6 Field Trials

On March 25, the day after the President's announcement, a meeting chaired by Meyer at the BoB—with CDC and NIAID and the producing laboratories represented—drew several key conclusions. These had been in the air March 10 or even earlier; this meeting tacked them down.

First, manufacturers should produce enough swine vaccine for everyone —roughly 200 million doses—and start deliveries in June for use from July on. Neither now nor later were dates for the mass immunization made precise. The aim was to start before August—as early in July as deliveries allowed—and to finish before winter. (In their April testimony, Sencer and Cooper said November; whereas Meyer, closer to production, said late December.)

Second, since this would fully occupy available facilities of active manufacturers, no more Victoria vaccine should be produced. What was at hand would be made bivalent by adding swine vaccine in bulk. This would produce some 30 million bivalent doses, to be used for high risk groups, mainly the elderly.

Third, the rest of the swine flu vaccine would be turned into monovalent doses and used on a one-person, one-dose basis, thus insuring wide availability. This assumed that one dose would give adequate protection without bothersome effects on adults and children alike. The assumption was colored by recent improvements in vaccine purification. But it rested fundamentally on logistical concerns: how could one hope to get vaccine and kids together twice?

Fourth, the needs of the armed forces, also those of the VA, although separately determined and contracted for (as usual), had to fit inside these targets, with deliveries coordinated in a fashion to which military doctors were distinctly unaccustomed. Production orders from still other sources, including other countries if they came, had to wait upon American deliveries. Diversions of American supplies would be a matter for the White House (so indeed was the compliance of DoD: Cavanaugh later got stuck with both).

Another assumption was hidden, or more precisely muffled, in these

calculations, namely that the manufacturers would grow the monovalent vaccine fast enough to guard against an early fall pandemic. In 1918, the virulent phase had begun in August. The manufacturers now argued, in Hilleman's words at the meeting:

> . . . you couldn't possibly have 200 million doses by fall. . . . If you are talking about one dose per egg, which is more what it looks like [instead of the hoped-for two doses] you are talking about a different situation.[6]

The day before, the President had pledged vaccine to everyone. A week later, Cooper, on the Hill, would state his goal as "95 percent of all Americans." Hilleman's discrepancy seems to have left Meyer untroubled.

On April 2, Sencer in Atlanta hosted a monster meeting to acquaint state health officials and representatives of private medicine with these targets (Congress willing) and with CDC's conception of administrative follow-through based on state immunization plans. Prompt filing of these plans was sought by CDC. Funding and technical assistance were to follow. Vaccine distribution would begin as soon as field trials, tests and bottling allowed, and states should start at once to put it into people. Taking maximum advantage of the time at hand, the states now had a chance to immunize the country, or most of it, before the next flu season.

Here was a challenge for the Public Health officialdom from coast to coast, an opportunity to do in 1976 precisely what had not been done in 1968 or 1957—and at Federal expense with the President responsible. Energy and time and personnel might have to be withdrawn from other uses, to be sure, but not much money begged from any legislature except Congress, his trouble not theirs. Besides, there was the vision of the Kilbournes and the Coopers: Preventive medicine raised high in public consciousness. Who could be against that?

Actually, there seem to have been many persons present who, in some degree or other, feared the swine flu program either as a dubious diversion from less speculative ventures—measles, polio—or as a likely failure in the public mind, the opposite of Kilbourne's view, or worse as a presumptive danger *to* the public health because of unknown side effects, the Alexander worry. Jonathan Fielding, Massachusetts Commissioner of Public Health, told us that he remembers disagreeing:

> I didn't favor a mass vaccination program because I thought the risk of an epidemic small and I didn't want to divert resources from other programs.

But Massachusetts had a long-standing feud with CDC and everybody knew it.

One Regional Director of the HEW who had come to the meeting with officials from "his" states wrote afterwards:

> How certain are we that an epidemic or pandemic will occur? There is a recognition that this decision [to proceed] is based on probability. Yet the recommendation to go forward was not wholly persuasive.
>
> How certain are we that this virus will be a "killer," or possibly a "normal" virus resulting in relatively mild illness? The answer seems to be the latter. . . . This answer also relates to the relative lack of certainty that the epidemic-pandemic will occur, thus combining to weaken the threshold assertion to go forward with the program.

This might have been interesting before decision; coming after, it was taken as spectator sportsmanship.

Alexander, hearing of the meeting, wrote Sencer a tactful note:

> I received the minutes of the ACIP meeting of March 10th and found them accurate and a good summary. . . . I have also seen newspaper reports of jousting with the state health officials. . . . I do not understand how practical political animals (which they should be) can be so short-sighted as not to appreciate the far bigger potential gain for the field of preventive medicine. . . .
>
> However, my reason for writing is to say once more that I strongly recommend some hesitation before beginning vaccine administration programs. . . . I realize that there is some risk to be taken in delaying in that, like A/Victoria, we may be one of the first countries to be hit—but we may not. And most of our recent experiences with new variants —and the experience in 1918—was with a longer period of warning before the first severe wave (called the second wave in December 1918). Furthermore, although there might be some morbidity and mortality in an initial wave, there would still be some opportunity to have a major effect in dampening or preventing the second, third and other waves. And in so doing, we would have experience to guide us concerning the age distribution of severe and fatal disease.
>
> As stated in the . . . minutes, "it was agreed that the production of vaccine must proceed and that a plan for vaccine administration must be developed." I, for one, do not agree that it need necessarily be carried out, unless there was another swine outbreak.
>
> It is prudent and necessary to protect the population against a potential threat. . . . We spend large sums of money . . . stockpiling for military defense of the continental United States . . . with well worked-out contingency plans for use. . . .
>
> I urge you to consider this. There still seems to be time to be cautious if there is no further evidence of significant swine outbreaks by September. Of course, if they do occur, here or in the Southern hemisphere—the subject is dead.
>
> With personal regards from your "half-a-hog" colleague. . . .

The tone tells volumes about the relations of advisers to directors in Sencer's world.

And Goldfield blew his top. Ignoring those relations, heedless of hierarchy, he expressed his opposition in the meeting, repeated it to the inquiring press and possibly to his surprise was featured on all network TV news shows. The CBS transcript quotes him on the April 2 Evening News:

> There are as many dangers to going ahead with immunizing the population as there are withholding. We can soberly estimate that approximately fifteen percent of the entire population will suffer disability reaction.[7]

Goldfield shared Alexander's view that mass immunization should not follow planning unless swine flu actually appeared again and showed itself to be more than a fluke. Unlike Alexander, Goldfield had a particular worry, the potential side-effects in pregnant mothers. Sharing this with his college-aged daughter, he had been sternly urged to go public. But this specific risk, unfortunately for him, was discounted by specialists, and he with it, obscuring Alexander's general point.

Goldfield thereupon became a source of professional controversy. He was admired in some quarters for his candor and lambasted in others for disloyalty. One of the country's senior epidemiologists told us he had admonished him: "Marty, you have some good points. I agree with much of what you say. But the decision's made. Now is the time to close ranks. You are wrong to go public." That was deemed unforgivable. By all accounts, including his own, Goldfield has *not* been forgiven.

Neither have the networks. At CDC, officials still shake their heads sadly as they think of it. One commented to us:

> There was 98 percent agreement with us in that audience. . . . Only a handful of people spoke on the other side. But they got more time on the screen. . . . The critics first. . . . Goldfield, of all people, had the most attention.

He also had the most impassioned manner and the special claim of coming from New Jersey. Each network balanced him with a supportive public health official from somewhere else. To us, the coverage seems both predictable and professional—professional, that is to say, in terms of news, not medicine.

CDC officials got a further jolt from the editorial page of the *New York Times*. The paper's reportage was comprehensive, factual, and careful, regarded as a model in Atlanta. This made the more painful a succession of editorials, which began by questioning and ended by denouncing the swine flu program. The first of these had come February 23, after the initial CDC press conference. The second, in a stiffer tone,

came April 6, four days after CDC's meeting with the states. At CDC, there was great puzzlement about one newspaper's ability to be so courtly on the news page and so nasty on the editorial. In fact, the editorials were written by one member of the Editorial Board, Harry Schwartz, entirely on his initiative, out of his own skepticism about public medicine. As he read the news reports, the scientific case had not been made and Ford had probably been panicked.

Five days after the meeting in Atlanta, the World Health Organization held a meeting in Geneva, and CDC attendees gave a briefing on American opinions and intentions. With no recorded outbreaks anywhere else, and still only one here, their auditors kept cool (which was convenient, since they mostly lacked funds or facilities to readily follow our lead). The relative calm was reflected in a CBS Evening News story from Geneva, April 8:

> . . . preparation for a possible swine flu epidemic next winter. The Geneva experts said inoculation supplies may run short in some countries and they urged other emergency measures, including the stockpiling of vaccine.

The British set up a program for high risk groups, along with a small stockpile, and some researchers undertook experiments with living subjects, testing the severity of the new virus. The Canadians took steps to interest their provincial health authorities in mass immunization. Unlike us, they dealt with the issue through usual channels where the provinces decide priorities in allocating limited funds. The national Health Ministry's equivalent of ACIP urged flu shots for half the population in a set of high-risk groups *excluding* healthy children and most adults between 40 and 65. The provinces acceded, scraping funds out of their regular health budgets.[8]

Meanwhile, American field trials were being planned. As usual, NIAID, BoB, and CDC had comfortably divided up responsibility. The trials were to start as soon as funds and vaccine were available. It would be necessary to include vaccine from every manufacturer and to test the uses of both "whole" and "split" (two different methods of preparing the killed-virus vaccine). Since immunization would be on a bigger scale than ever before, there was concern to make the field trials match. The sample was to be the biggest yet, with thousands of volunteers divided into different age groups receiving different doses of vaccine from different manufacturers.

Unfortunately, the trials made no provision for checking the responses of young volunteers as between one dose or two. The program had been predicated on one dose apiece for all. It was well understood that chil-

dren, lacking long exposure to related viruses, were likelier than adults to need stronger doses but to take a single dose with more discomfort. Yet one-person-one-dose was so well in mind, so much part of the program, that no one insisted on simultaneous trials of two.

Retrospectively, officials are regretful. Seal, for instance, said when interviewed:

> It would have been no trouble to bring back the volunteers in the right age groups for a second shot of split vaccine. The same subjects . . . no new selection process . . . the one consent form. . . . We just didn't think of it. . . .
> There's another lesson. . . .

Actually, it was thought of, but promptly discarded. The lesson lies in that. At the BoB meeting March 25, several outside scientists had urged inclusion of a two-dose test. The point was made, but the NIAID planners did not pick it up.

The field trials were launched April 21, with experimental lots of vaccine from the manufacturers; they for their part did what their own scientists, their laboratory specialists, said should be done. Mindful of the President's announcement, knowing that the funds had been appropriated, spurred by fellow professionals in PHS and sharing most of their concerns, the laboratories went full-tilt to meet governmental targets, rounding off Victoria while building up swine vaccine. They gambled on the field trials and counted on BoB licensing thereafter. One of them, Parke-Davis, mistakenly made several million doses of vaccine against a swine flu virus of a slightly different sort than CDC's Fort Dix strain. This was not discovered until June (and the source of the mistake, whether private lab or public, is now being judged in the courts).

Generally, production picked up smoothly though less rapidly than had been hoped in March. Low yield-per-egg was one problem. Other manufacturing impediments slowed some production labs, how much is hard to tell. Each company's vaccine is somewhat different from the others. Their products must meet the same FDA standards, but their processes are private. Taken as a whole, we know that their production rates fell below Sencer's (hence Cooper's) early expectations. Just how much and why is obscured by the privacy. The GAO Report has some suggestive data on how much. The answer to the why may be as simple as lack of realism in those expectations.

While NIAID prepared for field trials, Millar and his associates at CDC were seeking and then processing state plans. The states, along

with cities which had separate health departments, offered a variety of plans. Some, like Delaware and New Jersey, were state-wide; some, like California and Pennsylvania, were county-by-county (depending on state size and on the relative authority of local and state health agencies). Some sought guns for only a few roving teams; others sought to mount supplies for many. Pennsylvania and New Jersey are again in contrast. Some assumed use of the public schools (available in summer), others featured hospitals or other health facilities. Some stressed vaccination at the work place, planning a big role for corporations; others counted mainly on their public health facilities. And in a few jurisdictions, including New York City, where public health officials were most skeptical of flu, they produced plans, took the money, and postponed aggressive action until signs of a pandemic (which they doubted) should appear. One state commissioner who held back on implementation claimed to us:

> We could have mass vaccinated this state in six weeks, and would have, if the situation with swine flu had become critical. No problem. Well, sure, there are problems, but in a real emergency, volunteer help shows up. We could have gotten to everybody you could ever get to in six weeks.

We draw these characteristics from among four states and one city sampled by the GAO—Florida, Georgia, Missouri, Pennsylvania, and Philadelphia—together with some superficial sampling of our own in California, Delaware, Massachusetts, Minnesota, New Jersey, New York and Wisconsin.

While state plans were coming in, the field trials ended and evaluation began. That process took two weeks. By the time it was over some of the assumptions which the states had used (on CDC's say so) were in collapse. The evaluation implied that immunization should begin by leaving out all persons under 18, perhaps all those under 24; whether they were ever to be covered was now said to be dependent on another set of field trials. This news was particularly irritating to the many states, Pennsylvania for one, which had intended schools as immunization centers. They had to replan. The rest had to revise their estimates of need and of peak loads.

On June 21 and 22, NIAID played host in Bethesda to a joint meeting of the BoB Review Panel on Viral and Rickettsial Vaccine and the ACIP. CDC and BoB were amply represented. So were state health departments. Sabin was there; he had asked to be invited. Salk was there as well. So were doubters and detractors in observer status, Wolfe included. And the press was there in force. About 200 people came together for those days, another monster meeting—monstrous as some saw it (Sabin among them).

The purposes announced were first to brief advisers on the field trial findings, then to hear and discuss their views (with the consensus cranked up by two *ad hoc* subcommittees over lunch). Sabin had let it be known that he sought discussion also of an active form of stockpiling in lieu of the prospective immunization. In an informal way, this became the agenda item for the second day.

The story on the field trials was both simple and depressing: single doses worked poorly on children. For persons under 18, especially young children, "whole" vaccine was immunizing but caused many reactions ranging from sore arms to high fever. For the same group "split" vaccine did nothing of the sort, but also did not immunize. The obvious answer was half-strength doses of whole vaccine, given twice, some weeks apart. Quite possibly, a second dose of "split" vaccine would do as well, but this was not established. Yet how, if a pandemic came, get children back a second time? Besides, how get enough vaccine? All production schedules had assumed one child, one dose.

Discussions of the reactivity of whole vaccine and the potency of split led to an inevitable proposal. There should be another set of field trials to establish the results of second doses. The production question could be faced, and distribution also, after that was done. Sencer soon would say to an inquiring reporter for TV:

> What we're telling mothers for the next two months is that as scientists we don't know what to tell them, that we're doing the work that is going to be necessary to be able to give them good advice. And that's all we can say for the next two months because we just don't know the answers.[9]

But there also was, implicitly, a further answer. This, although not publicly acknowledged, seems to have been understood by all advisers and officials on the scene. As one of them told us:

> What Sencer meant but could not say is that if a pandemic came we'd use single shots of whole vaccine on children; no matter how uncomfortable it made them, mothers wouldn't mind. But in the absence of another outbreak, and a big one, no, we couldn't use it, mothers would mind too damn much. As for the split vaccine, it was all over for 1976. We had to go through field trials first; then how could we get twice as much vaccine as we originally ordered? In time, that is, for the flu season? Maybe 1978? So we knew in June that children were out unless the flu exploded, which by then was seeming more and more remote. But we had to order up new field trials . . . and we couldn't simply say "no kids."

They couldn't because they thought most Americans, recalling polio, expected kids and shots to go together like ham and eggs. Immunization

without children would sound crazy. What sort of preventive medicine was that? What sort of parental consciousness raising?

Both in what he said and in what he evidently thought, Sencer reflected the views of his colleagues.

On stockpiling, by contrast, Sencer squared off against Sabin who if not a colleague was at least a member of the club. Sabin had come to make two points quite separate from, although enlivened by, the children's problem. He argued, first, in terms like Alexander's, the case for watchful waiting now that no swine flu had shown up anywhere, not even in the southern hemisphere where flu season would shortly reach its peak. The case was only strengthened by the likelihood that we would not now immunize the children. In previous pandemics children had been the chief spreaders of disease. And second, Sabin argued that with proper preparation we could keep ahead of spread, inoculating quickly if the virus reappeared. The form of stockpiling was to be active, not passive, not mere warehousing. Proper measures in his view included both planning and training. He called for brigades of volunteers—high school age and up—recruited and trained locally, ready to immunize their neighborhoods the moment CDC should pass the word. In the minutes:

> We must be able to do [immunize] everybody in an area in 1 to 2 days. We need a total voluntary effort, training . . . students and others in an assembly-line technique. We cannot rely on health professionals and existing doctors' offices.[10]

Sencer, armed with a brief staff study, spoke out against this course on grounds of feasibility. His assistant director for operations, Dr. William Foege, strongly seconded him. The flu could move too fast, "jet-spread" again. That CDC staff study is the only written piece of staff work we can find on stockpiling; as such we include it in Appendix D. The study's objections to stockpiling centered on timing. Among its assumptions, three were questionable. The first was that many workers would have to be newly recruited and trained in an emergency; treating the whole of emergency staff like Army reservists was not explored. The second was that emergency clinics would work on a six-day week; working on Sundays was not discussed. The third was that "commitment" to a standby program would decline over time necessarily; the adrenal charge of a perceived emergency was nowhere recognized, nor was the draining effect of doubts about the program as it stood. Even so, Sencer argued hard (and probably still would).

The ACIP minutes for June 22 reflect his and Foege's views:

> . . . the infeasibility of achieving any measure of adequate immunization of the country once cases or clusters of cases were occurring . . .

> once operational, most immunization programs would take two to three months to complete even if all elements functioned smoothly and personnel, vaccine supplies and other program ingredients were ample . . . once identified as causing cases, pandemic strains can be expected to become widespread in less than two months, . . . no rational basis for a general 'stockpiling concept' . . . more risk in this concept when one adds a two-week period of antibody development onto the vaccination timetable.

Sencer also stressed that high school volunteers were bait for litigation. This last was a note to which all ears were just becoming sensitive. Besides, as several state officials said, plans now had gone too far to be revised wholesale in Sabin's fashion. Projects had momentum; break it and it would not soon revive.

In the minds of some committee members this turned the argument. Stallones, for one, recalled to us:

> I had talked to Alexander, and I was impressed by his point of view, although in March I had been an enthusiast for going all the way. But what Foege said was impressive too, and to have it reinforced by the state people themselves struck me personally as compelling.

At all events, a clear majority of the combined committees went along with CDC and state desires as expressed. Along with dosage recommendations, mass immunization was reaffirmed. Storing doses in people, not warehouses, as Salk said, won the day among those voting at Bethesda. Thereafter Cooper turned to Salk as once to Sabin.

The press found much of interest in these meetings, and the television news found interesting faces to present, both old and new. Postponement of the children caused wry comment on two networks, and the stockpiling debate was featured on all three. Sabin was the Goldfield of this coverage, but he was joined by others, notably Alexander, moved by three more months without a trace of swine flu. Uncharacteristically, Alexander went public:

> I think the issue is, as time goes on, there—it's becoming more evident that up till now there's no sign of swine influenza outbreaks like the one that occurred in Fort Dix, New Jersey occurring in the United States. Most people think that the probability is there will not be an epidemic in the 1976-77 season due to swine influenza.[11]

Other opponents cited in the newspapers, or shown on the TV, included those who had appeared when the program was first announced. But this was no mere replay of initial skepticism; Sabin and Alexander demonstrated that. The point was not lost in such places as the Editorial Board of the *New York Times,* or the Washington Bureau of CBS News. Nor was it lost in Congress. Congressman Henry A. Waxman of the Rogers subcommittee, an habitual watcher of CBS News, seems to have been

much struck by the whole proceeding; Senator Kennedy has told us he recalls stockpiling as an opportunity lost.

At CDC and Cooper's office, and indeed in Cavanaugh's, reactions against Sabin (who had been so eloquently their man on TV three months ago) remind us of White House reactions against favored columnists who come up with what staffers take as slurs upon their President. But White House aides, more royalist than the king, grow angry in defending *him*. The health officials here, excepting Cavanaugh, were not concerned with Ford. Their anger was indeed aroused but they defended something else: as best we can discern, it was the sanctity of hierarchical decisions in their profession. They are scornful of Sabin yet. Alexander they merely cold shouldered.

And the media in their view had distorted once again, with emphasis on controversy rather than agreement.

However, these officials did not have much time, just then, to dwell upon past grievances. For they were being threatened from another quarter. The Bethesda meetings were scarcely adjourned when word came that the casualty insurance industry could find no members willing to insure the manufacturers of swine vaccine. The manufacturers refused to bottle it until somebody did.