virus (HBV) would be considered an appropriate disinfectant provided the surfaces have not been contaminated with agent(s) or volumes of or concentrations of agent(s) for which higher-level disinfection is recommended.

5. Category II.

a. In units with high endemic *Clostridium difficile* infection rates or in an outbreak setting, the use of dilute solutions of 6% sodium hypochlorite (1:10 dilution of bleach) can be used for routine environmental disinfection.

b. Clean walls, blinds, and window curtains in patient-care areas when visibly contaminated or soiled.

c. Do not use high-level disinfectants/liquid chemical sterilants for disinfection of non-critical surfaces.

d. The contact time for low-level disinfection of non-critical items is at least 30 seconds.

6. Disinfection in Ambulatory Care and Home Care.

a. The same classification scheme described above should be followed (i.e., critical devices require sterilization, semi critical devices require high-level disinfection, and non-critical equipment requires low-level disinfection) in the ambulatory care (e.g., outpatient medical or surgical facilities) setting since there is a similar infection risk as in the hospital setting. Category IB

b. Reusable objects that touch mucous membranes (e.g., tracheostomy tubes) can be cleaned and disinfected by immersion in a 1:50 dilution of 6% sodium hypochlorite (household bleach) for 3 minutes, 70% isopropyl alcohol for 5 minutes, or 3% hydrogen peroxide for 30 minutes, because the home environment should be safer to the extent that person-to-person transmission is less likely. Category II

c. Non-critical items (e.g., crutches, blood pressure cuffs) in the home setting can be cleaned with a detergent. Category II.

APPENDIX F-5
Glossary of Decontamination Terms.

Bleach: Household bleach (6% to 6.15% sodium hypochlorite) is normally diluted in water at 1:10 or 1:100 (i.e., 1 part concentrated bleach to 10 or 100 parts water). Approximate dilutions are 1.5 cups of bleach in a gallon of water for a 1:10 dilution (6,000 ppm) and one-quarter cup of bleach in a gallon of water for a 1:100 dilution (600 ppm).

Cleaning: The removal, usually with detergent and water or enzymatic detergent and water, of adherent visible soil, blood, protein substances, and other debris from the surfaces, crevices, serrations, joints, and lumens of instruments, devices, and equipment by a manual or mechanical process that prepares the items for safe handling and/or further decontamination.

Contact time: The time a disinfectant is in direct contact with the surface or item to be disinfected. For surface disinfection, this time period is framed by the application to the surface until complete drying has occurred.

Contaminated: State of having been actually or potentially in contact with microorganisms. As used in healthcare, the term generally refers to the presence of microorganisms that could be capable of producing disease or infection.

Decontamination: A procedure that removes pathogenic microorganisms from objects so they are safe to handle.

Detergent: A cleaning agent that makes no antimicrobial claims on the label. They are composed of a hydrophilic component and a lipophilic component and can be divided into four types: anionic, cationic, amphoteric, and non-ionic detergents.

Disinfectant: An agent that frees from infection, usually a chemical agent but sometimes a physical one, that destroys disease-causing pathogens or other harmful microbes, but may not kill bacterial spores. It refers to substances applied to inanimate objects. The EPA groups disinfectants on whether the product label claims “limited,” “general,” or “hospital” disinfection.

Disinfection: Disinfection describes a process that eliminates many or all-pathogenic microorganisms on inanimate objects with the exception of bacterial spores. Disinfection is usually accomplished by the use of liquid chemicals. The efficacy of disinfection is affected by a number of factors, each of which may nullify or limit the efficacy of the process. These include the prior cleaning of the object; the organic and inorganic load present; the type and level of microbial contamination; the concentration of and exposure time to the germicide; the nature of the object (e.g., crevices, hinges, and lumens); the presence of biofilms; the temperature and pH of the disinfection process.

Germicide: An agent that can kill microorganisms, particularly pathogenic organisms ("germs"). It is like the word disinfectant with the difference that germicide applies to compounds used on both living tissue and inanimate objects, whereas disinfectants are applied only to inanimate objects.

Hospital disinfectant: A disinfectant registered for use in hospitals, clinics, dental offices, or any other medical-related facility. Efficacy is demonstrated against *Salmonella choleraesui*s, *Staphylococcus aureu*s, and *Pseudomonas aeruginosa.* EPA has registered about 1,200 hospital disinfectants.

Hospital-approved disinfectant (HAD): HAD disinfectants labeled as tuberculocidal approved by the healthcare facility.

Regulated Medical Waste: Liquid or semi-liquid blood or other potentially infectious materials; contaminated items that would release blood or other infectious materials in a liquid or semi-liquid state if compressed; items that are caked with dried blood or other potentially-infectious materials and are capable of releasing these materials during handling; contaminated sharps; and pathological and microbiological wastes containing blood or other potentially-infectious materials. Any waste defined by federal, state and local regulations capable of producing an infectious disease in humans.

Sterilization: The complete elimination or destruction of all forms of microbial life, accomplished in healthcare facilities by either physical or chemical processes. Steam under pressure, dry heat, ethylene oxide (ETO) gas, hydrogen peroxide gas plasma, and liquid chemicals are the principal sterilizing agents used in healthcare facilities.

ANNEX G TO SMALLPOX RESPONSE PLAN 29 September 2002
MEDICAL CARE OF SMALLPOX PATIENTS (VARIOLA INFECTION).

REFERENCES.

a. CDC Smallpox Response Plan, Annex 1. Overview Of Smallpox, Clinical Presentations, and Medical Care of Smallpox Patients, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

b. United States Army Medical Command. How-To" Guide for Command Surgeons: Implementation Guidelines for Investigational New Drug (IND) Protocols. Falls Church, VA, May 2002.

c. United States Army Medical Command. "How To" Guide for Unit Leaders and Unit Health Care Providers: Implementation Guidelines for Investigational New Drug (IND) Protocols. Falls Church, VA, May 2002.

d. United States Army Medical Command. "How To" Guide for Investigational New Drug (IND) Protocols, Supplement: Cidofovir (Vistide®, Gilead) to Treat Variola Infection (IND # 65,480). Falls Church, VA, publication pending.

e. CDC Smallpox Response Plan, Annex 2, Guidelines for Smallpox Vaccination Clinics, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

f. Breman JG, Henderson DA. Diagnosis and management of smallpox. *N Engl J Med* 2002; 346:1300-8. http://content.nejm.org/cgi/reprint/346/17/1300.pdf.

g. Army Regulation 40-535, Air Force Regulation 164-5, OPNAVINST 4630.9C, MCO P4630.9A. Worldwide Aeromedical Evacuation. 10 May 1979. http://www.usapa.army.mil/pdffiles/r40_535.pdf.

1. General. This DoD Annex augments CDC Annex 1 (reference a). Appendix G-1 summarizes CDC Annex 1 and this DoD Annex on one page.

a. Mission. Health-care workers will render supportive and life-sustaining care to treat patients diagnosed with smallpox (variola infection).

b. Assumptions.

(1) Although smallpox can spread widely across human populations, control measures will eventually slow and then stop epidemic spread. Depending upon the method, extent, and duration of smallpox transmission, restriction and control of the ensuing epidemic will be effective.

(2) Variola infection is not inevitably fatal. About 70% of unvaccinated people will survive, as will ~ 98% of vaccinated people. Adequate, conscientious, modern medical support may raise these survival probabilities (Appendix G-3).

(3) The US Army Medical Research & Materiel Command (USAMRMC) applied to the Food & Drug Administration (FDA) for permission to use the antiviral medication cidofovir (*Vistide*, Gilead Sciences, www.gilead.com/wt/sec/vistide) under an investigational new drug (IND) protocol to treat human variola infections. FDA accepted this IND protocol in Sep 02.

(4) Vaccinia immune globulin (VIG) is of no value and has no role in treating smallpox (variola infection).

c. Planning Factors.

(1) Disease Progression. Appendix G-2 outlines the clinical development of variola infection (smallpox). Medical management of a patient with smallpox is mainly supportive (Appendix G-3).

(2) Clinical Care. Good care consists of (a) isolation of the patient to prevent transmission of the smallpox virus to non-immune people, (b) monitoring and maintaining fluid and electrolyte balance, (c) skin care, and (d) monitoring for and treatment of complications. Unless the diagnosis of smallpox is laboratory confirmed, vaccinate the patient if he or she will be isolated with other confirmed or suspected smallpox cases. Vaccination of suspected cases of smallpox is done to prevent the accidental transmission of smallpox virus to any suspected smallpox patients who have been misdiagnosed as smallpox cases. See also Appendix G-3.

(3) Education and Awareness. Education and training of specialized treatment teams (T-Teams) must occur before a smallpox outbreak occurs. The education of healthcare providers of all specialties about the existence of specialized treatment teams will be necessary for timely alert and communication. Informing the military leadership and the public about these T-teams will aid morale.

(4) Training. Specialized treatment teams will be trained in the requirements of IND protocols in general and the cidofovir treatment protocol in particular, to allow prompt use of this agent. The US Army will coordinate such training.

(5) Personnel Resources. Services will be prepared to augment MTF medical capabilities overwhelmed by a large number of smallpox cases. MTF commanders will develop procedures for emergency credentialing of healthcare workers to assist with disease outbreaks. The specialized treatment team will travel to the MTF with the initial smallpox patients. The gaining MTF will assign additional personnel to the specialized treatment team, as requested by the treating physician(s). Additional DoD assets will be assigned, if requirements extend beyond the capabilities of the local MTF. Appendix G-6 provides additional considerations in mass care of smallpox patients.

(6) Access to Cidofovir.

(a) MTFs will not use on-hand stocks of cidofovir to treat patients infected with variola virus, nor order cidofovir from other sources, without first coordinating with the US Army Medical Research Institute of Infectious Diseases (USAMRIID). Upon notification that a smallpox outbreak has occurred anywhere in the world, all MTF pharmacies will sequester any stocks of cidofovir on hand to treat retinitis, and begin controlling the cidofovir as if it were a Schedule II narcotic (e.g., storage in a safe or vault, perpetual inventory). The pharmacy will dispense the drug only for its labeled indication, unless its use is pursuant to an FDA-accepted IND protocol.

(b) USAMRIID will establish a common point of access for telephonic requests for use of cidofovir for a named patient by a physician willing to comply with IND requirements (references b, c, and d). Access to cidofovir for eligible patients will be facilitated by specialized treatment teams (T-Teams). Healthcare providers from civilian institutions should contact the CDC Drug Service for cidofovir: CDC Drug Service, National Center for Infectious Diseases, Mail stop D-09, Atlanta, GA 30333; 404-639-3670, fax 404-639-3717.

(7) Other Medications. If therapy with cidofovir is ineffective, clinicians may be inclined to try other therapeutic modalities unavailable when routine smallpox vaccinations ceased in the 1970s and 1980s (e.g., interferons, other antivirals). Little or no data may exist to support the safety or effectiveness of such approaches and no Federal agency sanctions their use. Nonetheless, DoD clinicians reserve their individual prerogatives and responsibilities in the clinical practice of medicine for individual patients.

d. Coordinating Instructions.

(1) Command Relationships. The specialized treatment team will be assigned under the operational control (OPCON) of the local MTF commander.

(2) Communication. Information will be conveyed to other external sources, including the media, only with command approval and using risk-communication principles. If working in coordination with local treatment teams, no information will be conveyed to other external sources, including the media, without approval of, or simultaneous presentation with, the coordinating agency (CONUS--CDC, OCONUS--WHO).

e. Legal Considerations.

(1) All use of IND agents will be performed in accordance with IRB-approved guidelines and FDA regulations (see references b, c, and d, and Appendix G-4). MTFs will provide personnel and supply resources to the specialized treatment teams to satisfy regulatory requirements.

(2) Smallpox outbreaks may occur OCONUS. Travel of personnel into or out of the involved region may become difficult or impossible, for medical, legal, or political reasons. US unified commands will provide access by specialized treatment teams to patient needing treatment, as well as security for these T-Teams.

2. Execution.

a. Concept of Operations.

(1) The treatment of smallpox will occur within local medical facilities. Evacuation of smallpox patients will be avoided or minimized, to reduce contact with the patient and further spread of disease.

(2) Smallpox patients will be hospitalized, if adequate facilities permit. Adequate infection-control procedures (Annexes C and G) will be paramount. Negative airflow rooms are warranted. Cohorting (i.e., sharing of rooms/facilities by patients with similar disease categories) is recommended. Given adequate medical observation (at least daily physician visits) and restriction of further exposures, minimal care or out-of-hospital care is possible. See also Appendix G-6.

(3) Cidofovir is a medication licensed by the FDA for treatment of cytomegalovirus (CMV) retinitis in people infected with the human immunodeficiency virus (HIV) [see Appendix H-3]. For a different use, cidofovir is an investigational, moderately toxic antiviral agent projected to be given intravenously once a week in the treatment of variola infection. Side effects, especially renal insufficiency, occur. Animal-challenge experiments show the efficacy of cidofovir against orthopoxviruses (the group of viruses that includes variola and vaccinia viruses). It is presently unknown whether cidofovir will be effective in treating human smallpox infection. Cidofovir should be administered by an FDA-registered principal investigator or subinvestigator. Patient consent must be obtained before administration under IND protocol. See also Appendix G-4, for exceptions for unconscious patients. Actual use of cidofovir under the FDA-accepted protocol is specified within the treatment protocol (reference d). This protocol addresses dosage, expected side effects, physiologic and laboratory monitoring, and regulatory and reporting issues.

(4) Because of the administrative burden of implementing an IND protocol, and this drug's intravenous route of administration, multidisciplinary specialized treatment teams will be assembled to travel to areas affected by an outbreak, to administer cidofovir and assist with patient care. Prior vaccination against smallpox will be a condition of membership on these teams. Such T-Teams will include:

(a) Team leader – Senior medical officer.

(b) One or more infectious disease or dermatology physicians.

(c) One or more intensive-care physicians.

(d) Pharmacy officer and technician.

(e) Laboratory officer and technician.

(f) Nursing support – Two or more ICU-trained nurses.

(g) Preventive-medicine/Occupational-health specialist (physician or senior technician)

(h) Preventive-medicine technician

(i) Communications specialist

b. Tasks and Responsibilities.

(1) Identification and specific diagnosis of patients with smallpox will be the responsibility of healthcare providers at the MTF level, in consultation with regional infectious-diseases, dermatology, and pathology specialists, as needed. MTFs will make every attempt, using organic assets, to exclude the more common and probable diagnoses (e.g., chickenpox, allergic reactions, insect bites), using the CDC Generalized Vesicular or Pustular Rash Illness Protocol. See Annex A for the sequence when initiating an alert to the possible presence of a patient with smallpox.

(2) MTF commanders will be responsible for transporting patients between MTFs; provision of ancillary supply and personnel resources to specialized treatment teams; pharmacy and laboratory support; and communication support.

(3) The service member's unit will be responsible for initial transportation to the first-level MTF. Once within the medical system, it will be the responsibility of the medical-evacuation system for further patient transportation as needed. Evacuation of smallpox patients will be avoided or minimized, to reduce contact with the patient and further spread of disease.

(4) The MTF will provide routine medical care in accordance with standard practice, with laboratory, pharmacy, radiology, and pathology support. If the patient is treated with cidofovir, the treating team will have responsibility for the completion and maintenance of records and reports, and the processing or packaging of pathologic or autopsy materials.

(5) Once a definite or probable diagnosis of smallpox has been made, attending physicians will consider whether cidofovir treatment may be appropriate, consulting with local or regional infectious-disease (ID) or dermatology physicians. For clinical consultation with orthopoxvirus specialists, physicians may telephone USAMRIID at 1-888-USA-RIID or 301-619-2257. Alternately, page the USAMRIID staff duty officer at

301-631-4393 or the USAMRMC staff duty officer at 301-619-6092. USAMRIID will coordinate with specialized treatment teams, which will travel to the MTF caring for the diagnosed smallpox patient. These teams will be responsible for the treatment of patients with the indicated medications. IND-specific procedures will be followed carefully. To request cidofovir for a named patient, refer to Annex I.

c. Reporting.

(1) T-team leaders will periodically brief the MTF commander on the status of patients with smallpox, at a frequency directed by the commander.

(2) IND protocol reports will be submitted as detailed in reference d.

3. Operational Constraints.

a. Equipment. MTFs caring for smallpox patients can be expected to provide care up to and including intensive-care support. MTFs may expect this requirement to include appropriate equipment (e.g., ventilators, dialysis machines) and pharmacy support (e.g., vasopressors, and routine antibiotics).

b. Training. T-Teams will be trained in the use and monitoring of therapy with cidofovir. The US Army will coordinate such training. Periodic alert exercises, without travel, will be performed at least quarterly to sustain team proficiency.

c. Surge Capacity. Depending on the size of the smallpox outbreak, the number of people infected with smallpox may exceed the ability of specialized treatment teams to care for those infected with smallpox. Augmentation of T-Teams may occur by one or more of the following:

(1) Assignment of one or more additional regional treatment teams by USAMRIID, to the affected MTF or area;

(2) Augmentation of the team by local physician, pharmacy, nursing, and laboratory assets, with oversight of cidofovir administration remaining under the purview of the initial team’s subinvestigators; or

(3) Coordination with local civilian response teams, as needed. See paragraph 5 below.

d. Control of IND Agents. MTF pharmacy support to specialized treatment teams will include storage (see below), control, and security for both cidofovir and locally available medications. Pharmacy assets on the specialized treatment teams will prepare and dispense cidofovir for the team’s use.

e. Notification. Emergency use of an investigational drug for a named patient will comply with notification requirements to U.S. Army Medical Command, in accordance

with Army Regulation 40-7 (Use of Investigational Drugs and Devices in Humans and the Use of Schedule I Controlled Drug Substances, 4 January 1991), paragraph 4-9, and comparable regulations in other military Services.

f. Security. MTFs will coordinate with local military and local law enforcement personnel to protect patients, medical personnel, and the IND medications.

4. Administration and Logistics.

a. MTFs will provide administrative support for protocol performance by the teams (e.g., office space, copying, automation, communication support).

b. Shipping and Distribution. Either the T-Teams will transport the cidofovir themselves, or they will coordinate with the US Army Medical Materiel Agency (USAMMA) for transportation (see Annex I).

c. Supply and Storage. Supplies of cidofovir, delivered from USAMRIID, will be stored and maintained by the MTF pharmacy under the appropriate room-temperature conditions (reference d).

5. Special Situations.

a. Treatment of Military Personnel and Beneficiaries in CONUS. Military personnel and beneficiaries in CONUS will receive treatment in local military MTFs. Infection-control principles call for patients with smallpox to be cared for in designated Type-C treatment facilities. See also Annex C. At the beginning of a smallpox outbreak, this would likely be the first hospital(s) to which such patients are admitted.

b. Relation to Civilian Facilities. Members of specialized treatment teams will probably not be licensed under state regulations to provide medical care outside of a federal MTF. State regulations may be waived in time of emergency. Cidofovir and other IND medications may not be shared with or diverted to people not registered under the protocol, without the detailed knowledge and explicit agreement of USAMRIID and the principal investigator (who may also need FDA agreement).

c. Treatment of Military Personnel and Beneficiaries Outside of CONUS. Military personnel and beneficiaries OCONUS will receive treatment in local MTFs. Members of specialized treatment teams will probably not be licensed, by national laws or regulations, to provide medical care outside of the military MTF. These laws and regulations may be waived in time of emergency. Local civilian institutions may provide care to military personnel and beneficiaries under applicable Status of Forces Agreements or other agreements. Cidofovir and other IND medications may not be shared with or diverted to people not registered under the protocol, without the detailed knowledge and explicit agreement of USAMRIID and the principal investigator (who may also need FDA agreement).

d. Treatment of Military Personnel and Beneficiaries in Transit. If a patient started on cidofovir at one MTF is transferred to another medical facility, a physician at the gaining institution may continue cidofovir administration only if he or she agrees to join the IND protocol as a subinvestigator and takes responsibility for fulfilling FDA regulations for conducting an FDA-accepted IND protocol.

APPENDIX G-1
Medical Care Of Smallpox Patients (Variola Infection) – Summary.

1. Smallpox (variola infection) is not inevitably fatal. About 70% of unvaccinated people will survive infection, as will 95% of vaccinated people. The existence of a possible specific treatment for the disease, cidofovir (*Vistide*, Gilead Sciences), may increase survival.

2. The US Army Medical Research & Materiel Command (USAMRMC) is applying to the Food & Drug Administration (FDA) for permission to use cidofovir (*Vistide*, Gilead Sciences, Appendix G-5, Appendix H-3) under an investigational new drug (IND) protocol to treat human variola infections. This annex assumes FDA will accept this IND protocol.

3. Because of the administrative burden of implementing an IND protocol, and this drug's intravenous route of administration, multidisciplinary specialized treatment teams will be assembled to travel to areas affected by a smallpox outbreak, to administer cidofovir and assist with patient care. Prior vaccination against smallpox typically will be a condition of membership on these teams.

4. Once a definite or probable diagnosis of smallpox has been made, attending physicians will consider whether cidofovir treatment may be appropriate, consulting with local or regional infectious-disease (ID) or dermatology physicians. The physicians may request use of cidofovir for a named patient by telephoning USAMRIID at 1-888-USA-RIID or 301-619-2257. Alternately, page the USAMRIID staff duty officer at 301-631-4393 or the USAMRMC staff duty officer at 301-619-6092.

5. USAMRIID will coordinate with these specialized treatment teams (T-Teams), which will travel to the MTF caring for the diagnosed smallpox patient. IND-specific procedures will be followed carefully. The specialized treatment team will be assigned under the operational control (OPCON) of the local MTF commander.

6. Specialized treatment team leaders will periodically brief the MTF commander on the status of patients with smallpox, at a frequency directed by the commander. Team leaders and IND investigators will submit IND protocol reports as required by the FDA.

APPENDIX G-2
Stages of Smallpox Infection.

<table>
<tr><th>Communic-ability</th><th>Exposure = Day 0</th><th>Symptoms</th><th>Day of Symptoms</th><th>Disease Progress</th></tr>
<tr><td rowspan="14">Not contagious</td><td>Day 1</td><td rowspan="10">No symptoms</td><td rowspan="10"></td><td rowspan="3">Virus introduced to respiratory tract</td></tr>
<tr><td>2</td></tr>
<tr><td>3</td></tr>
<tr><td>4</td><td rowspan="2">Virus appears in lymph nodes</td></tr>
<tr><td>5</td></tr>
<tr><td>6</td><td rowspan="5">Virus replicates in lymph system</td></tr>
<tr><td>7</td></tr>
<tr><td>8</td></tr>
<tr><td>9</td></tr>
<tr><td>10</td></tr>
<tr><td>11</td><td rowspan="3">First symptoms</td><td>Day 1</td></tr>
<tr><td>12</td><td>2</td><td rowspan="3">Fever, backache, headache, nausea, malaise, enanthem</td></tr>
<tr><td>13</td><td>3</td></tr>
<tr><td>Contagious</td><td>14</td><td>4</td></tr>
<tr><td rowspan="2"></td><td>15</td><td rowspan="18">Rash</td><td>5</td><td>Macules (spots)</td></tr>
<tr><td rowspan="4">Very contagious</td><td>16</td><td>6</td><td rowspan="3">Papules (bumps, pimples)</td></tr>
<tr><td>17</td><td>7</td></tr>
<tr><td>18</td><td>8</td></tr>
<tr><td>19</td><td>9</td><td rowspan="2">Vesicles (blisters)</td></tr>
<tr><td>20</td><td>10</td></tr>
<tr><td rowspan="4">Contagious</td><td>21</td><td>11</td><td rowspan="4">Pustules (pus-filled blisters)</td></tr>
<tr><td>22</td><td>12</td></tr>
<tr><td>23</td><td>13</td></tr>
<tr><td>24</td><td>14</td></tr>
<tr><td rowspan="2"></td><td>25</td><td>15</td><td rowspan="5">Scabs</td></tr>
<tr><td rowspan="4">Scabs contagious</td><td>26</td><td>16</td></tr>
<tr><td>27</td><td>17</td></tr>
<tr><td>28</td><td>18</td></tr>
<tr><td>29</td><td>19</td></tr>
<tr><td rowspan="2">Not contagious</td><td>30</td><td>20</td></tr>
<tr><td>31</td><td colspan="2">Scars</td></tr>
<tr><td>32</td></tr>
</table>

From Fenn (2001, p.19), Breman & Henderson (2002), and Fenner et al (1988).

First symptoms may begin as soon as 7 days or as late as 17 days after exposure.

APPENDIX G-3
Considerations in Clinical Care of Variola Infection.

1. Fluid and Electrolyte Balance. During the vesicular and pustular stages of smallpox, patients may experience significant fluid losses and become hypovolemic or develop shock. Fluid loss can result from (a) fever, (b) nausea and vomiting, (c) decreased fluid intake due to swallowing discomfort from pharyngeal lesions, (d) body fluid shifts from the vascular bed into the subcutaneous tissue, and (e) massive skin desquamation in patients with extensive confluent lesions. Electrolyte and protein loss may also occur in these patients. Monitor fluid and electrolyte balance in hospitalized patients with appropriate oral or intravenous correction of imbalances. Encourage patients with less severe disease who do not require hospitalization to maintain good oral intake of fluids, educated on the signs/symptoms of hypovolemia/dehydration, and counsel them on when to seek medical attention if hypovolemia/dehydration occurs.

2. Skin Care. Keep the skin clean. Avoid rupturing vesicles or pustules. Do not apply salves or ointments. In general, allow scab lesions to heal and separate on their own. All scabs should separate by 3 to 4 weeks. But lesions on the palms and soles may persist longer than 3 to 4 weeks unless artificially removed. Bacterial superinfection of lesions may occur and should be treated with appropriate antibiotics.

3. Monitoring and Treatment of Complications. Several types of complications may occur during the course of a smallpox infection. These include: (a) hemorrhagic, (b) secondary bacterial infections, (d) corneal ulceration and/or keratitis, (d) arthritis or osteomyelitis variolosa, (e) respiratory, (f) encephalitis, (g) gastrointestinal, and (h) genitourinary. These complications and their treatment are described below.

a. Hemorrhagic. Minor hemorrhagic manifestations such as subconjunctival hemorrhages occur commonly in smallpox patients. If subconjunctival hemorrhages are isolated and not accompanied by consumption coagulopathy or active bleeding (e.g., decreasing hemoglobin, hematocrit, or platelets), no specific therapy is needed. However, if signs of more extensive hemorrhage are present (e.g., mucosal bleeding, bleeding into smallpox lesions, ecchymoses, hematemesis, hematuria), evaluate the patient for disseminated intravascular coagulation (DIC) and treat appropriately. Hemorrhagic complications may indicate a more severe form of the disease called hemorrhagic smallpox, which has a poor prognosis. Because of a high, sustained viremia coupled with mucosal hemorrhaging, these patients are highly infectious.

b. Secondary Bacterial Infections. Bacterial superinfections can include abscesses of skin lesions, pneumonia, osteomyelitis, joint infections, and septicemia. Perform laboratory diagnostics to help guide antibiotic therapy.

c. Corneal Ulceration and/or Keratitis. These complications occurred more frequently in hemorrhagic-type smallpox but were occasionally seen in the more typical ordinary-type smallpox. In a case series reported by Rao from Bombay in 1972, corneal ulcers

occurred in 1% of non-hemorrhagic type smallpox cases and keratitis occurred in 0.25%. Corneal ulcerations can appear around the second week of illness and begin at the corneal margins. Ulcers can heal rapidly, leaving a minor opacity, or on occasion, may cause severe corneal scarring. Keratitis and corneal ulceration was far more common in malnourished individuals. Topical idoxuridine has been used but its efficacy is undocumented.

d. Arthritis or Osteomyelitis Variolosa. This complication occurred in 1.7% of the cases in the Rao case series. It usually occurred after the 15th day, accompanied by a brief recurrence of fever during scabbing. The elbow is the most commonly affected joint. Symmetrical, bilateral involvement was frequently seen. This complication was most commonly due to viral infection of the metaphyses of growing bones. Most cases resolved without permanent deformity.

e. Respiratory. Viral bronchitis and pneumonitis can be common complications of severe smallpox. Treatment is symptomatic, treating hypoxemia with oxygen and/or intubation/ventilation as indicated. Secondary bacterial pneumonia can occur and should be treated with appropriate antibiotics as guided by laboratory diagnostics. Pulmonary edema is common in more severe forms of smallpox (i.e., hemorrhagic, flat-type), and should be treated with careful monitoring of oxygenation, fluid status, and blood pressure, with supplemental oxygen and diuretics administered as needed. Patients with cough during the first week of disease may transmit disease more readily than patients without cough. Patients who developed a cough after symptom day 10, when viral counts in secretions were lower, were not as infectious as those who developed coughs earlier.

f. Encephalitis. This complication occurred in about one out of every 500 cases of smallpox. It usually appeared between the sixth and tenth day of illness, when the rash was still in the papular or vesicular stage. During the smallpox era, this complication was a minor contributor to the case-fatality rate of variola major. Although sometimes slow, recovery was usually complete.

g. Gastrointestinal – Nausea and vomiting can occur in the earlier stages of smallpox, especially in the prodromal period before rash development and should be treated symptomatically. Diarrhea may occasionally occur in the prodromal period or in the second week of illness and should also be treated symptomatically. Acute distension of the stomach occurred rarely and was more common in infants. In some severe cases of smallpox (especially flat-type), extensive viral infection of intestinal mucosa occurred with sloughing of the mucosal membrane. Most of these cases were fatal.

h. Genitourinary System. Orchitis occurred in 0.1% of the Rao case series and was usually unilateral. Hematuria can be present in hemorrhagic type smallpox if bleeding into the pelvis of the kidney occurs.

4. Pathology.

5. For additional advice, seek appropriate medical consultations.

APPENDIX G-4
Exceptions to General Rule to Obtain Informed Consent for Unconscious or Incapacitated Patients.

1. PURPOSE. To describe conditions within federal regulation that provide for exceptions to the general requirement to obtain individual informed consent before use of investigational new drugs (IND).

2. FACTS.

a. Under normal circumstances, DoD health-care providers will obtain documentation of the individual informed consent of the recipients of investigational new drugs (INDs), under provisions of Title 21 Code of Federal Regulations (CFR) Section 50.20, 21 CFR 312, DOD Directive 3216.2 (Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research), and related regulations.

b. Under unusual circumstances, it may not be possible to obtain consent in this way. Individuals incapable of reaching their own reasoned decision on whether or not to grant consent include people incapacitated physically or mentally, such as people who are unconscious.

c. Title 21 CFR 50.23(a) specifies conditions for exception from the general requirement to obtain consent. Both the protocol investigator and a physician not otherwise participating in the IND protocol must certify in writing all the following:

(1) The human subject is confronted by a life-threatening situation necessitating the IND drug,

(2) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject,

(3) Time is not sufficient to obtain consent from the subject's legal representative, and

(4) There is no alternate method of approved or generally recognized therapy providing an equal or greater likelihood of saving the life of the subject.

d. If time is not sufficient to permit the physician not participating in the clinical investigation to render a review, it shall be made within 5 working days after use of the drug.

e. Title 10 United States Code (USC) Section 980 prohibits DoD research unless "the informed consent of the subject is obtained in advance" or "in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject is obtained in advance." This law does not apply to the

situation of individuals described in paragraphs 2b and 2c above, because the use of the IND drug would be for a treatment purpose and with individual life-saving intent, rather than as a function of a "research" undertaking within the meaning of 10 USC 980. This understanding of 10 USC 980 is supported by applicable case law (*Doe v. Sullivan*, 756 F. Supp. 12 (DDC 1991), affirmed, 938 F.2d 1370 (CADC 1991)).

f. Title 10 USC 1107 and 21 CFR 50.23(d) establish rules for waiver of informed consent by the President for IND drug use in particular military operations. As indicated in the legislative history of 10 USC 1107, these requirements for a Presidential waiver are not applicable to standard medical practice in the United States, such as authority to provide life-saving treatment to unconscious or incapacitated patients.

g. Title 21 CFR 50.24 discusses exception from informed-consent requirements for research of emergent conditions where it is anticipated that subjects will not be able to give their informed consent as a result of their medical conditions. In other words, 21 CFR 50.24 addresses situations where a large fraction of subjects will be unable to provide consent. This situation is not currently anticipated for any IND drug under evaluation by the Department of Defense.

APPENDIX G-5
Information Paper Describing Cidofovir.

INFORMATION PAPER

DASG-HCA
23 July 2002

SUBJECT: Cidofovir as a Treatment Against Vaccinia or Variola Viruses

1. Purpose. To describe the availability and potential value of the antiviral medication cidofovir in treating adverse events after smallpox vaccination or smallpox infection itself.

2. Facts.

a. Background. Cidofovir is an antiviral medication manufactured by Gilead Sciences (Foster City, California) with the brand name *Vistide*.

b. Approved Use. The Food & Drug Administration (FDA) approved cidofovir for the treatment of a viral infection of the eye that occurs among people with acquired immune deficiency syndrome (AIDS). This infection is known as cytomegalovirus (CMV) retinitis (inflammation of the retina). CMV retinitis is a relatively uncommon condition, so the standard commercial market for cidofovir is relatively small. As a result, available inventories of cidofovir could be exhausted by sudden increases in demand for the product.

c. Investigational Uses. Cidofovir has been proposed as (1) a treatment for adverse events caused by vaccinia virus, the active ingredient in smallpox vaccine, and (2) a treatment for variola infection (i.e., smallpox infection). The FDA has not approved these uses, so organized efforts to use cidofovir for either of these uses must fall under the investigational new drug (IND) provisions of FDA regulation and federal law. The US Army Medical Research Institute of Infectious Diseases is finalizing two IND protocols, one to support each of the two proposed uses of cidofovir.

d. Antiviral Effects. Using cidofovir against vaccinia or variola viruses is credible, because of laboratory and animal studies, including a study showing that cidofovir protects mice against lethal aerosol or intranasal cowpox virus challenge. However, there is no human experience with using cidofovir either for treating vaccine side effects or for treating smallpox infection.

e. Clinical Application. The proposed dose of cidofovir is 5 mg/kg, so an average patient will require one vial. A patient weighing more than 75 kg will require a second vial. About half of treated patients will need a second dose 7 days after the first. Cidofovir is diluted in 100 ml sodium chloride 0.9% (a common intravenous fluid) before

IV infusion. To minimize kidney damage, the oral medication probenecid plus intravenous fluids for hydration are administered before the cidofovir dose.

f. Logistical Characteristics. Cidofovir is stored at controlled room temperature (20º to 25ºC, 68º to 77ºF) with brief excursions permitted between 15º to 30ºC (59º to 86ºF). The federal contract price is $481.32 per vial as of July 2002. Unopened vials have up to a 3-year shelf life.

g. Stockpiles. About 2,500 vials of cidofovir are included in the National Pharmaceutical Stockpile managed by the Centers for Disease Control & Prevention (CDC). The Department of Defense does not maintain stocks of cidofovir beyond the small inventory at military hospitals available to treat CMV retinitis patients. Suitable warehousing space exists at Fort Detrick and other military installations.

h. Projection for Vaccination Reactions. Assuming that one person among 10,000 people vaccinated against smallpox develops an adverse event treatable with cidofovir and that each of these people needs an average of 1.5 vials of cidofovir, 150 vials costing $72,300 would be needed to support each 1 million vaccinations.

i. Projection for Smallpox Treatment. Assuming that 1,000 smallpox patients would need an average of 1.5 vials of cidofovir each for treatment, 1,500 vials costing $723,000 would be needed to treat each 1,000 smallpox patients.

LTC John D. Grabenstein/DASG-HCA/703-681-5059

Approved by COL Randolph

APPENDIX G-6
Mass Patient Care of Smallpox Patients: Planning Considerations.

1. Reference: CDC Smallpox Response Plan, Annex 3, Smallpox Vaccination Clinic Guide, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/.

2. Planning parameters for managing the consequences of the release of smallpox will include a variety of factors. All planning efforts must work in conjunction with established federal support planning. The primary consideration needs to be for the rapid expansion of capacity. This can be accomplished in a number of ways.

a. Expand existing personnel capacity by augmenting staff. Expansion of physical capacity can be accomplished by opening closed beds, wards, and floors. Converting large, interior spaces into patient care areas can develop further capacity. Some potential sources for augmenting staff may require the establishment of a memorandum of understanding. This must be done ahead of time. In addition to these local sources, the Department of Health and Human Services is initiating planning for the development of local Volunteer Medical Reserve Corps. Note that augmentation needs for mass patient care are in addition to those required for a mass vaccination program.

b. Use auxiliary facilities (e.g., hotels, schools). An important consideration in planning for the use of auxiliary facilities is that those facilities may not be able to be used again as originally intended. The use of auxiliary facilities may require that some standards of care be relaxed. Two major steps are required here: (a) Moving non-smallpox patients and other occupants out and (b) moving resources In (e.g., personnel, portable equipment).

c. Home care may be suitable for the type X and type R patient cohorts described in Annex A and below. Plan for the three facility types recommended by the CDC in the referenced document.

3. Command and Control. All elements of command and control must be exercised regularly. Use the incident command system. Use a centralized Communications Control Center. Centralize control of medical logistics and equipment. Centralize control of transportation assets. Consider using non-traditional (alternate) means of emergency transportation, such as public transportation, for patient movement. Establish procedures for patient movement to appropriate facilities and mobility of healthcare providers to and from treatment facilities. Develop a family support center, in coordination with the American Red Cross, to disseminate information to family members of victims.

4. Personnel Requirements. Preparing for the consequences of a smallpox outbreak will require a significant number of personnel associated with each component of the response. Resources provided by Federal and State agencies will not be sufficient to offset the medical human-resource needs associated with a large-scale smallpox

outbreak. Appropriate staffing of health and medical requirements will be critical for the success of this operation. Develop a plan for coordination with other local, state and federal agencies to avoid “double counting” potential augmentation resources.

a. Address credentialing issues to allow non-local physicians and other care providers to legally practice within the jurisdiction.

b. Ensure that during a smallpox response, unlicensed personnel can be utilized under the supervision of licensed personnel. Consider auxiliary personnel to assist with mass care (e.g., medical, nursing, veterinary students).

c. Identify in-hospital providers and first responders who would respond to a smallpox case. Identify personnel mobilization points.

d. Maintain adequate support staff (e.g., laundry, housekeeping, central supply) to provide mass care.

e. Identify hospital-based infectious-disease specialists for disease consultation.

f. Establish separate staffing to maintain normal medical functions, such as labor and delivery and injury care.

g. Provide for the segregation of providers treating smallpox victims from other providers. Establish control procedures to prevent medical personnel from fleeing from or flooding into medical treatment facilities. Consider the potential loss of healthcare providers due to smallpox exposure or fear of smallpox exposure.

h. Provide for the welfare and safety of emergency workers. Auxiliary response personnel for a city may number 5,000 or more people. Establish a vaccination plan for healthcare providers, public health officials, and their families. Provide appropriate personal protective equipment and infection control measures for personnel and train people in their use. Develop family support plan for medical providers and response personnel. Develop plan for the housing, feeding, and clothing needs of emergency responders.

5. Clinical Treatment and Advice.

a. Train medical staff to recognize and manage smallpox patients. Special considerations include immune-compromised patients and patients with adverse vaccination reactions.

b. Provide treatment protocols. Develop triaging procedures for smallpox victims. Utilize telemedicine for consultation.

c. Prepare to maintain appropriate documentation in mass-care setting.

d. Establish a hotline number to distribute information to vaccine recipients about what a vaccination take should look like. Provide information to those whose vaccinations do not take, including information about where to get revaccination.

e. Be prepared to treat persons with adverse reactions to vaccination. These patients should seek clinical care, which will probably not be available at mass vaccination sites.

6. Mental Health Services.

a. Plan for mental health services for victims and their families.

b. Plan for mental health services for emergency workers and their families.

c. Plan for the management of the worried well and psychological counseling for them.

7. Patient Tracking.

a. Match patients with appropriate medical facilities and other pre-selected treatment locations.

b. Track patients at all facilities.

8. Facilities.

a. Plan for the three facility types described in Annex A (i.e., type C facilities for contagious smallpox patients; type X facilities for vaccinated febrile patients without rash; type R facilities for asymptomatic contacts).

b. Home care may be suitable for the cohorts X and R noted above.

c. Plan for admission procedures for smallpox patients into hospitals or established treatment facility. Establish a standardized community reporting method to report bed availability.

d. Establish plans for the expedient expansion of the existing healthcare system capacity. Use isolation beds within existing facilities. Maximize use of existing healthcare facilities, by augmenting staff. Consider secondary treatment centers for temporary augmentation of healthcare capabilities. Consider using long-term care facilities. Consider using warehouses or schools, keeping in mind that such use may render the facilities contaminated and may require extensive decontamination. Consider the use of neighborhood-based treatment centers versus centralized treatment centers. Establish procedures to staff, equip and transport personnel and victims to and from secondary treatment facilities. Establish procedures for the movement of patients not infected with smallpox to other locales (e.g., National Defense Medical System).

e. Ensure adequate monitoring of the food, air and water within medical treatment facilities.

f. Enforce strict infection-control procedures (Annex C) and decontamination procedures (Annex F).

9. Patient Isolation.

a. Identify personnel responsible for local coordination of activities.

b. Identify appropriate facilities to be utilized for isolation and care.

c. Identify appropriate law-enforcement entities to enforce isolation and to control access to facilities.

d. Review and coordinate plan with Annex A.

10. Security. Provide security for medical treatment facilities and medical personnel (e.g., crowd control, preventing a rush of individuals wanting treatment and vaccinations). Provide security for medical supplies.

11. Training and Exercises.

a. Train personnel regarding the clinical aspects of a smallpox response.

b. Train healthcare and civilian personnel regarding the principles of homecare.

c. Train personnel on proper isolation techniques.

d. Exercise mechanisms to adapt and expand existing facilities.

e. Exercise all components of the local response system.

12. Planning Considerations for Mass Fatality Management.

a. Plan for vaccinating mortuary personnel and their families.

b. Maximize use of existing facilities.

c. Establish plans for the use of non-traditional facilities to augment existing facilities (e.g., cold storage, refrigerated vans).

d. Establish plans for requesting deployment of NDMS/DoD assets (e.g., portable morgue facilities and personnel to augment local capability).

e. Establish plans to identify the deceased. Prepare for and provide appropriate documentation.

f. Establish decontamination and isolation procedures for terminal-care providers.

g. Establish containment procedures for the deceased, following established protocols for double-body bagging/double taping. Exclude embalming procedures.

h. Consider use of vaults for burial purposes, if they are available and can handle more than one body. Do not use above-ground mausoleums.

i. Establish plans for engaging the religious community.

ANNEX H TO SMALLPOX RESPONSE PLAN 29 September 2002
MEDICAL CARE OF ADVERSE EVENTS AFTER SMALLPOX VACCINATION.

REFERENCES.

a. CDC Smallpox Response Plan, Annex 4. Vaccine Adverse Event Reporting, 23 September 2002. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-4.doc.

b. Advisory Committee on Immunization Practices. Vaccinia (smallpox) vaccine. *MMWR* 2001;50(RR-10):1-25. http://www.cdc.gov/mmwr/PDF/rr/rr5010.pdf [Appendix J-5].

c. United States Army Medical Command. Clinical Guidelines For Managing Adverse Events After Vaccination. Falls Church, VA, June 2002.

d. United States Army Medical Command. “How-To” Guide for Command Surgeons: Implementation Guidelines for Investigational New Drug (IND) Protocols. Falls Church, VA, May 2002.

e. United States Army Medical Command. “How To” Guide for Unit Leaders and Unit Health Care Providers: Implementation Guidelines for Investigational New Drug (IND) Protocols. Falls Church, VA, May 2002.

f. United States Army Medical Command. “How To” Guide for Investigational New Drug (IND) Protocols, Supplement: Vaccinia Immune Globulin (IND # 10664). Falls Church, VA, publication pending.

g. United States Army Medical Command. “How To” Guide for Investigational New Drug (IND) Protocols, Supplement: Cidofovir (Vistide®, Gilead) To Treat Vaccinia Reactions (IND # pending). Falls Church, VA, publication pending.

1. General. This DoD Annex augments CDC Annex 3. Appendix H-1 summarizes CDC Annex 3 and this DoD Annex on one page.

a. Mission. Health-care workers will take actions warranted to treat people who develop severe adverse events after smallpox vaccination.

b. Assumptions.

(1) An increased use of smallpox vaccine is expected, as part of the national program to prepare for the contingency of a smallpox outbreak. Mild to moderate adverse events after smallpox vaccination can be managed according to guidelines in references a, b, and c.

(2) Serious adverse events (AEs) associated with smallpox vaccine are expected, with an overall frequency of ~ 50 serious AEs per 1,000,000 vaccinations. Mild and moderate AEs occur more frequently after smallpox vaccination. The unique adverse events that follow smallpox vaccination chiefly involve progressive or complicated disease with this live-virus vaccine.

(3) Vaccinia immune globulin (VIG) was FDA-licensed until the 1990s as an effective treatment for some adverse events after smallpox vaccination (e.g., eczema vaccinatum, progressive vaccinia, severe generalized vaccinia) and ocular vaccinia (Appendix H-4). VIG is currently available only under an investigational new drug (IND) protocol (references b and f). VIG is in short supply.

(4) Although no human efficacy data are available yet, cidofovir (*Vistide*, Gilead Sciences, www.gilead.com/wt/sec/vistide, Appendix H-5) may be effective in treating adverse events associated with invasive or progressive disease after smallpox vaccination.

c. Planning Factors.

(1) Education and Awareness. Prompt recognition of serious adverse events after smallpox vaccination, especially those that benefit from specific therapy, is integral to the training of people who will administer smallpox vaccine and others who provide primary care. Appendix H-2 summarizes early symptoms of adverse reactions that warrant treatment with vaccinia immune globulin. Once a possible serious adverse event is recognized, vaccination staff and primary-care providers must have access to specialists in infectious diseases, dermatology, and/or allergy-immunology.

(2) Ophthalmic Antiviral Medications. The current status and clinical utility of antiviral medications intended for ophthalmic administration are summarized in Appendix H-3.

(3) Access to VIG and Cidofovir.

(a) MTFs will not use on-hand stocks of VIG or cidofovir to treat patients infected with variola virus, nor order them from other sources, without first coordinating with the US Army Medical Research Institute of Infectious Diseases (USAMRIID).

(b) USAMRIID will establish a common point of access for telephonic requests for use of VIG or cidofovir for a named patient by a physician willing to comply with IND requirements (references d, e, f, and g). Access to cidofovir for eligible patients will be facilitated by specialized treatment teams (T-Teams). Healthcare providers from civilian institutions should contact the CDC Drug Service for VIG or cidofovir: CDC Drug Service, National Center for Infectious Diseases, Mail stop D-09, Atlanta, GA 30333; 404-639-3670, fax 404-639-3717.

(3) Training. Specialized treatment teams will be trained in the requirements of IND protocols in general and the cidofovir treatment protocol in particular, to allow prompt use of this agent. The US Army will coordinate training.

(4) Personnel Resources. If warranted by available resources, a specialized treatment team may travel to the MTF to assist with cidofovir administration. The gaining MTF will assign additional personnel to the team, as requested by the treating physician(s). Additional DoD assets will be assigned, if requirements extend beyond the capabilities of the local MTF. Additional details about composition of specialized treatment teams appear in Annex G.

(5) Other Medications. If therapeutic approaches with VIG or cidofovir are inadequate, clinicians may be inclined to try other therapeutic modalities unavailable when routine smallpox vaccinations ceased in the 1970s and 1980s (e.g., immune globulin intravenous as an immunomodulator to treat encephalitis). Little or no data may exist to support the safety or effectiveness of such approaches and no Federal agency sanctions their use. Nonetheless, DoD clinicians reserve their individual prerogatives and responsibilities in the clinical practice of medicine for individual patients.

d. Coordinating Instructions.

(1) Command Relationships. The specialized treatment team will be assigned under the operational control (OPCON) of the local MTF commander.

(2) Communication. No information will be conveyed to other external sources, including the media, without command approval. If working in coordination with local clinicians, no information will be conveyed to other external sources, including the media, without approval of, or simultaneous presentation with, the coordinating agency (CONUS--CDC, OCONUS--WHO).

(3) VIG investigators and cidofovir investigators will coordinate with the Walter Reed National Vaccine Healthcare Center (VHC, 202-782-0411, DSN 662-0411) on status of individuals treated with VIG or cidofovir under IND protocol. Specialized treatment teams, investigators, and the VHC will assist in centralized tracking and case management and provide coordination with CDC's Clinical Immunization Safety Assessment (CISA) centers of excellence.

e. Legal Considerations.

(1) All use of IND agents will be performed in accordance with IRB-approved guidelines and FDA regulations (see references d, e, f, and Appendix G-4). MTFs will provide personnel and supply resources to the specialized treatment teams to satisfy regulatory requirements.

(2) Adverse events due to vaccination for occupational purposes are covered under provisions of the military medical review evaluation process and worker's

compensation benefits. Civilian employees should seek counsel from occupational health clinics in this regard.

2. Execution.

a. Concept of Operations.

(1) Recognition of a serious adverse event after smallpox vaccination will be infrequent, but of high consequence to the patient affected. Based on criteria in references a and b, the attending physician will consult with an infectious-disease, dermatology, and/or allergy-immunology specialist. If warranted the specialist may request use of either VIG or cidofovir, according to clinical circumstances, from USAMRIID, the unit staffed with the principal investigators for the IND protocols for these agents.

(2) Patients will be treated by a physician registered as a subinvestigator on the applicable IND protocol. Patients will be treated at the earliest possible opportunity, at the closest MTF possible. Movement of patients to capable MTFs, and specialized treatment teams to the same MTFs, will be expedited. Patient consent must be obtained before administration. See also Appendix G-4, for exceptions for unconscious patients.

(3) Patients with appropriate indications (i.e., not encephalitis, not keratitis) will be treated using available supplies of VIG under IND until the VIG supply is exhausted. Cidofovir, also under IND, will then be used for any subsequent serious adverse events (Appendix H-5). The rationale for this approach is that less effectiveness data is available for cidofovir, which is more prone to inducing adverse events than VIG. Nonetheless, cidofovir is in greater supply than VIG.

(4) Actual protocol use of these agents is specified in the pertinent treatment protocols (references f and g), including dosage, expected side effects, and regulatory and reporting issues.

(5) Because of the administrative burden of implementing an IND protocol, and cidofovir’s intravenous route of administration, multidisciplinary specialized treatment teams may travel to an MTF to administer the IND product and assist with patient care. During a smallpox outbreak, prior vaccination against smallpox will be a condition of membership on these teams.

b. Tasks and Responsibilities.

(1) Recognition of serious adverse events after smallpox vaccination is the responsibility of smallpox vaccination staff and primary-care providers. Any member of the medical team or the patient or patient’s contacts can alert the system to the possible presence of a vaccine-related adverse event.

(2) Once a definite or probable diagnosis of a medication-indicating adverse event has been made by a qualified provider (e.g., infectious-disease, dermatology, allergy-immunology physician), that provider may request use of VIG or cidofovir for a named patient by telephoning USAMRIID at 1-888-USA-RIID or 301-619-2257. Alternately, page the USAMRIID staff duty officer at 301-631-4393 or the USAMRMC staff duty officer at 301-619-6092. Healthcare providers from civilian institutions should contact the CDC Drug Service for VIG at 404-639-3670. USAMRIID will coordinate with specialized treatment teams, which will travel to the MTF caring for the diagnosed smallpox patient. These teams will be responsible for the treatment of patients with the indicated medications. IND-specific procedures will be followed carefully.

(3) The MTF will provide routine medical care in accordance with standard practice, with laboratory, radiology, and pathology support. If the patient is treated with an IND agent, the treating team will have responsibility for the completion and maintenance of records and reports, as well as the processing or packaging of pathologic or autopsy materials.

(4) MTF commanders will be responsible for transporting patients between MTFs; provision of ancillary supply and personnel resources to specialized treatment teams; pharmacy and laboratory support; and communication support.

(5) The service member's unit will be responsible for initial transportation to the first-level MTF. Once within the medical system, it will be the responsibility of the medical-evacuation system for further patient transportation as needed.

c. Reporting.

(1) T-team leaders will periodically brief the MTF commander on the status of patients with post-vaccination adverse events, at a frequency directed by the commander. Similar briefings will occur for and at the direction of the commander, USAMRIID.

(2) IND protocol reports will be submitted as detailed in the protocols.

(3) There is no need to report adverse events to VAERS that involve smallpox vaccine treated with vaccinia immune globulin (VIG) or cidofovir under IND protocol. The FDA will review all clinical data for patients treated with VIG or cidofovir under IND protocol under separate report filings. Filing reports to the Vaccine Adverse Event Reporting System (VAERS) in cases involving VIG or cidofovir under IND protocol is inappropriate, because filing a VAERS report will lead to double-counting of the case.

(4) Local requirements for reporting under quality-assurance programs (e.g., Patient Safety Program) will be observed.

3. Operational Constraints.

a. Equipment. No specialized equipment other than routine medical care in MTFs will be required.

b. Training. Specialized treatment teams will be trained in the requirements of IND protocols in general and the VIG and cidofovir treatment protocols in particular, to allow prompt use of this agent. The US Army will coordinate such training. Periodic alert exercises, without travel, will be performed to sustain team proficiency. During smallpox outbreaks, prior vaccination against smallpox will be a condition of membership on these teams.

c. Control of IND Agents. MTF pharmacy support to specialized treatment teams will include storage (see below), control, and security for both cidofovir and locally available medications. Pharmacy assets on the teams will prepare and dispense cidofovir for the team's use. Emergency use of an investigational drug for a named patient will comply with notification requirements to U.S. Army Medical Command, in accordance with Army Regulation 40-7 (Use of Investigational Drugs and Devices in Humans and the Use of Schedule I Controlled Drug Substances, 4 January 1991), paragraph 4-9, and comparable regulations in other military Services.

d. Medical Care of the Patient. General medical supportive care to a patient with an adverse event after vaccination will be given by the attending team organic to the MTF, supplemented by the specific therapy given by the treatment team, supplemented with MTF personnel as needed.

4. Administration and Logistics.

a. Shipping and Distribution. Either the T-Teams will transport the VIG or cidofovir themselves, or they will coordinate with the US Army Medical Materiel Agency (USAMMA) for transportation (see Annex I).

b. Supply and Storage. Supplies of VIG or cidofovir, delivered from USAMRIID, will be stored and maintained by the MTF pharmacy under the appropriate environmental conditions.

c. MTFs will provide administrative support for protocol performance by the specialized treatment teams (e.g., office space, copying, automation, communication support).

5. Special Situations.

a. Healthcare providers will attempt to periodically observe smallpox vaccine recipients through the duration of vaccine take and injection-site resolution. Nevertheless, recipients may be required to travel before this vulnerable window for complications has passed.

b. All situations in which a potential adverse event after vaccination is recognized in a recipient while outside of CONUS, or underway either in CONUS or outside of CONUS, should be handled by directing or transporting the recipient to the nearest MTF in an expedited manner. Once arrived, the medical consultation process described above will be implemented.

APPENDIX H-1
Medical Care Of Adverse Events After Smallpox Vaccination – Summary.

1. Recognition of a serious adverse event after smallpox vaccination will be infrequent, but of high consequence to the patient. The attending physician will consult with an infectious-disease, dermatology, and/or allergy-immunology specialist. If warranted, the specialist may request use of either vaccinia immune globulin (VIG) or cidofovir.

2. The US Army Medical Research & Materiel Command (USAMRMC) is applying to the Food & Drug Administration (FDA) for permission to use cidofovir (*Vistide*, Gilead Sciences, Appendix G-5, Appendix H-5) under an investigational new drug (IND) protocol to treat adverse events after smallpox vaccination. This annex assumes FDA will accept this IND protocol.

3. Patients with appropriate indications (e.g., eczema vaccinatum, progressive vaccinia, ocular vaccinia, febrile-"toxic" generalized vaccinia) (i.e., not encephalitis, not keratitis) will be treated using available supplies of VIG under IND until the VIG supply is exhausted. Cidofovir will then be used under IND for any subsequent serious adverse events. Less effectiveness data is available for cidofovir, which is more prone to inducing adverse events than VIG. Nonetheless, cidofovir may be in greater supply than VIG.

4. Because of the administrative burden of implementing an IND protocol, and cidofovir's intravenous route of administration, multidisciplinary specialized treatment teams may travel to an MTF to administer cidofovir and assist with patient care. During a smallpox outbreak, prior vaccination against smallpox will be a condition of membership on these teams.

5. Once a definite or probable diagnosis of a medication-indicating adverse event has been made by a qualified provider (e.g., infectious-disease, dermatology, allergy-immunology physician), that provider may request use of VIG or cidofovir for a named patient by telephoning USAMRIID at 1-888-USA-RIID or 301-619-2257. Alternately, page the USAMRIID staff duty officer at 301-631-4393 or the USAMRMC staff duty officer at 301-619-6092.

6. USAMRIID will coordinate with these specialized treatment teams (T-teams), which will travel to the MTF caring for the patient. IND-specific procedures will be followed carefully. The treatment team will be assigned under the operational control (OPCON) of the local MTF commander.

7. Specialized treatment team leaders will periodically brief the MTF commander on the status of patients, at a frequency directed by the commander. Team leaders and IND investigators will submit IND protocol reports as required by the FDA. VIG investigators and cidofovir investigators will coordinate with the Walter Reed National Vaccine Healthcare Center (VHC) on status of individuals treated with VIG or cidofovir.

APPENDIX H-2
Initial Symptoms of Conditions Warranting VIG Therapy.

1. In 1968, the Food & Drug Administration licensed vaccinia immune globulin intramuscular (VIG-IM) as a safe and effective treatment for some adverse events after smallpox vaccination, including eczema vaccinatum, progressive vaccinia, severe generalized vaccinia). VIG may be useful in treating ocular vaccinia resulting from inadvertent inoculation. VIG is neither effective nor indicated in treating post-vaccinial encephalitis. VIG is the immunoglobulin (antibody) fraction of plasma obtained from people vaccinated with smallpox (vaccinia) vaccine (Appendix H-4).

2. Current supplies of VIG-IM are limited, and limited supplies of an intravenous formulation of VIG (VIG-IV) are just becoming available. At present, both VIG-IM and VIG-IV are available only under investigational new drug (IND) protocols for patients who meet specific inclusion and exclusion criteria. Both forms of VIG should be reserved for treatment of vaccine complications with serious clinical manifestations. The recommended dosage of the currently available VIG for treatment of complications is 0.6 mL/kg of body weight. Because therapeutic doses of VIG might be substantial (e.g., 42 ml for a person weighing 70 kg), the product should be given in divided doses over a period of 24 to 36 hours. Doses can be repeated, usually at intervals of 2 to 3 days, until recovery begins.

3. VIG should be given as early as possible after the onset of symptoms. Consider hospitalization of any patient who requires VIG treatment. To assist primary-care providers in recognizing early symptoms of these conditions, the following information is provided.

4. Eczema vaccinatum.

a. Eczema vaccinatum is a localized or systemic dissemination of vaccinia virus, seen especially among people who have atopic dermatitis or eczema or a history of these conditions or other chronic exfoliative skin conditions. Usually, the illness is mild and self-limited, but can be severe or occasionally fatal. The most serious cases occur with primary vaccination and are independent of the activity of the underlying skin condition. Severe cases have also occurred after contact of recently vaccinated people with people who have active atopic dermatitis or eczema. Patient management includes supportive care as if the patient suffered extensive burns that denuded the skin, posing problems for secondary infection and fluid or electrolyte imbalances.

b. “Either concurrently with or shortly after the development of the local vaccinial lesion (or after an incubation period of about 5 days in unvaccinated eczematous contacts) a vaccinial eruption occurred at sites on the body that were at the time eczematous or had previously been so. These areas became intensely inflamed, and sometimes the eruption later spread to healthy skin. Constitutional symptoms were severe, with high temperature and generalized lymphadenopathy, and the prognosis

was grave in infants in whom large areas of skin were affected." Fenner, page 299. [Sic, atopic dermatitis rather than eczema.]

c. "Vaccinial lesions either generalized or as individual lesions elsewhere than at the vaccination site in a person who has eczema or a past history of eczema." Neff, et al., page 126. [Sic, atopic dermatitis rather than eczema.]

5. Progressive vaccinia

a. Progressive vaccinia (vaccinia necrosum) is a severe, potentially fatal illness characterized by progressive necrosis in the area of vaccination and other tissues at the vaccination site, often with metastatic lesions. It occurred almost exclusively among people with cellular immunodeficiency. Progressive vaccinia starts as a painless progressive enlargement of the vaccination site with scant inflammation and little or no discomfort. It is characterized by a vaccine site that fails to heal properly. The site may enlarge deeply, widely, and relentlessly with an ultimately fatal outcome.

b. "In these case the local lesion at the vaccination site failed to heal, secondary lesions sometimes appeared elsewhere on the body and all lesions spread progressively until—as was likely—the patient died, usually 2-5 months later." Fenner, page 299.

c. "Vaccinia necrosum (progressive vaccinia) is a rare, often fatal complication of vaccination, characterized by progressive necrosis in the area of vaccination, often with metastatic lesions. Although the lesions can be extensive, patients may not have fever, erythema, pain, or regional lymphadenopathy, and may not come to their physician's attention until several weeks after vaccination." Lane, et al., page 260.

d. "On very rare occasions, the growth of vaccinia virus in the skin is not halted at about the eighth or tenth day by the development of antibodies and the cellular reaction against the virus. The virus continues to grow for many weeks, producing large, destructive ulcers, the advancing edge being studded with typical primary-type vesicles, apparently growing in a fully susceptible skin. Although in the first few weeks the lesion may be limited to progress from the primary site, towards the end of the condition, which may last as long as three or four months, numerous secondary lesions occur on the face and on other parts of the body, which are most probably blood-borne, but may also be inoculated, and these again have all the appearances of primary vaccinations." Dixon, pages 153-154.

6. Severe generalized vaccinia)

a. Other less serious complications include generalized vaccinia, with a vesicular or pustular rash of varying extent away from the vaccination site, possibly the result of viremia. Lesions occur 6 to 9 days after vaccination and can be few or generalized. Generalized vaccinia in people without underlying illness is generally self-limiting and

requires little or no therapy. VIG is indicated for severe generalized vaccinia if the patient is extremely ill or has a serious underlying disease.

b. “Very rarely a generalized vaccinial rash, sometimes covering the whole body, occurred 6-9 days after vaccination. The course of the individual skin lesions resembled that of the lesion at the vaccination site, but if the rash was profuse the lesions sometimes varied greatly in size. The generalized eruption usually did not have the “centrifugal” distribution which was characteristic of the rash of smallpox.” Fenner, page 299.

c. “When systemic signs and symptoms lead one to suspect blood-borne virus dissemination, VIG may be of benefit.” Lane, et al., pages 258-259.

d. “There is general enlargement of the lymphatic glands, and the lesions normally commence in the abnormal areas of skin, but in this malignant form always involve normal skin as well. Usually, large areas of the skin are infected simultaneously, with a uniform development of the rash, not at all unlike that of malignant smallpox. Although in some areas the rash may be confluent, in closely adjoining areas of skin there may be no rash at all, and the characteristic centrifugal distribution of smallpox is absent, although the rash may be more developed on the limbs than on the trunk. The abrupt change in density is probably more characteristic than anything else. Although the rash on the face at first sight resembles smallpox, the absence of rash on the tip of the nose compared with the density on the cheeks rules this out.” Dixon, pages 151-152.

7. Ocular or peri-ocular vaccinia)

a. Vaccinia virus can be inadvertently transferred from the vaccination site to other parts of the body. A common site of autoinoculation is to the cutaneous surfaces surrounding the eye (the peri-ocular region). These lesions may occur either in vaccinees or close contacts. Usually these lesions heal without treatment, but severe untreated disease may heal with scarring of the lids causing subsequent ophthalmologic problems. Vaccinial infection of the cornea may cause blindness.

b. VIG was frequently used to treat peri-ocular vaccinia and possibly helps reduce its untoward consequences. On the other hand, VIG should be avoided if there is keratitis or corneal involvement because it increases the risk of corneal scarring. About 5 to 7% of patients with peri-ocular vaccinia developed corneal involvement (i.e., vaccinial keratitis), with resultant pain and significant blurring of the vision. These lesions usually result in scarring of the cornea. Use of VIG is generally contraindicated in vaccinial keratitis because it can lead to increased scarring. Therefore, VIG should be used with extreme caution is cases of ocular vaccinia and only after consultation with an ophthalmologist.

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APPENDIX H-3
Ocular Vaccinia & Ophthalmic Antiviral Medications.

1. Inadvertent Inoculation. Other than local pain, fever, and constitutional symptoms occurring in the first two weeks after smallpox vaccination, inadvertent inoculation (i.e., accidental infection) is the most frequently occurring type of adverse reaction. The most representative data regarding complications come from the 10-state survey of physicians in 1968 (Lane, et al., 1970). In that study, the overall rate of inadvertent inoculation was 529 cases per million people primarily vaccinated, and 42 cases per million for those re-vaccinated. Seven percent of all people with inadvertent inoculation were actually close contacts of vaccinees and not directly vaccinated. Of all complications recorded in the survey, 42% were due to inadvertent inoculation.

2. Inadvertent inoculation occurs on almost any part of the body, but the most frequently described areas include the face (particularly around the eye, nose or mouth), buttocks, and genitalia (ACIP, 2001; Goldstein, et al., 1975). In the 1963 and 1968 national studies, largely based on cases identified from vaccinia immune globulin (VIG) records, 308 cases of inadvertent inoculation were identified, of which 246 involved the eye (80%) (Neff, et al., 1967; Lane, et al., 1969).

3. Most ocular vaccinia presents as a few vesicular lesions with inflammation and swelling of the eyelids or conjunctiva. The cornea was affected in six percent (22/348) of the ocular vaccinia cases series from the 1960's (Ruben & Lane, 1970). Of six patients with keratitis from 1963 who could be followed up by slit-lamp examination in 1969, only two had no residua. The remainder had varying degrees of minor to more bothersome corneal and eyelid or eyelash abnormalities. There was also one case of chronic iritis. No other lasting problems were reported in the group with initial corneal involvement. The rate of residual complications in cases of ocular vaccinia without a history of keratitis was 2%. Most of these individuals either lost eyelashes or had other eyelid deformities.

4. Given the frequency of inadvertent inoculation and the potential sequelae of vaccinial keratitis, it is prudent to attempt to prevent this complication. As previously described, smallpox vaccination involves inoculation of a small amount of live virus into the skin. The potential exists for that virus to be disseminated directly to other areas of the body or even to other individuals. Current recommendations for smallpox vaccination recommend that recipients practice good hand hygiene to limit spread from the area of vaccination to themselves or others (ACIP, 2001). Simple detergent-type hand cleaners are adequate for this purpose, but alcohol-based gels are better as antiseptics, because alcohol inactivates vaccinia virus. These gels also cause less skin irritation after repetitive washing (Larson, 1995; Larson, 2001).

5. Historically, VIG was used with some success to treat ocular vaccinia. Because of currently limited supply, it is reserved for severe or life-threatening cases involving progressive vaccinia or eczema vaccinatum (ACIP, 2001; Henderson, et al., 1999). VIG

is contraindicated in cases of vaccinial keratitis, according to the Advisory Committee on Immunization Practices (ACIP, 2001), based on an animal study suggesting it may increase corneal scarring (Fulginiti, et al., 1965). At least one ophthalmologist specializing in viral diseases of the cornea disagrees with this position, advocating use of VIG to prevent progression to corneal melt with perforation.

6. Several pharmacologic agents show antiviral activity against orthopox and other DNA viruses, but few have been tested in either animals or humans, especially as an ophthalmic preparation (Clercq, 2001). The ACIP (2001) states that there is insufficient information to recommend any antiviral drug for treatment of complications of smallpox virus vaccination. Idoxuridine was the antiviral ophthalmic preparation typically used by clinicians for ocular vaccinia with keratitis in the past, but data on its efficacy were conflicting (Fulginiti, et al., 1965; Kaufman, et al., 1962; Kaufman, 1963; Jack & Sorenson, 1963; Focasi, et al, 1963). Breman & Henderson (2002) recently recommended idoxuridine topically to treat corneal lesions due to smallpox. However, this agent is no longer available in pharmacies in the United States, nor is vidarabine (Vira-A, Monarch Pharmaceuticals), both having gone out of production.

7. The FDA-approved therapeutic agent available for herpetic keratitis is trifluridine (Viroptic®, Monarch, also known as triflurothymidine), having displaced idoxuridine as a more effective treatment. Trifluridine is effective even in cases of idoxuridine-resistant herpetic keratitis. Trifluridine has been evaluated in animal models of experimentally induced vaccinial keratitis in comparison to idoxuridine or untreated controls and found to be significantly more effective in eliminating or reducing vaccinial ulcers on the cornea, as well as virus by culture (Hyndiuk, et al., 1976). The drug is administered in herpes simplex keratitis as a 1% ophthalmic solution, one drop every two hours while awake up to nine drops daily until the cornea is re-epithelialized, and then one drop every four hours up to five drops daily for seven more days. Ophthalmology consultation is warranted.

8. Use of trifluridine for ocular vaccinia (e.g., vaccinial conjunctivitis, vaccinial keratitis, vaccinial complications involving eyelid) would be off-label and, therefore, prescribed at the discretion of an individual physician after discussion with the patient. To change the product's FDA-approved labeling would require an investigational new drug (IND) protocol. Other antiviral agents have also been evaluated for use in vaccinia keratitis with promising results, but these are also not commercially available currently in the United States (Sidwell, et al, 1973). Cidofovir, active against some orthopox viruses and suggested for possible treatment of smallpox, has not been evaluated in ocular vaccinia or keratitis (ACIP, 2001; Clercq, 2001).

9. Summary. Inadvertent inoculation is one of the most common complications of smallpox vaccination and is usually manifested as a periorbital infection. Ocular vaccinia may result in deformities of the eyelid and eyelashes, and in the worst cases result in chronic iritis and or corneal scarring. Evidence of ocular vaccinia after vaccination should prompt ophthalmologic evaluation, including slit-lamp examination. Treatment of non-corneal ocular vaccinia may benefit from VIG if available, but until consensus is

obtained, VIG should not be used without advice of a corneal expert for vaccinial keratitis. Trifluridine ophthalmic solution is likely to be of benefit for this indication, but its use would be off-label.

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APPENDIX H-4
Product Labeling for Vaccinia Immune Globulin (VIG).

[reprinted verbatim from Hyland Therapeutics Division's VIG product labeling, circa 1983. Note that production methods in that era did not include viral-inactivation steps.]

Hyland®
Vaccinia Immune Globulin (Human)

DESCRIPTION

HYLAND Vaccinia Immune Globulin (Human) is a sterile 16.5 (±1.5) percent solution of the immunoglobulin fraction of plasma from individuals who were immunized with vaccinia virus. The solution is isotonic and contains 0.3M glycine as a stabilizer. It contains 0.01% thimerosal (a mercury derivative) as a preservative and 0 1% sodium chloride.

This product meets the FDA potency requirements for vaccinia antibody.

Each unit of plasma used in the preparation of this product has been found to be nonreactive for hepatitis B surface antigen (HBsAg) by counterelectrophoresis or radioimmunoassay. The product is prepared by the cold ethanol fractionation method; no instance of hepatitis transmission has been reported from the use of human immune globulins when prepared by this method.

This product has been processed and tested in accordance with requirements established by the Food and Drug Administration and is distributed under U.S. License No. 140.

INDICATIONS

Smallpox -Prevention or Modification:

Administration of Vaccinia Immune Globulin (Human) in conjunction with simultaneous vaccination or revaccination has been shown to reduce the incidence of smallpox in exposed individuals.[1]

Vaccinia Infections - Prevention or Modification:

Vaccinia Immune Globulin (Human) may be indicated in the following circumstances to prevent or modify aberrant infections induced by smallpox vaccine:[2-5]

a. Accidental implantation of vaccinia virus in eyes, mouth, or other areas where vaccinia infection would constitute a special hazard

b. Accidental vaccinia exposure of children who have extensive skin lesions such as eczema, burns, impetigo, or varicella.

c. Eczematous children where vaccination is indicated due to risk of exposure to smallpox.

Treatment of Postvaccinal Complications:

Vaccinia Immune Globulin (Human) may be effective for use in the following conditions: eczema vaccinatum, vaccinia necrosum, severe generalized vaccinia, vaccinia infections of the eyes or mouth, and vaccinia infections in the presence of other skin lesions such as burns, impetigo, varicella-zoster, or poison ivy.

This product is not of value in the treatment of postvaccinal encephalitis.

CONTRAINDICATIONS

Vaccinia Immune Globulin (Human) is contraindicated for use in the presence of vaccinal keratitis. The administration of a similar preparation in rabbits with vaccinal keratitis has been shown to cause increased scarring.[6]

WARNINGS

Do not give intravenously; this preparation is for intramuscular use only. Do not use if turbid.

PRECAUTIONS

A separate sterile syringe and needle or single-use disposable unit must be used for each individual patient to prevent the possible transmission of hepatitis or other infectious agents from one patient to another.

After cleansing the site for injection and inserting the needle in a muscle, draw back on the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel.

ADVERSE REACTIONS

A few instances of allergic or anaphylactoid systemic reactions have been reported following intramuscular injection of human immunoglobulin preparations. It is advisable that epinephrine or other suitable medication be available for treating such reactions should they occur.

Occasionally local tenderness and stiffness occur, persisting from a few hours to 1 to 2 days following injection (When the dosage is 10 ml or more, it should be divided and injected at 2 or more sites in order to reduce the trauma of injection).

DOSAGE

Smallpox - Prevention or Modification:

A dose of 0.3 ml per kg of body weight should be given within 24 hours of exposure. Exposed individuals should be simultaneously vaccinated or revaccinated with smallpox vaccine unless otherwise contraindicated.

Vaccinia Infections -Prevention or Modification:

A dose of 0.3 ml per kg of body weight should be given simultaneously with smallpox vaccination. In cases of accidental exposure to vaccinia virus, this dosage should be given as soon as possible after exposure has occurred.

Treatment of Postvaccinal Complications:

A dose of 0.6 ml per kg of body weight should be administered as soon as possible after symptoms appear. This dose may be repeated, depending upon the severity of symptoms and response to treatment.

No therapeutic effect may be expected from the use of this product in postvaccinal encephalitis.

ADMINISTRATION

Vaccinia Immune Globulin (Human) is to be administered intramuscularly, preferably in the buttock or the anterolateral aspect of the thigh.

When the dosage is 10 ml or more, it should be divided and injected at 2 or more sites.

HOW SUPPLIED

HYLAND Vaccinia Immune Globulin (Human) is available in a 5-ml size.

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Hyland Therapeutics Division
Travenol Laboratories, Inc.
Glendale, California 91202, U.S.A.
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APPENDIX H-5
Product Labeling for Cidofovir.

Vistide®, Gilead Sciences

Gilead Sciences
333 Lakeside Drive
Foster City, CA 94404

www.gilead.com/wt/sec/vistide

800-GILEAD-5 (800-445-3235)

VISTIDE® (cidofovir injection)

℞ only.

FOR INTRAVENOUS INFUSION ONLY.
NOT FOR INTRAOCULAR INJECTION.

WARNING:
RENAL IMPAIRMENT IS THE MAJOR TOXICITY OF VISTIDE. CASES OF ACUTE RENAL FAILURE RESULTING IN DIALYSIS AND/OR CONTRIBUTING TO DEATH HAVE OCCURRED WITH AS FEW AS ONE OR TWO DOSES OF VISTIDE. TO REDUCE POSSIBLE NEPHROTOXICITY, INTRAVENOUS PREHYDRATION WITH NORMAL SALINE AND ADMINISTRATION OF PROBENECID MUST BE USED WITH EACH VISTIDE INFUSION. RENAL FUNCTION (SERUM CREATININE AND URINE PROTEIN) MUST BE MONITORED WITHIN 48 HOURS PRIOR TO EACH DOSE OF VISTIDE AND THE DOSE OF VISTIDE MODIFIED FOR CHANGES IN RENAL FUNCTION AS APPROPRIATE (SEE DOSAGE AND ADMINISTRATION). VISTIDE IS CONTRAINDICATED IN PATIENTS WHO ARE RECEIVING OTHER NEPHROTOXIC AGENTS.

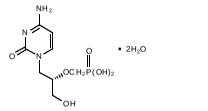
NEUTROPENIA HAS BEEN OBSERVED IN ASSOCIATION WITH VISTIDE TREATMENT. THEREFORE, NEUTROPHIL COUNTS SHOULD BE MONITORED DURING VISTIDE THERAPY.

VISTIDE IS INDICATED ONLY FOR THE TREATMENT OF CMV RETINITIS IN PATIENTS WITH ACQUIRED IMMUNODEFICIENCY SYNDROME.

IN ANIMAL STUDIES CIDOFOVIR WAS CARCINOGENIC, TERATOGENIC AND CAUSED HYPOSPERMIA (SEE CARCINOGENESIS, MUTAGENESIS, & IMPAIRMENT OF FERTILITY).

DESCRIPTION

VISTIDE® is the brand name for cidofovir injection. The chemical name of cidofovir is 1-[(*S*)-3-hydroxy-2-(phosphonomethoxy)propyl]cytosine dihydrate (HPMPC) , with the molecular formula of $C_8H_{14}N_3O_6P•2H_2O$ and a molecular weight of 315.22 (279.19 for anhydrous). The chemical structure is:



Cidofovir is a white crystalline powder with an aqueous solubility of ≥ 170 mg/mL at pH 6-8 and a log P (octanol/aqueous buffer, pH 7.1) value of -3.3.

VISTIDE is a sterile, hypertonic aqueous solution for intravenous infusion only. The solution is clear and colorless. It is supplied in clear glass vials, each containing 375 mg of anhydrous cidofovir in 5 mL aqueous solution at a concentration of 75 mg/mL. The formulation is pH-adjusted to 7.4 with sodium hydroxide and/or hydrochloric acid and contains no preservatives. The appropriate volume of VISTIDE must be removed from the single-use vial and diluted prior to administration (see DOSAGE AND ADMINISTRATION).

MICROBIOLOGY

Mechanism of Action: Cidofovir suppresses cytomegalovirus (CMV) replication by selective inhibition of viral DNA synthesis. Biochemical data support selective inhibition of CMV DNA polymerase by cidofovir diphosphate, the active intracellular metabolite of cidofovir. Cidofovir diphosphate inhibits herpesvirus polymerases at concentrations that are 8- to 600-fold lower than those needed to inhibit human cellular DNA polymerases alpha, beta, and gamma[1, 2, 3]. Incorporation of cidofovir into the growing viral DNA chain results in reductions in the rate of viral DNA synthesis.

In Vitro Susceptibility: Cidofovir is active *in vitro* against a variety of laboratory and clinical isolates of CMV and other herpesviruses (Table 1). Controlled clinical studies of efficacy have been limited to patients with AIDS and CMV retinitis.

Table 1. Cidofovir Inhibition of Virus Multiplication in Cell Culture

Virus	IC_{50} (µM)
Wild-type CMV Isolates	0.5 - 2.8
HSV-1, HSV-2	12.7 - 31.7

Resistance: CMV isolates with reduced susceptibility to cidofovir have been selected *in vitro* in the presence of high concentrations of cidofovir[4]. IC_{50} values for selected resistant isolates ranged from 7-15 µM.

There are insufficient data at this time to assess the frequency or the clinical significance of the development of resistant isolates following VISTIDE administration to patients.

The possibility of viral resistance should be considered for patients who show a poor clinical response or experience recurrent retinitis progression during therapy.

Cross Resistance: Cidofovir-resistant isolates selected *in vitro* following exposure to increasing concentrations of cidofovir were assessed for susceptibility to ganciclovir and foscarnet[4]. All were cross resistant to ganciclovir, but remained susceptible to foscarnet. Ganciclovir- or ganciclovir/foscarnet-resistant isolates that are cross resistant to cidofovir have been obtained from drug naive patients and from patients following ganciclovir or ganciclovir/ foscarnet therapy. To date, the majority of ganciclovir-resistant isolates are UL97 gene product (phosphokinase) mutants and remain susceptible to cidofovir[5]. Reduced susceptibility to cidofovir, however, has been reported for DNA polymerase mutants of CMV which are resistant to ganciclovir[6-9]. To date, all clinical isolates which exhibit high level resistance to ganciclovir, due to mutations in both the DNA polymerase and UL97 genes, have been shown to be cross resistant to cidofovir. Cidofovir is active against some, but not all, CMV isolates which are resistant to foscarnet[10-12]. The incidence of foscarnet-resistant isolates that are resistant to cidofovir is not known.

A few triple-drug resistant isolates have been described. Genotypic analysis of two of these triple-resistant isolates revealed several point mutations in the CMV DNA polymerase gene. The clinical significance of the development of these cross-resistant isolates is not known.

CLINICAL PHARMACOLOGY

PHARMACOKINETICS

VISTIDE must be administered with probenecid. The pharmacokinetics of cidofovir, administered both without and with probenecid, are described below.

The pharmacokinetics of cidofovir without probenecid were evaluated in 27 HIV-infected patients with or without asymptomatic CMV infection. Dose-independent pharmacokinetics were demonstrated after one hr infusions of 1.0 (n = 5), 3.0 (n = 10), 5.0 (n = 2) and 10.0 (n = 8) mg/kg (See Table 2 for pharmacokinetic parameters). There was no evidence of cidofovir accumulation after 4 weeks of repeated administration of 3 mg/kg/week (n = 5) without probenecid. In patients with normal renal function, approximately 80 to 100% of the VISTIDE dose was recovered unchanged in urine within 24 hr (n = 27). The renal clearance of cidofovir was greater than creatinine clearance, indicating renal tubular secretion contributes to the elimination of cidofovir.

The pharmacokinetics of cidofovir administered with probenecid were evaluated in 12 HIV-infected patients with or without asymptomatic CMV infection and 10 patients with relapsing CMV retinitis. Dose-independent pharmacokinetics were observed for cidofovir, administered with probenecid, after one hr infusions of 3.0 (n = 12), 5.0 (n = 6), and 7.5 (n = 4) mg/kg (See Table 2). Approximately 70 to 85% of the VISTIDE dose administered with concomitant probenecid was excreted as unchanged drug within 24 hr. When VISTIDE was administered with probenecid, the renal clearance of cidofovir was reduced to a level consistent with creatinine clearance, suggesting that probenecid blocks active renal tubular secretion of cidofovir.

Table 2. Cidofovir Pharmacokinetic Parameters Following 3.0 and 5.0 mg/kg Infusions, Without and With Probenecid*

PARAMETERS	VISTIDE ADMINISTERED WITHOUT PROBENECID		VISTIDE ADMINISTERED WITH PROBENECID	
	3 mg/kg (n = 10)	5 mg/kg (n = 2)	3 mg/kg (n = 12)	5 mg/kg (n = 6)
AUC (µg•hr/mL)	20.0 ± 2.3	28.3	25.7 ± 8.5	40.8 ± 9.0
Cmax (end of infusion) (µg/mL)	7.3 ± 1.4	11.5	9.8 ± 3.7	19.6 ± 7.2
Vdss (mL/kg)	537 ± 126 (n = 12)		410 ± 102 (n = 18)	
Clearance (mL/min/1.73 m^2)	179 ± 23.1 (n = 12)		148 ± 38.8 (n = 18)	
Renal Clearance (mL/min/1.73 m^2)	150 ± 26.9 (n = 12)		98.6 ± 27.9 (n = 11)	

* See DOSAGE AND ADMINISTRATION

In vitro, cidofovir was less than 6% bound to plasma or serum proteins over the cidofovir concentration range 0.25 to 25 µg/mL. CSF concentrations of cidofovir following intravenous infusion of VISTIDE 5 mg/kg with concomitant probenecid and intravenous hydration were undetectable (< 0.1 µg/mL, assay detection threshold) at 15 minutes after the end of a 1 hr infusion in one patient whose corresponding serum concentration was 8.7 µg/mL.

DRUG-DRUG INTERACTIONS

Zidovudine

The pharmacokinetics of zidovudine were evaluated in 10 patients receiving zidovudine alone or with intravenous cidofovir (without probenecid). There was no evidence of an effect of cidofovir on the pharmacokinetics of zidovudine.

SPECIAL POPULATIONS

Renal Insufficiency

Pharmacokinetic data collected from subjects with creatinine clearance values as low as 11 mL/min indicate that cidofovir clearance decreases proportionally with creatinine clearance.

High-flux hemodialysis has been shown to reduce the serum levels of cidofovir by approximately 75%.

Initiation of therapy with VISTIDE is contraindicated in patients with serum creatinine > 1.5 mg/dL, a calculated creatinine clearance ≤ 55 mL/min, or a urine protein ≥ 100 mg/dL (equivalent to ≥2+ proteinuria) (See CONTRAINDICATIONS).

Geriatric/Gender/Race

The effects of age, gender, and race on cidofovir pharmacokinetics have not been investigated.

INDICATION AND USAGE

VISTIDE is indicated for the treatment of CMV retinitis in patients with acquired immunodeficiency syndrome (AIDS). THE SAFETY AND EFFICACY OF VISTIDE HAVE NOT BEEN ESTABLISHED FOR TREATMENT OF OTHER CMV INFECTIONS (SUCH AS PNEUMONITIS OR GASTROENTERITIS), CONGENITAL OR NEONATAL CMV DISEASE, OR CMV DISEASE IN NON-HIV-INFECTED INDIVIDUALS.

DESCRIPTION OF CLINICAL TRIALS

Three phase II/II controlled trials of VISTIDE have been conducted in HIV-infected patients with CMV retinitis.

Delayed Versus Immediate Therapy (Study 105): In stage 1 of this open-label trial, conducted by the Studies of the Ocular Complications of AIDS (SOCA) Clinical Research Group, 29 previously untreated patients with peripheral CMV retinitis were randomized to either immediate treatment with VISTIDE (5 mg/kg once a week for 2 weeks, then 3 mg/kg every other week) or to have VISTIDE delayed until progression of CMV retinitis[13]. In stage 2 of this trial, an additional 35 previously untreated patients with peripheral CMV retinitis were randomized to either immediate treatment with VISTIDE (5 mg/kg once a week for 2 weeks, then 5 mg/kg every other week), immediate treatment with VISTIDE (5 mg/kg once a week for 2 weeks, then 3 mg/kg every other week), or to have VISTIDE delayed until progression of CMV retinitis. Of the 64 patients in this study, 12 were randomized to 5 mg/kg maintenance therapy, 26 to 3 mg/kg maintenance therapy, and 26 to delayed therapy. Of the 12 patients enrolled in the 5 mg/kg maintenance group, 5 patients progressed, 5 patients discontinued therapy and 2 patients had no progression at study completion. Based on masked readings of retinal photographs, the median [95% confidence interval (CI)] time to retinitis progression was not reached (25, not reached) for the 5 mg/kg maintenance group. Median (95% CI) time to the alternative endpoint of retinitis progression or study drug discontinuation was 44 days (24, 207) for the 5 mg/kg maintenance group. Patients receiving 5 mg/kg maintenance had delayed time to retinitis progression compared to patients receiving 3 mg/kg maintenance or deferred therapy.

Delayed Versus Immediate Therapy (Study 106): In an open-label trial, 48 previously untreated patients with peripheral CMV retinitis were randomized to either immediate treatment with VISTIDE (5 mg/kg once a week for 2 weeks, then 5 mg/kg every other week), or to have VISTIDE delayed until progression of CMV retinitis[14]. Patient baseline characteristics and disposition are shown in Table 3. Of 25 and 23 patients in the immediate and delayed groups respectively, 23 and 21 were evaluable for retinitis progression as determined by retinal photography. Based on masked readings of retinal photographs, the median [95% confidence interval (CI)] times to retinitis progression were 120 days (40, 134) and 22 days (10, 27) for the immediate and delayed therapy groups, respectively. This difference was statistically significant. However, because of the limited number of patients remaining on treatment over time (3 of 25 patients received VISTIDE for 120 days or longer), the median time to progression for the immediate therapy group was difficult to precisely estimate. Median (95% CI) times to the alternative endpoint of retinitis progression or study drug discontinuation (including adverse events, withdrawn consent, and systemic CMV disease) were 52 days (37, 85) and 22 days (13, 27) for the immediate and delayed therapy groups, respectively. This difference was statistically significant. Time to progression estimates from this study may not be directly comparable to estimates reported for other therapies.

Table 3. Patient Characteristics and Disposition (Study 106)

	Immediate Therapy (n = 25)	Delayed Therapy (n = 23)
Baseline Characteristics		
Age (years)	38	38
Sex (M/F)	24/1	22/1
Median CD4 Cell Count	6	9
Endpoints		
CMV Retinitis Progression	10	18
Discontinued Due to Adverse Event	6	0
Withdrew Consent	3[a]	1
Discontinued Due to Intercurrent Illness	2[b]	1[b]
Discontinued Based on Ophthalmological Examination	1[c]	1[c]
No Progression at Study Completion	1	0
Not Evaluable at Baseline	2	2

[a] One patient died 2 weeks after withdrawing consent.
[b] Two patients on immediate therapy were diagnosed with CMV disease and discontinued from study. One patient on delayed therapy was diagnosed with CMV gastrointestinal disease.
[c] CMV retinitis progression not confirmed by retinal photography.

Dose-response study of VISTIDE (Study 107): In an open-label trial, 100 patients with relapsing CMV retinitis were randomized to receive 5 mg/kg once a week for 2 weeks and then either 5 mg/kg (n = 49) or 3 mg/kg (n = 51) every other week. Enrolled patients had been diagnosed with CMV retinitis an average of 390 days prior to randomization and had received a median of 3.8 prior courses of systemic CMV therapy. Eighty-four of the 100 patients were considered evaluable for progression by serial retinal photographs (43 randomized to 5 mg/kg and 41 randomized to 3 mg/kg). Twenty-six and 21 patients discontinued therapy due to either an adverse event, intercurrent illness, excluded medication, or withdrawn consent in the 5 mg/kg and 3 mg/kg groups, respectively. Thirty-eight of the 100 randomized patients had progressed according to masked assessment of serial retinal photographs (13 randomized to 5 mg/kg and 25 randomized to 3 mg/kg). Using retinal photographs, the median (95% CI) times to retinitis progression for the 5 mg/kg and 3 mg/kg groups were 115 days (70, not reached) and 49 days (35, 52), respectively. This difference was statistically significant. Similar to Study 106, the median time to retinitis progression for the 5 mg/kg group was difficult to precisely estimate due to the limited number of patients remaining on treatment over time (4 of the 49 patients in the 5 mg/kg group were treated for 115 days or longer). Median (95% CI) times to the alternative endpoint of retinitis progression or study drug discontinuation were 49 days (38, 63) and 35 days (27, 39) for the 5 mg/kg and 3 mg/kg groups, respectively. This difference was statistically significant.

CONTRAINDICATIONS

Initiation of therapy with VISTIDE is contraindicated in patients with a serum creatinine > 1.5 mg/dL, a calculated creatinine clearance ≤ 55 mL/min, or a urine protein ≥ 100 mg/dL (equivalent to ≥ 2+ proteinuria).

VISTIDE is contraindicated in patients receiving agents with nephrotoxic potential. Such agents must be discontinued at least seven days prior to starting therapy with VISTIDE.

VISTIDE is contraindicated in patients with hypersensitivity to cidofovir.

VISTIDE is contraindicated in patients with a history of clinically severe hypersensitivity to probenecid or other sulfa-containing medications.

Direct intraocular injection of VISTIDE is contraindicated; direct injection of cidofovir has been associated with iritis, ocular hypotony, and permanent impairment of vision.

WARNINGS

Nephrotoxicity: Dose-dependent nephrotoxicity is the major dose-limiting toxicity related to VISTIDE administration. Cases of acute renal failure resulting in dialysis and/or contributing to death have occurred with as few as one or two doses of VISTIDE. Renal function (serum creatinine and urine protein) must be monitored within 48 hours prior to each dose of VISTIDE. Dose adjustment or discontinuation is required for changes in renal function (serum creatinine and/or urine protein) while on therapy. Proteinuria, as measured by urinalysis in a clinical laboratory, may be an early indicator of VISTIDE-related nephrotoxicity. Continued administration of VISTIDE may lead to additional proximal tubular cell injury, which may result in glycosuria, decreases in serum phosphate, uric acid, and bicarbonate, elevations in serum creatinine, and/or acute renal failure, in some cases, resulting in the need for dialysis. Patients with these adverse events occurring concurrently and meeting a criteria of Fanconi's syndrome have been reported. Renal function that did not return to baseline after drug discontinuation has been observed in clinical studies of VISTIDE.

Intravenous normal saline hydration and oral probenecid must accompany each VISTIDE infusion. Probenecid is known to interact with the metabolism or renal tubular excretion of many drugs (see PRECAUTIONS). The safety of VISTIDE has not been evaluated in patients receiving other known potentially nephrotoxic agents, such as intravenous aminoglycosides (e.g., tobramycin, gentamicin, and amikacin), amphotericin B, foscarnet, intravenous pentamidine, vancomycin, and non-steroidal anti-inflammatory agents (see DOSAGE AND ADMINISTRATION).

Preexisting Renal Impairment: Initiation of therapy with VISTIDE is contraindicated in patients with a baseline serum creatinine > 1.5 mg/dL, a creatinine clearance ≤ 55 mL/min, or a urine protein ≥ 100 mg/dL (equivalent to ≥ 2+ proteinuria).

Hematological Toxicity: Neutropenia may occur during VISTIDE therapy. Neutrophil count should be monitored while receiving VISTIDE therapy.

Decreased Intraocular Pressure/Ocular Hypotony: Decreased intraocular pressure may occur during VISTIDE therapy, and in some instances has been associated with decreased visual acuity. Intraocular pressure should be monitored during VISTIDE therapy.

Metabolic Acidosis: Decreased serum bicarbonate associated with proximal tubule injury and renal wasting syndrome (including Fanconi's syndrome) have been reported in patients receiving VISTIDE (see ADVERSE REACTIONS). Cases of metabolic acidosis in association with liver dysfunction and pancreatitis resulting in death have been reported in patients receiving VISTIDE.

PRECAUTIONS

General

Due to the potential for increased nephrotoxicity, doses greater than the recommended dose must not be administered and the frequency or rate of administration must not be exceeded (see DOSAGE AND ADMINISTRATION).

VISTIDE is formulated for intravenous infusion only and must not be administered by intraocular injection. Administration of VISTIDE by infusion must be accompanied by oral probenecid and intravenous saline prehydration (see DOSAGE AND ADMINISTRATION).

Uveitis/Iritis

Uveitis or iritis was reported in clinical trials and during postmarketing in patients receiving VISTIDE therapy. Treatment with topical corticosteroids with or without topical cycloplegic agents should be considered. Patients should be monitored for signs and symptoms of uveitis/iritis during VISTIDE therapy.

Information for Patients

Patients should be advised that VISTIDE is not a cure for CMV retinitis, and that they may continue to experience progression of retinitis during and following treatment. Patients receiving VISTIDE should be advised to have regular follow-up ophthalmologic examinations. Patients may also experience other manifestations of CMV disease despite VISTIDE therapy.

HIV-infected patients may continue taking antiretroviral therapy, but those taking zidovudine should be advised to temporarily discontinue zidovudine administration or decrease their zidovudine dose by 50%, on days of VISTIDE administration only, because probenecid reduces metabolic clearance of zidovudine.

Patients should be informed of the major toxicity of VISTIDE, namely renal impairment, and that dose modification, including reduction, interruption, and possibly discontinuation, may be required. Close monitoring of renal function (routine urinalysis and serum creatinine) while on therapy should be emphasized.

The importance of completing a full course of probenecid with each VISTIDE dose should be emphasized. Patients should be warned of potential adverse events caused by probenecid (e.g., headache, nausea, vomiting, and hypersensitivity reactions). Hypersensitivity/allergic reactions may include rash, fever, chills and anaphylaxis. Administration of probenecid after a meal or use of antiemetics may decrease the nausea. Prophylactic or therapeutic antihistamines and/or acetaminophen can be used to ameliorate hypersensitivity reactions.

Patients should be advised that cidofovir causes tumors, primarily mammary adenocarcinomas, in rats. VISTIDE should be considered a potential carcinogen in humans (See Carcinogenesis, Mutagenesis, & Impairment of Fertility). Women should be advised of the limited enrollment of women in clinical trials of VISTIDE.

Patients should be advised that VISTIDE caused reduced testes weight and hypospermia in animals. Such changes may occur in humans and cause infertility. Women of childbearing potential should be advised that cidofovir is embryotoxic in animals and should not be used during pregnancy. Women of childbearing potential should be advised to use effective contraception during and for 1 month following treatment with VISTIDE. Men should be advised to practice barrier contraceptive methods during and for 3 months after treatment with VISTIDE.

Drug Interactions

Probenecid: Probenecid is known to interact with the metabolism or renal tubular excretion of many drugs (e.g., acetaminophen, acyclovir, angiotensin-converting enzyme inhibitors, aminosalicylic acid, barbiturates, benzodiazepines, bumetanide, clofibrate, methotrexate, tamotidine, furosemide, nonsteroidal anti-inflammatory agents, theophylline, and zidovudine). Concomitant medications should be carefully assessed. Zidovudine should either be temporarily discontinued or decreased by 50% when coadministered with probenecid on the day of VISTIDE infusion.

Nephrotoxic agents: Concomitant administration of VISTIDE and agents with nephrotoxic potential [e.g., intravenous aminoglycosides (e.g., tobramycin, gentamicin, and amikacin), amphotericin B, foscarnet, intravenous pentamidine, vancomycin, and non-steroidal anti-inflammatory agents] is contraindicated. Such agents must be discontinued at least seven days prior to starting therapy with VISTIDE.

Carcinogenesis, Mutagenesis, & Impairment of Fertility

Chronic, two-year carcinogenicity studies in rats and mice have not been carried out to evaluate the carcinogenic potential of cidofovir. However, a 26-week toxicology study evaluating once weekly subscapular subcutaneous injections of cidofovir in rats was terminated at 19 weeks because of the induction, in females, of palpable masses, the first of which was detected after six doses. The masses were diagnosed as mammary adenocarcinomas which developed at doses as low as 0.6 mg/kg/week, equivalent to 0.04 times the human systemic exposure at the recommended intravenous VISTIDE dose based on AUC comparisons.

In a 26-week intravenous toxicology study in which rats received 0.6, 3, or 15 mg/kg cidofovir once weekly, a significant increase in mammary adenocarcinomas in female rats as well as a significant incidence of Zymbal's gland carcinomas in male and female rats were seen at the high dose but not at the lower two doses. The high dose was equivalent to 1.1 times the human systemic exposure at the recommended dose of VISTIDE, based on comparisons of AUC measurements. In light of the results of these studies, cidofovir should be considered to be a carcinogen in rats as well as a potential carcinogen in humans.

Cynomolgus monkeys received intravenous cidofovir, alone and in conjunction with concomitant oral probenecid, intravenously once weekly for 52 weeks at doses resulting in exposures of approximately 0.7 times the human systemic exposure at the recommended dose of VISTIDE. No tumors were detected. However, the study was not designed as a carcinogenicity study due to the small number of animals at each dose and the short duration of treatment.

No mutagenic response was observed in microbial mutagenicity assays involving *Salmonella typhimurium* (Ames) and *Escherichia coli* in the presence and absence of metabolic activation. An increase in micronucleated polychromatic erythrocytes *in vivo* was seen in mice receiving ≥ 2000 mg/kg, a dosage approximately 65-fold higher than the maximum recommended clinical intravenous VISTIDE dose based on body surface area estimations. Cidofovir induced chromosomal aberrations in human peripheral blood lymphocytes *in vitro* without metabolic activation. At the 4 cidofovir levels tested, the percentage of damaged metaphases and number of aberrations per cell increased in a concentration-dependent manner.

Studies showed that cidofovir caused inhibition of spermatogenesis in rats and monkeys. However, no adverse effects on fertility or reproduction were seen following once weekly intravenous injections of cidofovir in male rats for 13 consecutive weeks at doses up to 15 mg/kg/week (equivalent to 1.1 times the recommended human dose based on AUC comparisons). Female rats dosed intravenously once weekly at 1.2 mg/kg/week (equivalent to 0.09 times the recommended human dose based on AUC)

or higher, for up to 6 weeks prior to mating and for 2 weeks post mating had decreased litter sizes and live births per litter and increased early resorptions per litter. Peri- and post-natal development studies in which female rats received subcutaneous injections of cidofovir once daily at doses up to 1.0 mg/kg/day from day 7 of gestation through day 21 postpartum (approximately 5 weeks) resulted in no adverse effects on viability, growth, behavior, sexual maturation or reproductive capacity in the offspring.

Pregnancy: Category C

Cidofovir was embryotoxic (reduced fetal body weights) in rats at 1.5 mg/kg/day and in rabbits at 1.0 mg/kg/day, doses which were also maternally toxic, following daily intravenous dosing during the period of organogenesis. The no-observable-effect levels for embryotoxicity in rats (0.5 mg/kg/day) and in rabbits (0.25 mg/kg/day) were approximately 0.04 and 0.05 times the clinical dose (5 mg/kg every other week) based on AUC, respectively. An increased incidence of fetal external, soft tissue and skeletal anomalies (meningocele, short snout, and short maxillary bones) occurred in rabbits at the high dose (1.0 mg/kg/day) which was also maternally toxic. There are no adequate and well-controlled studies in pregnant women. VISTIDE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether cidofovir is excreted in human milk. Since many drugs are excreted in human milk and because of the potential for adverse reactions as well as the potential for tumorigenicity shown for cidofovir in animal studies, VISTIDE should not be administered to nursing mothers. The U.S. Public Health Service Centers for Disease Control and Prevention advises HIV-infected women not to breast-feed to avoid postnatal transmission of HIV to a child who may not yet be infected.

Pediatric Use

Safety and effectiveness in children have not been studied. The use of VISTIDE in children with AIDS warrants extreme caution due to the risk of long-term carcinogenicity and reproductive toxicity. Administration of VISTIDE to children should be undertaken only after careful evaluation and only if the potential benefits of treatment outweigh the risks.

Geriatric Use

No studies of the safety or efficacy of VISTIDE in patients over the age of 60 have been conducted. Since elderly individuals frequently have reduced glomerular filtration, particular attention should be paid to assessing renal function before and during VISTIDE administration (see DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS

1. ***Nephrotoxicity:*** Renal toxicity, as manifested by ≥ 2+ proteinuria, serum creatinine elevations of ≥ 0.4 mg/dL, or decreased creatinine clearance ≤ 55 mL/min, occurred in 79 of 135 (59%) patients receiving VISTIDE at a maintenance dose of 5 mg/kg every other week. Maintenance dose reductions from 5 mg/kg to 3 mg/kg due to proteinuria or serum creatinine elevations were made in 12 of 41 (29%) patients who had not received prior therapy for CMV retinitis (Study 106) and in 19 of 74 (26%) patients who had received prior therapy for CMV retinitis (Study 107). Prior foscarnet use has been associated with an increased risk of nephrotoxicity; therefore, such patients must be monitored closely (see CONTRAINDICATIONS, WARNINGS, DOSAGE AND ADMINISTRATION).
2. ***Neutropenia:*** In clinical trials, at the 5 mg/kg maintenance dose, a decrease in absolute neutrophil count to ≤ 500 cells/mm^3 occurred in 24% of patients. Granulocyte colony stimulating factor (GCSF) was used in 39% of patients.
3. ***Decreased Intraocular Pressure/Ocular Hypotony:*** Among the subset of patients monitored for intraocular pressure changes, a ≥ 50% decrease from baseline intraocular pressure was reported in 17 of 70 (24%) patients at the 5 mg/kg maintenance dose. Severe hypotony (intraocular pressure of 0-1 mm Hg) has been reported in 3 patients. Risk of ocular hypotony may be increased in patients with preexisting diabetes mellitus.
4. ***Anterior Uveitis/Iritis:*** Uveitis or iritis has been reported in clinical trials and during postmarketing in patients receiving VISTIDE therapy. Uveitis or iritis was reported in 15 of 135 (11%) patients receiving 5 mg/kg maintenance dosing. Treatment with topical corticosteroids with or without topical cycloplegic agents may be considered. Patients should be monitored for signs and symptoms of uveitis/iritis during VISTIDE therapy.
5. ***Metabolic Acidosis:*** A diagnosis of Fanconi's syndrome, as manifested by multiple abnormalities of proximal renal tubular function, was reported in 1% of patients. Decreases in serum bicarbonate to ≤ 16 mEq/L occurred in 16% of cidofovir-treated patients. Cases of metabolic acidosis in association with liver dysfunction and pancreatitis resulting in death have been reported in patients receiving VISTIDE.

In clinical trials, VISTIDE was withdrawn due to adverse events in 39% of patients treated with 5 mg/kg every other week as maintenance therapy.

The incidence of adverse reactions reported as serious in three controlled clinical studies in patients with CMV retinitis, regardless of presumed relationship to drug, is listed in Table 4.

Table 4. Serious Clinical Adverse Events or Laboratory Abnormalities Occurring in > 5% of Patients

	N = 135[b] # patients (%)	
Proteinuria (≥ 100 mg/dL)	68	(50)
Neutropenia (≤ 500 cells/mm^3)	33	(24)
Decreased Intraocular Pressure[a]	17	(24)
Decreased Serum Bicarbonate (≤ 16 mEq/L)	21	(16)
Fever	19	(14)
Infection	16	(12)
Creatinine Elevation (≥ 2.0 mg/dL)	16	(12)
Pneumonia	12	(9)
Dyspnea	11	(8)
Nausea with Vomiting	10	(7)

[a] Patients receiving 5 mg/kg maintenance regimen in Studies 105, 106 and 107.

[b] Defined as decreased intraocular pressure (IOP) to ≤ 50% that at baseline. Based on 70 patients receiving 5 mg/kg maintenance dosing (Studies 105, 106 and 107), for whom baseline and follow-up IOP determinations were recorded.

The most frequently reported adverse events regardless of relationship to study drugs (cidofovir or probenecid) or severity are shown in Table 5.

The following additional list of adverse events/intercurrent illnesses have been observed in clinical studies of VISTIDE and are listed below regardless of causal relationship to VISTIDE. Evaluation of these reports was difficult because of the diverse manifestations of the underlying disease and because most patients received numerous concomitant medicines.

Body as a Whole: abdominal pain, accidental injury, AIDS, allergic reaction, back pain, catheter blocked, cellulitis, chest pain, chills and fever, cryptococcosis, cyst, death, face edema, flu-like syndrome, hypothermia, injection site reaction, malaise, mucous membrane disorder, neck pain, overdose, photosensitivity reaction, sarcoma, sepsis

Cardiovascular System: cardiomyopathy, cardiovascular disorder, congestive heart failure, hypertension, hypotension, migraine, pallor, peripheral vascular disorder, phlebitis, postural hypotension, shock, syncope, tachycardia, vascular disorder, edema

Digestive System: cholangitis, colitis, constipation, esophagitis, dyspepsia, dysphagia, fecal incontinence, flatulence, gastritis, gastrointestinal hemorrhage, gingivitis, hepatitis, hepatomegaly, hepatosplenomegaly, jaundice, abnormal liver function, liver damage, liver necrosis, melena, pancreatitis, proctitis, rectal disorder, stomatitis, aphthous stomatitis, tongue discoloration, mouth ulceration, tooth caries

Endocrine System: adrenal cortex insufficiency

Hemic & Lymphatic System: hypochromic anemia, leukocytosis, leukopenia, lymphadenopathy, lymphoma like reaction, pancytopenia, splenic disorder, splenomegaly, thrombocytopenia, thrombocytopenic purpura

Metabolic & Nutritional System: cachexia, dehydration, edema, hypercalcemia, hyperglycemia, hyperkalemia, hyperlipemia, hypocalcemia, hypoglycemia, hypoglycemic reaction, hypokalemia, hypomagnesemia, hyponatremia, hypophosphatemia, hypoproteinemia, increased alkaline phosphatase, increased BUN, increased lactic dehydrogenase, increased SGOT, increased SGPT, peripheral edema, respiratory alkalosis, thirst, weight loss, weight gain

Musculoskeletal System: arthralgia, arthrosis, bone necrosis, bone pain, joint disorder, leg cramps, myalgia, myasthenia, pathological fracture

Nervous System: abnormal dreams, abnormal gait, acute brain syndrome, agitation, amnesia, anxiety, ataxia, cerebrovascular disorder, confusion, convulsion, delirium, dementia, degression, dizziness, drug dependence, dry mouth, encephalopathy, facial paralysis, hallucinations, hemiplegia, hyperesthesia, hypertonia, hypotony, incoordination, increased libido, insomnia, myoclonus, nervousness, neuropathy, paresthesia, personality disorder, somnolence, speech disorder, tremor, twitching, vasodilatation, vertigo

Respiratory System: asthma, bronchitis, epistaxis, hemoptysis, hiccup, hyperventilation, hypoxia, increased sputum, larynx edema, lung disorder, pharyngitis, pneumothorax, rhinitis, sinusitis

Skin & Appendages: acne, angioedema, dry skin, eczema, exfoliative dermatitis, furunculosis, herpes simplex, nail disorder, pruritus, rash, seborrhea, skin discoloration, skin disorder, skin hypertrophy, skin ulcer, sweating, urticaria

Special Senses: abnormal vision, amblyopia, blindness, cataract, conjunctivitis, corneal lesion, corneal opacity, diplopia, dry eyes, ear disorder, ear pain, eye disorder, eye pain, hyperacusis, iritis, keratitis, miosis, otitis externa, otitis media, refraction disorder, retinal detachment, retinal disorder, taste perversion, tinnitus, uveitis, visual field defect, hearing loss

Urogenital System: decreased creatinine clearance, dysuria, glycosuria, hematuria, kidney stone, mastitis, metorrhagia, nocturia, polyuria, prostatic disorder, toxic nephropathy, urethritis, urinary casts, urinary incontinence, urinary retention, urinary tract infection

Table 5. All Clinical Adverse Events, Laboratory Abnormalities or Intercurrent Illnesses Regardless of Severity Occurring in > 15% of Patients

	N = 115[a] # patients (%)	
Any Adverse Event	115	(100)
Proteinuria (≥ 30 mg/dL)	101	(88)
Nausea +/- Vomiting	79	(69)
Fever	67	(58)
Neutropenia (< 750 cells/mm^3)	50	(43)
Asthenia	50	(43)
Headache	34	(30)
Rash	34	(30)
Infection	32	(28)
Alopecia	31	(27)
Diarrhea	30	(26)
Pain	29	(25)
Creatinine Elevation (> 1.5 mg/dL)	28	(24)
Anemia	28	(24)
Anorexia	26	(23)
Dyspnea	26	(23)
Chills	25	(22)
Increased Cough	22	(19)
Oral Moniliasis	21	(18)

[a] Patients receiving 5 mg/kg maintenance regimen in Studies 106 and 107.

Reporting of Adverse Reactions

Malignancies or serious adverse reactions that occur in patients who have received VISTIDE should be reported to Gilead in writing to the Director of Clinical Research, Gilead Sciences, Inc., 333 Lakeside Drive, Foster City, CA 94404 or by calling 1-800-GILEAD-5 (445-3235), or to FDA MedWatch 1-800-FDA-1088/fax 1-800-FDA-0178.

OVERDOSAGE

Two cases of cidofovir overdose have been reported. These patients received single doses of VISTIDE at 16.3 mg/kg and 17.4 mg/kg, respectively, with concomitant oral probenecid and intravenous hydration. In both cases, the patients were hospitalized and received oral probenecid (one gram three times daily) and vigorous intravenous hydration with normal saline for 3 to 5 days. Significant changes in renal function were not observed in either patient.

DOSAGE AND ADMINISTRATION

VISTIDE MUST NOT BE ADMINISTERED BY INTRAOCULAR INJECTION.

Dosage

THE RECOMMENDED DOSAGE, FREQUENCY, OR INFUSION RATE MUST NOT BE EXCEEDED. VISTIDE MUST BE DILUTED IN 100 MILLILITERS 0.9% (NORMAL) SALINE PRIOR TO ADMINISTRATION. TO MINIMIZE POTENTIAL NEPHROTOXICITY, PROBENECID AND INTRAVENOUS SALINE PREHYDRATION MUST BE ADMINISTERED WITH EACH VISTIDE INFUSION.

Induction Treatment The recommended induction dose of VISTIDE for patients with a serum creatinine of ≤ 1.5 mg/dL, a calculated creatinine clearance > 55 mL/min, and a urine protein < 100 mg/dL (equivalent to < 2+ proteinuria) is 5 mg/kg body weight (given as an intravenous infusion at a constant rate over 1 hr) administered once weekly for two consecutive weeks. Because serum creatinine in patients with advanced AIDS and CMV retinitis may not provide a complete picture of the patient's underlying renal status, it is important to utilize the Cockcroft-Gault formula to more precisely estimate creatinine clearance (CrCl). As creatinine clearance is dependent on serum creatinine and patient weight, it is necessary to calculate clearance prior to initiation of VISTIDE. CrCl (mL/min) should be calculated according to the following formula:

$$\text{Creatinine clearance for males} = \frac{[140\text{-age (years)}] \times [\text{body wt (kg)}]}{72 \times [\text{serum creatinine (mg/dL)}]}$$

$$\text{Creatinine clearance for females} = \frac{[140\text{-age (years)}] \times [\text{body wt (kg)}] \times 0.85}{72 \times [\text{serum creatinine (mg/dL)}]}$$

Maintenance Treatment The recommended maintenance dose of VISTIDE is 5 mg/kg body weight (given as an intravenous infusion at a constant rate over 1 hr), administered once every 2 weeks.

Dose Adjustment

Changes in Renal Function During VISTIDE Therapy: The maintenance dose of VISTIDE must be reduced from 5 mg/kg to 3 mg/kg for an increase in serum creatinine of 0.3 - 0.4 mg/dL above baseline. VISTIDE therapy must be discontinued for an increase in serum creatinine of ≥ 0.5 mg/dL above baseline or development of ≥ 3+ proteinuria.

Preexisting Renal Impairment: VISTIDE is contraindicated in patients with a serum creatinine concentration > 1.5 mg/dL, a calculated creatinine clearance ≤ 55 mL/min, or a urine protein ≥ 100 mg/dL (equivalent to ≥ 2+ proteinuria).

Probenecid Probenecid must be administered orally with each VISTIDE dose. Two grams must be administered 3 hr prior to the VISTIDE dose and one gram administered at 2 and again at 8 hr after completion of the 1 hr VISTIDE infusion (for a total of 4 grams).

Ingestion of food prior to each dose of probenecid may reduce drug-related nausea and vomiting. Administration of an antiemetic may reduce the potential for nausea associated with probenecid ingestion. In patients who develop allergic or hypersensitivity symptoms to probenecid, the use of an appropriate prophylactic or therapeutic antihistamine and/or acetaminophen should be considered (see CONTRAINDICATIONS).

Hydration Patients must receive at least one liter of 0.9% (normal) saline solution intravenously with each infusion of VISTIDE. The saline solution should be infused over a 1-2 hr period immediately before the VISTIDE infusion. Patients who can tolerate the additional fluid load should receive a second liter. If administered, the second liter of saline should be initiated either at the start of the VISTIDE infusion or immediately afterwards, and infused over a 1 to 3 hr period.

Method of Preparation and Administration

Inspect vials visually for particulate matter and discoloration prior to administration. If particulate matter or discoloration is observed, the vial should not be used. With a syringe, extract the appropriate volume of VISTIDE from the vial and transfer the dose to an infusion bag containing 100 mL 0.9% (normal) saline solution. Infuse the entire volume intravenously into the patient at a constant rate over a 1 hr period. Use of a standard infusion pump for administration is recommended.

It is recommended that VISTIDE infusion admixtures be administered within 24 hr of preparation and that refrigerator or freezer storage not be used to extend this 24 hr limit.

If admixtures are not intended for immediate use, they may be stored under refrigeration (2-8°C) for no more than 24 hr. Refrigerated admixtures should be allowed to equilibrate to room temperature prior to use.

The chemical stability of VISTIDE admixtures was demonstrated in polyvinyl chloride composition and ethylene-propylene copolymer composition commercial infusion bags, and in glass bottles. **No data are available to support the addition of other drugs or supplements to the cidofovir admixture for concurrent administration.**

VISTIDE is supplied in single-use vials. Partially used vials should be discarded (see Handling and Disposal).

Compatibility with Ringer's solution, Lactated Ringer's solution or bacteriostatic infusion fluids has not been evaluated.

Handling and Disposal

Due to the mutagenic properties of cidofovir, adequate precautions including the use of appropriate safety equipment are recommended for the preparation, administration, and disposal of VISTIDE. The National Institutes of Health presently recommends that such agents be prepared in a Class II laminar flow biological safety cabinet and that personnel preparing drugs of this class wear surgical gloves and a closed front surgical-type gown with knit cuffs. If VISTIDE contacts the skin, wash membranes and flush thoroughly with water. Excess VISTIDE and all other materials used in the admixture preparation and administration should be placed in a leak-proof, puncture-proof container. The recommended method of disposal is high temperature incineration.

Patient Monitoring

Serum creatinine and urine protein must be monitored within 48 hours prior to each dose. White blood cell counts with differential should be monitored prior to each dose. In patients with proteinuria, intravenous hydration should be administered and the test repeated. Intraocular pressure, visual acuity and ocular symptoms should be monitored periodically.

HOW SUPPLIED

VISTIDE (cidofovir injection) 75 mg/mL for intravenous infusion, is supplied as a non-preserved solution in single-use clear glass vials as follows:

NDC 61958-0101-1 375 mg in a 5 mL vial in a single-unit carton

VISTIDE should be stored at controlled room temperature 20°-25°C (68°-77°F).

Manufactured by:
Ben Venue Laboratories, Inc.
Bedford, OH 44146-0568

Manufactured for and distributed by:
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

VISTIDE® (cidofovir injection) is covered by U.S. Patent No. 5,142,051 and its foreign counterparts. Other patents pending.

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ANNEX I TO SMALLPOX RESPONSE PLAN 29 September 2002
MEDICAL LOGISTICS & PRODUCT DISTRIBUTION.

REFERENCES.

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b. United States Army Medical Command. “How To” Guide for Unit Leaders and Unit Health Care Providers: Implementation Guidelines for Investigational New Drug (IND) Protocols. Falls Church, VA, May 2002.

c. United States Army Medical Command. “How To” Guide for Investigational New Drug (IND) Protocols, Supplement: Smallpox Vaccination (IND # 10664). Falls Church, VA, publication pending.

1. General. This annex describes instructions from the U.S. Army Medical Materiel Agency (USAMMA) for ordering, shipping, storing, controlling, accounting, and disposition of expired or suspended products. Appendix I-1 summarizes this DoD Annex on one page.

2. Mission. USAMMA will coordinate the distribution of the smallpox (vaccinia) vaccine and ancillary supplies to all medical supply activities of each of the Armed Services or other supported organizations. USAMMA will also coordinate the distribution of vaccinia immune globulin (VIG), cidofovir, and other critical medical logistic items that might be needed in implementing the DoD Smallpox Response Plan.

3. Assumptions:

a. The smallpox (vaccinia) vaccine may be either (a) licensed by the Food & Drug Administration (FDA) at the time of vaccination or (b) unlicensed but permitted by FDA to be used under Investigational New Drug (IND) provisions of the Food Drug & Cosmetic Act. If smallpox vaccine is used as an IND medication within the constructs of the DoD Smallpox Response Plan, additional education, documentation, and consent requirements apply. This iteration of Annex I assumes that smallpox vaccine is in IND status.

b. If the licensing status of these products changes during the course of the DoD response, IND products will be removed from inventory and replaced with licensed product as soon as possible.

c. In the event of a smallpox outbreak, DoD will supplement its inventory of smallpox vaccine from the National Pharmaceutical Stockpile (NPS). Appendix I-7 describes

some features of the NPS vaccine distribution planning and describes four potential types of smallpox vaccine that may be used. Nonetheless, vaccine requisitioning procedures through DoD channels described elsewhere in this annex will be used.

4. Planning Factors:

a. References a, b, and c provide guidance on applicable education, documentation, and consent issues for IND medications, including smallpox vaccine and two medications to treat adverse events after smallpox vaccination (i.e., vaccinia immune globulin (VIG) and cidofovir).

b. IND products require strict procedures for logistical tracking. Medical supply activities will track these medications like controlled substances (e.g., morphine). Activities must document all product movement from the wholesale level down to patient administration.

c. Customers must ensure they have appropriate refrigeration available for storage of the vaccine or the USAMMA's Distribution Operations Center (DOC) cannot ship to the site.

d. The intent of DoD vaccine distribution operations is to arrange door-to-door transportation from supply depot to the pharmacy supporting the clinic that will administer the vaccine. In case distribution operations are overwhelmed by excessive simultaneous demand, less direct arrangements may be required. In such cases, installations may be required to send a courier and vehicle to a prearranged location (e.g., a commercial airhead) to take possession of a vaccine shipment. Depending on circumstances, it may be appropriate for the installation courier to be accompanied by a security detail.

5. Contracting and Sources of Supply.

a. Linen & Waste Management. MTFs will develop plans for handling linens and regulated medical waste (RMW), as well as ensuring adequate medical supplies. All waste generated by smallpox patients will be treated as RMW. Linen may be handled through normal in-house or contract mechanisms as long as provisions have been made for the appropriate protection of the personnel who will be handling the linen (i.e. vaccination and appropriate personal protective equipment).

b. Sources of Supply. MTFs will identify Prime Vendor (PV) capabilities for increased deliveries of all medical supplies and equipment. MTFs will develop contingency plans for requisitioning medical supplies, in case standard channels are inadequate. Just-in-time delivery by prime vendors may not be sufficient to meet needs during outbreaks, based on the large volume of supplies that may be needed throughout a region. Establish delivery protocols for delivery of key supplies and equipment.

c. Transport of Regulated Medical Waste. Logistics or housekeeping division will be responsible for collecting, packaging, and disposing of RMW according to local, state, and federal regulations, as well as maintaining required documentation (manifests). The environmental science officer or preventive-medicine staff provides guidance as needed. Facilities that perform regulated medical waste handling on site will ensure appropriate coordination with local and state officials.

6. Requisitioning.

a. USAMMA's DOC will not accept automated requisitions for smallpox (vaccinia) vaccine, VIG, or cidofovir. Vaccination sites submit requests to their supporting medical logistics activity, which will validate the requirement and submit a formal request to their strategic logistics agency (i.e., their Service Vaccine Control Center) using a DD Form 1348-6 or acceptable written alternative. A sample DD Form 1348-6 is attached as Appendix I-2.

b. Units may order VIG or cidofovir only in conjunction with IND protocols for their use, except in limited prepositioning situations. Use of VIG or cidofovir is discussed in Annexes B, G, and H.

c. The Service Vaccine Control Centers are:

(1) Navy & Marine Corps – Naval Medical Logistics Command (NAVMEDLOGCOM)

(2) Air Force – Air Force Medical Logistics Office (AFMLO)

(3) Army – U.S. Army Medical Materiel Agency (USAMMA).

(4) Coast Guard -- U.S. Army Medical Materiel Agency (USAMMA).

d. Provide the following information on the DD Form 1348-6 or alternate form:

Item Requested	National Stock Number (NSN)	Unit of Issue (UI)
Smallpox vaccine (*Dryvax*), full-strength	6505-00-903-8173	PG (100-dose vial with diluent, 100 bifurcated needles, and 100 transfer needles)
Smallpox vaccine (*Dryvax*), diluted 1:5	6505-01-499-9118	PG (500-dose vial with diluent, 500 bifurcated needles, and 500 transfer needles)
Vaccinia immune globulin, intramuscular (VIG-IM)	6505-01-053-2600	VI (5 ml vial)

Vaccinia immune globulin, intravenous (VIG-IV)	NSN pending	pending
Cidofovir (*Vistide*)	6505-01-501-0628	VI (375 mg/5 ml vial)

e. Also enter:

(1) Document Number (including requisitioner, date, and serial number) (Army sites only),
(2) Priority – 02
(3) Quantity – quantity of units of issue required
(4) Requester's name,
(5) Requester's telephone number (commercial and DSN if available),
(6) Requester's fax number,
(7) Person who will be the shipment point of contact (POC),
(8) POC telephone number (commercial and DSN if available),
(9) POC fax number,
(10) POC e-mail (if available),
(11) Alternate POC information (identical information as requested for POC), and
(12) Shipping address (unit or facility, street address, city, state and zip code).

f. Individuals experiencing difficulties providing this information should contact the DOC at (301) 619-4121, -4128, -4411, -4318, -4198, or –4320 (DSN 343). Updated information appears at https://usamma-extranet.detrick.army.mil/cpp/index.html.

g. The Service Vaccine Control Center will provide approved requests to the DOC at fax (301) 619-4468.

h. The DOC will contact customers promptly if requests are incomplete or illegible.

7. Shipping.

a. The DOC will contact the receiving units before their scheduled shipment. During this call, the DOC and the receiving unit will discuss handling requirements. The activity will notify personnel in their receiving area and central receiving mail drop-off area. The activity will clear all gate or installation requirements for shipment delivery. For OCONUS shipments, the DOC will assist the local action officer in preparing documentation required from the Food and Drug Administration or Ministry of Health before the package arrives at Customs for clearance.

b. After calling the activity, the DOC will fax them a copy of the product receipt matrix and handling instructions. A sample of each is attached at Appendix I-3 and Appendix I-4.

c. The DOC will coordinate packaging and shipping of product(s) directly to the requesting site. In some cases, shipment escorts may be required.

d. The DOC advises the activity to track the shipment using either DHL, Federal Express, or the Defense Logistics Agency (DLA) Distribution Standard System (DSS) Material Release Order (MRO) or Global Transportation Network (GTN) web sites or operators.

(1) DHL: www.DHL.com or 1-800-345-3579.

(2) FedEx: www.fedex.com or 1-800-463-3339.

(3) DLA DSS MRO: http://wegal.ogden.disa.mil/mrostatus/query.html.

(4) GTN: http://gtn.transcom.mil.

The DOC also tracks each shipment and provides the activity their tracking numbers upon notification of shipment.

e. Upon receipt of the product, the activity inspects the package for damage. If the package is damaged, the activity should call the DOC immediately. If shipment was completed through the DoD supply system, a report of discrepancy (ROD) should be completed for any damaged shipment. The receiving activity must complete all requirements specified on the receiving matrix faxed from the DOC earlier (Appendix I-3).

f. If the receiving activity has an urgent need to use the shipped product(s) immediately upon receipt, follow these steps:

(1) Upon receiving the shipment, the site contacts the DOC before opening the package.

(2) The DOC staff will explain procedures for conducting a check on the shipment's cold-chain maintenance status, recorded by the TempTale® temperature-monitoring device, enclosed in each shipment needing refrigeration.

(3) The receiving activity promptly removes the TempTale® from the shipping container and follow the steps exactly as described by the DOC staff (within 5 minutes of opening the shipping container).

(4) The response from the TempTale® (either Green Light or Red Light) will be relayed back to the DOC staff person, who will either provide verbal authorization to release the product for immediate use, or will tell the receiving activity that further inspection is required.

(5) The receiving activity will inspect the product and place it in an approved storage container. This is a refrigerator for smallpox vaccine and VIG (2° to 8°C, 36° to 46°F). Cidofovir is stored at controlled room temperature (25°C or 77°F), although refrigeration is acceptable.

g. If immediate release of the product is not necessary, activities should remove the product, inspect it, and store as above. If more than one container arrives, the vials from each container should be segregated and marked with the corresponding TempTale® monitor number. This provides accurate identification in case one container's monitor reads outside of required temperature parameters and is determined to be unusable. Contact the DOC to acknowledge receipt of the shipment, confirm quantity received, and confirm the express-mail air bill number for the return envelope.

h. The receiving site express-mail returns the TempTale® monitor to USAMMA's DOC, using the enclosed pre-addressed, overnight express mail envelope.

i. Upon receipt, the DOC will download the temperature data from the TempTale®. Once validated, the DOC will inform the site it may use the product, first telephonically, then with a follow-up faxed confirmation.

j. If the receiving site is located in CONUS, it returns all shipping and packaging materials using the enclosed, pre-addressed shipping label. Attach the pre-addressed shipping label to the box and send it back to the stockpile location. OCONUS locations may retain the shipping and packaging materials.

k. The DOC will not provide release of product for administration unless a proper green-light release is performed on the TempTale® monitor or the monitor is received, downloaded and approved by the USAMMA Pharmacy Consultant.

8. Storing.

a. Like most vaccines and antibody products, smallpox (vaccinia) vaccine and vaccinia immune globulin are stored in the refrigerator at 2 to 8 degrees Celsius (36–46 degrees Fahrenheit). If smallpox vaccine or VIG is exposed to temperatures above or below this level for more than 1 hour, contact the DOC at 301-619-4128, -4121, -4411, -4198, -4318, -4320 (DSN 343) for disposition instructions. Smallpox (vaccinia) vaccine and VIG can tolerate short exposures to other temperatures without degradation.

b. Cidofovir is stored at controlled room temperature (25°C or 77°F).

c. The DOC provides guidance on unusual storage conditions or distribution emergencies. Track all critical products by lot number and quantity.

9. Emergency Storage.

a. During situations when normal refrigeration systems break down, take every effort to minimize loss of product due to breaks in the cold-chain.

b. In the case of power failure or breakdown of proper storage facilities, the DOC will assist in establishing alternative emergency storage plans. The DOC has several VaxiCool® temporary-storage refrigeration units located around the world. These VaxiCools® can be used until existing storage facilities return to proper operating order or are replaced. When a power failure or loss of storage is discovered, notify the DOC immediately. DOC personnel will assist with risk assessment, recommend actions to be taken, and assist with redistribution of product or delivery of a VaxiCool® for temporary storage. Service POCs also should be contacted shortly after the initial contact with the DOC to inform them of the situation.

10. Redistribution. Guidance for product redistribution can be obtained from the USAMMA website: https://usamma-extranet.detrick.army.mil/cpp/index.html. Contact the DOC before redistributing smallpox vaccine, VIG, or cidofovir. The effective movement of product requires constant maintenance of the appropriate storage temperature. To ensure this requirement, the product will be moved in a refrigerated container. DOC personnel must ensure maintenance of cold-chain throughout redistribution and will provide release authorization when redistribution is completed. Information on these containers can be obtained from the above-mentioned web site.

a. The DOC will provide the losing activity detailed packing instructions for the VaxiCool® or VaxiPac® container or Endurotherm Box. Gaining activities will be provided receiving and processing matrix for the transported product.

b. The DOC will send an empty container with shipping labels and a serial numbered security band to the losing activity. If the container is damaged, notify DOC immediately. If the container is in satisfactory condition, receive and process documents and pack product according to information provided.

c. With the pre-addressed, overnight express-mail label, send the VaxiCool® or VaxiPac® to the gaining unit. Call DOC to confirm overnight express-mail label account number, air bill and security band serial number for the shipment.

d. Upon receipt of the product, the gaining activity will immediately inspect the container and contents for damage and the security band for serial number accuracy. If the container or contents are damaged, notify the DOC immediately with details. If container is in satisfactory condition, receive and immediately secure product in the required refrigerated storage environment (2° to 8° Celsius or 36° to 46° Fahrenheit). Call DOC to confirm receipt and document the lot number and quantity received.

e. Process documents and product in accordance with the information provided. Call commercial carrier to schedule pickup of VaxiCool®, VaxiPac® or Endurotherm Box. Ship container back to the DOC, using the provided pre-addressed, overnight, express-

mail label. Call the DOC to confirm overnight express-mail label account number and air bill serial number for the container.

f. Establish stock-record accountability of product in accordance with Service regulations.

g. Do not release the product to end-user until authorized by the DOC.

11. Control and Accountability. The lots of IND products must be handled in accordance with the control and accountability procedures of an investigational pharmaceutical.

a. Logistics activities must maintain readily retrievable records showing receipts and issues to supported activities, clinics, or other vaccination sites. This information includes the lot number and expiration date (if applicable) of the vials received or issued. Logistics sites not possessing an automated method that can readily retrieve reports of this information should implement manual procedures similar to those used for controlled substances (e.g., morphine).

b. Clinics and vaccination sites must also maintain readily retrievable records showing receipts from their supporting logistics activities, including lot number and expiration date, and local administration records showing consumption of the product they have received (i.e., number of doses administered). Vaccination sites not possessing an automated method that can readily retrieve reports on the receipt and gross usage of product should implement manual procedures as would be used for controlled substances. A sample form for a manual process is attached at Appendix I-5.

c. Clinics and vaccination sites will record individual dosage administration in Service-specific medical documentation systems, as discussed in DoD Annex B.

d. The DOC and all activities receiving IND products must provide hard-copy supply status reports to the US Army Medical Materiel Development Agency (USAMMDA) on a monthly basis. These data will include the information discussed above (receipts, issues and vaccination documentation) as well as an updated, validated inventory and will be gathered with a closing date of the last day of each month. Activities will forward/fax these data to USAMMDA for inclusion in the protocol case files not later than the seventh of each month. The USAMMDA fax number is (301) 619-2304 (DSN – 343).

12. Recovery of Unused IND Products. All unopened vials of IND medication will be accounted for and returned to USAMMA. Contact the DOC before movement of any IND medication. DOC personnel will ensure the use of appropriate packing materials and shipping containers, maintenance of cold chain, and will coordinate the movement of all smallpox vaccine to be recovered. Activities may not ship any IND medication without explicit guidance from USAMMA’s DOC.

13. Disposal of Unused Non-IND Products. Activities have responsibility for disposal and destruction of unusable products other than IND products. Contact the DOC before

destruction of any product issued under the DoD Smallpox Response Plan. Activities will report on-hand product inventories to be destroyed to their respective logistic agencies. The report will include information regarding lot numbers and quantities. FDA-licensed smallpox product must be handled as infectious waste. Do not discharge this item into a sanitary sewer.

a. The disposal code for FDA-licensed smallpox vaccine and FDA-licensed vaccinia immune globulin is CA01. [If used in IND status, refer to paragraph 12 above.]

b. Methods for disposal are as follows:

(1) Autoclave/Sanitary Landfill. Autoclave this item at 120 degrees Celsius for 60 minutes at 15 psi before burial in a permitted sanitary landfill.

(2) Incineration. Mix this disposal item with other combustibles and incinerate. To prevent the production of excessive air pollutants, the disposal item or combination of similar items shall not exceed 10% by weight of the total waste load charged to the incinerator at any one time.

(3) Use the following procedures if the aforementioned disposal methods are not available or immediate disposal is necessary:

(a) Contact the DOC and provide information regarding lot numbers and quantities. The DOC will provide a pre-addressed, overnight, express-mail container with packing procedures.

(b) Deface the label on each vial with red permanent marker.

(c) The activity will pack the container according to instructions provided and mail the container to DOC.

(d) The activity will call DOC to confirm overnight express-mail account number and air bill serial number for the container.

c. The disposal code for FDA-licensed cidofovir is AC01. [If used in IND status, refer to paragraph 12 above.]

d. Methods for disposal are as follows:

(1) Sanitary Landfill. This item and its container should be crushed/broken prior to burial in a permitted sanitary landfill. Rate shall not exceed 1% by weight per day of the total quantity of refuse collected and buried.

(2) Incineration. Mix this disposal item with relatively dry combustible material and incinerate. To prevent the production of excessive air pollutants, the disposal item or

combination of similar items shall not exceed 1% by weight of the total waste load charged to the incinerator at any one time.

(3) Use the following procedures if the aforementioned disposal methods are not available or immediate disposal is necessary:

(a) Contact the DOC and provide information regarding lot numbers and quantities. The DOC will provide a pre-addressed, overnight, express-mail container with packing procedures.

(b) Deface the label on each vial with red permanent marker.

(c) The activity will pack the container according to instructions provided and mail the container to DOC.

(d) The activity will call DOC to confirm overnight express-mail account number and air bill serial number for the container.

e. Activities will prepare a certificate of disposition/destruction on DA Form 3161, Request for Issue or Turn-In, to document disposal actions and fax a copy to the DOC within 24 hours after final disposition. A sample DA Form 3161 is attached at Appendix I-6. Activities must also prepare an executive summary that documents the circumstances surrounding the wasting of the product and what actions have been taken to prevent loss of product in the future and fax to the DOC at 301-619-4468 (DSN 343).

f. Those charged with the disposal and destruction should address all questions or concerns to USAMMA Pharmacy Consultant.

14. Special Situations.

a. Ships Underway. Naval units requisition via responsible Type Commander (TYCOM) to (NAVMEDLOGCOM.

b. OCONUS Units. Procedures apply as above. For OCONUS shipments, USAMMA will assist the local action officer in preparing documentation required from the Food and Drug Administration or Ministry of Health before the package arrives at Customs for clearance. After delivery, the receiving official must complete a Customs Invoice for the TempTale® monitor to be shipped to USAMMA.

c. IND medications may not be shared or diverted without the knowledge and agreement of USAMRIID or the IND sponsor.

APPENDIX I-1
Medical Logistics & Product Distribution – Summary.

1. The U.S. Army Medical Materiel Agency (USAMMA) Distribution Operations Center (DOC) will coordinate distribution of smallpox vaccine, vaccinia immune globulin (VIG), cidofovir, and other critical medical logistic items to all medical supply activities of each of the Armed Services.

2. Coordinate with the DOC at (301) 619-4121, -4128, -4411, -4318, -4198, or –4320 (DSN 343). Updated information appears at https://usamma-extranet.detrick.army.mil/cpp/index.html. The DOC works closely with the Naval Medical Logistics Command (NAVMEDLOGCOM) and the Air Force Medical Logistics Office (AFMLO).

3. Annex I assumes that smallpox vaccine is in Investigational New Drug (IND) status. VIG and cidofovir are in IND status. Medications in IND status involve education, documentation, and consent issues addressed in greater detail in “How To” guides for command surgeons and unit health-care providers, available separately (references a, b, and c).

4. Smallpox vaccine, VIG, and cidofovir require strict logistical tracking. This annex details USAMMA instructions for ordering, shipping, storing, controlling, accounting, and disposition of expired or suspended products.

a. Ordering. Submit requests to supporting medical logistics activity, which validates requirement and submits a formal requisition (e.g., DD Form 1348-6).

b. Shipping. Requesting activities coordinate individually with USAMMA’s DOC before shipment and immediately after receipt. Prevent shipments from sitting unattended at receipt, leading to product exposure to extreme temperatures and resultant wastage. For shipment overseas, plan ahead to prevent delays in customs clearance.

c. Storing. Refrigerate vaccine and VIG. Check refrigerator temperatures at least daily. Consider backup power supply. Store cidofovir at controlled room temperature.

d. Control & Accounting. Logistics activities, clinics, and vaccination sites must maintain readily retrievable records of receipts and issues. All activities must report supply status reports for IND medications monthly to USAMMA.

e. Disposition. Unused IND products must be returned to USAMMA. Unused non-IND products, if expired or suspended, may be disposed of according to USAMMA instructions. Empty containers may be disposed of according to USAMMA instructions.

APPENDIX I-2

Sample DD Form 1348-6, DoD Single Line Item Requisition System Document.

DOCUMENT IDENTIFIER	ROUTING IDENTIFIER	M & S	ITEM IDENTIFICATION* (NSN, FSCM, Part No., Other) FSCM	PART NUMBER	UNIT OF ISSUE	QUANTITY	DOCUMENT NUMBER SERV	REQUISITIONER
1 2 3	4 5 6	7	8 9 10 11 12	13 14 15 16 17 18 19 20 21 22	23 24	25 26 27 28 29	30	31 32 33 34 35

DOCUMENT NO. DATE	DOCUMENT NO. (Cont.) SERIAL	DEMAND	SUPPLEMENTARY ADDRESS SERV	SUPPLEMENTARY ADDRESS	SIGNAL	FUND CODE	DISTRIBUTION CODE	PROJECT CODE	PRIORITY	REQUIRED DELIVERY DAY OF YEAR	ADVIC ECODE	BLANK
36 37 38 39	40 41 42 43	44	45	46 47 48 49 50	51	52 53	54 55 56	57 58 59	60 61	62 63 64	65 66	67 68 69

	REJECT CODE (FOR USE BY SUPPLY SOURCE ONLY)	IDENTIFICATION DATA
70 71 72 73 74 75 76 77 78 79 80	65 66	*1. MANUFACTURER'S CODE AND PART NO. (When they exceed card columns 8 thru 22)
		2. MANUFACTURER'S NAME

3. MANUFACTURER'S CATALOG IDENTIFICATION	4. DATE (YYMMDD)	5. TECHNICAL ORDER NUMBER
6. TECHNICAL MANUAL NUMBER	7. NAME OF ITEM REQUESTED Vaccinia Vaccine	
8. DESCRIPTION OF ITEM REQUESTED		8a. COLOR 8b. SIZE
9. END ITEM APPLICATION		9a. SOURCE OF SUPPLY
9b. MAKE	9c. MODEL NUMBER / 9d. SERIES	9e. SERIAL NUMBER
10. REQUISITIONER (Clear text name and address)	11. REMARKS	

FOLD LINE

FOLD LINE

DD FORM 1348-6, *Edition of Apr 77 may be used until exhausted*

DOD SINGLE LINE ITEM REQUISITION SYSTEM DOCUMENT ***(MANUAL - LONG FORM)***

USAPPC

APPENDIX I-3
Smallpox Vaccine Receiving and Processing Matrix.

1. PURPOSE. To give detailed instructions on the receiving and processing of smallpox (vaccinia) vaccine.

2. GENERAL INFORMATION. The Secretary of Defense assigned the U.S Army as the Executive Agent for DoD's Immunization Program for Biological Warfare Defense, including protocol management for smallpox vaccination. The Surgeon General of the Army is responsible for implementation of this vaccination program.

3. SPECIFIC RESPONSIBILITIES. The local activity's chief of medical logistics designates a Receiving Official and alternate(s). The delegated Receiving Official or Authorized Alternate official is responsible for the receipt, processing, storage, security, and subsequent release to the end-user of this vaccine. This matrix details the necessary receiving and handling instructions to be followed by each Receiving Official or Authorized Alternate. This product must be handled as a critical medical materiel item requiring close control. Due to the sensitivity of this product, the Receiving Official or Authorized Alternate is personally responsible to prevent damage or spoilage caused by negligence.

STEP	CRITICAL EVENTS
1	Service Medical Logistics Agency (USAMMA, AFMLO, NAVMEDLOGCOM) contacts Receiving Official before shipment, to verify ship-to address and convey any special preliminary receipt instructions.
2	DOC calls Receiving Official or Alternate before shipment and verifies: a. Address and any other alternate receiving official(s). b. Receipt time of product (typically 1000-1200 the next day). c. Expected time of phone call (1500-1630 on day of shipment) from DOC with FedEx or DHL tracking/air bill number. d. Receiving Official has been contacted by their Medical Logistics Agency (USAMMA, AFMLO, NAVMEDLOGCOM) to confirm delivery.
3	DOC provides the Receiving Official a briefing on the details and potential risk associated with receipt of this shipment: a. All personnel in receiving area are aware of the incoming product shipment and a policy is in place to contact the Receiving Official or Authorized Alternate immediately for signature. b. Receiving Official must clear all facility (e.g., post, installation, clinic) security requirements (e.g., gate guards notified). c. Receiving Official notifies central receiving mail drop off locations of incoming product shipment from FedEx or DHL. d. Receiving Official verifies that proper refrigeration is available in the receiving area, with constant temperature monitoring capability and

STEP	CRITICAL EVENTS
	proper backup plans. e. Start tracking shipment. Call FedEx or DHL by 0800 the next day (www.DHL.com or 800-345-3579 or www.fedex.com or 800-463-3339). f. Contact DOC if delivery is not made by 1200.
4	USAMMA Distribution Operations Center (DOC) faxes Receiving Official a copy of this matrix and handling instructions a day before shipment.
5	Upon receipt of product, Receiving Official or Authorized Alternate will: a. Ask FedEx/DHL courier to wait for return shipment of TempTale® device included inside package, if possible. b. Check package for signs of damage, then open it and check for damage. If contents are damaged, notify USAMMA immediately. c. Remove handling instruction information paper, FedEx/DHL envelope (for TempTale® return to USAMMA), and FedEx/DHL label from the top of box. Note the airway bill numbers for the FedEx/DHL envelope for returning the TempTale and the FedEx/DHL label for returning the box. You will need to provide this information to the DOC in step 5(e). d. Remove top layers of gel packs, locate and remove the TempTale®, and place it in the FedEx/DHL envelope. If shipment is OCONUS, complete Customs Invoice provided for the return of the TempTale® monitor. Call FedEx or DHL for pickup. e. Call DOC to confirm receipt. If damaged, describe damage to DOC. Provide DOC with TempTale® FedEx/DHL tracking/air bill numbers for both the TempTale return envelope and the shipping box return label. f. Immediately secure product in the required refrigerated storage environment (2 to 8° Celsius, which is equivalent to 36 to 46° Fahrenheit). DO NOT FREEZE. g. Enclose all remaining packaging materials in shipping box and put FedEx/DHL label on box. Call FedEx or DHL for pickup. h. Assure stock record accountability for product is established in accordance with Service regulations. Track lot number and quantity. i. DO NOT RELEASE THE PRODUCT TO END-USER UNTIL AUTHORIZED BY THE DOC.
6	After receiving and downloading the TempTale®, the DOC will: a. Telephone the Receiving Official or Authorized Alternate with results. b. Fax Smallpox Vaccine Release Form to Receiving Official.
7	After receiving release authorization from the DOC, Receiving Official will: a. Notify pharmacy, immunization clinic, or other end user that product is available for clinical use. b. Report receipt of shipment to their Service Medical Logistics Agency.

APPENDIX I-4
Handling Instructions Of Smallpox Vaccine (Insert Into Product Shipments).

1. PURPOSE. To give detailed instructions on the receiving and processing of the smallpox (vaccinia) vaccine.

2. GENERAL INFORMATION. The Secretary of Defense assigned the U.S Army as the Executive Agent for DoD's Immunization Program for Biological Warfare Defense, including protocol management for smallpox vaccination. The Surgeon General of the Army is responsible for implementation of this vaccination program.

3. SPECIFIC RESPONSIBILITIES. This paper details the necessary receiving and handling instructions to be followed by each activity. This product must be handled as a critical medical materiel item requiring the utmost control. Accountability by lot number and quantity is required.

4. SMALLPOX (VACCINIA) VACCINE INFORMATION. The product must be refrigerated and maintained at temperatures between 2 to 8 degrees Centigrade (36 to 46 degrees Fahrenheit). DO NOT FREEZE. The refrigerator's temperature must be monitored electronically or manually and recorded on a routine basis. The National Stock Number (NSN) for this vaccine is 6505-01-399-6828.

4. SHIPPING. The carrier will be DHL or FedEx. Shipment tracking information for DHL is available at www.DHL.com or 1-800-225-5345 and for Federal Express at www.fedex.com or 1-800-463-3339. USAMMA's Distribution Operations Center (DOC) will notify each receiving activity with the shipment tracking number (air bill number).

5. RECEIPT INFORMATION. Upon receipt of the package:

a. Check package for signs of damage, then open it and check for damage. If contents are damaged, notify the DOC immediately.

b. Remove handling instruction information paper, FedEx/DHL envelope (for TempTale® return to USAMMA), and FedEx/DHL label from the top of box. Note the airway bill numbers for the FedEx/DHL envelope for returning the TempTale and the FedEx/DHL label for returning the box. You will need to provide this information to the DOC in step 5(e).

c. Remove top layers of gel packs, locate and remove the TempTale®, and place it in the FedEx/DHL envelope. If shipment is OCONUS, complete Customs Invoice provided for the return of the TempTale® monitor. Call FedEx or DHL for pickup.

d. Call DOC to confirm receipt. If damaged, describe damage to DOC. Provide DOC with TempTale® FedEx/DHL tracking/air bill numbers for both the TempTale return envelope and the shipping box return label.

e. Immediately secure product in the required refrigerated storage environment (2 to 8° Celsius, which is equivalent to 36 to 46° Fahrenheit). DO NOT FREEZE. If more than one container arrives, segregate the vials from each shipping container with the corresponding TempTale® monitor number. This provides accurate identification in case one container's monitor reads outside of required temperature parameters and is determined to be unusable.

f. Enclose all remaining packaging materials in shipping box and put FedEx/DHL label on box. Call FedEx or DHL for pickup.

g. If contents are in satisfactory condition, receive and process documents in accordance with local procedures. Assure stock record accountability for product is established in accordance with Service regulations. Track lot number and quantity.

h. DO NOT RELEASE PRODUCT TO END-USER UNTIL AUTHORIZED BY USAMMA's DOC. Release authorization will be electronically transmitted to the receiving activity once the temperature control monitors are received, downloaded and approved by USAMMA staff pharmacist.

6. SECURING SHIPMENT. DO NOT FREEZE! Products must be refrigerated at temperatures between 2 to 8 degrees Celsius (36-46 degrees Fahrenheit).

7. FINAL STEPS. After receiving release authorization from the DOC:

a. Notify pharmacy, immunization clinic, or other end user that product is available for clinical use.

b. Report receipt of shipment to your Service Medical Logistics Agency.

APPENDIX I-5
Sample Investigational Drug Accountability Record.

Investigational Drug Accountability Record for _____(product) Organization / Unit _____							
Line #	Date	Recipient / Patient's Name	Recipient / Patient's ID #	Quantity Dis-pensed or Re-ceived	Balance Forward _____ Balance	Manu-facturer & Lot #	Initials of person dis-pensing drug
X		XXXXXXXXX	XXXXXXXXX	XXXXX		XXXXXXX	XXXXXXX
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							
16							
17							
18							
19							
20							

APPENDIX I-6
Sample DA Form 3161, Request for Issue or Turn-In.

REQUEST FOR ISSUE OR TURN-IN (DA PAM 710-2-1)		ISSUE / X TURN-IN	SHEET NO. 1	NO. SHEETS	3. REQUEST NO.		4. VOUCHER NO.			
1. SEND TO:		5. DATE MATERIAL REQUIRED			6. DODAAC	7. PRIORITY	8. ACCOUNTING/FUNDING DATA			
2. REQUEST FROM:		9. END ITEM IDENT			9a. NAME/MANUFACTURER		9b. MODEL		9c. SERIAL NO.	
* CODE — ISSUE: I-Initial, R-Replacement; TURN-IN: FWT-Fair Wear And Tear, RS-Report of Survey, EX-Excess, SC-Stmt of Charges					10. PUBLICATION				11. JOB ORDER NO.	
12. ITEM NO. *a*	STOCK NO. *b*	ITEM DESCRIPTION *c*	UNIT OF ISSUE *d*	QUANTITY *e*	CODE* *f*	SUPPLY ACTION *g*	UNIT PRICE *h*	TOTAL COST *i*	*j.* POSTED DATE	*j.* POSTED BY
		Vaccinia Vaccine								
							SHEET TOTAL		GRAND TOTAL	
13. ISSUE/TURN-IN "QUANTITY" COLUMN IS REQUESTED	DATE	BY	14. ISSUE QTY IN "SUPPLY ACTION" COLUMN	DATE	BY		15. REC QTY IN "SUPPLY ACTION" COLUMN	DATE	BY	

DA FORM 3161, MAY 83 — REPLACES EDITION OF JUN 73 WHICH WILL BE USED UNTIL EXHAUSTED — USAPPC V2.10

APPENDIX I-7
Mass Vaccination: Vaccine Delivery & Packaging Logistics.

1. In a smallpox outbreak, after federal authorities authorize release of smallpox vaccine for mass vaccination, the initial vaccine shipment to a location may be provided in a self-contained shipping and storage unit called a Vaxicool®. One Vaxicool unit contains approximately 300 vials of vaccine and can also be used for continued storage of up to 300 vials of vaccine with an appropriate 110-volt power source. The number of vaccine vials contained within a Vaxicool unit may depend upon the specific brand of smallpox vaccine dispensed from the National Pharmaceutical Stockpile (e.g., Wyeth, Aventis, Acambis, or Baxter vaccine) and the potential need for refrigeration of the specific diluent during shipping.

2. Diluent for vaccine reconstitution and needles for single-use vaccine administration will be included in all vaccine shipments, but may be in containers separate from the vaccine. Shipments will contain vial holders to secure the vial and prevent accidental tipping during preparation and vaccination.

3. Subsequent vaccine shipments will be in Styrofoam® shipping containers. These Styrofoam shippers can support 100 to 1500 vials of vaccine, depending upon the shipment size required. Vaccine shipped in Styrofoam containers will require arrangements for refrigerated storage at 2 to 8°C upon arrival. The need to store subsequent vaccine shipments should be incorporated into all vaccine storage plans at the installation and clinic levels.

4. Current plans for rapid, large-scale shipment of vaccine through the National Pharmaceutical Stockpile (NPS) system allow for shipment of up to 500 Vaxicool systems on the first day (75 million vaccine doses), with up to 615 additional vaccine shipments per day in Styrofoam shipping containers on days 2 through 6. This plan provides for distribution of 280 million doses of smallpox vaccine from the NPS storage sites to field sites within 5 to 7 days.

5. Security Considerations. Incorporate specific security needs into planning efforts for large-scale vaccination programs. Appropriate security should provide for the following:

a. Vaccine storage sites (clinic and non-clinic), including security personnel and locked, limited access areas for vaccine storage.

b. Identify backup power sources (e.g., generators) for all sites where vaccine is stored (i.e., vaccination clinics, storage sites).

c. Vaccination clinic sites: Security personnel for crowd control, traffic movement, clinic personnel safety, and related security issues.

d. Vaccine transportation to storage sites and dispensing clinics.

Potential Smallpox Vaccine Formulations for Mass Vaccination.

Vaccine (Manufacturer)	Doses per Vial	Standard Storage	Reconstitution/Storage
ACAM1000 (Acambis)	100	2 to 8ºC	0.25 ml of accompanying diluent. Store at 2 to 8ºC once reconstituted.
ACAM2000 (Baxter)	100	2 to 8ºC	0.25 ml of accompanying diluent. Store at 2 to 8ºC once reconstituted.
generic (Aventis Pasteur)	100 (see also later instructions)	0ºC or below (see also later instructions)	0ºC or below (see also later instructions).
Dryvax (Wyeth)	500	2 to 8ºC	1.25 ml of accompanying diluent. Store at 2 to 8ºC once reconstituted.

NOTE: Because the brand of vaccine to be used will not be known beforehand, review storage and handling instructions for the specific vaccine being used with *all* staff before they begin their shift.

ANNEX J TO SMALLPOX RESPONSE PLAN 29 September 2002
RESOURCES.

APPENDIX J-1
Acronyms and Abbreviations.

ACAM – Acambis
ACC – Acute Care Center
ACIP - Advisory Committee on Immunization Practices
AE - Adverse Event
AFCITA - Air Force Complete Immunization Tracking Application
AFMAN – Air Force Manual
AFMLO - Air Force Medical Logistics Office
AFMOA - Air Force Medical Operations Agency
AHA – American Hospital Association
AIA – American Institute of Architects
AIDS - Acquired Immune Deficiency Syndrome
AIIR – Airborne Infectious Isolation Room (or area, AIIA)
AMA - American Medical Association
AMSA - Army Medical Surveillance Activity
AO – Area of Operations
AOI – Area of Interest
AOR – Area of Responsibility
AP - Aventis Pasteur
APHIS – Anaimal and Plant Health Inspection Service
APIC - Association for Professionals in Infection Control & Epidemiology
AHA- American Hospital Association
ASHE – American Society for Healthcare Engineering
ATI – Air Transportable Isolator (a chamber to contain patients with infectious diseases)
ATOC – Air Transportation Operations Center
BAT - Biological Augmentation Team
BioMedAC-Biological Medical Advisory Committee
BMBL - Biosafety in Microbiological and Biomedical Laboratories
BSC – BIOLOGICAL safety Cabinets
BSL - Bio-Safety Level
BPRP - Bioterrorism Preparedness & Response Program, CDC
BW- Biological Weapon/ Warfare
C-type Facility - (C for confirmed) Mode of shelter and care for people diagnosed with smallpox
CBRN - Chemical Biological Radiologic Nuclear
CBRNE – Chemical Biological Radiologic Nuclear Explosive
CDC - Centers for Disease Control & Prevention
CENTCOM - Central Command
CFR - Code of Federal Regulations

CINC - Commander-In-Chief
CIL- Critical Information Lists
CIO - Center/Institute/Office
CISA - Clinical Immunization Safety Assessment centers of excellence
CHPPM - Center for Health Promotion & Preventive Medicine
CM – Consequence Management
CMV - Cytomegalovirus
CONUS - Contiguous United States
CPR – Cardiopulmonary resuscitation
CXR – Chest radiograph X-ray
DA - Department of Army
DD - Department of Defense
DEERS - Defense Eligibility Enrollment Reporting System
DEPMEDS - Deployable Medical Systems
DIC – Disseminated Intravascular Coagulation
DGR - Dangerous Goods Regulations
DHHS - Department of Health & Human Services
DLA – Defense Logistics Agency
DMDC - Defense Manpower Data Center
DMAT – Disaster Medical Assistance Teams
DNA – Deoxyribonucleic Acid
DNIF – Duties Not Including Flying
DOC - Distribution Operations Center, USAMMA
DOT - Department of Transportation
DOMS- Directorate of Military Support
DoD - Department of Defense
DRG – Dangerous Goods Regulations
DSN - Defense Switch Network
DSS – Distribution Standard System
DVC - DynPort Vaccine Company
DVRD - Division of Viral & Rickettsial Diseases, CDC
DWI-Disaster Welfare Information
DQ - Division of Quarantine, CDC
EHBS - Enhanced Hospital-Based Surveillance
EISO - Epidemic Intelligence Service Officer
EPA - Environmental Protection Agency
Epi-Team - Epidemiologic Response Team
EPO - Epidemiology Program Office, CDC
EPRB - Emergency Preparedness & Response Branch, CDC
ESF – Emergency Support Function
ER - Emergency Room
ESSENCE - Electronic Surveillance System for the Early Notification of Community Based Epidemics
EUCOM - European Command
FBI - Federal Bureau of Investigations
FDA - Food & Drug Administration

FEMA - Federal Emergency Management Agency
FMP – Family Member Prefix
FPCON – Force Protection Condition
FOSC- Federal On-Scene Coordinator
FRP - Federal Response Plan
GCFS – Granulocyte Colony Stimulating Factor
GFVPRI - Generalized Febrile Vesicular-Pustular Rash Illness
GTN – Global Transportation Network
GVPRI - Generalized Vesicular-Pustular Rash Illness
HAD – Hospital-Approved Disinfectant
HCP - Health Care Providers
HCW – Healthcare Worker
HEPA - High-Efficiency Particulate Air (filter)
HHS - Health & Human Services, Department of
HICPAC – Hospital Infection Control Practices Advisory Committee
HIP - Hospital Infections Program, CDC
HIV/STD/TB - National Center for HIV, STD, & TB Prevention, CDC
HQ – Headquarters
HSRRB - Human Subjects Research Review Board (Army Surgeon General's IRB)
HSV - Herpes Simplex Virus
HVAC – Heating Ventilation and Air Conditioning
IATA - International Air Transportation Association
IAW – In Accordance With
ICAO – International Civil Aviation Organization
ICD9 – International Classification of Diseases, 9th edition
ICP – Infection Control Professionals
ICU - Intensive Care Unit
ICRA – Infection Control Risk assessments
ID - Infectious disease
IDSA – Infectious Diseases Society of America
IERA - Institute for ESOH (Environmental, Safety & Occupational Health) Risk Analysis, USAF
ICU – Intensive Care Unit
IGIV - Immune globulin intravenous
IM – Intramuscular
IND - Investigational New Drug
IRB – Institutional Review Board (medical research ethics committee)
IV – Intravenous
IVIG - see IGIV
JAMA - Journal of the American Medical Association
JIC - Joint Information Center
JPMPG - Joint Preventive Medicine Policy Group
JS - Joint Staff
JSSED – Joint Service Sensitive Equipment Decontamination
JVAP - Joint Vaccine Acquisition Program, DoD
LACUC - Laboratory Animal Care & Use Committee

LRMC – Landstuhl Regional Medical Center
LFA – Lead Federal Agency
LRN - Laboratory Response Network
MADCP – Mortuary Affairs Decontamination Collection Point
MEDCEN - Medical Center (US Army)
MEDCOM - Medical Command (US Army)
MHS - Military Health System
MMWR - Morbidity & Mortality Weekly Report
MEDPROS - Medical Protection System (US Army software application)
MRO – Materiel Release Order
MTF - Military Treatment Facility
NACI - National Advisory Committee on Immunization, Canada
NAME – National Association of Medical Examiners
NAVMED - Naval Medical Command
NAVMEDLOGCOM - Navy Medical Logistics Command
NBC - Nuclear, Biological & Chemical
NCEH - National Center for Environmental Health, CDC
NCID - National Center for Infectious Diseases, CDC
NCR – National Capital Region
NDC - National Drug Code
NDMS- National Disaster Medical System
NEHC - Navy Environmental Health Center
NEO- Non Combatant Evacuation Operations
NEPMU-6 - Navy Environmental & Preventive Medicine Unit-6
NHRC - Naval Health Research Command, San Diego
NIOSH - National Institute for Occupational Safety & Health
NIP - National Immunization Program, CDC
NPS - National Pharmaceutical Stockpile, CDC
NPSB - National Pharmaceutical Stockpile Branch, CDC
NSN - National Stock Number
NYCBOH - New York City Board of Health
OASD(HA) - Office of the Assistant Secretary of Defense for Health Affairs
OASD(PA) - Office of the Assistant Secretary of Defense for Public Affairs
OCONUS - Outside the Contiguous United States
OEP - Office of Emergency Preparedness, DHHS
OHS - Office of Health & Safety, CDC
OGC - Office of General Council (either CDC or DoD)
OPCON – Under Operational Control
OSHA – Occupational Safety and Health Administration
OTSG - Office of the Surgeon General, US Army
PACOM - Pacific Command
PAG – Public Affairs Guidance
PAHO- Pan American Health Organization
PAO – Public Affairs Officers
PAPR – Powered Air Purifying Respirations
PAR - Population at Risk

PCR- Polymerase Chain Reaction(Laboratory test method)
PDF - Portable document format
PFU - Pock-forming units
PHA- Public Health Advisor
PHPPO- Public Health Practice Program Officer, CDC
PHS- Public Health Service
PI- Principal Investigator/Product Insert(Package insert)
PM- Preventive Medicine
PPE – Personal Protective Equipment\
ppm – parts per million
PV- Prime Vendor
PAHO - Pan-American Health Organization
PAO - Public Affairs Office or Officers
PCR – Polymerase Chain Reaction (laboratory test method)
PHA - Public Health Advisor
PHPPO - Public Health Practice Program Office, CDC
PHS - Public Health Service
PI - Principal investigator, product insert (package insert)
PM - Preventive Medicine
PPE – Personal Protective Equipment
PV – Prime Vendor
R-type Facility - Residential mode of housing for surveillance of vaccinated contacts of smallpox cases
RC - Reserve Component
ROM – Restriction of Movement
RUC – Reporting Unit Codes
RMW - Regulated Medical Waste
RRAT - Rapid Response & Advanced Technology Laboratory, CDC
SACEUR- Supreme Allied Commander- Europe
SAMS - Shipboard Automated Medical System
SHEA – Society of Healthcare Epidemiologists of America
SIR - Serious Incident Report
SMART - Special Medical Augmentation Response Team, US Army
SOFA - Status Of Forces Agreement
SRT - Smallpox Response Teams
TAML - Theater Army Medical Laboratory
TEU - Technical Escort Unit
T-TEAMS – Treatment Teams
TYCOM – Type Commander (Naval)
Type C Facility - (C for confirmed) Mode of shelter and care for people diagnosed with smallpox
Type R Facility - Residential mode of housing for surveillance of vaccinated contacts of smallpox cases
Type X Facility - (X for Uncertain) Mode of shelter for surveillance of contacts of smallpox cases with fever but without signs and symptoms diagnostic of smallpox

UI - Unit of Issue
UIC - Unit Identification Code
UPS - United Parcel Service
URL - Universal Resource Locator
USAMMA - United States Army Medical Materiel Agency
USAMMDA - United States Army Medical Materiel Development Activity
USACHPPM - United States Army Center for Health Promotion & Preventive Medicine
USAMRIID - United States Army Medical Research Institute of Infectious Diseases
USAMRMC – United States Army Medical Research and Materiel Command
USC - United States Code
USDA – United States Department of Agriculture
USPS - United States Postal Service
USUHS - Uniformed Services University of the Health Sciences
UV – Ultraviolet
VAERS - Vaccine Adverse Event Reporting System
VEHB - Viral Exanthems & Herpesvirus Branch, CDC
VIG - Vaccinia Immune Globulin
VHC – Vaccine Healthcare Center
WMD - Weapons of Mass Destruction
WHO - World Health Organization
WRAMC - Walter Reed Army Medical Center
X-type Facility - (X for Uncertain) Mode of shelter for surveillance of contacts of smallpox cases with fever but without signs and symptoms diagnostic of smallpox

APPENDIX J-2
URLs for CDC Smallpox Response Plan Document. http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/index.asp

	Source of Exposure		
Docu-ment	**Title / Subject**	**PDF URL**	**HTML URL**
	Executive Summary plus parts II through VI	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/FrontPgs/Sections-i-iv.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/FrontPgs/Sections-i-iv.doc
CDC Guide A	**Surveillance, Contact Tracing, and Epidemiological Investigation**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a.doc
	Smallpox Case Investigation		
Form 1A	Page 1 of 2	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1a-pg1.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1a-pg1.ppt
Form 1A	Page 2 of 2	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1a-pg2.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1a-pg2.ppt
Form 1B	Page 1 of 2	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1b-pg1.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1b-pg1.ppt
Form 1B	Page 2 of 2	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1b-pg2.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-1b-pg2.ppt
	Contact Tracing		
Form 2	Interviewer Checklist / Contact Information	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2.doc
Form 2a	Case Travel / Activity Calendar	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2a.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2a.doc
Form 2b	Interviewer Contact / Site Summary Worksheet	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2b.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2c.doc
Form 2c	Contact Transportation	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2c.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2c.doc
Form 2d	Out of Area Travel Log	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2d.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-2d.xls

Form 4	Source of Exposure	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-4.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-4-now-3.doc
Form 6	Daily Case Status Tracking	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-6.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-6.xls
Form 7	Daily Case Status Tracking	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-7.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-7.doc
Form 8	Contact Interview	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-8.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-8.doc
Form 9	Contact Vaccination Referral	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-9.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-9.doc
Form 10	Individual Contact Surveillance	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-10.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-10.doc
Form 11	Contact Tracking (Daily Record Master form)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-11.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/guideA/guide-a-form-11.doc
CDC Guide B	**Vaccination Guidelines for State and Local Health Agencies**		
	Part 1 (pages 1 to 12)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideB/guide-b-part1of2.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideB/guide-b-part1of2.doc
	Part 2 (pages 13 to 19)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideB/guide-b-part2of2.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideB/guide-b-part2of2.doc
CDC Guide C	**Isolation and Quarantine Guidelines**		
	Part 1 (pages 1 to 18)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideC/guide-C-pages1-18only.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideC/guide-C-pages1-18only.doc
	Part 2 (pages 1 to 21)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideC/guide-C-pages19-21only.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideC/guide-C-pages19-21only.doc
CDC Guide D	**Specimen Collection and Transport Guidelines**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideD/Guide-D.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideD/Guide-D.doc

CDC Guide E	**Communications Plans and Activities**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideE/Guide-E.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideE/Guide-E.doc
CDC Guide F	**Decontamination Guidelines**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideF/Guide-F.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/GuideF/Guide-F.doc
CDC Annex 1	**Annex 1: Overview of Smallpox, Clin. Present-ation, Medical Care of Smallpox Patients**		
	Part 1 (pages 1 to 9)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-1-part1of3.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-1-part1of3.doc
	Part 2 (pages 10 to 16)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-1-part2of3.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-1-part2of3.doc
	Part 3 (pages 17 to 19)	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-1-part3of3.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-1-part3of3.doc
CDC Annex 2	**Guidelines for Smallpox Vaccination Clinics**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-2.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-2.doc
CDC Annex 3	**Vaccine Adverse Event Reporting**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-3.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-3.doc
CDC Annex 4	**Suggested Pre-Event Activities for State & Local Health Authorities**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-4.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-4.doc
	Generalized Vesicular or Pustular Rash Illness Protocol	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-4-rash-color.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-4-rash-color.ppt
CDC Annex 5	**Glossary of Abbreviations and Smallpox References**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-5.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-5.doc
CDC Annex 6	**Miscellaneous Forms in development**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-6.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-6.doc
CDC Annex 7	**Checklists for State/ Local/ CDC Personnel Actions in a Smallpox Emergency**	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-7.pdf	http://www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/annex/annex-7.doc

APPENDIX J-3
Professional Resources on Smallpox.

Agency for Healthcare Research and Quality Bioterrorism Education Site, www.bioterrorism.uab.edu/

American College of Physicians and American Society of Internal Medicine (ACCP-ASIM), Bioterrorism Resource Center, www.acponline.org/bioterro/index.html

American Society for Microbiology (ASM), Resources Related to Biological Weapons Control and Bioterrorism Preparedness, www.asmusa.org/pcsrc/bioprep.htm

Association for Infection Control and Epidemiology, Inc. (APIC), (202) 789-1890, (202) 789-1890, http://www.apic.org/bioterror/, www.apicelearn.org

Centers for Disease Control and Prevention, http://www.bt.cdc.gov/ or http://www.cdc.gov/, (404) 639-3311

Centers for Disease Control and Prevention (CDC). Facts about smallpox., www.bt.cdc.gov/DocumentsApp/FactSheet/SmallPox/About.asp

Centers for Disease Control and Prevention (CDC). Frequently asked questions, www.bt.cdc.gov/DocumentsApp/SmallPox/10242001faqs/10242001SmallpoxFAQs.asp

CDC Responds series: Smallpox: What Every Clinician Should Know, www.phppo.cdc.gov/phtn/default.asp

CDC Public Health Emergency & Response site, www.bt.cdc.gov, cdc.gov/ncidod/diseases/bioterr.htm

Department of Defense, http://www.defenselink.mil/, (703) 697-5737

DoD; Improving Local And State Agency Response To Terrorist Incidents Involving Biological Weapons, http://www2.sbccom.army.mil/hld/downloads/bwirp/bwirp_interim_planning_guide.pdf

Department of Health and Human Services, http://www.dhhs.gov/, 1-877-696-6775

Domestic Preparedness Helpline: 1-800-368-6498
Domestic Preparedness Website: http://www.nbc-prepare.org/

Environmental Protection Agency, http://www.epa.gov/, (202) 260-2090

Federal Bureau of Investigation, http://www.fbi.gov/, (202) 324-3000

Federal Emergency Management Agency, http://www.fema.gov/, (202) 646-4600

Infectious Disease Society of America (IDSA), Bioterrorism Preparedness (includes links to useful articles), www.idsociety.org/PA/PS&P/BT_Preparedness_10-2-01.htm

Johns Hopkins Center for Civilian Biodefense Studies, http://www.hopkins-biodefense.org/pages/agents/agentsmallpox.html

National Domestic Preparedness Office, http://www.ndpo.gov/, (202) 324-9026

Society for Healthcare Epidemiology of America, Inc., http://www.shea-online.org/BTprep.html

University of Alabama – Birmingham, Emerging Infections and Potential Bioterrorist Agents, www.bioterrorism.uab.edu/

UCLA Department of Epidemiology, www.ph.ucla.edu/epi/bioter/bioterrorism.html

U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), www.usamriid.army.mil

USAMRIID's Medical Management of Biological Casualties Handbook, www.usamriid.army.mil/education/bluebook.html

US Army Medical NBC Information Server, www.nbc-med.org/others/Default.html

US Army NBC Information Server, www.nbc-med.org/others/Default.html

APPENDIX J-4
Reference Publications on Smallpox.

Advisory Committee on Immunization Practices. Vaccinia (smallpox) vaccine. *MMWR* 2001;50(RR-10):1-25. http://www.cdc.gov/mmwr/PDF/rr/rr5010.pdf. See Appendix J-7.

Advisory Committee on Immunization Practices. Draft supplemental recommendations on smallpox (vaccinia) vaccine. 2002 June 20. www.cdc.gov/nip/smallpox/supp_recs.htm

Atkinson W, Wolfe C, Humiston S, Nelson R, ed. Chapter 18, Smallpox. In: *Epidemiology & Prevention of Vaccine-Preventable Diseases*, 7th ed. Atlanta: Centers for Disease Control & Prevention, Apr 2002. http://www.cdc.gov/nip/publications/pink/#download.

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Redfield RR, Wright DC, James WD, Jones TS, Brown C, Burke DS. Disseminated vaccinia in a military recruit with human immunodeficiency virus (HIV) disease. *N Engl J Med* 1987;316:673-676.

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APPENDIX J-5
Restriction of Movement as a Tool for the Control of Contagious Disease on the Battlefield.

Adapted from: Joint Venture Oversight Group (a joint US/UK bilateral collaboration), November 2001.

Introduction

1. Military personnel face a serious threat from disease during military operations. Historically, disease, not warfare, was the greatest source of casualties on the battlefield. Unchecked, casualties from disease have the potential to seriously degrade the operational effectiveness of deployed forces or, in the worst case, endanger the achievement of mission goals.

2. Disease in humans originates from some naturally occurring micro-organisms such as bacteria and viruses. Some of these organisms are highly contagious (i.e., have the capacity to spread from person to person). Others are infrequent causes of illness in man in normal conditions (e.g., anthrax), but may be highly contagious when introduced to the environment deliberately (e.g., in a biological weapon, BW). The control of contagious diseases presents particular problems in a military operational setting. Warfare inevitably involves large numbers of personnel working and living closely together for extended periods of time under stressful conditions. In these circumstances, a contagious disease has the potential to spread rapidly whether due to poor public or environmental health and hygiene or as a result of introduction by release from a biological weapon.

Principles of Disease Control

3. Whatever its source, contagious disease on the battlefield must be managed and controlled in order to maintain the operational effectiveness of forces. Modern medical science, public-health practices and good environmental health management provide many effective disease control tools.

4. Preventing, or controlling, the spread of contagious disease is accomplished by rendering those at risk resistant to the disease and limiting their exposure. In general, this is effected by medical intervention, such as immunization, or by restricting contact between healthy individuals and sources of the disease (other individuals, animals, insects etc.).

5. This guide focuses on one tool available to a Commander for the control of contagious disease - Restriction of Movement (ROM). The use of ROM will present him with a number of unique challenges and dilemmas. However, in reading this guide, it is important to bear in mind that contagious disease control relies on the co-ordinated use of a number of techniques.

What is Restriction of Movement (ROM)?

6. ROM is a tool for maintaining operational effectiveness in the face of a contagious disease, whether natural or artificial (for example, a biological-weapon attack). It aims to control the spread of the disease by restricting contact between healthy groups of personnel and those who have, or are suspected of having, contracted it. Personnel covered by ROM do not necessarily need to be removed from operations; wherever possible it should be implemented in such a way as to allow them to continue their mission. ROM may also be necessary to reduce the risk that a contagious disease is transferred back to the home base. A separate paper ("Decision making tool for the evacuation of military casualties following suspect BW exposure") provides guidance on the evacuation of casualties following a suspected or confirmed attack using BW.

7. A note on terminology: The terms 'quarantine' and 'isolation' are often used in the context of preventing contact between healthy populations and those either infected, or suspected of being infected, with a contagious disease. Quarantine involves the detention of an individual, or group, who is suspected of having been exposed to a contagious disease, until it is deemed that they have escaped infection. Isolation is the separation of an infected individual from a healthy population. Both rely on restricting the movement of individuals to some degree. During military operations where personnel have contracted, or are suspected of having been exposed to, a contagious disease, a Commander may need to consider using either, or both. Throughout this guide we will therefore use the more universal term, restriction of movement, or ROM.

Overview of Approach to Disease Control

8. Before considering ROM in detail, it is necessary to understand the overall approach to disease control in a theatre of operations (see figure). Before deployment, general Nuclear, Biological & Chemical (NBC) and medical **intelligence** and **reconnaissance** is required in order to assess threats to health of the deploying force from disease. This information forms an integral part of the intelligence preparation of the battlespace and will be incorporated into the operational estimate. It provides a baseline against which to assess any subsequent disease outbreaks. This may be particularly important in assessing whether an outbreak is naturally occurring rather than the result of a biological attack. On the basis of the resulting **health risk assessment**, medical staff will advise the Commander on the **force health protection** options available to him. The aim should be to reduce the risk of disease exposure to as low as reasonably practical. Typical steps that the Commander will need to consider prior to, and during, deployment include:

- Appropriate theatre surveillance measures to ensure early detection of potential exposures to disease. This includes pre-deployment surveillance.

- Measures to avoid, or minimize, exposure to potential sources of disease. In many cases, operational considerations will make this difficult, in which case the steps

below should be taken in order to minimize the risks.

- Ensuring that all personnel receive appropriate pre-deployment health advice and training concerning the in-theatre disease risks and the measures required to minimize the risks of exposure.

- Ensuring that personnel are offered appropriate medical countermeasures (for example, immunization) prior to deployment and that adequate supplies are available for use in-theatre as required.

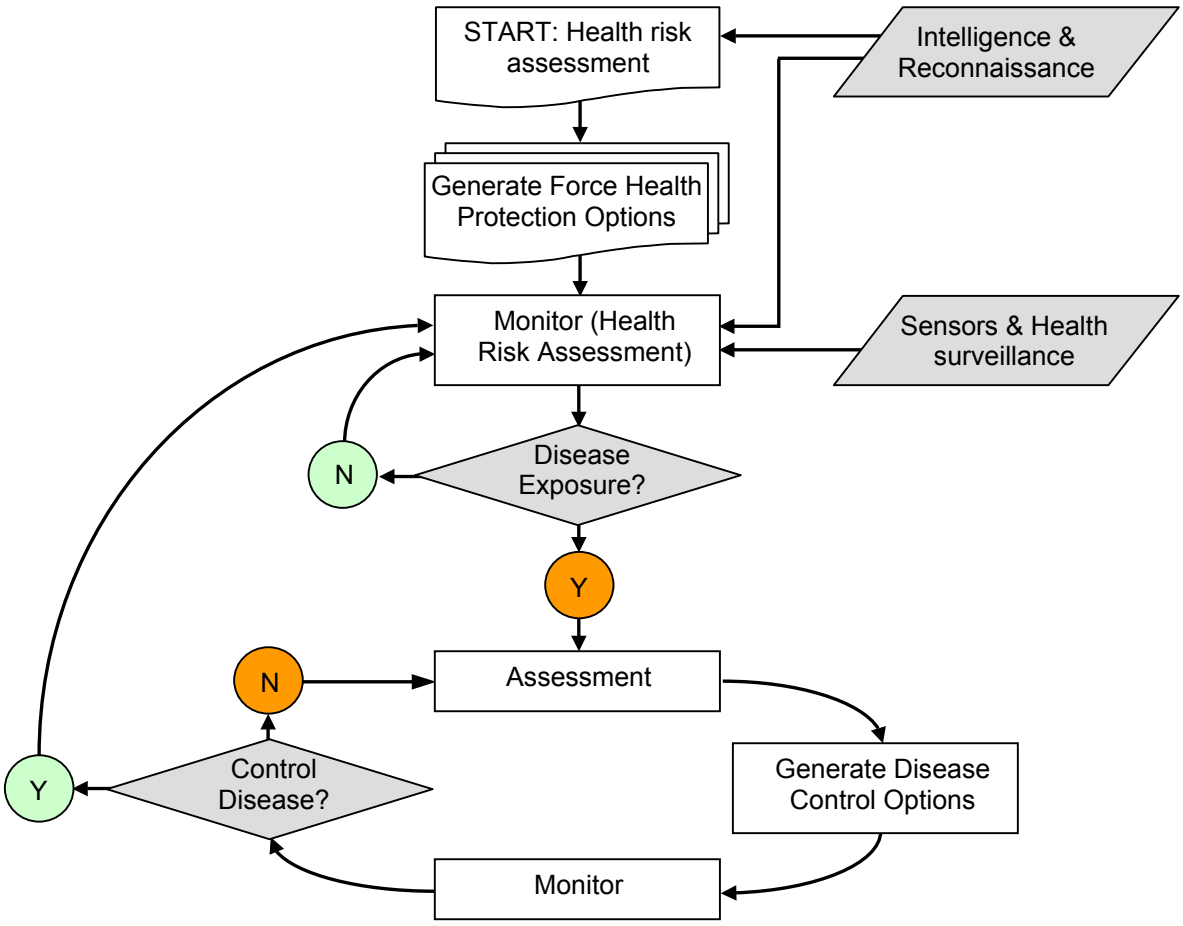

Figure: Overall approach to in-theatre disease control.

9. During deployment, the risks to the health of personnel are continuously **monitored** to ensure force health protection. Intelligence and reconnaissance continue to play an important role, and medical staff will provide the Commander with a health risk assessment. The first indication that personnel have been exposed to disease will be from one of two sources:

- Health surveillance and morbidity analysis picking up unusually high numbers, or distributions of illness amongst personnel, local civilians or others in theatre (e.g.

NGOs).

- Biological Warfare (BW) sensor alarms.

10. It may take some time to establish whether personnel have been exposed to a disease-causing agent, what that agent is and whether it is contagious. Until a definitive diagnosis or identification can be made, the Commander should assume that personnel have been exposed to, and infected by, a contagious disease and take all possible steps, balanced against wider operational imperatives, to limit the spread of that disease. It may, in the initial stages, also be difficult to distinguish between a naturally occurring disease event and one as the result of a BW attack. All disease events will therefore require careful investigation involving a variety of medical and NBC specialists.

11. Based on the evidence available and medical advice, the Commander must, as a matter of priority, **assess** the likely extent of exposure and infection and then in close consultation with the medical staff, taking the operational situation into account, generate **options** for controlling the disease event. These might include:

- Removing individuals showing disease symptoms for treatment as soon as possible.

- Instructing personnel within affected areas (or zones) on steps to minimize disease spread. Depending on the circumstances these might include decontamination procedures and environmental health controls such as enhanced monitoring of food and water supplies, more stringent hygiene measures, removing personnel from possible disease sources etc.

- Distributing, and instructing personnel to take, available medical countermeasures.

- Enhancing health surveillance of personnel within the suspected areas of exposure.

- Taking steps to minimize contact between personnel in the affected and non-affected areas by the use of ROM (see below).

12. A period of continuous **monitoring** and **assessment** follows during which the success of **disease control measures** are monitored and progressively refined or modified. A high priority must be to obtain a definitive diagnosis or identification of the disease-causing agent so that the Commander and medical staff are able to tailor control measures to that particular pathogen and its mode of transmission. In particular, ROM will not be necessary for diseases that are not contagious, and may not be necessary for diseases against which physical protection (such as oro-nasal masks), or available medical countermeasures, provide an adequate level of protection.

Implementing Restriction of Movement (ROM)

13. A Commander will need to consider ROM following evidence that personnel have been exposed to disease. As described at Appendix J-5, paragraph 9, this evidence could come from BW sensors or health surveillance. Plans of action for these two eventualities are given at addendum A and addendum B respectively. Further considerations in implementing ROM are below.

General Operational Considerations

14. If the use of ROM is contemplated at any stage during an operation, it must be with the full knowledge that the impact on operational effectiveness is likely to be significant. The only stage of an operation when ROM is unlikely to play a significant deleterious role is during the close of an operation when personnel are being returned home. Here, ROM would be aimed not at preserving the fighting integrity of the force but, rather, reducing the risk of introducing contagious disease into the home base.

15. The implementation of ROM will restrict the ability of the Commander to use affected force elements and the fighting effectiveness of those units. There is also the danger that a perception on the part of an aggressor that ROM is likely to be used in response to a BW attack may make the use (or threatened use) of biological agents more attractive. In practice, the operational impact of disease control measures will need to be balanced against the potential consequences of the spread of a contagious disease. Operational pressures may dictate a policy that accepts the limited spread of a contagious disease because the implementation of ROM would result in the loss of the military objective. Special attention will need to be paid to highly mobile battlefield assets such as logistical units and Special Forces since these could inadvertently spread a contagious disease widely across the force structure or back to the home base.

<u>Scale of Restriction of Movement (ROM)</u>

16. The scale of ROM will depend on the precise set of circumstances surrounding any decision to implement it. It is most likely that ROM will be based around a particular geographic area or group of personnel. Personnel who may have been exposed to a BW agent should be instructed to carry out standard BW decontamination procedures. Most BW agents decay quickly when exposed to sunlight and drying, so contamination of the environment is unlikely to pose a significant hazard for an extended period (days or weeks) following an attack. Definition of ROM by geographic area is therefore unlikely to be useful beyond defining those force elements that may have been exposed to an agent. The general guideline is that, wherever possible, ROM should cover autonomous force elements so that they are able to continue their operational tasks while minimizing their contact with other unaffected units. This preserves the integrity of the chain of command, which will be critical both for ensuring that ROM is properly enforced and communication (see below).

17. One priority, whether or not ROM is used, is to ensure that any contagious disease is not spread back to the home base. As a minimum, it will be necessary to ensure that those returning home from a theatre of operation where a contagious disease is confirmed, or suspected, are the subjects of rigorous follow-up health surveillance. Special procedures

may be need to be implemented for personnel and assets that cycle in and out of theatre with high frequencies, for example strategic lift aircrew.

Treatment of Civilians

18. Civilians play an increasing role in the support of military operations. It is therefore very likely that the use of ROM will also affect civilians. DoD civilian workers and contractors likely will be treated in the same fashion as military personnel. However, where ROM affects other civilians (e.g. those of a host nation) its imposition and enforcement will be particularly problematic – for example, it may be necessary to segregate forces from the local populace. Close liaison with host nation authorities will be necessary in order to implement ROM successfully.

Duration of ROM

19. Once the decision to implement ROM has been taken, the criteria under which it will be lifted should also be identified. These 'exit criteria' will need to be based on medical advice and will primarily depend on the biological agent involved. The duration of ROM might be tailored to the projected incubation period of the disease following infection. As a minimum, this period should elapse without cases of disease occurring amongst personnel before ROM can be lifted. However, caution is needed since projections about the incubation time of contagious diseases are often imprecise and based on observations of naturally occurring forms of the disease. They may also be modified when biological agents are used as BW weapons or when personnel have used medical countermeasures. Once ROM is lifted, additional health surveillance for personnel should continue for an extended period to ensure that any subsequent outbreak, or re-emergence, of disease is quickly detected.

Morale & Communication

20. The use of ROM is likely to have far reaching psychological consequences on the personnel directly affected, the local civilian population and the perceptions of those at home. The successful prosecution of the operation may depend on dealing with the very natural feelings of fear, confusion, panic, indignation and anger likely to be displayed by different groups.

- Personnel affected by ROM. The imposition of ROM is likely to have a severe psychological impact on those groups who are directly affected, particularly if some of their number begin to fall ill. As suggested above, ROM should, wherever possible, be based around autonomous force elements that can continue some, or all, of their operational activities. This will ensure that personnel are focussed on continuing to perform their operational tasks rather than the implications of ROM. Clear communication is key and this approach also preserves the chain of command which has a crucial role to play in this respect. A decision to withhold information in order to reduce anxiety, although well intentioned, is likely to be counterproductive since rumour and confusion will spread quickly. Clear, concise and realistic messages should therefore be conveyed by a skilled health risk communicator as

soon as possible. These should cover:

- Why ROM has been implemented;
- The threat or risk faced by personnel – factual, realistic assessments of the risks faced by personnel (including any details of the agents that might be involved);
- What precisely ROM involves – clear explanation of how it will affect personnel and their operational activities;
- Other measures being taken – including the delivery of medical assistance (medicines and treatment).
- When ROM will be lifted.
- The Main Force. Knowledge that ROM has been implemented on a component of the force is likely to be damaging. Again, clear and timely information will be vital and should be along the same lines as that for those directly affected.
- Local Civilian Population. Knowledge that a contagious disease is a problem amongst a locally deployed force has the potential to cause panic and disorder. Extremely close liaison with host nation civil and military authorities will be required to ensure that the situation is contained. All communication with the local civilian population should employ risk-communication principles.
- The Home Base. The media, perhaps as the result of a BW attack, will seize on news that personnel have been exposed to disease. Outrage, frustration, demands for action (and retaliation in the case of a BW attack), perhaps even calls for withdrawal will quickly follow. Many will fear the disease being spread back home. Relatives will be particularly anxious for news and information that the movements of apparently healthy personnel are being deliberately restricted, perhaps placing them at greater risk, will not be well received. The news media will need careful and professional handling. Commanders should take advice on this as soon as a decision to implement ROM is taken. Key messages will need to cover:
- Why ROM is necessary - a broad explanation of the threat/risks faced by personnel;
- The aim of ROM – protecting personnel and ensuring the success of the operation;
- Ensuring that any casualties get the best possible treatment.
- Ending ROM.

Summary

- The basic principles of the control of contagious disease on the battlefield are broadly the same whether the disease is naturally occurring or artificially introduced.

- ROM is one tool that may be considered by the Commander during an operation in order to control the spread of an infection amongst personnel. It should be used in concert with other measures and its use needs to be carefully balanced against its operational impact.

- Where ROM is implemented, it should, as far as possible, involve autonomous units that preserve the chain of command. Clear, precise and timely communication to personnel affected is critical.

Useful References

Joint NBC Defence Doctrine	JWP 3-61
Joint Medical Doctrine	JWP 4-03
Joint Doctrine for Operations in NBC Environments	JP 3-11

ADDENDUM A: Evidence from BW Sensor Alarms

In this case, the priority will be to establish whether a biological weapons attack has taken place but, until confirmed otherwise, the Commander should assume that personnel have been exposed to a contagious disease. Action should be taken as follows:

STEP 1: Carry out standard BW defence procedures. Establish the zone(s) within which it is most likely that personnel have been exposed to the BW agent (or, alternatively, where exposure is unlikely to have taken place).

STEP 2: With medical staff, immediately review force health protection options with the assumption that the disease is contagious. See Appendix J-5, paragraph 11.

STEP 3: Identify the agent used. This may be accomplished either by direct detection by BW sensors or may require the analysis of samples from the environment, or personnel, in a laboratory.

STEP 4: Once the agent is identified, seek medical advice and review and refine the disease control measures taken at STEP 2, including the use of ROM. For all contagious disease there is a delay between exposure and the point at which infected individuals become contagious (i.e. are capable of passing the disease to others). This period depends on the disease, but ranges from one to several days. During this period personnel who have been exposed may have dispersed to different locations and may be difficult to track. A Commander therefore has up to 24 hours following initial detection in order to seek advice, reach a decision and, if necessary, prepare for the introduction of ROM, but should aim to do so as soon as possible. This process should include the generation of criteria for lifting ROM (see Appendix J-5, paragraph 19). These exit criteria will be based on the typical incubation period following exposure for the disease caused by the agent. For example, it may be possible to consider lifting ROM if no cases occur within several days of initial detection.

STEP 5. Implement ROM (if required) and other disease control measures. In the initial instance, ROM is likely to be based on the zones identified at STEP1, but needs to take into account operational practicalities. For example, where only part of a unit has been exposed to a contagious agent, it may make more sense to apply ROM to the whole unit. Units within this area can continue to operate, but contact with other elements of the force should be limited as far as possible. However, the operational situation will determine whether unexposed personnel should be deployed in a ROM area.

STEP 6. Enhance health surveillance and monitor success of control measures. This continues until the exit criteria identified at STEP 3 are satisfied (in which case

ROM can be lifted) or the first cases of disease amongst personnel are identified (proceed to STEP 1 in Addendum B).

ADDENDUM B: Evidence from Health Surveillance

In this case, the fact that personnel have been infected by disease is likely to become apparent over a period of days, even weeks. Even where the introduction of disease takes place as the result of a single event (e.g. the use of a single biological weapon) as well as being spread over a long period of time, cases may have a large geographic distribution caused by the movement of personnel and secondary spread of infection. A decision to implement ROM will be more difficult in these circumstances because the seriousness and extent of any disease outbreak may not be clear. If health surveillance indicates that personnel may have been infected, action should be as follows:

STEP 1. Prompt isolation and treatment of those with the symptoms of disease. Consideration will need to be given to how medical support will be delivered to the sick. It may be feasible to remove casualties, with appropriate precautions, to field hospitals, but where large numbers of personnel are affected this may not be possible. In this case medical facilities may need to be deployed into ROM areas.

STEP 2. With medical staff, immediately review force health protection options. See Appendix J-5, paragraph 11.

STEP 3. Definitive identification of the agent responsible. This will be arrived at based on medical diagnosis of the symptoms of infected individuals and laboratory analysis of patient samples. This may require the evacuation of a single case, under rigorously controlled conditions, back to the UK and/or US.

STEP 4. Once the agent is identified, seek medical advice and review and refine the disease control measures taken at STEP 2, including the use of ROM. If the agent does not cause a contagious disease, ROM is not required. If, however, the agent is confirmed as contagious the introduction of ROM will need to be considered (if not already implemented in STEP 2) to limit any potential spread amongst healthy personnel. In this case, the imperative will be to make an early decision concerning whether or not to use ROM, since the disease is already spreading amongst personnel. In the case of a highly contagious agent, delay may make the situation far worse than it may otherwise have been. Criteria for the lifting of ROM will also need to be generated (see Appendix J-5, paragraph 19).

STEP 5. Implement ROM (if required) in concert with other control measures. Here ROM is likely to be based on individuals or groups who have come into close contact with confirmed cases. As the disease runs its course, the groups affected by ROM may need to be expanded, or reduced. The operational impact of ROM can be minimized by basing it around autonomous force elements that are able to sustain their military functions.

STEP 6. Enhance health surveillance and monitor success of control measures.

STEP 7. Based on exit criteria, lift ROM. This may take place progressively as units, or force elements are confirmed disease free.

APPENDIX J-6
Considerations In Air-Evacuation Of A Smallpox Patient from Overseas

Adapted from: Decision Making Tool For Evacuation Of Military Casualties Following Suspect BW Exposure, Joint Venture Oversight Group (a joint US/UK bilateral collaboration), November 2001.

1. Introduction. Patients with an infection caused by a biological warfare (BW) attack can be medically managed in the same manner as those with a disease caused by natural exposure to the same agent. The route of acquisition of the infection does not bear any relationship to the risk of secondary transmission. However, a suspected BW attack on any military deployed operation would have significant political, operational and medical implications. Medical factors will include the need for:

a. Rapid and accurate identification of the agent in order to ensure appropriate prophylaxis of non-exposed personnel and treatment of those exposed.

b. Provision of adequate medical resources in theatre. This will include diagnosis, treatment, specialist nursing, infection control and the ability, if required, to hold BW casualties.

c. Confirmation of the risk of secondary infection.

2. Aim. The aim of this paper is to identify the actions that need to be taken to prevent the spread of a contagious disease from a deployed theatre of operations to the home base from the aeromedical evacuation of casualties.

3. Scope. This paper is concerned only with medical issues. It does not address the need or provision for forensic sampling. Detailed guidance on Restriction of Movement (ROM) is addressed in Appendix 7.

4. Attack Indicators. The following are indicators that BW agents have been used:

a. Intelligence.

b. Activation of detectors.

c. Medical surveillance. For example, the sudden onset of illness with large numbers of personnel military or civilians or animals, unusual distribution or types of illness in the theatre of operations (e.g., localized or widespread, multiple foci).

5. Restriction of Movement (ROM). In the event of a suspected BW incident, the theatre commander may impose ROM along with other disease-control measures. The presence of positive intelligence (i.e., both the possession of BW agents by a nation of concern and an indication of intention to use) together with the occurrence of 4b or 4c above will almost certainly be treated as a BW attack until proved otherwise. Where a contagious disease is

suspected it will, at a minimum, be necessary to ensure that those returning home from a theatre of operations (including casualties) are the subjects of rigorous follow-up health surveillance. As a general rule, the movement of personnel and casualties back to the home base should be minimized until any disease is definitively diagnosed. Where ROM is implemented, a decision to evacuate casualties from the theatre of operation will need to be taken in consultation with the theatre commander and operational HQ. Any decision to evacuate casualties needs to be balanced against the risk of spreading a contagious disease to the home base and the needs of the casualties. ROM may be applied to the movement of casualties.

6. Actions. A simple decision-making tool covering the steps that need to be taken in order to avoid the inadvertent spread a contagious disease back to the home base is attached at Addendum A, Evidence from BW Sensor Alarms (just ahead of this appendix). This tool will be implemented under ROM or where there is suspicion of a contagious disease affecting personnel in-theatre. Up to three steps may be required to accurately diagnose a disease:

Step 1: Diagnosis in theatre. Ideally, disease diagnosis will be made in theatre. This might be based on clinical observations of symptomatic cases or the analysis of suitable samples from symptomatic patients using in-theatre analysis capabilities.

Step 2: Returning Specimens to the UK/US. If diagnosis cannot be made within the theatre of operations, specimens must be sent out of theatre. Take samples only from patients who are symptomatic. There is no benefit in taking samples from healthy individuals who may have been exposed to a contagious agent. Consider sample collection from corpses. Veterinary and/or environmental-health assistance may be required to collect samples from dead animals.

Step 3: Evacuation of an Index Case to the UK/US.

a. The initial clinical picture of natural and weaponized agents is often non-specific and the analysis of samples may not result in a definitive diagnosis. A patient may therefore need to be moved to a reference facility for confirmation of diagnosis and guidance on treatment. In order to facilitate the diagnosis process, it may be necessary to evacuate an index case along with the transmission of samples at Step 2.

b. Evacuation of an Index Case–Mechanism. The patient should be transported in a patient Air Transportable Isolator (ATI) chamber because of:

(1) Risk of airborne transmission.

(2) Risk of contamination of the airframe.

c. Selection of Index Patient. Senior medical officer in charge of the patient, following consultation with the theatre medical commander, will make the choice of individual. In general, the patient should be representative of the clinical syndrome involved, early in the natural history of the illness and physically accessible to the ATI team. Ideally the patient

should be self-caring and unlikely to deteriorate in the time it takes to reach the reference facility. The evacuation of an index case will comply, whenever possible, with IATA and WHO Regulations.

Step 4: Risk Assessment. The implementation of the above steps should safeguard the home base against inadvertent spread of contagious disease from the aeromedical evacuation of casualties. Once an accurate diagnosis has been made, the theatre medical Commander and his staff will need to:

a. Identify the health protection options and medical resources required, including the most appropriate prophylaxis and treatments for any personnel who may have been exposed and/or infected with a contagious disease. This process will assist the commander in deciding what force health protection measures, including the use of ROM, need be implemented in-theatre.

b. Carry out an assessment of the risks of evacuating casualties, some of who may be contagious, back to the home base. It may be possible to evacuate casualties with appropriate precautions in place, however where it is judged that the risks of doing this are too great treatment will need to be delivered in theatre.

7. Personnel & Casualties Already Evacuated. It is possible that Steps 1-4 above will take several days to effect. By the time a definitive diagnosis is obtained, some casualties may already have been evacuated to the home base. Where a contagious disease is confirmed, evacuated casualties and contacts will need to be the subject of rigorous medical surveillance.

APPENDIX J-7
Advisory Committee on Immunization Practices (ACIP) Guidelines:

Part 1, Draft Supplemental Recommendation of the ACIP, Use of Smallpox (Vaccinia) Vaccine, June 2002.

Draft approved by ACIP on June 20, 2002

Now under consideration by CDC and DHHS

http://www.cdc.gov/nip/smallpox/supp_recs.htm

Part 2, ACIP Recommendations for Use of Smallpox Vaccine, June 2001

Advisory Committee on Immunization Practices (ACIP).

Vaccinia (smallpox) vaccine.

MMWR—Morbidity & Mortality Weekly Report 2001;50(RR-10)(June 22):1-25.

http://www.cdc.gov/mmwr/PDF/rr/rr5010.pdf.

The documents appear on following pages.

Smallpox

Draft Supplemental Recommendation of the ACIP

Use of Smallpox (Vaccinia) Vaccine, June 2002

Draft approved by ACIP on June 20, 2002
Now Under Consideration by CDC and DHHS

http://www.cdc.gov/nip/smallpox/supp_recs.htm

- Introduction
- Smallpox transmission and control
- Critical considerations
- Smallpox vaccines and VIG availability
- Surveillance
- Recommendations
  - Pre-release vaccination of the general population
  - Pre-release vaccination of selected groups to enhance smallpox response readiness
- Comments

Introduction

In June 2001, the Advisory Committee on Immunization Practices (ACIP) made recommendations for use of smallpox (vaccinia) vaccine to protect persons working with Orthopoxviruses, to prepare for a possible bioterrorism attack and respond to an attack involving smallpox. Because of the terrorist attacks in the fall of 2001, the Centers for Disease Control and Prevention (CDC) asked the ACIP to review their previous recommendations for smallpox (vaccinia) vaccination. As a result of this review, these supplemental recommendations update those for vaccination of 1) the general population and 2) persons designated to respond or care for a suspected or confirmed case of smallpox. In addition, they clarify and expand the primary strategy for control and containment of smallpox in the event of an outbreak.

Recommendations for vaccination of laboratory workers who directly handle recombinant vaccinia viruses derived from non-highly attenuated vaccinia strains, or other orthopoxviruses that infect humans (e.g., Monkeypox, cowpox, vaccinia, and variola) remain unchanged. Other aspects of the previous recommendations (e.g., screening for contraindications, care of the vaccination site) are being reviewed, and until new recommendations are published, the June 2001 recommendations should be consulted.

Prior to the terrorist attacks in the fall of 2001, the Department of Health and Human Services (DHHS) began to increase public health preparedness through expansion of the existing stockpile of smallpox (vaccinia) vaccine (Dryvax, Wyeth) by purchase of vaccine produced in cell culture (Acambis). The additional purchase of vaccine was initiated to address perceived vulnerability to future terrorist attacks. The anthrax attacks in the fall of 2001 resulted in increased activities to enhance preparedness and response capabilities, including those involving the deliberate release of smallpox and resulted in the accelerated production of additional doses of smallpox (vaccinia) vaccine. This increased supply of vaccine allows for consideration of expanded vaccination options.

The following recommendations were developed after formation of a joint Working Group of the ACIP and the National Vaccine Advisory Committee (NVAC) and a series of public meetings and forums to review available data on smallpox, smallpox (vaccinia) vaccine, smallpox control strategies, and other issues related to smallpox (vaccinia) vaccination. A website was established to solicit public opinion and input on options for smallpox (vaccinia) vaccine use.

The ACIP will review these recommendations periodically, or more urgently if necessary. These reviews will include new information or developments related to smallpox disease, smallpox (vaccinia) vaccines (including vaccine licensure), risk of smallpox attack, smallpox (vaccinia) vaccine adverse events, and the experience gained in the implementation of the current recommendations. Revised recommendations will be developed as needed.

Smallpox Transmission and Control

Smallpox is transmitted from an infected person once a rash appears. Transmission does not occur during the prodromal period that precedes the rash. Infection is transmitted by large droplet nuclei and only rarely has airborne transmission been documented. Epidemiologic studies have shown that smallpox has a lower rate of transmission than diseases such as measles, pertussis, and influenza. The greatest risk of infection occurs among household members and close contacts of persons with smallpox, especially those with prolonged face-to-face exposure. Vaccination and isolation of contacts of cases at greatest risk of infection has been shown to interrupt transmission of smallpox. However, poor infection control practices resulted in high rates of transmission in hospitals.

The primary strategy to control an outbreak of smallpox and interrupt disease transmission is surveillance and containment, which includes ring vaccination and isolation of persons at risk of contracting smallpox. This strategy involves identification of infected persons through intensive surveillance, isolation of infected persons, vaccination of household contacts and other close contacts of infected persons (i.e., primary contacts), and vaccination of household contacts of the primary contacts (i.e. secondary contacts). This strategy was instrumental in the ultimate eradication of smallpox as a naturally occurring disease even in areas that had low vaccination coverage.
Depending upon the size of the smallpox outbreak and the resources that were available for rapid and thorough contact tracing, surveillance and containment activities in areas with identified smallpox cases was sometimes supplemented with voluntary vaccination of other individuals. This was done in order to expand the ring of immune individuals within an outbreak area and to further reduce the chance of secondary transmission from smallpox patients before they could be identified and isolated. Regardless of the geographic distribution, number of cases, or number of concurrent outbreaks, surveillance and containment activities remained the primary disease control strategy.

Critical Considerations

A number of factors and assumptions were used in developing these supplemental recommendations.

- **Level of disease risk and threat**
  Information provided to the ACIP indicated that the risk for smallpox occurring as a

result of a deliberate release by terrorists is considered low, and the population at risk for such an exposure cannot be determined. It was further assumed that regardless of the mode of a bioterrorism release, the epidemiology of subsequent person-to-person transmission would be consistent with prior experience. These recommendations also assumed that in addition to vaccination, health care workers and others would be afforded protection from infection through appropriate infection control measures, including the use of appropriate personal protective equipment.

- **Expected severe adverse reactions to vaccination**
  These supplemental recommendations assume that appropriate screening for contraindications to vaccination would be implemented and would include both the vaccinated persons, as well as their contacts. It is further assumed that recommended precautions would be taken to minimize the risk of adverse events among vaccinees as well as their close contacts (e.g., patients, household members).
- **Vaccine and vaccinia immune globulin (VIG) supply**
  The supplemental recommendations assume that both would be available for use, in sufficient supply, and handled and administered correctly. Smallpox (vaccinia) vaccine and VIG are currently available only under Investigational New Drug (IND) protocols (i.e., protocols for products that are not yet licensed). As such, it was assumed that appropriate informed consent, patient follow-up, and administrative oversight by federal, state, and local public health officials would be required. Further, any administration of smallpox (vaccinia) vaccine would be voluntary.
- **State and local vaccination capacity and capability**
  Surveillance and containment, including ring vaccination, is the primary strategy for the control and containment of smallpox. In addition, state and local health departments would be able, if necessary, to expand immunization to additional groups, up to and including their entire population, in a timely manner.

Smallpox Vaccines and VIG Availability

Currently, there are no commercially available (e.g., licensed) smallpox vaccines. Smallpox vaccines previously produced by Wyeth (Dryvax) and Aventis-Pasteur are available under Investigational New Drug (IND) protocols held by CDC. Both vaccines were prepared from calf lymph with a seed virus derived from the New York City Board of Health strain of vaccinia virus. Studies conducted among young adults with no previous smallpox vaccination history showed that a 1:5 dilution of Dryvax (Wyeth Laboratories, Inc) produced take rates among vaccinees equivalent to those of the undiluted vaccine.
In October 2001, the federal government contracted with Acambis and Acambis-Baxter Pharmaceuticals for at least 209 million doses of smallpox vaccine produced in cell-culture. These vaccines use a clone of the same strain of vaccinia virus (New York City Board of Health), which was utilized in the smallpox vaccines produced from calf lymph. These doses are expected to be available at the end of 2002 or soon thereafter.
Smallpox vaccines are formulated and packaged for administration with a bifurcated needle, which provides a fast, easy, and effective means for administration. All vaccines are packaged in 100 dose vials, except when Dryvax is diluted 1:5 resulting in vials that contain 500 doses.
The CDC National Pharmaceutical Stockpile (NPS) has developed protocols to allow for the rapid, simultaneous delivery of smallpox vaccine to every state and US territory within 12-

24 hours. State and local bioterrorism response plans should provide for the rapid distribution of vaccine within their jurisdiction.
Currently, there is enough VIG available under an IND protocol to treat about 600 serious adverse events. This is enough VIG doses to treat the adverse reactions that would be expected to result from the vaccination of 4 million to 6 million people. Contracts for additional supplies of VIG are in progress.

Surveillance

Currently, cases of febrile rash illnesses, for which smallpox is considered in the differential diagnosis, should be immediately reported to local and/or state health departments. Following evaluation by local/state health departments, if smallpox laboratory diagnostics are considered necessary, the CDC Rash Illness Evaluation Team should be consulted at 770-488-7100 or 404-639-2888. As smallpox was eradicated in 1980 and no longer occurs naturally, an initial case of smallpox must be laboratory confirmed. At this time, laboratory confirmation for smallpox is available only at CDC. Clinical consultation and a preliminary laboratory diagnosis can be completed within 8-24 hours.
To assist medical and public health personnel in evaluating the likelihood of smallpox in patients with febrile rash illnesses, CDC has developed a rash illness assessment algorithm. Poster copies of this algorithm are available from state health departments and on the CDC website Orders for copies of the poster can be made over the Internet at: https://www2.cdc.gov/nchstp_od/PIWeb/niporderform.asp

Surveillance activities, including notification procedures and laboratory confirmation of cases, would change if smallpox is confirmed. Additional information regarding surveillance activities following laboratory confirmation of a smallpox outbreak can be found in the CDC Interim Smallpox Response Plan and Guidelines.

Recommendations

Pre-Release Vaccination of the General Population

Under current circumstances, with no confirmed smallpox, and the risk of an attack assessed as low, vaccination of the general population is not recommended, as the potential benefits of vaccination do not outweigh the risks of vaccine complications.

Recommendations regarding pre-outbreak smallpox vaccination are being made on the basis of an assessment that considers the risks of disease and the benefits and risks of vaccination. The live smallpox (vaccinia) vaccine virus can be transmitted from person to person. In addition to sometimes causing adverse reactions in vaccinated persons, the vaccine virus can cause adverse reactions in the contacts of vaccinated persons. It is assumed that the risk of serious adverse events with currently available vaccines would be similar to those previously observed and could be higher today due to the increased prevalence of persons with altered immune systems.

Pre-Release Vaccination of Selected Groups to Enhance Smallpox Response Readiness

Smallpox Response Teams

Smallpox vaccination is recommended for persons pre-designated by the appropriate bioterrorism and public health authorities to conduct investigation and follow-up of initial smallpox cases that would necessitate direct patient contact.

To enhance public health preparedness and response for smallpox control, specific teams at the federal, state and local level should be established to investigate and facilitate the diagnostic work-up of the initial suspect case(s) of smallpox and initiate control measures. These Smallpox Response Teams might include persons designated as medical team leader, public health advisor, medical epidemiologists, disease investigators, diagnostic laboratory scientist, nurses, personnel who would administer smallpox vaccines, and security/law enforcement personnel. Such teams may also include medical personnel who would assist in the evaluation of suspected smallpox cases.

The ACIP recommends that each state and territory establish and maintain at least one Smallpox Response Team. Considerations for additional teams should take into account population and geographic considerations and should be developed in accordance with federal, state, and local bioterrorism plans.

Designated Smallpox Healthcare Personnel at Designated Hospitals

Smallpox vaccination is recommended for selected personnel in facilities pre-designated to serve as referral centers to provide care for the initial cases of smallpox. These facilities would be pre-designated by the appropriate bioterrorism and public health authorities, and personnel within these facilities would be designated by the hospital.

As outlined in the CDC Interim Smallpox Response Plan and Guidelines, state bioterrorism response plans should designate initial smallpox isolation and care facilities (e.g., type C facilities). In turn, these facilities should pre-designate individuals who would care for the initial smallpox cases. To staff augmented medical response capabilities, additional personnel should be identified and trained to care for smallpox patients.

Implementation of Recommendations

The ACIP recognizes that the implementation of the supplemental recommendations presented in this document requires addressing a number of issues, and that this will take time. The issues include provider and public education, health care provider training, availability of vaccine and VIG, developing the appropriate investigational new drug protocols, screening, strategies to minimize vaccine wastage, vaccine adverse event surveillance, and other logistical and administrative issues.

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Inside: Continuing Education Examination

Vaccinia (Smallpox) Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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Vaccinia (Smallpox) Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

Summary

*These revised recommendations regarding vaccinia (smallpox) vaccine update the previous Advisory Committee on Immunization Practices (ACIP) recommendations (*MMWR 1991;40; No. RR-14:1–10*) and include current information regarding the nonemergency use of vaccinia vaccine among laboratory and health-care workers occupationally exposed to vaccinia virus, recombinant vaccinia viruses, and other Orthopoxviruses that can infect humans. In addition, this report contains ACIP's recommendations for the use of vaccinia vaccine if smallpox (variola) virus were used as an agent of biological terrorism or if a smallpox outbreak were to occur for another unforeseen reason.*

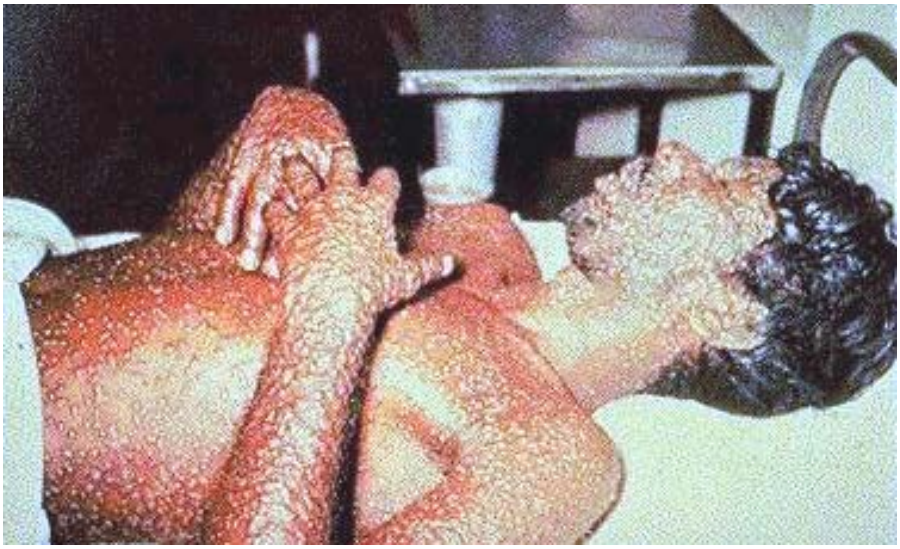
INTRODUCTION

Variola virus is the etiological agent of smallpox. During the smallpox era, the only known reservoir for the virus was humans; no known animal or insect reservoirs or vectors existed. The most frequent mode of transmission was person-to-person, spread through direct deposit of infective droplets onto the nasal, oral, or pharyngeal mucosal membranes, or the alveoli of the lungs from close, face-to-face contact with an infectious person. Indirect spread (i.e., not requiring face-to-face contact with an infectious person) through fine-particle aerosols or a fomite containing the virus was less common (*1,2*).

Symptoms of smallpox begin 12–14 days (range: 7–17) after exposure, starting with a 2–3 day prodrome of high fever, malaise, and prostration with severe headache and backache. This preeruptive stage is followed by the appearance of a maculopapular rash (i.e., eruptive stage) that progresses to papules 1–2 days after the rash appears; vesicles appear on the fourth or fifth day; pustules appear by the seventh day; and scab lesions appear on the fourteenth day (Figures 1,2) (*3*). The rash appears first on the oral mucosa, face, and forearms, then spreads to the trunk and legs (*3,4*). Lesions might erupt on the palms and soles as well. Smallpox skin lesions are deeply embedded in the dermis and feel like firm round objects embedded in the skin. As the skin lesions heal, the scabs separate and pitted scarring gradually develops (Figure 2) (*4*). Smallpox patients are most infectious during the first week of the rash when the oral mucosa lesions ulcerate and release substantial amounts of virus into the saliva. A patient is no longer infectious after all scabs have separated (i.e., 3–4 weeks after the onset of the rash).

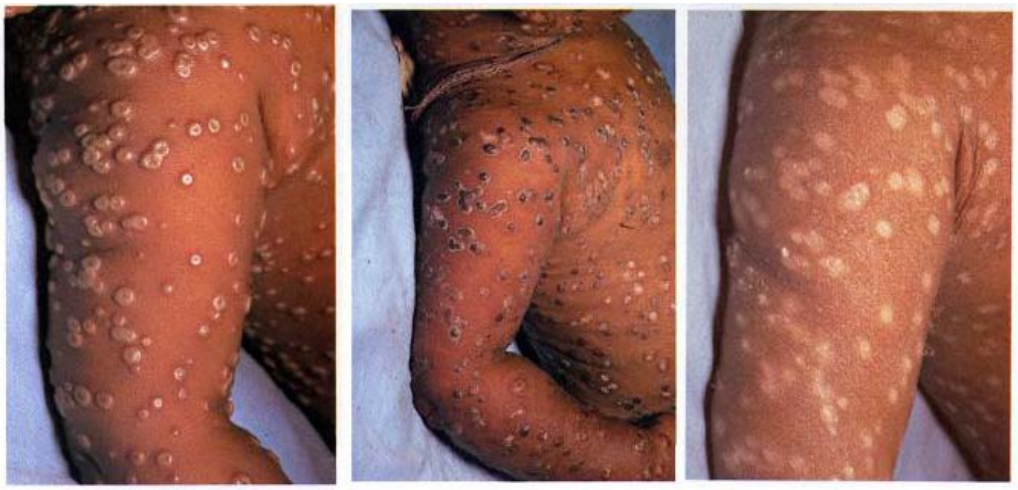
During the smallpox era, overall mortality rates were approximately 30%. Other less common but more severe forms of smallpox included a) flat-type smallpox with a mortality rate >96% and characterized by severe toxemia and flat, velvety, confluent lesions that did not progress to the pustular stage; and b) hemorrhagic-type smallpox, characterized by severe prodromal symptoms, toxemia, and a hemorrhagic rash that was almost always fatal, with death occurring 5–6 days after rash onset (*4*).

FIGURE 1. Man with smallpox



Source: CDC/Public Health Images Library, identification no. 131. Photographer: Barbara Rice. Available at <http://phil.cdc.gov/Phil/>; accessed on May 16, 2001.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp> (accessed April 20, 2001).

FIGURE 2. Progression of smallpox lesions from, left to right, pustules to scabs to scars



Source: Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and its eradication. Geneva, Switzerland: World Health Organization (WHO), 1988. Reprinted with permission from WHO.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp> (accessed April 20, 2001).

Vaccinia vaccine is a highly effective immunizing agent that enabled the global eradication of smallpox. The last naturally occurring case of smallpox occurred in Somalia in 1977. In May 1980, the World Health Assembly certified that the world was free of naturally occurring smallpox (*5*). By the 1960s, because of vaccination programs and quarantine regulations, the risk for importation of smallpox into the United States had been reduced. As a result, recommendations for routine smallpox vaccination were rescinded in 1971 (*6*). In 1976, the recommendation for routine smallpox vaccination of health-care workers was also discontinued (*7*). In 1982, the only active licensed producer of vaccinia vaccine in the United States discontinued production for general use, and in 1983, distribution to the civilian population was discontinued (*8*). All military personnel continued to be vaccinated, but that practice ceased in 1990. Since January 1982, smallpox vaccination has not been required for international travelers, and International Certificates of Vaccination forms no longer include a space to record smallpox vaccination (*9*).

In 1980, the Advisory Committee on Immunization Practices (ACIP) recommended the use of vaccinia vaccine to protect laboratory workers from possible infection while working with nonvariola Orthopoxviruses (e.g., vaccinia and monkeypox) (*10*). In 1984, those recommendations were included in guidelines for biosafety in microbiological and biomedical laboratories (*11*). The guidelines expanded the recommendations to include persons working in animal-care areas where studies with Orthopoxviruses were being conducted. They further recommended that such workers have documented evidence of satisfactory smallpox vaccination within the preceding 3 years. CDC has provided vaccinia vaccine for these laboratory workers since 1983 (*12*). In 1991, ACIP further expanded smallpox vaccination recommendations to include health-care workers involved in clinical trials using recombinant vaccinia virus vaccines and lengthened the recommendations for revaccination for persons working with vaccinia virus, recombinant vaccinia viruses, or other nonvariola Orthopoxviruses to every 10 years (*13*).

Currently, international concern is heightened regarding the potential use of smallpox (variola) virus as a bioterrorism agent (*14,15*). Because of these concerns, ACIP has developed recommendations for vaccinia (smallpox) vaccine regarding the potential use of smallpox virus as a biological weapon. Additionally, recommendations regarding vaccination of persons working with highly attenuated strains or recombinant vaccines derived from highly attenuated strains of vaccinia virus have been revised.

VACCINIA VACCINE

Dryvax,® the vaccinia (smallpox) vaccine currently licensed in the United States, is a lyophilized, live-virus preparation of infectious vaccinia virus (Wyeth Laboratories, Inc., Marietta, Pennsylvania). Vaccinia vaccine does not contain smallpox (variola) virus. Previously, the vaccine had been prepared from calf lymph with a seed virus derived from the New York City Board of Health (NYCBOH) strain of vaccinia virus and has a minimum concentration of 10^8 pock-forming units (PFU)/ml. Vaccine was administered by using the multiple-puncture technique with a bifurcated needle. A reformulated vaccine, produced by using cell-culture techniques, is now being developed.

Vaccine Efficacy

Neutralizing antibodies induced by vaccinia vaccine are genus-specific and cross-protective for other Orthopoxviruses (e.g., monkeypox, cowpox, and variola viruses) (*16–18*). Although the efficacy of vaccinia vaccine has never been measured precisely during controlled trials, epidemiologic studies demonstrate that an increased level of protection against smallpox persists for ≤5 years after primary vaccination and substantial but waning immunity can persist for ≥10 years (*19,20*). Antibody levels after revaccination can remain high longer, conferring a greater period of immunity than occurs after primary vaccination alone (*3,19*). Administration of vaccinia vaccine within the first days after initial exposure to smallpox virus can reduce symptoms or prevent smallpox disease (*2–4*).

Although the level of antibody that protects against smallpox infection is unknown, after percutaneous administration of a standard dose of vaccinia vaccine, >95% of primary vaccinees (i.e., persons receiving their first dose of vaccine) will experience neutralizing or hemagglutination inhibition antibody at a titer of ≥1:10 (*21*). Neutralizing antibody titers of ≥1:10 persist among 75% of persons for 10 years after receiving second doses and ≤30 years after receiving three doses of vaccine (*22,23*). The level of antibody required for protection against vaccinia virus infection is unknown also. However, when lack of local skin response to revaccination with an appropriately administered and potent vaccine dose is used as an indication of immunity, <10% of persons with neutralizing titers of ≥1:10 exhibit a primary-type response at revaccination, compared with >30% of persons with titers <1:10 (*24*). Lack of major or primary-type reaction can indicate the presence of neutralizing antibody levels sufficient to prevent viral replication, although it can also indicate unsuccessful vaccination because of improper administration or less potent vaccine.

Recombinant Vaccinia Viruses

Vaccinia virus is the prototype of the genus Orthopoxvirus. It is a double-stranded DNA (deoxyribonucleic acid) virus that has a broad host range under experimental conditions but is rarely isolated from animals outside the laboratory (*25,26*). Multiple strains of vaccinia virus exist that have different levels of virulence for humans and animals. For example, the Temple of Heaven and Copenhagen vaccinia strains are highly pathogenic among animals, whereas the NYCBOH strain, from which the Wyeth vaccine strain was derived, had relatively low pathogenicity (*3*).

Vaccinia virus can be genetically engineered to contain and express foreign DNA with or without impairing the ability of the virus to replicate. Such foreign DNA can encode protein antigens that induce protection against one or more infectious agents. Recombinant vaccinia viruses have been engineered to express immunizing antigens of herpesvirus, hepatitis B, rabies, influenza, human immunodeficiency virus (HIV), and other viruses (*27–32*).

Recombinant vaccinia viruses have been created from different strains of vaccinia virus. In the United States, recombinants have been made from a nonattenuated NYCBOH strain, or a mouse neuroadapted derivative, the WR strain. Recombinants have also been made by using the Copenhagen and Lister vaccinia strains, which are more pathogenic among animals than the NYCBOH strain. Additionally, certain highly attenuated, host-restricted, non- or poorly replicating poxvirus strains have been developed for use as substrates in recombinant vaccine development. These strains include the

Orthopoxviruses, modified vaccinia Ankara (MVA) and NYVAC (derived from the Copenhagen vaccinia strain), and the Avipoxviruses, ALVAC and TROVAC (derived from canarypox and fowlpox viruses, respectively) (*33–36*) (Table 1).

TABLE 1. Highly attenuated poxvirus strains used for recombinant vaccine development

Strain	Parent virus strain	Biosafety level
MVA	Vaccinia virus (Ankara)	2
NYVAC	Vaccinia virus (Copenhagen)	1
TROVAC	Fowlpox virus	1
ALVAC	Canarypox virus	1

Animal studies indicate that recombinants are less pathogenic than the parent strain of vaccinia virus (*37*). Laboratory-acquired infections with nonhighly attenuated vaccinia and recombinant viruses derived from nonhighly attenuated vaccinia strains have been reported (*38–41*). However, highly attenuated poxvirus strains (MVA, NYVAC, ALVAC, and TROVAC) are unable to replicate (MVA, ALVAC, and TROVAC) or replicate poorly (NYVAC) in mammalian host cells; therefore, highly attenuated poxvirus strains do not create productive infections (*36*).

These highly attenuated strains have also been reported to be avirulent among normal and immunosuppressed animals (MVA, NYVAC, ALVAC, or TROVAC) and safe among humans (MVA) (*33,35,42,43*). Although no formal surveillance system has been established to monitor laboratory workers, no laboratory-acquired infections resulting from exposure to these highly attenuated strains or recombinant vaccines derived from these strains have been reported in the scientific literature or to CDC. Because of the biological properties and accumulated attenuation data for NYVAC, ALVAC, and TROVAC, the Recombinant DNA Advisory Committee of the National Institutes of Health (NIH) reduced the biosafety level for these viruses to biosafety level 1 (*44*). The Occupational Safety and Health Board of NIH no longer requires vaccinia (smallpox) vaccination for personnel manipulating MVA or NYVAC in a laboratory where no other vaccinia viruses are being manipulated (*45*).

During human trials of recombinant vaccines, physicians, nurses, and other health-care personnel who provide clinical care to recipients of these vaccines could be exposed to both vaccinia and recombinant viruses. This exposure could occur from contact with dressings contaminated with the virus or through exposure to the vaccine. Although the risk for transmission of recombinant vaccinia viruses to exposed health-care workers is unknown, no reports of transmission to health-care personnel from vaccine recipients have been published. If appropriate infection-control precautions are observed (*46,47*), health-care workers are at less risk for infection than laboratory workers because of the smaller volume and lower titer of virus in clinical specimens compared with laboratory material. However, the potential does exist of nonhighly attenuated vaccinia viruses or recombinant viruses derived from these strains being transmitted to health-care personnel. Therefore, those workers who have direct contact with contaminated dressings or other infectious material from volunteers in clinical studies where such strains are used can be offered vaccination. Vaccination is not indicated for health-care personnel who are exposed to clinical materials contaminated with highly attenuated poxvirus strains used to develop vaccine recombinants.

Laboratory and other health-care personnel who work with highly attenuated strains of vaccinia virus (e.g., MVA and NYVAC) do not require routine vaccinia vaccination. Laboratory and other health-care personnel who work with the Avipoxvirus strains ALVAC and TROVAC also do not require routine vaccinia vaccination because these viruses do not grow in mammalian cells and, therefore, do not produce clinical infections among humans. In addition, antibodies induced by vaccinia vaccine are genus-specific (*16*) and would probably not inhibit the expression of genes incorporated into recombinant vaccines derived from ALVAC and TROVAC. Therefore, vaccination would provide no theoretical benefit in preventing seroconversion to the foreign antigen expressed by a recombinant virus if an inadvertent exposure occurred. Laboratory and other health-care personnel who work with viral cultures or other infective materials should always observe appropriate biosafety guidelines and adhere to published infection-control procedures (*46–48*).

Routine Nonemergency Vaccine Use

Vaccinia vaccine is recommended for laboratory workers who directly handle a) cultures or b) animals contaminated or infected with, nonhighly attenuated vaccinia virus, recombinant vaccinia viruses derived from nonhighly attenuated vaccinia strains, or other Orthopoxviruses that infect humans (e.g., monkeypox, cowpox, vaccinia, and variola). Other health-care workers (e.g., physicians and nurses) whose contact with nonhighly attenuated vaccinia viruses is limited to contaminated materials (e.g., dressings) but who adhere to appropriate infection control measures are at lower risk for inadvertent infection than laboratory workers. However, because a theoretical risk for infection exists, vaccination can be offered to this group. Vaccination is not recommended for persons who do not directly handle nonhighly attenuated virus cultures or materials or who do not work with animals contaminated or infected with these viruses.

Vaccination with vaccinia vaccine results in high seroconversion rates and only infrequent adverse events (see Side Effects and Adverse Reactions). Recipients of standard potency vaccinia vaccine (Dryvax) receive controlled percutaneous doses (approximately 2.5×10^5 PFU [*3*]) of relatively low pathogenicity vaccinia virus. The resulting immunity should provide protection to recipients against infections resulting from uncontrolled, inadvertent inoculation by unusual routes (e.g., the eye) with a substantial dose of virus of higher or unknown pathogenicity. In addition, persons with preexisting immunity to vaccinia might be protected against seroconversion to the foreign antigen expressed by a recombinant virus if inadvertently exposed (*41*). However, persons with preexisting immunity to vaccinia might not receive the full benefit of recombinant vaccinia vaccines developed for immunization against other infections (*31,49*).

Routine Nonemergency Revaccination

According to data regarding the persistence of neutralizing antibody after vaccination, persons working with nonhighly attenuated vaccinia viruses, recombinant viruses developed from nonhighly attenuated vaccinia viruses, or other nonvariola Orthopoxviruses should be revaccinated at least every 10 years (*13*). To ensure an increased level of protection against more virulent nonvariola Orthopoxviruses (e.g., monkeypox), empiric revaccination every 3 years can be considered (*17*).

Side Effects and Adverse Reactions

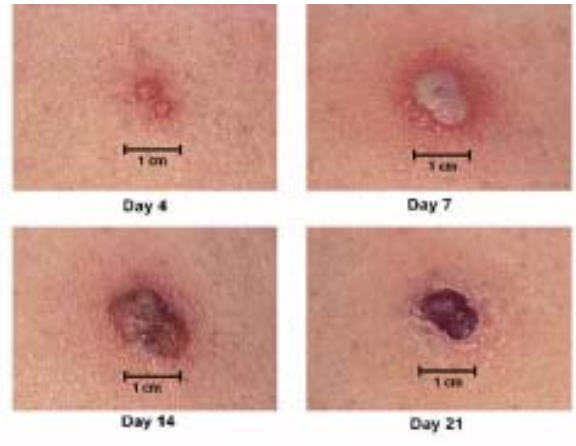
Vaccine Recipients

Side Effects and Less Severe Adverse Reactions. In a nonimmune person who is not immunosuppressed, the expected response to primary vaccination is the development of a papule at the site of vaccination 2–5 days after percutaneous administration of vaccinia vaccine. The papule becomes vesicular, then pustular, and reaches its maximum size in 8–10 days. The pustule dries and forms a scab, which separates within 14–21 days after vaccination, leaving a scar (Figure 3). Primary vaccination can produce swelling and tenderness of regional lymph nodes, beginning 3–10 days after vaccination and persisting for 2–4 weeks after the skin lesion has healed. Maximum viral shedding from the vaccination site occurs 4–14 days after vaccination, but vaccinia can be recovered from the site until the scab separates from the skin (*50*).

A fever is also common after the vaccine is administered. Approximately 70% of children experience ≥1 days of temperatures ≥100 F for 4–14 days after primary vaccination (*21*), and 15%–20% of children experience temperatures ≥102 F. After revaccination, 35% of children experience temperatures ≥100 F, and 5% experience temperatures of ≥102 F (*24*). Fever is less common among adults after vaccination or revaccination (CDC, unpublished data, undated).

Inadvertent inoculation at other sites is the most frequent complication of vaccinia vaccination and accounts for approximately half of all complications of primary vaccination and revaccination (Tables 2,3). Inadvertent inoculation usually results from autoinoculation of vaccinia virus transferred from the site of vaccination. The most common sites involved are the face, eyelid, nose, mouth, genitalia, and rectum (Figure 4). Most lesions heal without specific therapy, but vaccinia immunoglobulin (VIG) can be useful for cases of ocular implantation (see Treatment for Vaccinia Vaccine Complications). However, if vaccinial keratitis is present, VIG is contraindicated because it might increase corneal scarring (*51*).

FIGURE 3. Vaccine site major reaction and progression after primary smallpox vaccination or revaccination after a prolonged period between vaccinations, using multiple-puncture technique



Source: CDC

* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp> (accessed April 20, 2001).

TABLE 2. Vaccine adverse reactions and vaccinia immunoglobulin (VIG) indications

Adverse reactions	VIG treatment
Mild to moderate	
Inadvertent inoculation	Usually not required; might be indicated for ocular implantation*
Erythematous or urticarial rashes	Not indicated†
Bullous erythema multiforme (Stevens-Johnson syndrome)	Not indicated†
Moderate to severe	
Eczema vaccinatum	Indicated in severe cases
Generalized vaccinia	Usually not required but might be indicated if patient is severely ill or has serious underlying illness
Progressive vaccinia (vaccinia necrosum)	Might be effective, depending on immune defect
Postvaccinial encephalitits	Not indicated†
Vaccinial keratitis	Contraindicated*

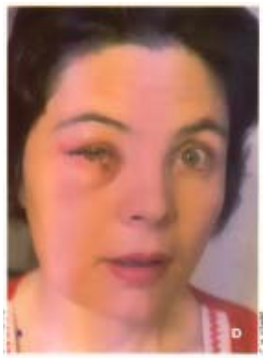
* VIG contraindicated if vaccinial keratitis present because increased scarring can occur.
† VIG is not effective in treatment of these adverse reactions.

TABLE 3. Rates of reported complications* associated with vaccinia vaccinations† (cases/million vaccinations)

Age (yrs) and status	Inadvertent inoculation§	Generalized vaccinia	Eczema vaccinatum	Progressive vaccinia¶	Postvaccinial encephalitis	Total**
Primary vaccination						
<1	507.0	394.4	14.1	—††	42.3	**1549.3**
1–4	577.3	233.4	44.2	3.2	9.5	**1261.8**
5–19	371.2	139.7	34.9	—††	8.7	**855.9**
≥20	606.1	212.1	30.3	—††	—††	**1515.2**
Overall rates††	**529.2**	**241.5**	**38.5**	**1.5**	**12.3**	**1253.8**
Revaccination						
<1	—††	—††	—††	—††	—††	**—††**
1–4	109.1	—††	—††	—††	—††	**200.0**
5–19	47.7	9.9	2.0	—††	—††	**85.5**
>20	25.0	9.1	4.5	6.8	4.5	**113.6**
Overall rates§§	**42.1**	**9.0**	**3.0**	**3.0**	**2.0**	**108.2**

* See text for descriptions of complications.
† Adapted from Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968: results of ten statewide surveys. J Infect Dis 1970;122:303–9.
§ Referenced as accidental implantation.
¶ Referenced as vaccinia necrosum.
** Rates of overall complications by age group include complications not provided in this table, including severe local reactions, bacterial superinfection of the vaccination site, and erythema multiforme.
†† No instances of this complication were identified during the 1968 10-state survey.
§§ Overall rates for each complication include persons of unknown age.

FIGURE 4. Inadvertent autoinoculation of lower eyelid with vaccinia virus



Source: Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and its eradication. Geneva, Switzerland: World Health Organization (WHO), 1988. Reprinted with permission from WHO.

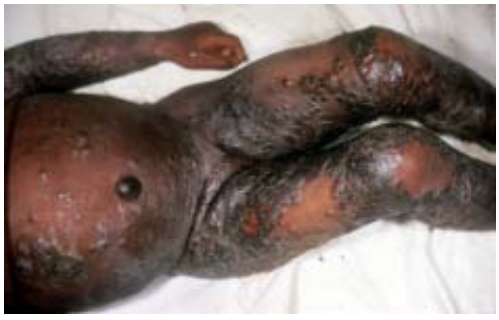
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

Erythematous or urticarial rashes can occur approximately 10 days after primary vaccination and can be confused with generalized vaccinia. However, the vaccinee is usually afebrile with this reaction, and the rash resolves spontaneously within 2–4 days. Rarely, bullous erythema multiforme (i.e., Stevens-Johnson syndrome) occurs (*52*).

Moderate to Severe Adverse Reactions. Moderate and severe complications of vaccinia vaccination include eczema vaccinatum, generalized vaccinia, progressive vaccinia, and postvaccinial encephalitis (Table 2). These complications are rare but occur ≥10 times more often among primary vaccinees than among revaccinees and are more frequent among infants than among older children and adults (*53–55*) (Table 3). A study of Israeli military recruits aged ≥18 years, who were vaccinated during 1991–1996, reported rates of the severe complications progressive vaccinia (i.e., vaccinia necrosum rate: 0/10,000 vaccinees) and postvaccinial encephalitis (rate: 0/10,000 vaccinees) similar to those reported in previous studies (*56*).

Eczema vaccinatum is a localized or systemic dissemination of vaccinia virus among persons who have eczema or a history of eczema or other chronic or exfoliative skin conditions (e.g., atopic dermatitis) (Figure 5). Usually, illness is mild and self-limited but can be severe or fatal. The most serious cases among vaccine recipients occur among

FIGURE 5. Eczema vaccinatum

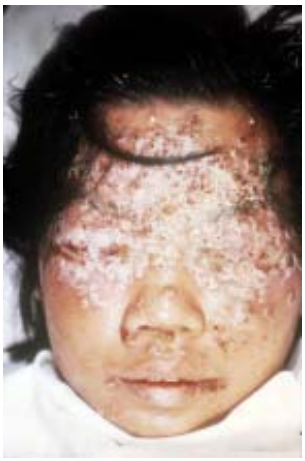


Source: John M. Leedom, M.D.

* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

primary vaccinees and are independent of the activity of the underlying eczema (*57*). Severe cases have been observed also after contact of recently vaccinated persons with persons who have active eczema or a history of eczema (see Contacts of Vaccinees) (Figure 6).

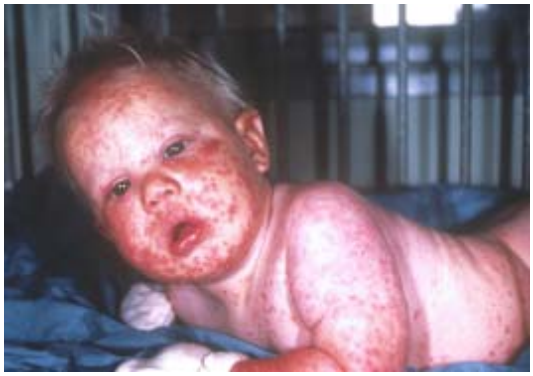
FIGURE 6. Eczema vaccinatum resulting from contact with recently vaccinated child; patient recovered without sequelae or permanent ocular damage



Photographer: John M. Leedom, M.D.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

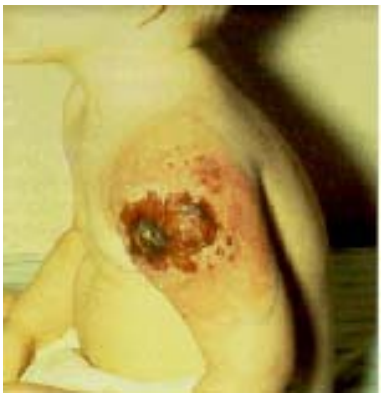
Generalized vaccinia is characterized by a vesicular rash of varying extent that can occur among persons without underlying illnesses (Figure 7). The rash is generally self-limited and requires minor or no therapy except among patients whose conditions might be toxic or who have serious underlying immunosuppressive illnesses (e.g., acquired immunodeficiency syndrome [AIDS]) (*58*).

FIGURE 7. Generalized vaccinia in an otherwise healthy child; the child recovered without sequelae



Photographer: John M. Leedom, M.D.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

FIGURE 8. Progressive vaccinia (vaccinia necrosum), which was fatal, in a child with an immunodeficiency



Source: Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and its eradication. Geneva, Switzerland: World Health Organization (WHO), 1988. Reprinted with permission from WHO.

* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

Progressive vaccinia (vaccinia necrosum) is a severe, potentially fatal illness characterized by progressive necrosis in the area of vaccination, often with metastatic lesions (Figure 8). It has occurred almost exclusively among persons with cellular immunodeficiency. The most serious complication is postvaccinial encephalitis. In the majority of cases, it affects primary vaccinees aged <1 year or adolescents and adults receiving a primary vaccination (*3*). Occurrence of this complication was influenced by the strain of vaccine virus and was higher in Europe than in the United States. The principle strain of vaccinia virus used in the United States, NYCBOH, was associated with the lowest incidence of postvaccinial encephalitis (*3*). Approximately 15%–25% of affected vaccinees with this complication die, and 25% have permanent neurological sequelae (*52–54*). Fatal complications caused by vaccinia vaccination are rare, with approximately 1 death/million primary vaccinations and 0.25 deaths/million revaccinations (*54*). Death is most often the result of postvaccinial encephalitis or progressive vaccinia.

Contacts of Vaccinees

Transmission of vaccinia virus can occur when a recently vaccinated person has contact with a susceptible person. In a 1968 10-state survey of complications of vaccinia vaccination, the risk for transmission to contacts was 27 infections/million total vaccinations; 44% of those contact cases occurred among children aged ≤5 years (*53*). Before the U.S. military discontinued routine smallpox vaccination in 1990, occurrences of contact transmission of vaccinia virus from recently vaccinated military recruits had been reported, including six cases resulting from transmission from one vaccine recipient (*59–61*).

Approximately 60% of contact transmissions reported in the 1968 10-state survey resulted in inadvertent inoculation of otherwise healthy persons. Approximately 30% of the eczema vaccinatum cases reported in that study were a result of contact transmission (*53*). Eczema vaccinatum might be more severe among contacts than among vaccinated persons, possibly because of simultaneous multiple inoculations at several sites (*54,62*). Contact transmission rarely results in postvaccinial encephalitis or vaccinia necrosum.

Precautions and Contraindications

Routine Nonemergency Laboratory and Health-Care Worker Contraindications

The following contraindications to vaccination apply to routine nonemergency use of vaccinia vaccine (see Smallpox Vaccine for Bioterrorism Preparedness for information regarding precautions and contraindications to vaccination during a smallpox outbreak emergency) (Table 4). Before administering vaccinia vaccine, the physician should complete a thorough patient history to document the absence of vaccination contraindications among both vaccinees and their household contacts. Efforts should be made to identify vaccinees and their household contacts who have eczema, a history of eczema, or immunodeficiencies. Vaccinia vaccine should not be administered for routine nonemergency indications if these conditions are present among either recipients or their household contacts.

TABLE 4. Vaccination contraindications and precautions for nonemergency and emergency use contraindications*

Contraindications for nonemergency vaccine use	Contraindications during smallpox emergency
History or presence of eczema†	Exposure to smallpox virus — no contraindications
Other acute, chronic, or exfoliative skin conditions†§	No virus exposure — same contraindications as nonemergency use
Immunosuppression†¶	—
Pregnancy†	—
Aged <18 yrs	—
Vaccine component allergy	—

* See text for explanation.

† Vaccination also not recommended for persons who live in household with others who have these conditions.

§ Vaccination may be administered after condition resolves.

¶ Conditions include human immunodeficiency virus, acquired immunodeficinecy syndrome, leukemia, lymphoma, generalized malignancy, solid organ transplantation, cellular or humoral immunodeficiencies, or therapy with alkylating agents, antimetabolites, radiation, or high-dose corticosteroids.

History or Presence of Eczema or Other Skin Conditions

Because of the increased risk for eczema vaccinatum, vaccinia vaccine should not be administered to persons with eczema of any degree, those with a past history of eczema, those whose household contacts have active eczema, or whose household contacts have a history of eczema. Persons with other acute, chronic, or exfoliative skin conditions (e.g., atopic dermatitis, burns, impetigo, or varicella zoster) might also be at higher risk for eczema vaccinatum and should not be vaccinated until the condition resolves.

Pregnancy

Live-viral vaccines are contraindicated during pregnancy; therefore, vaccinia vaccine should not be administered to pregnant women for routine nonemergency indications. However, vaccinia vaccine is not known to cause congenital malformations (*63*). Although <50 cases of fetal vaccinia infection have been reported, vaccinia virus has been reported to cause fetal infection on rare occasions, almost always after primary vaccination of the mother (*64*). Cases have been reported as recently as 1978 (*55,65*). When fetal vaccinia does occur, it usually results in stillbirth or death of the infant soon after delivery.

Altered Immunocompetence

Replication of vaccinia virus can be enhanced among persons with immunodeficiency diseases and among those with immunosuppression (e.g., as occurs with leukemia, lymphoma, generalized malignancy, solid organ transplantation, cellular or humoral immunity disorders, or therapy with alkylating agents, antimetabolites, radiation, or high-dose corticosteroid therapy [i.e., ≥2 mg/kg body weight or 20 mg/day of prednisone for ≥2 weeks] [*66*]). Persons with immunosuppression also include hematopoietic stem cell transplant recipients who are <24 months posttransplant, and hematopoietic stem cell transplant recipients who are ≥24 months posttransplant but who have graft-versus-host disease or disease relapse. Persons with such conditions or whose household contacts have such conditions should not be administered vaccinia vaccine.

Persons Infected with HIV

Risk for severe complications after vaccinia vaccination for persons infected with HIV is unknown. One case of severe generalized vaccinia has been reported involving an asymptomatic HIV-infected military recruit after the administration of multiple vaccines that included vaccinia vaccine (*58*). Additionally, a 1991 report indicated that two HIV-infected persons might have died of a progressive vaccinia-like illness after treatment with inactivated autologous lymphocytes infected with a recombinant HIV-vaccinia virus (*67*). No evidence exists that smallpox vaccination accelerates the progression of HIV-related disease. However, the degree of immunosuppression that would place an HIV-infected person at greater risk for adverse events is unknown. Because of this uncertainty, until additional information becomes available, not vaccinating persons (under routine nonemergency conditions) who have HIV infection is advisable.

Infants and Children

Before the eradication of smallpox, vaccinia vaccination was administered routinely during childhood. However, smallpox vaccination is no longer indicated for infants or children for routine nonemergency indications.

Persons with Allergies to Vaccine Components

The currently available vaccinia vaccine (i.e., Dryvax) contains trace amounts of polymyxin B sulfate, streptomycin sulfate, chlortetracycline hydrochloride, and neomycin sulfate. Persons who experience anaphylactic reactions (i.e., hives, swelling of the mouth and throat, difficulty breathing, hypotension, and shock) to any of these antibiotics should not be vaccinated. Vaccinia vaccine does not contain penicillin. Future supplies of vaccinia vaccine will be reformulated and might contain other preservatives or stabilizers. Refer to the manufacturer's package insert for additional information.

Treatment for Vaccinia Vaccine Complications

Using VIG

The only product currently available for treatment of complications of vaccinia vaccination is VIG, which is an isotonic sterile solution of the immunoglobulin fraction of plasma from persons vaccinated with vaccinia vaccine. It is effective for treatment of eczema vaccinatum and certain cases of progressive vaccinia; it might be useful also in the

treatment of ocular vaccinia resulting from inadvertent implantation (*68,69*). However, VIG is contraindicated for the treatment of vaccinial keratitis (*51,54*). VIG is recommended for severe generalized vaccinia if the patient is extremely ill or has a serious underlying disease. VIG provides no benefit in the treatment of postvaccinial encephalitis and has no role in the treatment of smallpox. Current supplies of VIG are limited, and its use should be reserved for treatment of vaccine complications with serious clinical manifestations (e.g., eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, and severe ocular viral implantation) (Table 2).

The recommended dosage of the currently available VIG for treatment of complications is 0.6 ml/kg of body weight. VIG must be administered intramuscularly and should be administered as early as possible after the onset of symptoms. Because therapeutic doses of VIG might be substantial (e.g., 42 ml for a person weighing 70 kg), the product should be administered in divided doses over a 24- to 36-hour period. Doses can be repeated, usually at intervals of 2–3 days, until recovery begins (e.g., no new lesions appear). Future reformulations of VIG might require intravenous administration, and health-care providers should refer to the manufacturer's package insert for correct dosages and route of administration. CDC is currently the only source of VIG for civilians (see Vaccinia Vaccine Availability for contact information).

Other Treatment Options for Vaccinia Vaccine Complications

The Food and Drug Administration has not approved the use of any antiviral compound for the treatment of vaccinia virus infections or other Orthopoxvirus infections, including smallpox. Certain antiviral compounds have been reported to be active against vaccinia virus or other Orthopoxviruses in vitro and among test animals (*70–75*). However, the safety and effectiveness of these compounds for treating vaccinia vaccination complications or other Orthopoxvirus infections among humans is unknown. Questions also remain regarding the effective dose and the timing and length of administration of these antiviral compounds. Insufficient information exists on which to base recommendations for any antiviral compound to treat postvaccination complications or Orthopoxvirus infections, including smallpox. However, additional information could become available, and health-care providers should consult CDC to obtain up-dated information regarding treatment options for smallpox vaccination complications (see Consultation Regarding Complications of Vaccinia Vaccine).

Consultation Regarding Complications of Vaccinia Vaccine

CDC can assist physicians in the diagnosis and management of patients with suspected complications of vaccinia vaccination. VIG is available when indicated. Physicians should telephone CDC at (404) 639-3670 during Mondays–Fridays, except holidays, or (404) 639-3311 during evenings, weekends, and holidays. Health-care workers are requested to report complications of vaccinia vaccination to the Vaccine Adverse Event Reporting System at (800) 822-7967, or to their state or local health department.

PREVENTING CONTACT TRANSMISSION OF VACCINIA VIRUS

Vaccinia virus can be cultured from the site of primary vaccination beginning at the time of development of a papule (i.e., 2–5 days after vaccination) until the scab separates from the skin lesion (i.e., 14–21 days after vaccination). During that time, care must be

taken to prevent spread of the virus to another area of the body or to another person by inadvertent contact. Thorough hand-hygiene with soap and water or disinfecting agents should be performed after direct contact with the site or materials that have come into contact with the site to remove virus from the hands and prevent accidental inoculation to other areas of the body (*76*). In addition, care should be taken to prevent contact of the site or contaminated materials from the site by unvaccinated persons. The vaccination site can be left uncovered, or it can be loosely covered with a porous bandage (e.g., gauze) until the scab has separated on its own to provide additional barrier protection against inadvertent inoculation. An occlusive bandage should not be routinely used because maceration of the site might occur. Bandages used to cover the vaccination site should be changed frequently (i.e., every 1–2 days) to prevent maceration of the vaccination site secondary to fluid buildup. Hypoallergenic tape should be used for persons who experience tape hypersensitivity. The vaccination site should be kept dry, although normal bathing can continue. No salves or ointments should be placed on the vaccination site. Contaminated bandages and, if possible, the vaccination site scab, after it has fallen off, should be placed in sealed plastic bags before disposal in the trash to further decrease the potential for inadvertent transmission of the live virus contained in the materials. Clothing or other cloth materials that have had contact with the site can be decontaminated with routine laundering in hot water with bleach (*2,4*).

Recently vaccinated health-care workers should avoid contact with unvaccinated patients, particularly those with immunodeficiencies, until the scab has separated from the skin at the vaccination site. However, if continued contact with unvaccinated patients is unavoidable, health-care workers can continue to have contact with patients, including those with immunodeficiencies, as long as the vaccination site is well-covered and thorough hand-hygiene is maintained. In this setting, a more occlusive dressing might be required. Semipermeable polyurethane dressings (e.g., Opsite®) are effective barriers to vaccinia and recombinant vaccinia viruses (*31*). However, exudates can accumulate beneath the dressing, and care must be taken to prevent viral contamination when the dressing is removed. In addition, accumulation of fluid beneath the dressing can increase the maceration of the vaccination site. Accumulation of exudates can be decreased by first covering the vaccination site with dry gauze, then applying the dressing over the gauze. The dressing should also be changed at least once a day. To date, experience with this type of containment dressing has been limited to research protocols. The most critical measure in preventing inadvertent implantation and contact transmission from vaccinia vaccination is thorough hand-hygiene after changing the bandage or after any other contact with the vaccination site.

VACCINATION METHOD

The skin over the insertion of the deltoid muscle or the posterior aspect of the arm over the triceps muscle are the preferred sites for smallpox vaccination. Alcohol or other chemical agents are not required for skin preparation for vaccination unless the area is grossly contaminated. If alcohol is used, the skin must be allowed to dry thoroughly to prevent inactivation of the vaccine by the alcohol. The multiple-puncture technique uses a presterilized bifurcated needle that is inserted vertically into the vaccine vial, causing a droplet of vaccine to adhere between the prongs of the needle. The droplet contains the recommended dosage of vaccine, and its presence within the prongs of the bifurcated needle should be confirmed visually. Holding the bifurcated needle perpendicular to the

skin, 15 punctures are rapidly made with strokes vigorous enough to allow a trace of blood to appear after 15–20 seconds (*3*). Any remaining vaccine should be wiped off with dry sterile gauze and the gauze disposed of in a biohazard waste container.

EVIDENCE OF IMMUNITY AND VACCINATION-RESPONSE INTERPRETATION

Appearance of neutralizing antibodies after vaccination with live vaccinia virus indicates an active immune response that includes the development of antibodies to all viral antigens and increased vaccinia-specific cell-mediated immunity. In a person with normal immune function, neutralizing antibodies appear approximately 10 days after primary vaccination and 7 days after revaccination (*3*). Clinically, persons are considered fully protected after a successful response is demonstrated at the site of vaccination.

The vaccination site should be inspected 6–8 days after vaccination and the response interpreted at that time. Two types of responses have been defined by the World Health Organization (WHO) Expert Committee on Smallpox. The responses include a) major reaction, which indicates that virus replication has taken place and vaccination was successful; or b) equivocal reaction, which indicates a possible consequence of immunity adequate to suppress viral multiplication or allergic reactions to an inactive vaccine without production of immunity.

Major Reaction

Major (i.e., primary) reaction is defined as a vesicular or pustular lesion or an area of definite palpable induration or congestion surrounding a central lesion that might be a crust or an ulcer. The usual progression of the vaccination site after primary vaccination is as follows:

- The inoculation site becomes reddened and pruritic 3–4 days after vaccination.
- A vesicle surrounded by a red areola then forms, which becomes umbilicated and then pustular by days 7–11 after vaccination.
- The pustule begins to dry; the redness subsides; and the lesion becomes crusted between the second and third week. By the end of approximately the third week, the scab falls off, leaving a permanent scar that at first is pink in color but eventually becomes flesh-colored (*77*).

Skin reactions after revaccination might be less pronounced with more rapid progression and healing than those after primary vaccinations. Revaccination is considered successful if a pustular lesion is present or an area of definite induration or congestion surrounding a central lesion (i.e., scab or ulcer) is visible upon examination 6–8 days after revaccination (*3*).

Equivocal Reaction

Equivocal reaction, including accelerated, modified, vaccinoid, immediate, early, or immune reactions, are defined as all responses other than major reactions. If an equivocal reaction is observed, vaccination procedures should be checked and the vaccination repeated by using vaccine from another vial or vaccine lot, if available. Difficulty in determining if the reaction was blunted could be caused by immunity, insufficiently po-

tent vaccine, or vaccination technique failure. If the repeat vaccination by using vaccine from another vial or vaccine lot fails to elicit a major reaction, health-care providers should consult CDC or their state or local health department before attempting another vaccination.

MISUSE OF VACCINIA VACCINE

Vaccinia vaccine should not be used therapeutically for any reason. No evidence exists that vaccinia vaccine has any value in treating or preventing recurrent herpes simplex infection, warts, or any disease other than those caused by human Orthopoxviruses (*78*). Misuse of vaccinia vaccine to treat herpes infections has been associated with severe complications, including death (*54,79,80*).

VACCINIA VACCINE AVAILABILITY

CDC is the only source of vaccinia vaccine and VIG for civilians. CDC will provide vaccinia vaccine to protect laboratory and other health-care personnel whose occupations place them at risk for exposure to vaccinia and other closely related Orthopoxviruses, including vaccinia recombinants. Vaccine should be administered under the supervision of a physician selected by the institution. Vaccine will be shipped to the responsible physician. Requests for vaccine and VIG, including the reason for the request, should be referred to

Centers for Disease Control and Prevention
Drug Services, National Center for Infectious Diseases
Mailstop D-09
Atlanta, GA 30333
Telephone: (404) 639-3670
Facsimile: (404) 639-3717

SMALLPOX VACCINE FOR BIOTERRORISM PREPAREDNESS

Although use of biological agents is an increasing threat, use of conventional weapons (e.g., explosives) is still considered more likely in terrorism scenarios (*81*). Moreover, use of smallpox virus as a biological weapon might be less likely than other biological agents because of its restricted availability; however, its use would have substantial public health consequences. Therefore, in support of current public health bioterrorism preparedness efforts, ACIP has developed the following recommendations if this unlikely event occurs.

Surveillance

A suspected case of smallpox is a public health emergency. Smallpox surveillance in the United States includes detecting a suspected case or cases, making a definitive diagnosis with rapid laboratory confirmation at CDC, and preventing further smallpox transmission. A suspected smallpox case should be reported immediately by telephone to state or local health officials and advice obtained regarding isolation and laboratory specimen collection. State or local health officials should notify CDC immediately at (404) 639-2184, (404) 639-0385, or (770) 488-7100 if a suspected case of smallpox is reported.

Because of the problems encountered previously in Europe with health-care–associated smallpox transmission from imported cases present in a hospital setting (*82,83*), health officials should be diligent regarding use of adequate isolation facilities and precautions (see Infection Control Measures). Currently, specific therapies with proven treatment effectiveness for clinical smallpox are unavailable. Medical care of more seriously ill smallpox patients would include supportive measures only. If the patient's condition allows, medical and public health authorities should consider isolation and observation outside a hospital setting to prevent health-care–associated smallpox transmission and overtaxing of medical resources. Clinical consultation and a preliminary laboratory diagnosis can be completed within 8–24 hours. Surveillance activities, including notification procedures and laboratory confirmation of cases, might change if smallpox is confirmed.

Prerelease Vaccination

The risk for smallpox occurring as a result of a deliberate release by terrorists is considered low, and the population at risk for such an exposure cannot be determined. Therefore, preexposure vaccination is not recommended for any group other than laboratory or medical personnel working with nonhighly attenuated Orthopoxviruses (see Routine Nonemergency Vaccine Use).

Recommendations regarding preexposure vaccination should be on the basis of a calculable risk assessment that considers the risk for disease and the benefits and risks regarding vaccination. Because the current risk for exposure is considered low, benefits of vaccination do not outweigh the risk regarding vaccine complications. If the potential for an intentional release of smallpox virus increases later, preexposure vaccination might become indicated for selected groups (e.g., medical and public health personnel or laboratorians) who would have an identified higher risk for exposure because of work-related contact with smallpox patients or infectious materials.

Postrelease Vaccination

If an intentional release of smallpox (variola) virus does occur, vaccinia vaccine will be recommended for certain groups. Groups for whom vaccination would be indicated include

- persons who were exposed to the initial release of the virus;
- persons who had face-to-face, household, or close-proximity contact (<6.5 feet or 2 meters) (*84*) with a confirmed or suspected smallpox patient at any time from the onset of the patient's fever until all scabs have separated;
- personnel involved in the direct medical or public health evaluation, care, or transportation of confirmed or suspected smallpox patients;
- laboratory personnel involved in the collection or processing of clinical specimens from confirmed or suspected smallpox patients; and
- other persons who have an increased likelihood of contact with infectious materials from a smallpox patient (e.g., personnel responsible for medical waste disposal, linen disposal or disinfection, and room disinfection in a facility where smallpox patients are present).

Using recently vaccinated personnel (i.e., <3 years) for patient care activities would be the best practice. However, because recommendations for routine smallpox vaccination in the United States were rescinded in 1971 and smallpox vaccination is currently recommended only for specific groups (see Routine Nonemergency Vaccine Use), having recently vaccinated personnel available in the early stages of a smallpox emergency would be unlikely. Smallpox vaccine can prevent or decrease the severity of clinical disease, even when administered 3–4 days after exposure to the smallpox virus (*2,4,85*). Preferably, healthy persons with no contraindications to vaccination, who can be vaccinated immediately before patient contact or very soon after patient contact (i.e., ≤3 days), should be selected for patient care activities or activities involving potentially infectious materials. Persons who have received a previous vaccination (i.e., childhood vaccination or vaccination >3 years before) against smallpox might demonstrate a more accelerated immune response after revaccination than those receiving a primary vaccination (*3*). If possible, these persons should be revaccinated and assigned to patient care activities in the early stages of a smallpox outbreak until additional personnel can be successfully vaccinated.

Personnel involved with direct smallpox patient care activities should observe strict contact and airborne precautions (*47*) (i.e., gowns, gloves, eye shields, and correctly fitted N-95 masks) for additional protection until postvaccination immunity has been demonstrated (i.e., 6–8 days after vaccination). Shoe covers should be used in addition to standard contact isolation protective clothing to prevent transportation of the virus outside the isolation area. After postvaccination immunity has occurred, contact precautions with shoe covers should still be observed to prevent the spread of infectious agents (see Infection Control Measures). If possible, the number of personnel selected for direct contact with confirmed or suspected smallpox patients or infectious materials should be limited to reduce the number of vaccinations and to prevent unnecessary vaccination complications.

Children who have had a definite risk regarding exposure to smallpox (i.e., face-to-face, household, or close-proximity contact with a smallpox patient) should be vaccinated regardless of age (*20,52*). Pregnant women who have had a definite exposure to smallpox virus (i.e., face-to-face, household, or close-proximity contact with a smallpox patient) and are, therefore, at high risk for contracting the disease, should also be vaccinated (*52*). Smallpox infection among pregnant women has been reported to result in a more severe infection than among nonpregnant women (*3*). Therefore, the risks to the mother and fetus from experiencing clinical smallpox substantially outweigh any potential risks regarding vaccination. In addition, vaccinia virus has not been documented to be teratogenic, and the incidence of fetal vaccinia is low (*52,63,86,87*). When the level of exposure risk is undetermined, the decision to vaccinate should be made after assessment by the clinician and patient of the potential risks versus the benefits of smallpox vaccination.

In a postrelease setting, vaccination might be initiated also for other groups whose unhindered function is deemed essential to the support of response activities (e.g., selected law enforcement, emergency response, or military personnel) and who are not otherwise engaged in patient care activities but who have a reasonable probability of contact with smallpox patients or infectious materials. If vaccination of these groups is initiated by public health authorities, only personnel with no contraindications to vaccination should be vaccinated before initiating activities that could lead to contact with suspected smallpox patients or infectious materials. Steps should be taken (e.g.,

reassignment of duties) to prevent contact of any unvaccinated personnel with infectious smallpox patients or materials.

Because of increased transmission rates that have been described in previous outbreaks of smallpox involving aerosol transmission in hospital settings (*1,82,83*), potential vaccination of nondirect hospital contacts should be evaluated by public health officials. Because hospitalized patients might have other contraindications to vaccination (e.g., immunosuppression), vaccination of these nondirect hospital contacts should occur after prudent evaluation of the hospital setting with determination of the exposure potential through the less-common aerosol transmission route.

Contraindications to Vaccination During a Smallpox Emergency

No absolute contraindications exist regarding vaccination of a person with a high-risk exposure to smallpox. Persons at greatest risk for experiencing serious vaccination complications are also at greatest risk for death from smallpox (*20,52*). If a relative contraindication to vaccination exists, the risk for experiencing serious vaccination complications must be weighed against the risk for experiencing a potentially fatal smallpox infection. When the level of exposure risk is undetermined, the decision to vaccinate should be made after prudent assessment by the clinician and the patient of the potential risks versus the benefits of smallpox vaccination.

Infection Control Measures

Isolation of confirmed or suspected smallpox patients will be necessary to limit the potential exposure of nonvaccinated and, therefore, nonimmune persons. Although droplet spread is the major mode of person-to-person smallpox transmission, airborne transmission through fine-particle aerosol can occur. Therefore, airborne precautions using correct ventilation (e.g., negative air-pressure rooms with high-efficiency particulate air filtration) should be initiated for hospitalized confirmed or suspected smallpox patients, unless the entire facility has been restricted to smallpox patients and recently vaccinated persons (*88,89*). Although personnel who have been vaccinated recently and who have a demonstrated immune response should be fully protected against infection with variola virus (see Evidence of Immunity and Vaccination-Response Interpretation), they should continue to observe standard and contact precautions (i.e., using protective clothing and shoe covers) when in contact with smallpox patients or contaminated materials to prevent inadvertent spread of variola virus to susceptible persons and potential self-contact with other infectious agents. Personnel should remove and correctly dispose of all protective clothing before contact with nonvaccinated persons. Reuseable bedding and clothing can be autoclaved or laundered in hot water with bleach to inactivate the virus (*2,4*). Laundry handlers should be vaccinated before handling contaminated materials.

Nonhospital isolation of confirmed or suspected smallpox patients should be of a sufficient degree to prevent the spread of disease to nonimmune persons during the time the patient is considered potentially infectious (i.e., from the onset of symptoms until all scabs have separated). Private residences or other nonhospital facilities that are used to isolate confirmed or suspected smallpox patients should have nonshared ventilation, heating, and air-conditioning systems. Access to those facilities should be limited to recently vaccinated persons with a demonstrated immune response. If suspected small-

pox patients are placed in the same isolation facility, they should be vaccinated to guard against accidental exposure caused by misclassification as someone with smallpox.

In addition to isolation of infectious smallpox patients, careful surveillance of contacts during their potential incubation period is required. Transmission of smallpox virus rarely occurs before the appearance of the rash that develops 2–4 days after the prodromal fever (*3*). If a vaccinated or unvaccinated contact experiences a fever >101 F (38 C) during the 17-day period after his or her last exposure to a smallpox patient, the contact should be isolated immediately to prevent contact with nonvaccinated or nonimmune persons until smallpox can be ruled out by clinical or laboratory examination.

VIG for Prophylaxis and Treatment of Adverse Reactions During a Smallpox Emergency

If vaccination of persons with contraindications is required because of exposure to smallpox virus after an intentional release as a bioterrorism agent, current stores of VIG are insufficient to allow its prophylactic use with vaccination. Because of the limited stores of VIG, its use in such a scenario should be reserved for severe, life-threatening complications (e.g., progressive vaccinia, eczema vaccinatum, or severe, toxic generalized vaccinia). If additional VIG becomes available in sufficient quantities to allow its prophylactic use, VIG should be administered intramuscularly as a dose of 0.3 mg/kg along with vaccinia vaccine to persons with contraindications who require vaccination.

RESEARCH PRIORITIES

Development and Evaluation of New Vaccinia Vaccine

Current supplies of vaccinia vaccine are limited to remaining stores of vaccine that were produced before the discontinuation of production by Wyeth Laboratories, Inc., in 1981. Although viral titer evaluations have indicated that the vaccine has remained potent, additional quantities of vaccine are needed to augment the current stores and replace expired vaccine. Previous methods of vaccine production that used calf lymph are no longer available; therefore, virus produced for use in a new vaccine must be grown by using a Food and Drug Administration-approved cell-culture substrate. Any new cell-culture vaccine should be evaluated for safety and efficacy by direct comparison with Dryvax by using appropriate animal models, serologic and cell-mediated immunity methods, and cutaneous indicators of successful vaccination (major reaction).

Treatment and Prevention Alternatives for Vaccine Adverse Reactions

Regarding alternatives to VIG for potential treatment and prevention of vaccine adverse reactions, research priorities include a) evaluating antivirals for activity against vaccinia virus by using in vitro assays and test animals that demonstrate vaccinia virus pathogenicity, and b) developing and evaluating monoclonal antibodies against vaccinia virus. Antivirals or monoclonal antibodies that demonstrate activity against vaccinia virus in vitro and efficacy in protecting against dissemination of vaccinia virus among test animals without compromising vaccine effectiveness could provide medical personnel with alternatives to VIG.

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MORBIDITY AND MORTALITY
WEEKLY REPORT

June 22, 2001 / Vol. 50 / No. RR-10

Recommendations and Reports

Continuing Education Activity Sponsored by CDC

Vaccinia (Smallpox) Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

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GOAL AND OBJECTIVES

This *MMWR*\t provides recommendations regarding vaccinia (smallpox) vaccine. These recommendations were developed by CDC staff and the Smallpox Vaccine Working Group of the Advisory Committee on Immunization Practices (ACIP). The goal of this report is to provide guidance for the use of vaccinia (smallpox) vaccine in the United States. Upon completion of this educational activity, the reader should be able to a) describe the characteristics of the currently licensed vaccinia (smallpox) vaccine; b) identify groups recommended for routine, nonemergency vaccination with vaccinia vaccine; c) list precautions and contraindications for the use of vaccinia vaccine under routine, nonemergency conditions; and d) describe recommended infection control measures for a suspected or confirmed case of smallpox.

To receive continuing education credit, please answer all of the following questions.

1. What is the primary reason that routine vaccinia (smallpox) vaccination is not recommended for the general public?

A. The frequency of adverse events following vaccination is unacceptably high.
B. The cost of vaccination programs prohibits routine vaccination.
C. The supply of vaccine is insufficient to meet demand.
D. Smallpox disease has been eradicated.
E. All the above are reasons that routine vaccinia vaccination is not recommended for the general public.

2. Which of the following groups is recommended to receive vaccinia (smallpox) vaccine under routine, nonemergency conditions?

A. All health-care providers.
B. Military personnel.
C. Laboratory workers who handle cultures containing a nonhighly attenuated strain of vaccinia virus.
D. Emergency medical personnel (e.g., paramedics).
E. All the above groups are recommended to receive vaccinia vaccine under routine, nonemergency conditions.

3. What is the most common adverse reaction or complication after vaccinia (smallpox) vaccination?

A. Generalized vaccinia.
B. Eczema vaccinatum.
C. Progressive vaccinia.
D. Severe allergic reaction.
E. Inadvertent inoculation.

4. Which of the following conditions is a precaution or contraindication for the use of vaccinia (smallpox) vaccine under routine, nonemergency conditions?

A. Immunosuppression.
B. Severe allergy to a component of the vaccine.
C. Household contact with a person with eczema.
D. Pregnancy.
E. All of the above are precautions or contraindications to the use of vaccinia vaccine.

5. Which of the following best describes the currently licensed vaccinia (smallpox) vaccine?

A. Live attenuated smallpox virus.
B. Inactivated smallpox virus.
C. Live vaccinia virus.
D. Inactivated vaccinia virus.
E. Reassortant vaccine containing both vaccinia and smallpox viruses.

6. What is a critical measure in preventing contact transmission of vaccinia virus?

A. Thorough hand washing after contact with the vaccination site.
B. Isolation of the vaccinated person.
C. Use of a porous bandage to cover the vaccination site.
D. Antibacterial ointment applied to the vaccination site.
E. Application of the vaccine at an anatomic site normally covered by clothing.

7. For which of the following conditions is treatment with vaccinia immunoglobulin (VIG) of no benefit?

A. Severe generalized vaccinia.
B. Progressive vaccinia.
C. Postvaccinal encephalitis.
D. Eczema vaccinatum.
E. Ocular vaccinia.

8. What infection control measures are recommended for a person with suspected or confirmed smallpox?

A. Isolation of the person in a negative-air pressure room.
B. Protective clothing for health-care workers in contact with that patient.
C. Vaccination of persons involved in direct medical care of suspected cases.
D. Monitoring contacts of suspected smallpox cases for febrile illness.
E. All the above infection control measures are recommended for a person with suspected or confirmed smallpox.

9. At what point is a vaccinated person considered to be fully protected from smallpox?

A. Ten days after the first dose of vaccine, regardless of the response at the site of administration.
B. Ten days after the second dose of vaccine, regardless of the response at the site of administration.
C. After the appearance of any reaction at the site of administration.
D. After the appearance of a vesicular or pustular lesion at the site of administration.
E. After the appearance of a generalized rash in the vaccinated person.

10. Indicate your work setting.

A. State/local health department.
B. Other public health setting.
C. Hospital clinic/private practice.
D. Managed care organization.
E. Academic institution.
F. Other work setting.

11. Which best describes your professional activities?

A. Patient care — emergency or urgent care.
B. Patient care — inpatient.
C. Patient care — primary-care clinic or office.
D. Laboratory or pharmacy.
E. Public health.
F. Other.

12. I plan to use these recommendations as the basis for . . . (*Indicate all that apply.*)

A. health education materials.
B. insurance reimbursement policies.
C. local practice guidelines.
D. public policy.
E. other uses.

13. Have you administered one or more doses of vaccinia (smallpox) vaccine during the past 12 months?

A. Yes.
B. No.

14. How much time did you spend reading this report and completing the exam and evaluation?

A. <1 hour.
B. 1–1.5 hours.
C. 1.5–2 hours.
D. >2 hours.

15. After reading this report, I am confident I can describe the characteristics of the currently licensed vaccinia (smallpox) vaccine.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

16. After reading this report, I am confident I can identify groups recommended for routine, nonemergency vaccination with vaccinia vaccine.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

17. After reading this report, I am confident I can list precautions and contraindications for the use of vaccinia vaccine under routine, nonemergency conditions.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

18. After reading this report, I am confident I can describe recommended infection control measures for a suspected or confirmed case of smallpox.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

19. The objectives are relevant to the goal of this report.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

20. The tables are useful.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree
E. Strongly disagree.

21. The figures are useful.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree
E. Strongly disagree.

22. Overall, the presentation of the report enhanced my ability to understand the material.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

23. These recommendations will affect my practice.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

24. The availability of continuing education credit influenced my decision to read this report.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

25. How did you learn about this continuing education activity?

A. Internet.
B. Advertisement (e.g., fact sheet *MMWR* cover, newsletter, or journal).
C. Coworker/supervisor.
D. Conference presentation.
E. *MMWR* subscription.
F. Other.

Correct answers for questions 1–9

1. D; 2. C; 3. E; 4. E; 5. C; 6. A; 7. C; 8. E; 9. D.

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June 22, 2001/Vol. 50/No. RR-10

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Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

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Fill in the appropriate blocks to indicate your answers. Remember, you must answer <u>all</u> of the questions to receive continuing education credit!

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2. [ ] A [ ] B [ ] C [ ] D [ ] E
3. [ ] A [ ] B [ ] C [ ] D [ ] E
4. [ ] A [ ] B [ ] C [ ] D [ ] E
5. [ ] A [ ] B [ ] C [ ] D [ ] E
6. [ ] A [ ] B [ ] C [ ] D [ ] E
7. [ ] A [ ] B [ ] C [ ] D [ ] E
8. [ ] A [ ] B [ ] C [ ] D [ ] E
9. [ ] A [ ] B [ ] C [ ] D [ ] E
10. [ ] A [ ] B [ ] C [ ] D [ ] E [ ] F
11. [ ] A [ ] B [ ] C [ ] D [ ] E [ ] F
12. [ ] A [ ] B [ ] C [ ] D [ ] E
13. [ ] A [ ] B
14. [ ] A [ ] B [ ] C [ ] D
15. [ ] A [ ] B [ ] C [ ] D [ ] E
16. [ ] A [ ] B [ ] C [ ] D [ ] E
17. [ ] A [ ] B [ ] C [ ] D [ ] E
18. [ ] A [ ] B [ ] C [ ] D [ ] E
19. [ ] A [ ] B [ ] C [ ] D [ ] E
20. [ ] A [ ] B [ ] C [ ] D [ ] E
21. [ ] A [ ] B [ ] C [ ] D [ ] E
22. [ ] A [ ] B [ ] C [ ] D [ ] E
23. [ ] A [ ] B [ ] C [ ] D [ ] E
24. [ ] A [ ] B [ ] C [ ] D [ ] E
25. [ ] A [ ] B [ ] C [ ] D [ ] E

Signature ***Date I Completed Exam***

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