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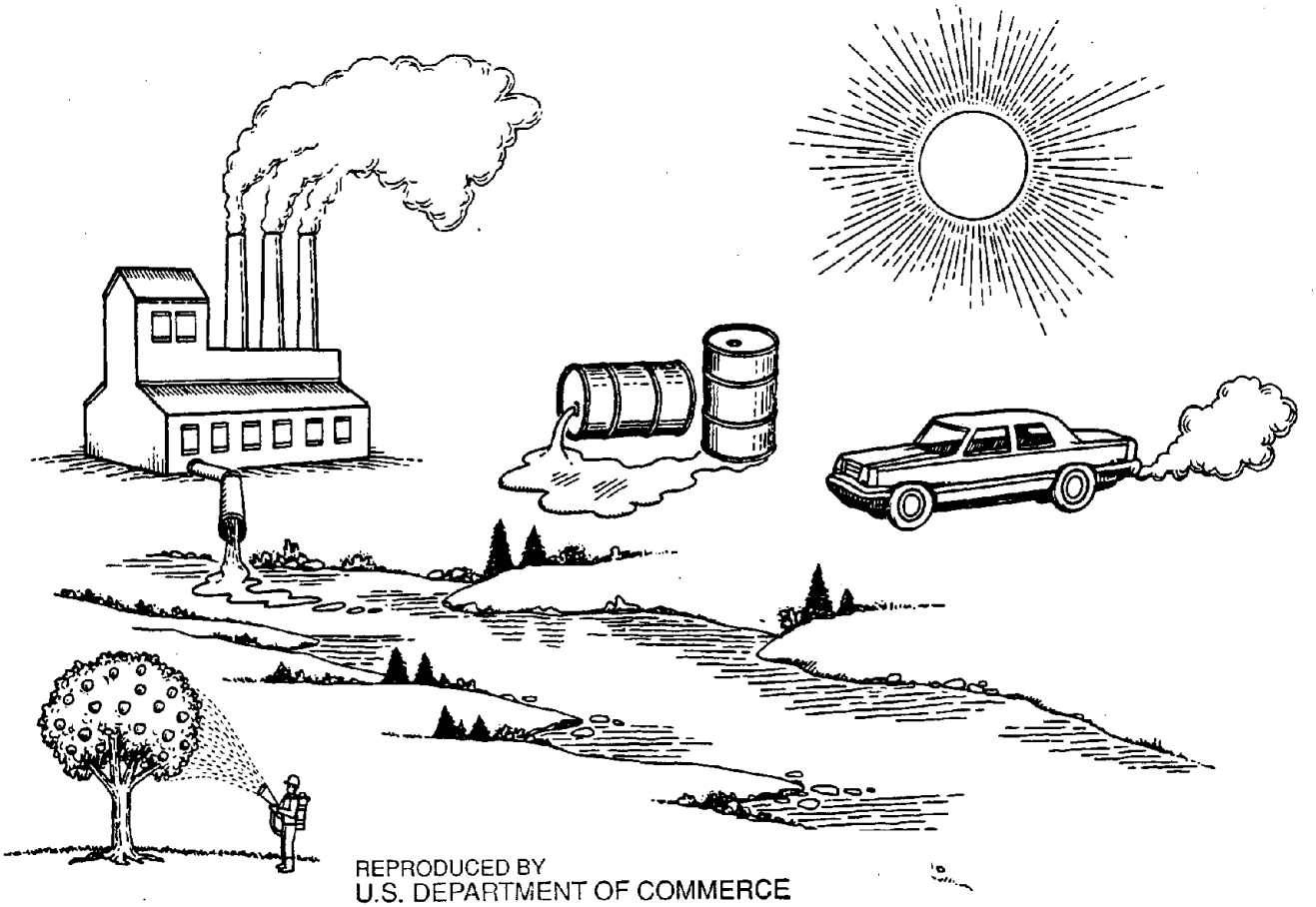
Unfinished Business: A Comparative Assessment of Environmental Problems

Appendix II Non-Cancer Risk Work Group



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16. ABSTRACT

This report is one of four reports comparing risks currently associated with major environmental problems.

A ranking methodology was devised and 31 environmental problems areas under EPA's jurisdiction were ranked according to the relative magnitude of the non-cancer health risks they pose. Chapter 2 of the report summarizes the results of the ranking of the non-cancer health risks associated with major environmental problem areas, and Chapter 3 reviews the process used to produce these rankings. Chapter 4 presents some overall observations on the project and recommendations resulting from it. The steps and issues in the ranking methodology are described in further detail in the Appendix.

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COMPARATIVE RISK PROJECT

Report of the Non-Cancer Work Group

February, 1987

NOTICE

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Chapter 1: Introduction

The non-cancer work group was asked to devise a ranking methodology and to rank the 31 environmental problems according to the relative magnitude of the non-cancer health risks they pose. This task was exceedingly difficult.

There are thousands of different chemicals* in the environment that may cause adverse human health effects. Many of the 31 environmental problems involve large numbers of these chemicals: at least 129 priority pollutants are of concern in surface water, there are some 600 registered pesticide active ingredients, about 75 chemicals are under study as hazardous air pollutants, and Appendix VIII lists 400 hazardous constituents of concern at hazardous waste management units. Little is known about the toxicological properties of most of these chemicals; only a few have good information on their health effects and potency and on the extent of human exposure to them.

Even if such data did exist for all chemicals, reaching a judgment on aggregate risks from a group of chemicals constituting an environmental problem would be difficult. Different chemicals produce different adverse effects, ranging from effects of lesser concern (e.g., dental mottling from fluoride in drinking water) to severe ones (e.g., death from pesticide poisoning). Entirely different health effects may arise from a single chemical when exposure occurs at different levels or by different routes. Dose-response functions are generally non-linear, with most, but not all, non-cancer health effects thought to involve thresholds. Effects for a given dose may differ depending on whether the exposure was acute, subchronic, or chronic. Different individuals may react differently to the same chemical; some substances at typical ambient concentrations are of concern only to sensitive subpopulations such as asthmatics or infants. And, a health effect may even be more specific; for example, it may show up only when the asthmatic is exercising.

In short, to the extent we do have knowledge about non-cancer health effects from toxic chemicals, it is highly particularized and difficult to aggregate. There is no accepted common denominator by which to compare different health effects. (In contrast, when analyzing cancer effects, the generally accepted method is to treat different sorts of cancers as equivalent and estimate aggregate cancer incidence. In analyzing welfare effects, diverse problems can be expressed in common terms as dollar losses.) We can make no simplifying linear assumptions to allow us to aggregate non-cancer effects over time and across populations.

EPA therefore has had great difficulty in analyzing non-cancer health effects. In September 1986, EPA promulgated a series of risk assessment guidelines in the Federal Register. Conspicuously missing from the set (both proposed and final) were the guidelines on how to assess risks from "systemic toxicants" (i.e., non-cancer effects excluding reproductive, developmental and mutagenic effects). One reason was that members of the work group on these guidelines

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* In this report, we use the term "chemicals" or "substances" very loosely, to refer generally to a wide variety of agents -- including chemicals, radiation, pathogens, and other things -- that can cause adverse non-cancer health effects through environmental exposure.

from different offices within EPA approached assessment of these effects differently. The work group has recently reconvened to complete work on the guidelines.

Most program offices do not actually assess risks from non-carcinogens. Instead, they identify a "safe" level for which no adverse effects are expected to occur in humans. This is often determined by reducing the no observed adverse effects level (NOAEL) seen in animals by one or more uncertainty factors. Most programs aim to control levels down to this "safe" level, sometimes known as an acceptable daily intake (ADI) or reference dose (RfD)*. Most programs merely evaluate the extent to which a regulatory option prevents exposures above the RfD without an explicit calculation of risk. This type of analysis may not be well suited to comparisons of aggregate risks across environmental problem areas because RfDs for different chemicals may protect against different health effects that vary widely in their severity. In addition, the shape of the dose-response function at levels above the RfD probably varies substantially across chemicals.

A few EPA programs do use methods for assessing and/or aggregating non-cancer risks. The Office of Air and Radiation's program for National Ambient Air Quality Standards (NAAQS) uses a probabilistic approach to calculate the uncertainty and expected incidence of various health effects associated with alternative exposure levels. The Office of Policy, Planning and Evaluation's Integrated Environmental Management Program and the Office of Solid Waste and Emergency Response's WET and Liner-Location models use slightly varying approaches to establishing no-effects thresholds and dose-response functions for exposures above the thresholds. But each of these approaches is controversial, and each applies at most to only about 100 of the thousands of potentially toxic chemicals.

As a result, the non-cancer effects work group had to break new ground to compare the non-cancer risks associated with major environmental problem areas. There was no established procedure for doing this. And even if there were an acceptable method for aggregating and comparing non-cancer health effects, the data with which to do so was certainly not available for the vast majority of toxic chemicals.

With established methods and data lacking, the work group has relied extensively on its judgment. We have ordered this judgment by whatever assessment methods we have been able to develop and by whatever information we have been able to marshall. The conclusions reached by the work group therefore represent judgment and not verifiable fact. In this report we are offering our opinion, or our best bet, as to the relative magnitude of the non-cancer health risks associated with the environmental problem areas examined, and we will lay out the reasoning that has led us to this opinion.

Recognizing that we would be relying heavily on our judgments, we have been careful to create conditions that would make these judgments as informed,

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* The official EPA term for these levels is the reference dose. The term RfD, however, implies Agency approval, which in fact many of the ADIs do not yet have. In this paper, we will refer to these "safe" levels as RfDs whether or not they are approved.

expert and systematic as possible. We think we have been very successful in this effort. The work group consists of senior agency health scientists and program managers from each major EPA program office, all of whom are expert on the data and/or techniques available for assessing non-cancer health risks. The work group has gathered relevant data through extensive canvassing. Its judgments have all been arrived at collegially, and most, after some discussion, have been unanimous.

In sum, the results of this project represent the judgment of a knowledgeable and careful group of EPA professionals. We are the first to admit that critical data and methods necessary to accurately respond to our charge are lacking. Our methods combine qualitative and quantitative factors in rough and probably non-replicable fashion. Despite these caveats, though, we are confident that there really are substantial relative differences in non-cancer risks across major environmental problem areas, and that our relative rankings reflect the gist of these differences. The work group participants feel satisfied with the process they created to rank the problem areas and with the results of the process.

At the same time, the work group emphasizes that none of the assessments, opinions or judgments included in this report were developed for regulatory decision-making purposes, and that they should not be used for such purposes. While the report is based on Agency information used in making scientific assessments and regulatory decisions, this information was evaluated here for different purposes, using different procedures. In particular, the scientific assessments have not been reviewed by any of the Agency's formally constituted groups such as the Office of Research and Development or the Steering Committee, nor have they been peer reviewed by external experts. Also, there has been no public process such as notice and comment. Finally, this report which covers a vast subject area was developed relatively quickly by a selected inter-office work group without full involvement of senior Agency management. For all of these reasons, the work group believes that the report should be used only for priority setting activities and not for other purposes, such as guidance or regulation.

The remainder of this report is organized as follows. Chapter 2 summarizes the results of our ranking of the non-cancer health risks associated with major environmental problem areas. Chapter 3 reviews the process we used to produce these rankings. Chapter 4 presents some overall observations on the project and recommendations resulting from it. The appendix describes the steps and issues in the ranking methodology in further detail.

Chapter 2: Relative Ranking of Environmental Problem Areas

Table 2-1 shows our relative ranking of the non-cancer health effects associated with the 31 environmental problems. We do not feel confident in suggesting a more detailed ranking than into the three categories of high, medium and low. No inferences should be drawn from the order in which the problems are listed within a category. Although the rankings are qualitative, they were developed partly from a quantitative scoring system that suggests that there is a difference in aggregate risk from one category to the next of about two or more orders of magnitude. Thus we believe the differences in risk between the categories are substantial.

The table also characterizes our degree of confidence in the ranking assigned to each problem. The degree of confidence notation reflects the extent and quality of data that were available to us in making this assignment. In most cases, we have not let our degree of confidence affect our ranking of a problem. If, for example, a problem appears to be high risk but on the basis of only sketchy information, we leave it ranked as high risk. But we would not be overly surprised if further information came to light at some point that would cause its ranking to change. In two cases -- indoor radon and radiation other than radon -- we moved a problem down from the ranking it otherwise would have had because of some uncertainty about the data responsible for the initial high placement. (And also because the major effect in question [mutagenesis] is very closely related to carcinogenesis, which is covered by another group.)

Finally, Table 2-1 also shows the approximate percentage of the non-cancer risks for a problem area that are associated with the specific chemicals we studied. This is important because we ranked a problem area mostly by considering a few specific chemicals that we thought represented the problem area. Where the chemicals we studied represent most of the problem, the entire problem is not much different from the sum of the components we studied. For example, for criteria air pollutants we studied six chemicals -- ozone, sulfur oxides, particulate matter, acid aerosols, carbon monoxide and lead -- leaving out only nitrogen dioxide. With the six studied chemicals, we are confident that we have considered the bulk of the non-cancer risk associated with criteria air pollutants. For pesticide residues on food, though, we studied only three chemicals (EPN, aldicarb and diazinon) of the perhaps 160 that may show some problem with dietary residues exceeding a level of concern for non-cancer health effects. In this case, the sum of the chemicals we studied constitutes only a small fraction of the total risks attributable to pesticide residues on food. In another case, although we studied only six of the hundreds or thousands of chemicals of concern in indoor air, we thought environmental tobacco smoke was such a large component of the total risk that the chemicals we studied represented perhaps half of the risks from indoor air pollutants.

Our final ranking of the 31 problem areas incorporates the proportion of the problem we had covered with the chemicals we studied. In performing sensitivity analyses involving different ways of scaling up from individual chemicals to entire problems (see Chapter 3), four problem areas moved between the high and medium risk categories depending on the approach chosen. These problem areas included: hazardous air pollutants, pesticide residues in food, worker exposures and consumer exposures. We decided ultimately to rank each of these four in the high risk category; partly because the chemicals we had studied in each were such a small fraction of the problem, and partly because some of the different mathematical approaches suggested a high ranking in the first place.

Table 2-1 Relative Ranking of Environmental Problem Areas

Problem Area	Level of Confidence*	% of Problem Covered*
High Non-Cancer Risks		
Criteria air pollutants (#1)	High	30-100
Hazardous air pollutants (#2)	Medium	<3
Indoor air pollutants - not radon (#5)	Medium	30-100
Drinking water (#15)	High	30-100
Accidental releases - toxics (#21)	High	30-100
Pesticide residues on food (#25)	Medium	<3
Application of pesticides (#26)	High	3-10
Consumer product exposure (#30)	Medium	3-10
Worker exposure to chemicals (#31)	High	<3
Medium Non-Cancer Risks		
Radon - indoor air (#4)	Low	30-100
Radiation - not radon (#6)	Medium	30-100
UV radiation/ozone depletion (#7)	Low	30-100
Indirect discharges (POTWs) (#10)	Medium	3-10
Non-point sources (#11)	--	--
To estuaries, coastal waters, oceans (#13)	Medium	30-100
Municipal non-hazardous waste sites (#18)	Medium	10-30
Industrial non-hazardous waste sites (#19)	Low	30-100
Other pesticide risks (#27)	Medium	10-30
Low Non-Cancer Risks		
Direct discharges (industrial) (#9)	Medium	3-10
Contaminated sludge (#12)	Medium	30-100
To wetlands (#14)	--	--
Active hazardous waste sites (#16)	Medium	10-30
Inactive hazardous waste sites (#17)	Medium	10-30
Mining waste (#20)	Low	30-100
Releases from storage tanks (#23)	--	--
Unranked		
Other air pollutants (#3)	--	--
CO_2 and global warming (#8)	--	--
Accidental releases - oil spills (#22)	--	--
Other ground-water contamination (#24)	--	--
New toxic chemicals (#28)	--	--
Biotechnology (#29)	--	--

* For some problem areas, the work group did not believe it had sufficient information to fill out these columns.

Although there are other problem areas where we studied only a small portion of the problem (e.g., direct and indirect discharges to surface water), we did not believe that this alone provided a sufficient reason to move them to a higher risk category.

As noted, our ranking of a problem area depends primarily on an evaluation of a few chemicals we thought were representative of the problem area. For each chemical we studied, we accumulated data on the health effects it can cause, the potency of the chemical in causing these health effects, and the amount of exposure to the chemical. We devised a scoring system to combine data for multiple chemicals on severity of health effects, potencies and exposures into a single ranking for an environmental problem area. In a few cases we used data on the incidence of health effects from a chemical rather than data on potency and exposure. And in some cases where data were lacking we proceeded directly to ranking a problem area without detailed consideration of individual chemicals. Table 2-2 summarizes our rationale for ranking each of the 31 environmental problem areas as we did.

Observations on the Ranking:

- Criteria air pollutants and indoor air pollutants other than radon ranked high generally because of large numbers of people exposed and because ambient levels are frequently well above levels of concern.

- Drinking water risks were high, because of the very large numbers of people exposed to levels often above RfDs. However, the pollutants that resulted in a high ranking for drinking water may surprise the general public (although the drinking water program office has for some time been aware of this pattern). In general high risks do not seem to come from chemical contaminants entering drinking water from waste disposal, but instead from disinfection by-products, lead from pipes, and pathogens.

- Risks to applicators from pesticides were high because of serious health effects, frequent high levels of exposure, and high documented incidence. These risks rank high despite the limited number of applicators exposed.

- Risks from hazardous air pollutants, pesticide residues on food, and consumer exposures were ranked high because of large numbers of people exposed and potentially serious health effects. Although exposure concentrations associated with these problems are not usually high relative to RfDs, the work group thought that it was probably observing only "the tip of the iceberg" among the thousands of potentially toxic chemicals in these areas.

- Nearly all of the environmental problems that were ranked as low or medium risk were characterized generally by indirect routes of human exposure. Such problems included direct and indirect discharges to surface water, non-point sources, pesticide runoff, estuaries, wetlands, hazardous and non-hazardous waste disposal, sludge, mining waste, and storage tanks. In all these areas, moderate to small numbers of people were exposed to pollutants, at levels usually not far above RfDs. In these areas, there is usually substantial opportunity for pollutants released into the environment to degrade,

Table 2-2 Rationale for Ranking of Environmental Problem Areas

Problem Area and Rank	Substances Studied	Comments
1. Criteria air pollutants [Ranked HIGH]	o Lead o Carbon monoxide o Sulfur dioxide o Particulate matter o Acid aerosols o Ozone	Problem area ranking dependent mostly on ozone and acid aerosols. Ozone has large numbers of people exposed at levels far above safe levels. Acid aerosols has large numbers of people exposed, with a severe health effect (increased mortality) possible. In general, large populations exposed to most criteria air pollutants with moderate to severe health effects.
2. Hazardous air pollutants [Ranked HIGH]	o Benzene o Carbon tetrachloride o Chlorine o Chromium o Formaldehyde o Hydrogen sulfide	Exposed populations are again large, but endpoints are less severe (generally pulmonary irritation). Benzene has large population exposed, with a more significant health effect possible (bone marrow hypoplasia), but with typical ambient concentration only slightly above the RfD. Ranked high partially because of low proportion of problem covered by the substances studied.
3. Other air pollutants [Unranked]	--	Thought to be low risk. No serious health risks suggested from noise, odor, fluorides.
4. Indoor radon [Ranked MEDIUM]	o Radon	Incidence modeling suggests high ranking; perhaps 200 cases per year of serious mutagenic and teratogenic effects. Ranking revised to medium because of some uncertainty about this estimate and because effects are closely related to cancer. Effects are spread over many generations. Very large population exposed, with severe endpoints but low probability of effects.
5. Indoor Air - other than radon [Ranked HIGH]	o Benzene o Carbon tetrachloride o Environmental tobacco smoke	Large populations exposed to these pollutants above levels of concern. Endpoints are moderate to severe (from jaundice to mortality and teratogenicity), and ambient levels are often substantially above RfDs.

Table 2-2 (Continued)

Problem Area and Rank	Substances Studied	Comments
5. Continued	o Formaldehyde o Nitrogen dioxide o Xylene	Environmental tobacco smoke thought to contribute the largest portion of total risk.
6. Radiation - other than radon [Ranked MEDIUM]	o Occupational o Consumer	Incidence modeling suggests high ranking; perhaps 160 to 220 serious mutagenic and teratogenic effects per year. Ranking revised to medium because of some uncertainty about this estimate, and because effects are so closely related to cancer. Very large populations exposed to consumer radiation, with severe endpoints but low probability of effects. Assessment does not consider possible non-cancer effects due to non-ionizing radiation such as microwaves or powerlines.
7. Ozone depletion [Ranked MEDIUM]	o Ultraviolet radiation	Ozone depletion and increased UV radiation will increase risks of moderately serious eye damage (e.g., cataracts) to the entire population. One percent ozone depletion estimated to increase incidence of senile cataracts by 10,000-30,000 per year. Other effects on immune systems possible but not considered.
8. CO_2 and global warming [Unranked]	--	Considered mostly an ecological problem.
9. Direct discharges to surface water [Ranked LOW]	--	Ranked as an entire problem without data on specific substances. Problem area defined to exclude POTWs, which are included in problem area # 10. Risks via consumption of fish and shellfish that have bioaccumulated toxics or that are contaminated by pathogens thought to be low. Risks via consumption of drinking water contaminated by surface water discharges thought to be minimal.

Table 2-2 (Continued)

Problem Area and Rank	Substances Studied	Comments
10. Indirect discharges to surface water [Ranked MEDIUM]	--	Ranked as an entire problem without data on specific substances. Problem area defined to include POTWs and indirect dischargers that contribute to them. Moderate concern for bacteriological contamination of fish and shellfish from inadequate sewage treatment, including combined sewer overflows.
11. Nonpoint discharges to surface water [Ranked MEDIUM]	--	Ranked as an entire problem without data on specific substances. Moderate concern for bacteriological contamination of fish and shellfish from agricultural and urban runoff. Some concern for runoff and bioaccumulation of pesticides in fish and shellfish. Some concern for toxics in sediment and effects via fish or drinking water.
12. Contaminated sludge [Ranked LOW]	o Lead o Cadmium	Human exposure to contaminants in sludge thought to be indirect and extremely limited.
13. Discharges to estuaries, coastal waters, oceans [Ranked MEDIUM]	--	Ranked as an entire problem without data on specific substances. Primary exposure route is through consumption of contaminated fish and shellfish. Both pathogens and toxic chemicals are important concerns.
14. Discharges to wetlands [Ranked LOW]	--	Ranked as an entire problem without data on specific substances. Same concerns as for estuaries, but much lower consumption of contaminated food or water from wetlands.
15. Drinking water [Ranked HIGH]	o Lead o Pathogens o Legionella o Nitrates o Chlorine disinfectants	Generally very large exposed population and serious health effects (neurotoxicity, mortality) are possible, but exposures not often far above levels of concern. Primary concerns were over disinfection byproducts, lead, and pathogens.

Table 2-2 (Continued)

Problem Area and Rank	Substances Studied	Comments
16. Active hazardous waste sites [Ranked LOW]	—	Ranked as an entire problem without reference to specific substances. Very low number of humans potentially exposed around active hazardous waste sites. Exposure concentrations also thought to be low relative to levels of concern. Substances involved are generally of moderate toxicity.
17. Inactive hazardous waste sites [Ranked LOW]	--	Ranked as an entire problem without reference to specific substances. Moderate number of people potentially exposed around inactive hazardous waste sites, but exposure concentrations thought to be usually low relative to levels of concern. Substances involved are generally of moderate toxicity.
18. Municipal non-hazardous waste sites [Ranked MEDIUM]	--	Ranked as an entire problem without reference to specific substances. Large number of people potentially exposed, due to large number of such sites and proximity to populations. Exposure concentrations thought to be very low relative to levels of concern because of low concentration of hazardous constituents in such sites and indirect routes of exposure. Substances involved are generally of moderate toxicity.
19. Industrial non-hazardous waste sites [Ranked MEDIUM]	--	Ranked as an entire problem without reference to specific substances. Moderate number of people potentially exposed. Exposure concentrations may not always be low relative to levels of concern because wastes are concentrated in these sources and controls are often not extensive. Substances involved are generally of moderate toxicity.

Table 2-2 (Continued)

Problem Area and Rank	Substances Studied	Comments
20. Mining waste [Ranked LOW]	--	Ranked as an entire problem without reference to specific substances. Low number of people potentially exposed due to distance of sites from population. Low concentrations when exposure does occur. Low toxicity substances.
21. Accidental releases (toxics) [Ranked HIGH]	--	Ranked as an entire problem without reference to specific substances. Incidence data show very substantial morbidity and mortality. Working lifetime risks to chemical plant and transportation workers estimated at about 8×10^{-4} for death and 2.7×10^{-2} for morbidity. Chronic risks are believed to be small compared with acute risks (most incidents counted result from fires and explosions). Perhaps 1-5% of risks are borne by individuals other than chemical workers.
22. Accidental releases (oil spills) [Unranked]	--	Risks thought to be small and primarily of ecological concern.
23. Releases from storage tanks [Ranked LOW]	--	Ranked as an entire problem without reference to specific substances. Risks thought to be small. Relatively few health impacts reported, controls fairly good, and people take averting behavior to avoid chronic risks when motor fuel contaminates drinking water.
24. Other ground-water contamination [Unranked]	--	Risks exclusive of those covered under other source categories are generally thought to be small. Difficult to assess magnitude of problem involving bacteriological contamination of private wells by septic systems.

Table 2-2 (Continued)

Problem Area and Rank	Substances Studied	Comments
25. Pesticide residues on foods [Ranked HIGH]	o Aldicarb o Diazinon o EPN	Large populations exposed. Potentially serious health effects (acetylcholinesterase inhibition). Level of exposure not often much higher than levels of concern. Could have been ranked as medium risk but for the fact that these three pesticides represent only a very small fraction of the problem.
26. Application of pesticides [Ranked HIGH]	o Dinoseb o Ethyl parathion o Paraquat	Modest applicator populations exposed (10,000-250,000). Potentially very serious health effects (acute poisoning, fetotoxicity, teratogenicity). Exposures often far above levels of concern. Substantial incidence estimates: 350 annual poisonings from ethyl parathion, 100 from paraquat.
27. Other pesticide risks [Ranked MEDIUM]	o Aldicarb o Carbofuran o Chlordane	Large populations exposed to pesticides in drinking water, very large number exposed to pesticides in indoor air. Potential health effects moderate (increased liver weight) to serious (acetylcholinesterase inhibition). Exposures typically low relative to levels of concern.
28. New toxic chemicals [Unranked]	--	No satisfactory method for projecting what risks will be. Risks may be low, as new chemical review program weeds out many potential problems.
29. Biotechnology [Unranked]	--	No satisfactory method for projecting risks. Suspect risks to be low.
30. Consumer product exposure [Ranked HIGH]	o 2-ethoxyethanol o Methylene chloride o Formaldehyde	Large populations exposed to all these substances. Ambient exposures can be at levels well above RfDs. Serious health effects possible, including teratogenicity and hepatotoxicity. Methylene chloride seems to present greatest risks. Substances studied represent very small portion of the problem.

Table 2-2 (Continued)

Problem Area and Rank	Substances Studied	Comments
31. Worker exposure to chemicals [Ranked HIGH]	o 2-ethoxyethanol o Methylene chloride o Perchloroethylene o Formaldehyde	Exposed population of workers somewhat smaller than the consumer category, but still at least 300,000 for each substance. Workplace concentrations can be extremely high, exceeding RfDs by over three orders of magnitude in some cases. Substances studied represent very small portion of the problem.

dissipate, or be diluted before exposure occurs. The problems among this group that ranked higher than the others (non-point sources, indirect discharges to surface water, estuaries and non-hazardous waste sites) did so primarily because of greater proximity to potentially exposed populations and/or large volumes of pollutants.

- Worker exposures entailed very high risks, despite the limited numbers of people exposed in occupational settings. Occupational exposures appear to rank as high risk even on a population-risk basis. This is because of the far higher concentrations at which contaminants can be found in the workplace relative to those observed in the environment.

- Three problem areas -- accidental releases of toxics, radiation other than radon, and indoor radon -- were initially ranked as high risk on the basis of incidence data. Observed incidence of mortality and morbidity from accidental releases clearly place it in the high risk category. Estimates of the effects from radiation exposures accounted for their initially high ranking, and were considered by the work group to be more uncertain. One reason these results were surprising is that these sorts of risks (e.g., injuries from accidents in transporting hazardous substances, risks from radiation in building materials and televisions) are conceptually familiar and small from the standpoint of personal risk. But this does not mean that such risks are negligible; exposures to these risks occur with such frequency in our society that they may add up to very substantial problems. Ultimately, because of the uncertainty associated with the estimates of genetic effects from radiation and because these effects are so closely related to carcinogenic effects that will be considered by another work group, the work group revised the initial rankings of the two radiation problem areas from "high" to "medium".

Upon reflection, the work group continues to agree with the high rankings given to occupational exposures and accidental releases of toxics.

Chapter 3: Methodology for Ranking Non-Cancer Health Risks

In the absence of any conventional method for assessing and aggregating non-cancer health risks, we developed our own procedure. This chapter briefly describes the method used by the work group to rank the 31 problem areas. A full description of this process is included in the appendix to this report.

Shortly after starting this project, we realized that the 31 problem areas involved numerous different substances with the ability to cause numerous different health effects. There appeared to be no strong pattern to the sorts of health effects associated with a particular environmental problem; the association was much stronger between health effects and chemicals, with a problem representing the sum of the diverse effects caused by its component chemicals. We made an early decision to focus on a limited number of substances associated with each environmental problem that are representative of the problem and are reasonably well understood. We would then try to scale up from the representative substances to the entire problem.

The work group developed a format for recording existing data on representative substances. These "summary sheets" were prepared for nearly all of the 31 environmental problems. They included the following information:

- A selection of 3-6 substances to represent the environmental problem, and a description of the rationale for selecting these substances.
- An estimate of the proportion of risk associated with the entire problem that is accounted for by the selected substances.
- Data on health endpoints, levels of toxicological concern (RfDs, NOELs, etc.), ambient concentrations, exposed populations, incidence, and other information bearing on the magnitude and severity of the risks from each selected substance.
- Sources and methods for the data on the selected substances.

To assess the risks from each selected substance, we used a logic akin to that used in calculating the number of cases expected from a chemical:

Exposure x Potency = Incidence

We could then aggregate the differing health effects caused by a single substance into a total risk from that chemical through use of a severity index.

The data available on health effects from and exposures to toxic substances were far from adequate to perform these calculations in a quantitatively precise way. Exposure or potency data were frequently not available for the substances of interest. When data were available, they were of highly variable quality. They were often generated using different and incompatible procedures by different programs, and they reflected very different degrees of conservatism.

Thus, the work group added its judgment to these data and developed a semi-quantitative scoring system with which to represent key attributes for each selected substance. Scores were developed to cover:

- o The severity of the health endpoints caused by the substance. A subcommittee of health scientists developed a severity index that assessed the extent to which any health effect threatens the viability of the individual subjected to it. Over 100 health endpoints associated with the selected substances were scored as to their relative severity.

- o The population exposed to the substance.

- o The potency of the substance at the ambient concentration or dose to which this population is exposed. This potency was represented by the ratio between the dose at which exposure occurs and the RfD for the substance. The higher this ratio, the greater the probability of the health effect occurring, or the greater the potency. This ratio can also be thought of as an index of the individual risk at a specific concentration of a substance. The work group debated basing this index on the LOAEL or NOEL rather than on the RfD. This decision may have influenced the final rankings somewhat (see Appendix), but no sensitivity analysis was performed on it.

We tried to develop these three scores consistently for all the selected substances. We used a different method when available data covered incidence of a health effect from a substance rather than exposure and potency (see Appendix). When data on individual substances were lacking, the work group used its best judgement to score a problem area as a whole without reference to its component substances. In a few other cases when available information was minimal, the entire problem area was ranked without developing component scores. Finally, we did not rank at all some problem areas where we could not develop any way to estimate risks.

We combined these three scores -- representing the severity of the endpoints, the exposed population, and the likelihood of an effect given an exposure-in various alternative ways to produce tentative risk rankings of substances and of problem areas. We paid special attention in sensitivity analysis to ascertaining whether ranking by individual risk would yield results much different from ranking by population risk. It did not. In addition, different approaches were used to aggregate scores from selected substances into scores for an entire problem. With different approaches, a few problems (hazardous air pollutants, drinking water, worker and consumer exposures) moved between the medium and high risk categories. All were ultimately ranked high.

We reviewed the various tentative rankings of problem areas and developed our own qualitative ranking of problem areas that was consistent with most of the tentative rankings. We assigned problem areas to categories of high, medium or low non-cancer risks. The available quantitative data underlying the scores suggest that there is about a 2+ order of magnitude difference in risk between each successive risk category. As a final step in the ranking, we adjusted the rankings slightly to reflect the quality of data on each problem and the proportion of each problem we had covered with the substances we studied.

The appendix includes a full discussion of the major methodological or data problems we encountered, how we resolved them, and how satisfied we are with their resolution.

Chapter 4: Observations and Recommendations

In this concluding chapter we present summary observations and recommendations from the project. Chapter 2 included our final rankings of non-cancer health risks associated with the 31 environmental problem areas. In this chapter, we present conclusions of a broader nature; ones that are not specific to a particular problem area. We have divided our observations and recommendations into substantive and procedural categories.

Substantive Conclusions:

1. There is a wide disparity between the amount of risk we estimate for many problem areas and the amount of attention EPA gives these areas. High-risk areas to which EPA devotes relatively little attention include:

   - o Indoor air
   - o Accidental releases of toxics
   - o Consumer product exposure
   - o Worker exposure to chemicals

   Low-risk areas to which EPA devotes relatively large amounts of attention include:

   - o Direct point source discharges (industrial)
   - o Active hazardous waste sites (RCRA Subtitle C)
   - o Inactive hazardous waste sites (Superfund)
   - o Releases from storage tanks (UST)

   There are undoubtedly some good reasons for this disparity between risk and program attention:

   - o We have assessed only one class of risks. A program that ranks high or low in non-cancer risks may rank differently when other sorts of risks are considered, such as ecological, welfare, or cancer risks.

   - o We have assessed the residual risks remaining now in each environmental problem area. That is, we have taken credit for all of EPA's previous activities and incorporated their effects into the baseline. A large program effort may still be necessary (e.g., in enforcement) to hold future risks to these residual levels.

   - o We have not considered the controllability of the risks in our ranking. It may make sense to focus EPA resources where we can have the largest impact in risk reduction. This may not correlate precisely with relative risk.

   - o Other factors besides risk are also important determinants of the appropriate level of effort to devote to a problem area. These include statutory mandates, public demands, and the responsibilities of other agencies and governments.

   One principle in allocating resources is that EPA should put resources where they will "do the most good." More precisely, a marginal increment of resources in dollars or manpower should be allocated to the activity

where it will result in the greatest reduction in risk. We can evaluate the potential for the greatest reduction in risk by determining: (1) the existing risk in each problem area, (2) the availability of technical methods to reduce that risk, and (3) the availability of regulatory tools that will lead to the use of the technical solutions to reduce the risk. Our ranking concentrates only on the first of these three components. An evaluation of all three is essential in order to make a logical decision on resources.

We believe another distinction is important regarding the relationship between the non-cancer analysis (as well as this risk project as a whole) and EPA resource allocation. Our work suggests areas to which additional resources should be devoted, but does not suggest areas from which existing resources should be withdrawn. We focused only on residual risks given existing regulatory programs. We did not attempt to estimate the risks that existed before application of these programs. Without estimates of these risks, we cannot judge the value of these programs at current resource levels, nor can we guess what the effect of reductions in these programs would be.

In sum, we support organizing environmental protection more around the fundamental goal of reducing demonstrable risks. EPA management should consider providing incremental program resources to areas promising higher risk reduction. At a minimum, EPA should devote substantially more R&D resources to the seemingly high risk areas that are not already getting them, in order to confirm or refute judgments about these areas. Such areas should include indoor air, accidental releases of toxics, and consumer and worker exposures. EPA should also engage the public and the Congress in a dialogue on this so that over time, environmental statutes will represent risk priorities.

2. In many of the areas we identify as high risk, EPA has vague or non-existent regulatory authority to prevent emissions or limit exposures. In fact, EPA seems more likely to have explicit regulatory authority in areas that we rank as medium or low risk than in areas of high risk. Often this occurs because EPA's regulatory authorities in these other areas have helped reduce their risks.

   In important areas where EPA has only tenuous or indirect regulatory authority — indoor air, accidental releases, consumer product exposure, and occupational exposures — EPA should intensify its use of broad non-regulatory authorities. Such authorities include research and development, information gathering (TSCA Sections 4 and 8), technical assistance, referral to other agencies (TSCA Section 9), and public education. All available statutes should be used to solve problems. These authorities may be very effective in reducing risks. In particular, EPA now conducts little public health education, and should do more. Successful efforts in areas including radon, health advisories (on drinking water contaminants and on used oil) and misfueling suggest the effectiveness of public education.

3. Workplace exposures to toxic chemicals were often extremely high relative to ambient exposures. EPA should make much more extensive use of TSCA's authorities to address this area.

4. A few chemicals were cited as major concerns in multiple problem areas.

These chemicals include lead most prominently, and also cadmium, carbofuran, chromium, dinoseb and formaldehyde. EPA should consider developing cross-program integrated strategies for dealing with these key toxics. The integrated strategies might include comprehensive information gathering on sources and total exposure, cross-program comparison of cost-effectiveness of options to reduce exposure, and promulgation of regulatory programs drawing upon authorities under multiple statutes.

5. Our analyses of exposures in different problem areas point out some important relationships between programs. Many programs aim to prevent the release of pollutants that can eventually find their way into drinking water and cause health risks. These prevention programs include primarily the surface water (direct, indirect, and non-point discharges), hazardous and non-hazardous waste (RCRA C and D, CERCLA), storage tank, other ground-water contamination and pesticide runoff programs. The drinking water program provides summary information on the risks that are missed or not abated by these prevention programs. These prevention programs, though, take little advantage of the information available on contaminants ultimately in drinking water. The information on drinking water contaminants should be critical in establishing priorities within a prevention program (e.g., the contaminants eventually causing highest risks should be of greatest priority) and between prevention programs (e.g., the programs that can abate eventual drinking water risks most effectively should be of greatest priority).

   A similar observation might be made about indoor air as another program with a growing data base on health risks. Prevention programs involving consumer product exposures, pesticides (indoor), drinking water (VOCs), and radon should use data on comparative risks of different indoor exposures for priority setting.

6. Concern about health impacts from radiation has traditionally focused on cancer. Modeling of mutagenic and teratogenic effects, primarily because of the large populations exposed, results in substantial projected incidence. Further research on these non-cancer effects of radiation, as well as on effects from non-ionizing radiation, is appropriate.

Procedural Conclusions:

1. EPA should make a concerted effort to increase its knowledge about non-cancer risks to human health as they relate to EPA's responsibilities. In general, we possess only poor data and inadequate methods for assessing non-cancer risks.

2. All programs need higher-quality data on exposure to substances capable of causing non-cancer health effects. Exposure information currently is shamefully poor, even on the highest-priority chemicals that are objects of major regulatory efforts. Exposure information, when it exists, is often based upon inconsistent methods. Exposure estimates in different areas exhibit fundamentally different degrees of conservatism. Even in areas when EPA has a relatively greater amount of good information (e.g., criteria air pollutants), there still remain major uncertainties with respect to dose-response and exposure relationships for many of the pollutants examined. EPA should dedicate resources to collect the data needed to assess non-cancer risks. EPA should consider getting stronger statutory authority and using existing authority more fully to have others (e.g., manufacturers, dischargers)

also generate exposure data.

3. EPA has no consistent methods for assessing non-cancer risk, making it difficult to compare results across programs. A few general methods are in limited use -- OSW's WET and Liner-Location Models and OPPE's Integrated Environmental Management approach -- but they are not widely accepted. This lack of a consistent methodology does not characterize assessment of cancer risks. The Risk Assessment Forum should make development of general methods of assessing non-cancer risks a high priority.

4. A particular methodological problem is the lack of a dose-based model of non-cancer effects that is able to deal with both severity and incidence. EPA's traditional focus on NOELs, LOELs, RfDs, and margins of safety is insufficient. Characterizing a dose-response function at levels above the RfD is important. Scientists should be encouraged to report differences in severity of effect, as well as incidence, at varying doses in animal and human studies.

5. The results of our ranking reflect great uncertainties about appropriate methods, exposed populations, exposure levels, dose-response functions, and comparison of health effects. The quality of data used also varies greatly. Large amounts of qualitative judgment have gone into the rankings. While the rankings represent the disciplined opinions of experts, they are still only opinions. These rankings would not withstand rigorous scientific peer review or judicial review. The Agency should be very careful about how the non-cancer study is portrayed in the final report on this risk project, and how the rankings are used.

6. Despite the extensive difficulties and uncertainties in assessing non-cancer risks in the 31 problem areas, we are reasonably confident that there <u>are</u> major differences in non-cancer risks between problem areas, and that our rankings have accurately captured these differences. We believe that there are generally about two orders of magnitude difference in risk between problems that we have placed in different categories.

7. Very large amounts of valuable staff time have been spent on this project. On the whole, we believe this investment was worthwhile. However, this effort should not be repeated again within the next few years. It will take a substantial period of time before data and methods for non-cancer risk assessment can be meaningfully improved. And, many of our conclusions seem robust enough to resist major changes, should we perform this project again in the near future.

8. During the work group meetings, it became apparent that most of us knew little about each others' program areas. One of the most effective ways that EPA can move toward a more integrated view of environmental protection is for staff and managers to have a comprehensive appreciation of environmental problems and programs. Personnel transfers, training, and other means of encouraging a cross-media and cross-program perspective should be increased.

9. The Risk Assessment Forum and the Risk Management Council should be directed to monitor progress EPA is making in collecting necessary information, developing methodologies, and using non-cancer risks in decision-making.

APPENDIX

METHOD FOR ASSESSING NON-CANCER HEALTH RISKS

In the absence of any conventional method for assessing and aggregating non-cancer health risks, the work group developed its own procedure. This chapter describes the steps the work group went through.

1. Establishing the Work Group

The work group consisted of at least one representative from each of EPA's program offices, the regions, the Office of Research and Development and the Office of Policy, Planning and Evaluation. Most of these individuals are health scientists with extensive experience at EPA. All have access to relevant data, studies and other experts in their individual program areas. The chairperson of the work group was Marcia Williams, the Director of the Office of Solid Waste and formerly the Deputy Assistant Administrator of the Office of Pesticides and Toxic Substances. In short, the work group was chaired and staffed by individuals with broad and appropriate expertise for the task.

2. Initial Decisions on Project Methodology

The work group's assignment was to assess the non-cancer health risks associated with the 31 environmental problem areas, and to produce a relative ranking of the 31 areas by non-cancer risk. The 31 areas were defined in a common fashion for this and the other three work groups (cancer, ecological and welfare).

In general, the work group planned to go as far as it could in assessing non-cancer risks quantitatively. It would use the standard approach (exposure x potency = incidence) to calculate cases of adverse health effects from exposures to a chemical, and then sum across chemicals to obtain total risks for a problem area. Cases of different health effects might be aggregated if an appropriate severity index could be agreed upon. Gaps in quantitative knowledge would be filled through qualitative analysis or Delphi procedures. The work group was ultimately unable to get very far with the quantitative approach alone.

An initial effort was made to collect easily available data on non-cancer health effects in major environmental program areas. After reviewing this information, the work group reached three conclusions about further work:

- A common format should be used for acquiring and organizing existing data on the different problem areas.

- Particular health effects are associated more with particular substances than they are with broad problem areas. Information collection should focus on the effects of a substance within a problem area (e.g., the effects of lead in drinking water, the effects of pathogens in drinking water, the effects of lead as a criteria air pollutant) rather than on the problem area as a whole.

- Most environmental problems involve numerous toxic chemicals. Any attempt to be comprehensive and assess the risks from every toxic chemical for a problem area would necessarily fail -- such a task would be too large, and data would be inadequate for a large proportion of the chemicals.

The work group thus decided to focus for each environmental problem on a limited number of chemicals that are representative of the problem and are reasonably well understood. The work group would then try to scale up from the representative chemicals to the entire problem.

3. Summary Sheets

The work group developed "summary sheets" for recording existing data on representative chemicals. These sheets were to be filled out by the program office most knowledgeable about each environmental problem area.

Each summary sheet required the following information on an environmental problem area:

- o Select 3-6 substances representative of the environmental problem and describe the rationale for selecting these specific substances.
- o Estimate the proportion of risk associated with the entire problem that is accounted for by the selected substances. Describe the rationale.
- o Describe the overall approach and sources of data for estimating health effects and exposures in this problem area.

For each of the selected substances, the summary sheet also described the:

- o Most important health endpoints, including the:
  - assumptions used in deciding on endpoints -- for example, whether there are sensitive subpopulations, the nature and quality of the studies providing evidence, etc;
  - particular endpoint that drives regulatory concern for the substance. The particular endpoint for which the RfD is established, or which is observed at the LOAEL; and
  - level at which the substance is of toxicological concern, such as an RfD, ADI, NOEL, LOAEL, potency, NAAQS or other standard or benchmark.
- o Magnitude and severity of the problem, including the:
  - populations exposed to different concentrations of the substance;
  - ratio of the concentration at which environmental exposure occurs to the level at which the substance is of toxicological concern, (the higher this ratio is, the more likely there are to be adverse health effects from actual ambient exposures);
  - effects and severity expected from actual ambient exposures;
  - time dimensions to these exposures: chronic, subchronic, one-hour, 24-hour, etc; and
  - available data on the incidence of the health effect.

Backup pages to each summary sheet were also requested. They were to explain the basis for all these estimates: whether concentration data were modeled or monitored, which models were used, what type of monitoring occurred, where the population data came from, what methods were used in exposure assessment, etc..

Summary sheets were produced for 22 of the 31 environmental problem areas. The work group had decided not to request summary sheets for three problem areas (other air pollutants, CO_2 and global warming and oil spills) because it thought non-cancer health risks in these areas were likely to be minimal and virtually impossible to estimate. For another five problem areas (wetlands, releases from storage tanks, other ground-water contamination, new toxic chemicals and biotechnology) the work group requested summary sheets. However, the program offices did not prepare them because they were unable to develop a method for projecting substances of concern, health effects and exposures for new toxic chemicals and biotechnology and they thought that the non-cancer risks from the other three problem areas were low and simply were not worth the effort of producing summary sheets.

The final data base in the summary sheets included information on 50 chemicals. Many chemicals were selected because they caused concern in more than one problem area. For example, lead appeared in six problem areas, and cadmium, chromium, carbofuran, dinoseb and formaldehyde in four areas. Table A-1 lists the chemicals selected. In all cases the health effects and exposure information on a substance were specific to the problem area for which it was chosen. Thus when lead was chosen to represent criteria air pollutants, the summary sheet included information on effects via inhalation, concentrations in ambient air, etc. When lead was selected to represent drinking water problems, the information pertained to ingestion risks, concentrations in drinking water, etc.

The summary sheets differed very widely in quality. This was largely a function of the amount of pre-existing information available on concentrations, exposures, health effects and risks in each program area. The extent to which information already existed depended in turn, on the historical amount of attention each program office had given to learning about exposure to and the health impacts of substances under its purview. To generalize, the Office of Air and Radiation has the most extensive information on the air pollutants that have been assessed for regulatory purposes. The Office of Water, with the exception of contaminants in drinking water, has very little information available. The Office of Solid Waste and Emergency Response also has little information available, but has recently made a substantial effort to model exposures and health effects via pathways within their purview. The Office of Toxic Substances has good data available on particular existing chemicals with the exception of limited available data on consumer exposures. The Office of Pesticide Programs has extensive data on health effects (including incidence) from pesticides, but is weaker on exposure data.

The summary sheets highlighted some data problems that the work group always knew it would have to deal with. The nature of the data problems varied widely:

- At one extreme were some large, insoluble problems. There is only a small proportion of the thousands of substances in our environment about which we have any toxicological understanding. In the future, numerous substances that we know nothing about today will be found

TABLE A-1 OCCURRENCE OF SUBSTANCES REPORTED IN SUMMARY SHEETS (a)

Substance	Frequency	Problem Areas
Aldicarb	3	11,25,27
Benzene	2	2,5
Cadmium	4	12,16,17,18
Carbofuran	4	9,10,11,27
Carbon tetrachloride	2	2,5
Chlordane, Aldrin, Heptachlor	1	27
Chlorine	2	2,21
Chlorobenzene	1	16
Chromium	4	2,16,17,19
Diazinon	1	25
Dinoseb	4	9,10,11,26
Environmental tobacco smoke	1	5
EPN	1	25
2-ethoxyethanol	2	30,31
Ethyl parathion	1	26
Fluoride	1	20
Formaldehyde	4	2,5,30,31
Hydrogen sulfide	1	2
Lead	6	1,11,12,15,17,18
Legionella	1	15
Mercury	3	9,10,17
Nitrate/Nitrite	2	11,15
Nitrobenzene	1	16
Nitrogen dioxide	1	5
Paraquat	1	26
Pathogens (Giardia/Viruses)	1	15
Phenol	3	16,17,19
Radiation	1	6
2,4,6-Trinitrotoluene	1	16
UV Radiation (Ozone depletion)	1	7
Xylene	1	5
Methylene chloride	2	30,31
Chlorine disinfectants	1	15
Perchloroethylene	1	31
Carbon monoxide	1	1
Sulfur dioxide	1	1
Particulate matter	1	1
Acid aerosols	1	1
Ozone	1	1
Copper	1	11
Zinc	1	11
Radon/Radon daughters	1	4
Endothall	2	9,10
Oxamyl	2	9,10
Glycol ethers	2	30,31
Asbestos	2	30,31
Anhydrous ammonia	1	21
Hydrochloric acid	1	21
Sulfuric acid	1	21

(a) This list consists of chemicals that were mentioned in the summary sheets. Because of significant data gaps in some problem areas, the workgroup scored these entire problem areas rather than individual, representative substances. Therefore, some chemicals listed here do not appear in Tables 2-2 and A-6 which summarize the final rankings.

to have toxic effects. The work group's attitude about such issues was not to try and assess risks that we know nothing about.

- For many substances on which there was sufficient toxicological knowledge, exposure information was incomplete. Gaps would have to be guessed at.

- Where some data existed on a substance in all relevant areas -- health effects, levels of concern, ambient concentrations and exposed populations -- the data frequently did not mesh well. For example, an estimated ambient concentration and an estimated exposed population might not have been generated under identical assumptions. The ambient concentration might derive from monitoring in urban areas, while the exposed population consists of some individuals subjected to lower concentrations in rural areas as well as those subjected to the higher urban ones.

- Even if a reasonably consistent data set could be obtained for a single substance, making the comparisons across substances that are necessary in assessing relative risks can be very difficult. Data on different substances have often been generated under different ground rules. For some chemicals ADIs or RfDs were available, for others there were only NOELs or LOAELs. Some exposure estimates were very conservative upper-bound estimates, while some were maximum likelihood estimates.

- A final data problem related to the variable quality of the estimates. Some estimates were good, precise and generated by reliable methods, while others were little more than guesses. How could they be compared? We are not referring here to comparing estimates of different things where we know there will be some bias in making the comparison (e.g., comparing a conservative worst-case estimate of exposure in one area with an annual average sort of estimate in another area). The work group instead was worried about putting side-by-side and comparing two estimates that were generated under identical ground rules but were nevertheless of substantially different precision. Should we compare the two estimates and simply note the level of uncertainty associated with each? Or should we downgrade the less certain estimate to reflect our lack of confidence in it?

  The most pointed example of this issue ultimately arose in the final ranking of the 31 problems, when criteria air pollutants and indoor radon both seemed to present high non-cancer risks. The data underlying the ranking for criteria air pollutants were strong and reliable. The data behind the radon ranking were sparse, the model used to estimate radon effects was unfamiliar, and the results were surprising. But our best, albeit imprecise, estimate of radon risks were that they were high. The work group had a lengthy argument in this case about whether criteria air pollutants and radon had to be ranked similarly, or could we account for the much lower certainty of the radon estimate by moving radon down in the ranking.

Some of these data problems evidenced in the summary sheets could be mitigated through more effort -- trying harder to find appropriate data, reworking existing estimates to make them more comparable, and developing some quantitative

way for expressing the quality of data, for example. The work group took some of these steps. Some summary sheets were written two or three times, and some estimates were revised to reduce inconsistencies. But the work group decided generally not to go to extreme lengths to improve the data that were available.

In general, time and available resources did not permit extensive reworking of the data base. Instead, the work group adapted the nature of the process it planned to use for ranking the 31 problem areas to the quality of the available data. It was clear that the ideal of quantitatively estimating the number of cases of adverse health effects for each problem area was not feasible. Judgment and qualitative evidence had to be substituted frequently where data were unavailable. As long as existing data were sufficiently accurate to give a rough impression of the magnitude of the quantity being assessed, they were used. If a piece of existing data was probably wrong in some way (e.g., "I'll bet that really is an overestimate"), the work group decided not to spend the time to rework the piece of data, but instead only to appreciate the nature of the likely error. The nature of the ranking process the work group initially wanted to pursue dictated the information that was requested via the summary sheets. But once the summary sheets had been developed, it is fair to say that the nature of the information they contained dictated the further development of the ranking process.

Although it appeared impossible to explicitly estimate the number of cases of health effects as the workgroup had initially hoped, the steps involved in trying to estimate the number of cases continued to provide the organizing principles in the group's ranking process. Cases are a function of exposure to a substance and the potency of the substance. Cases of different health endpoints could be aggregated if they were weighted by some acceptable index of severity. The work group proceeded to evaluate the risks from each representative substance by assessing these three factors: health endpoints, exposure and potency.

4. Health Endpoints

The workgroup had decided to classify all health effects into one of 11 categories: cardiovascular, developmental, hematopoietic, immunological, kidney, liver, mutagenic, neurotoxic/behavioral, reproductive, respiratory and other. At one point the workgroup considered not making distinctions between different effects within a category; counting, for example, all respiratory effects as similar. The ultimate risk ranking might then assess how many respiratory effects a particular problem might cause, how many cardiovascular effects, etc. After some consideration, though, the workgroup decided that it ought to preserve the distinctions among health effects within a category. It made little sense to lump effects of such disparate severity as nasal irritation and emphysema simply because they both involved the respiratory system.

In reviewing the summary sheets, there were 106 different health endpoints listed as being caused by exposure to the selected representative chemicals. These endpoints, cross-referenced to the substances causing them, are listed in Table A-2. However, ranking each of the 31 problem areas by comparing their impacts on 106 different classes of effects was clearly impossible. Some common denominator or sorting procedure had to be developed for these disparate health effects. With aggregating effects by organ or function having been rejected, the work group decided to develop a severity index. Each health endpoint would be assigned a score representing its relative severity.

TABLE A-2 CHARACTERIZATION OF SPECIFIC ENDPOINTS (a)

Specific endpoints	Problem Area (Substance)
Cardiovascular	
unspecified	30[Methylene chloride], 17[Lead], 15[Lead], 31[Methylene chloride]
increased heart attacks	1[Carbon monoxide]
aggravation of angina	1[Carbon monoxide]
increased blood pressure	1[Lead]
mort. from ischemic heart dis.	5[Environmental tobacco smoke]
Developmental	
fetotoxicity	2[Benzene], 5[Benzene]
low birth weight	5[Environmental tobacco smoke], 30[2-Ethoxyethanol], 31[2-Ethoxyethanol], 1[Carbon monoxide]
teratogenicity	26[Dinoseb], 30[2-Ethoxyethanol], 17[Lead], 17[Cadmium], 6[Radiation], 31[2-Ethoxyethanol], 5[Xylene], 2[Carbon tetrachloride], 5[Carbon tetrachloride], 4[Radon]
Hematopoietic	
unspecified	18[Lead], 16[Nitrobenzene]
decreased heme production	17[Lead]
bone marrow hypoplasia	2[Benzene], 5[Benzene]
impaired heme synthesis	2[Hydrogen sulfide], 1[Lead]
methemoglobinemia	15[Nitrate], 11[Nitrate]
leukopenia	2[Benzene], 5[Benzene]
anemia	2[Benzene], 5[Benzene]
thrombocytopenia	2[Benzene], 5[Benzene]
Immunological	
unspecified	15[Chlorine disinfectants], 1[Particulate matter]
herpes	7[UV Radiation/Ozone depletion]
allergic reactions	2[Formaldehyde], 5[Formaldehyde]
increased infections	5[Nitrogen dioxide], 1[Ozone]
Kidney effects	
unspecified	19[Chromium], 19[Phenol], 30[Methylene chloride], 17[Chromium], 16[Chlorobenzene], 16[Chromium], 16[Phenol], 16[Nitrobenzene], 16[Cadmium], 31[Methylene chloride], 30[Methylene chloride]
tubular degeneration	2[Carbon tetrachloride], 5[Carbon tetrachloride], 18[Cadmium], 12[Cadmium], 12[Lead]
dysfunction	17[Cadmium], 17[Mercury]
hyperplasia	17[Phenol]
hypertrophy	17[Mercury], 17[Phenol]
atrophy	17[Mercury], 17[Phenol]
necrosis	17[Mercury]
histopathological alterations	31[Perchloroethylene]
Liver effects	
unspecified	16[Cadmium], 19[Chromium], 17[Chromium], 15[Chlorine disinfectants], 16[Chlorobenzene], 16[Chromium], 16[Phenol], 16[Nitrobenzene]
hepatitis A	15[Pathogens (Giardia/Viruses)]
jaundice	2[Carbon tetrachloride], 5[Carbon tetrachloride]
increased weight	27[Chlordane/Aldrin/Heptachlor]
increased enzymes	27[Chlordane]
necrosis	27[Chlordane]
histopathological alterations	31[Perchloroethylene], 30[Methylene chloride], 31[Methylene chloride]

Note: Problem Area numbers are given in Tables 2-1 and 2-2.

Mutagenicity	
unspecified	2[Carbon tetrachloride], 5[Carbon tetrachloride], 1[Particulate matter], 2[Chromium]
cytogenetic	2[Benzene], 5[Benzene]
hereditary disorders	6[Radiation], 4[Radon]
Neurotoxic/Behavioral	
unspecified	2[Formaldehyde], 25[EPN], 30[2-Ethoxyethanol], 18[Lead], 17[Lead], 15[Chlorine disinfectants], 30[Methylene chloride], 31[2-Ethoxyethanol], 31[Perchloroethylene], 31[Methylene chloride], 9[Mercury], 10[Mercury]
retardation	15[Lead], 6[Radiation], 4[Radon]
reduced corneal sensitivity	2[Carbon tetrachloride], 5[Carbon tetrachloride]
retinal disorders	26[Ethyl parathion], 7[UV Radiation/Ozone depletion]
visual aging	7[UV Radiation/Ozone depletion]
AChE inhibition	27[Aldicarb], 27[Carbofuran], 26[Ethyl parathion], 25[EPN], 25[Aldicarb], 25[Diazinon], 11[Aldicarb], 11[Carbofuran]
learning disabilities (red. cogn.)	15[Lead], 1[Lead], 1[Carbon monoxide], 12[Lead]
neuropathy	17[Mercury], 12[Lead]
irritability	27[Chlordane]
tremors	27[Chlordane]
convulsions	27[Chlordane]
sensory irritation	30[Formaldehyde], 31[Formaldehyde]
micromecurialism	9[Mercury], 10[Mercury]
Reproductive	
unspecified	17[Mercury]
post implantation losses	5[Xylene]
testicular degeneration	2[Carbon tetrachloride], 5[Carbon tetrachloride], 27[Carbofuran], 26[Dinoseb]
spermatocyte damage	30[2-Ethoxyethanol], 31[2-Ethoxyethanol]
decreased testicular weight	30[2-Ethoxyethanol], 31[2-Ethoxyethanol]
aspermia	27[Carbofuran]
increased resorptions	30[2-Ethoxyethanol], 31[2-Ethoxyethanol]
giant cell formation	27[Carbofuran]
increased spontan.abortions	1[Carbon monoxide]
male sterility	11[Dinoseb]
oligospermia	26[Dinoseb]
decreased sperm motility	26[Dinoseb]
Respiratory	
unspecified	1[Particulate matter]
emphysema	18[Cadmium], 12[Cadmium]
nasal irritation	5[Environmental tobacco smoke]
pulmonary irritation	5[Environmental tobacco smoke], 2[Chlorine], 2[Formaldehyde], 2[Hydrogen sulfide], 5[Formaldehyde]
nasal ulceration	2[Chromium]
mucosal atrophy	2[Chromium]
bronchitis	2[Chromium], 5[Environmental tobacco smoke]
pulmonary impairment	5[Nitrogen dioxide], 5[Environmental tobacco smoke]
lung injury	5[Nitrogen dioxide], 1[Ozone]
pneumonia	5[Formaldehyde], 15[Legionella], 12[Cadmium], 5[Environmental tobacco smoke]
pulmonary edema	5[Formaldehyde], 26[Paraquat], 2[Formaldehyde], 2[Hydrogen sulfide], 2[Chlorine]
pontiac fever	15[Legionella]
congestion	26[Paraquat]
hemorrhage	26[Paraquat]
alveolar collapse	26[Paraquat]
fibrosis	26[Paraquat]
lung structure changes	5[Nitrogen dioxide], 1[Ozone], 1[Acid Aerosols], 1[Particulate matter]
aggravation of asthma	1[Sulfur dioxide], 5[Environmental tobacco smoke]

Note: Problem Area numbers are given in Tables 2-1 and 2-2.

increased resp. disease	1[Acid Aerosols]
bronchoconstriction	5[Environmental tobacco smoke]
decreased mid-expiratory flow rates	5[Environmental tobacco smoke]
increased respiratory infections	5[Environmental tobacco smoke], 1[Ozone], 5[Nitrogen dioxide]
altered lung function	1[Particulate matter], 5[Nitrogen dioxide], 2[Chromium], 1[Ozone]
aggrav. of resp. diseases	1[Particulate matter], 1[Sulfur dioxide], 1[Acid Aerosols]
decreas. small airway function	5[Environmental tobacco smoke]
ciliary effects	30[Formaldehyde], 31[Formaldehyde]
infant hospital. for resp. disease	5[Environmental tobacco smoke]
squamous metaplasia	30[Formaldehyde], 31[Formaldehyde]
Other	
unspecified organ effects	16[2,4,6-Trinitrotoluene]
unspecified acute effects	26[Dinoseb]
mortality	5[Environmental tobacco smoke], 15[Legionella], 15[Pathogens (Giardia/Viruses)], 21[Accidental Releases - Toxics (b)] 1[Particulate matter], 1[Acid Aerosols], 1[Sulfur dioxide], 26[Ethyl parathion], 26[Paraquat]
morbidity	21[Accidental releases - Toxics (b)
eye irritation	2[Formaldehyde], 2[Hydrogen sulfide], 5[Environmental tobacco smoke], 5[Formaldehyde]
dental erosion	2[Chlorine]
cataracts	7[UV Radiation/Ozone depletion]
leishmaniasis	7[UV Radiation/Ozone depletion]
adrenal	16[Nitrobenzene]
gastrointestinal disease	15[Pathogens (Giardia/Viruses)], 15[Lead]
bone damage	20[Fluoride]
dental mottling	20[Fluoride]
symptomatic effects(headache)	5[Environmental tobacco smoke]
Legionnaires' disease	15[Legionella]

Note:Problem Area numbers are given in Tables 2-1 and 2-2.

(a) Endpoints listed in this table represent all endpoints specified in the summary sheets; not just the driving endpoints. Health endpoints were not reported for some substances listed in Table A-1. Thus, they are not included in this table. Because of significant data gaps in some problem areas, the workgroup scored these entire problem areas rather than individual, representative substances. Therefore, some chemicals listed here do not appear in Tables 2-2 and A-6.

(b) Examples include chlorine, anhydrous ammonia, hydrochloric acid, and sulfuric acid.

Severity indexes have been developed in many ways, and they are invariably controversial. One approach involves estimating severity in economic terms -- how much does each different health effect cost for treatment, or how much would each different health effect reduce an individual's expected lifetime earnings. The first of these approaches tends to assign low severity scores to effects that are quickly fatal, and high scores to illnesses needing protracted treatment. The second approach assigns low scores to diseases affecting older people and high scores to those affecting the young. Another approach to severity scores involves polling people about which effects they would least like to suffer. This has the disadvantage of asking laymen to speculate about effects about which they have little technical understanding.

A subcommittee of the work group developed an approach to assess the disparate health endpoints. The subcommittee began with a severity index that had been developed for a contract report to the EPA Environmental Criteria and Assessment Office in Cincinnati. The index basically ranked health effects by how threatening they were to the viability of the organism. The index involved two steps:

- A ranking of organs. Category I organs (most important) include those whose impairment or loss is fatal. Gradations extend to Category IV organs, which include those found in animals which have no counterparts in humans.

- A seven-point endpoint severity scale. A score of 1 (lowest) is given to functional impairment of Category IV organs. A score of 4 is given to mild functional impairment in Category I organs or major impairment in Category II organs, etc.

A full description of this severity index appears in Table A-3. This index has in no way been approved by EPA; in fact, it is highly controversial. Many reviewers have disagreed strongly with the idea of ranking or comparing organs by importance. There is much less reluctance to compare different effects to the same organ.

With misgivings, the subcommittee nevertheless used this index as the starting point in assigning severity scores to the health endpoints. The scores assigned by the subcommittee ranged from 1 (least severe) to 7 (most severe). While the index provided a guide in developing scores, the assigned score for a health endpoint depended primarily on the subcommittee's qualitative judgments about the extent to which the health effect was life threatening, permanent, reversible and manageable therapeutically. The severity scores assigned by the subcommittee are listed in Table A-4. Table A-5 indicates how the assigned severity scores are distributed. The distribution of scores looks surprisingly like a normal distribution, with very few endpoints ranked as either extremely benign (score of 1) or extremely severe (score of 7) and most clustering around a score of 4.

One important point about the severity scores is they are ordinal but not cardinal. A score of six is not twice as bad as a score of three. Although it is difficult to be quantitative about such a qualitative concept as severity, the subcommittee believes that there is a large difference in severity (perhaps up to an order of magnitude difference) involved in a one point difference in ranking.

Table A-3

Ranking of Organs

Category I - Includes organs, impairment or loss of which is fatal and cannot be compensated for at all, or only with heroic measures (i.e., expensive mechanical devices, transplantation). Also includes gonads, loss of which prevents reproduction.

Lung, Heart, Brain/Spinal Cord, Kidney, Liver, Bone Marrow, Gonads

Category II - Includes organs whose loss or impairment may be fatal, but which can be compensated for by replacement therapy. Also includes organs, impairment or loss of which indicates an adverse effect on immune function or hematopoietic function which may be life threatening.

Adrenal, Thyroid, Parathyroid, Pituitary, Pancreatic Islets, Pancreas, Esophagus, Stomach, Small Intestine, Large Intestine, Lymph Node, Spleen, Thymus, Trachea, Pharynx, Urinary Bladder, Skin

Category III - Impairment or loss of any of these organs is not life threatening but may result in severe functional or emotional handicaps.

Accessory reproductive organs (Oviduct, Epididymis, Uterus, Prostate, Coagulating Gland, Seminal Vesicle, Ductus Deferens, Penis, Vagina), Eye, Bone, Nose, Nerve, Muscle, Urinary Bladder, Blood Vessel, Ear, Gall Bladder, Harderian and Lacrimal Gland, Larynx, Mammary Gland, Salivary Gland, Tongue, Tooth, Ureter, Urethra

Category IV - These organs are not found in humans and toxic lesions (noncarcinogenic) in these organs are not readily extrapolable to humans.

Clitoral/Preputial Gland, Zymbal's Gland, Anal Glands

Table A-3 (Continued)

Toxicity Test Endpoint Severity Scores

Toxicity Test Endpoint Severity Score (T)	Toxicity Test Endpoints
1.0	Body wt. change, food and/or water consumption changes, minor serum electrolyte changes, minor clinical changes, functional impairment of category IV organs
2.0	Small hematological changes, functional impairment in category III organs, organ weight change in category II-IV organs
3.0	Mild function impairment in category II organs, severe impairment in category III organ, minor organ weight changes in category I organs
4.0	Mild functional impairment in category I organs (small increases in urine concentration, proteniuria, enzymuria; changes in conjugated and unconjugated bilirubin, increases in sleeping time; small changes in ECG; minor changes in pulmonary function tests; mild behavioral changes; mild alterations in reproductive function), major impairment in category II organs, major organ weight changes in category I organs
5.0	Definite functional impairment in category I organs (moderate increases in urine concentration, proteinuria, enzymuria; serum increases in SGPT, SGOT, LDH, ICDH; increases in BSP retention; moderate changes in ECG; moderate impairments of pulmonary and reproductive function; definite behavioral changes; developmental toxicity with maternal toxicity

Table A-3 (Continued)

6.0	Major degree of functional impairment in category I organs (substantial increases in proteinuria, enzymuria, BUN; substantial increases in serum levels of SGPT, SGOT, LDH, ICDH, albumin; severe changes in ECG, and pulmonary and reproductive function; substantial behavioral alterations)
7.0	Severe central nervous system, respiratory or cardiovascular depression, mortality, developmental toxicity without maternal toxicity

TABLE A-4: RANKING OF SPECIFIC NON-CANCER HEALTH ENDPOINTS

SPECIFIC ENDPOINTS	SCORE (1-7)
Cardiovascular	
- unspecified	
- increased heart attacks	7
- aggravation of angina	5-6
- increased blood pressure	4
Developmental	
- fetotoxicity	6
- abnormal ossification (see teratogenicity)	
- low birth weight	4
- teratogenicity	7
Hematopoietic	
-unspecified	
- decreased heme production	4
- bone marrow hypoplasia	5
- impaired heme synthesis	4
- methemoglobinemia	5
Immunological	
- unspecified	
- herpes	1
- allergic reactions	3
- increased infections	4
Kidney effects	
- unspecified	
- tubular degeneration	5
- dysfunction	3
- hyperplasia	3
- hypertrophy	3
- atrophy	4
- necrosis	6
Liver effects	
- unspecified	
-hepatitis A	5
-jaundice	4
-increased weight	3
-increased enzymes	2
-necrosis	6
Mutagenicity	
-unspecified	
-cytogenetic	4
-heriditary disorders	7
Neurotoxic/Behavioral	
- unspecified	
- retardation	7
- reduced corneal sensitivity	2
- retinal disorders	4
- visual aging	2
- AChe inhibition	5
- learning disabilities	6
- neuropathy	6
- decreased sensory perception	3
- irritability	3
- tremors	4
- convulsions	6
- sensory irritation	2
Reproductive	
- unspecified	
- post implantation losses	4
- testicular degeneration	4
- spermatocyte damage	4
- decreased testicular weight	3
- uterine hypoplasia	3
- aspermia	6
- increased resorptions	4
- giant cell formation	2
- increased spontan. abortions	5

TABLE A-4 CONT'D: RANKING OF SPECIFIC NON-CANCER HEALTH ENDPOINTS

SPECIFIC ENDPOINTS	SCORE (1-7)
Respiratory	
- unspecified	
- emphysema	6
- nasal irritation	2
- pulmonary irritation	3
- nasal ulceration	3
- mucosal atrophy	3
- bronchitis	4
- pulmonary impairment	4
- lung injury	4
- pneumonia	5
- pulmonary edema	6
- Pontiac fever	5
- congestion	3
- hemorrhage	4
- alveolar collapse	5
- fibrosis	5
- nasal cellular irritation	2
- lung structure changes	5
- aggravation of asthma	4
- increased resp. disease	4
- bronchoconstriction	4
- decreased mid-expiratory flow rates	3
- increased respiratory infections	4

SPECIFIC ENDPOINTS	SCORE (1-7)
Other	
- unspecified organ effects	
- unspecified acute effects	
- mortality	7
- eye irritation	2
- dental erosion	3
- cataracts	5
- leishmaniasis	3
- adrenal	
- gastrointestinal disease	4
- bone damage dental mottling	2
- symptomatic effects (headache)	3
- Legionnaires dis.	5

TABLE A-5: DISTRIBUTION OF RANKINGS FOR NON-CANCER HEALTH ENDPOINTS

SCOPE: 1	2	3	4	5	6	7
herpes (non-infectious)	- liver-increased enzymes - reduced corneal sensitivity - sensory irritation - giant cell formation - nasal irritation - nasal cellular irritation - eye irritation - dental mottling	- allergic reactions - kidney-hyperplasia - kidney-hypertrophy - liver-increased weight - decreased sensory perception - irritability - decreased testicular weight - uterine hypoplasia - pulmonary irritation - nasal ulceration - mucosal atrophy - pulmonary congestion - decreased mid-expiratory flow rates - dental erosion - leishmaniasis - symptomatic effects (headache)	- increased blood pressure - low birth weight - decreased heme production - impaired heme synthesis - increased infections (immun.) - kidney-atrophy - jaundice - mutagenicity-cytogenetic - retinal disorders - tremors - post implantation losses - testicular degeneration - spermatocyte damage - increased resorptions - bronchitis - pulmonary impairment - lung injury - respiratory-hemorrhage - aggravation of asthma - increased respiratory disease - bronchoconstriction - increased respiratory infections - gastrointestinal disease	- aggravation of angina - - bone marrow hypoplasia - methemoglobinemia - kidney-tubular degeneration - hepatitis A - AChE inhibition - increased spontaneous abortion - pneumonia - Pontiac fever - alveolar collapse - fibrosis - lung structure changes - cataracts - Legionnaires disease	- fetotoxicity - kidney-necrosis - liver-necrosis - learning disabilities - neuropathy - convulsions - aspermia - emphysema - pulmonary edema	- increased heart atta - teratogenicity - mutagenicity-heredit disorders - retardation - mortality

The subcommittee members expressed strong reservations about the endpoint severity scores they had developed. They were willing to go out on this shaky limb and develop severity scores because completion of the non-cancer risk project required making such rough judgments in many areas besides this one. Developing severity scores seemed no more far-fetched or unfounded than other steps in assessing non-cancer risks. But the subcommittee cannot support use of these severity scores in other contexts or for other purposes. The scores are highly subjective, and have been reviewed and approved by no one. The base index has not been peer-reviewed or in any way approved by EPA. The subcommittee developed the scores for the endpoints in many cases without a detailed understanding of the endpoint and without reference to the studies reporting observation of the endpoint. In many cases the endpoint has been observed only under experimental conditions in animals; the subcommittee could only assume generally similar responses in humans.

In addition to developing severity scores, the endpoints subcommittee resolved another difficult issue for the non-cancer work group. Many toxic chemicals can produce more than one type of health effect. Cadmium, for example, can cause renal disfunction at low doses, but can also cause teratogenic effects at higher doses. The severity of the health effect may also vary with the dose: as cadmium dosage increases, renal disfunction may instead become renal tubular degeneration. The instructions to the program offices on generating the summary sheets were not specific on which of multiple endpoints to report and how to describe gradations of effects. Some summary sheets in fact reported multiple endpoints with experimental data for each, while others reported data only on a single driving endpoint (the endpoint that drives regulatory concern, or the significant endpoint that occurs at the lowest dose). Some summary sheets reported only a single gradation of effect, while others reported ranges.

The endpoints subcommittee suggested two simplifying rules that the workgroup agreed to try to follow in assessing health effects:

- Deal with the driving endpoint only. All summary sheets have consistently reported on driving endpoints, while inclusion of data on other endpoints is erratic.

- Focus on the grade of the effect as it would occur at the dose for which ambient exposures occur. If a dose at a level far above the LOEL is being considered, for example, grade the effect as it would occur at that high dose.

5. Exposure

In theory, for any chemical there is an entire distribution that relates the size of the exposed population to the ambient concentration or dose. In general there will be large numbers of people exposed to small amounts of the chemical, and smaller numbers of people exposed to larger amounts of the chemical. Such an exposure distribution is illustrated in Figure A-1.

For the substances covered by the summary sheets, there was rarely enough exposure information available to specify much of the exposure distribution. For most substances, only one data point was available; the exposed population had been estimated for only one ambient concentration or corresponding dose. For a few substances (mostly air pollutants), multiple data points were available. For many substances, no data points were available, or estimates were

very rough (e.g., somewhere between 1 and 10 million people are exposed to a specified ambient concentration of the pollutant).

Figure A-1: Example of an Exposure Distribution

A further problem was that the ambient concentrations and the exposed populations reported on the summary sheets frequently had been estimated under inconsistent assumptions. For example, a summary sheet might claim that the entire U.S. population of 240 million is exposed to ambient levels of the pollutant of concern. The concentration at which this exposure is assumed to occur is then estimated by reference to annual average monitored levels of the pollutant in urban areas, the only places where the pollutant is routinely monitored for. In fact, though, urban ambient levels of the pollutant are probably much higher than rural levels. In reality the entire U.S. population of 240 million is actually exposed to ambient levels lower than the urban average, or only the urban fraction of the 240 million people are actually exposed to the urban average monitored concentration.

More generally, a problem in reviewing exposure estimates across different chemicals was use of widely differing levels of conservatism. For example, the Superfund estimate was initially generated under a conservative assumption that all people served by ground water within a three mile radius of a Superfund site drank contaminated water. By contrast, the RCRA estimate was generated by modeling contaminant transport and potential exposure at actual RCRA sites, allowing contaminants to affect only downgradient water users, and providing for degradation, retardation, dilution, etc.. The result was a RCRA estimate of exposed population many orders of magnitude smaller than Superfund's. This result was due primarily to differences in conservatism of the modeling assumptions, and Superfund's approach was eventually revised.

Another sort of problem involved the distinction between the population exposed to a substance and the population at risk of suffering adverse health effects from the substance. If only sensitive subgroups (e.g., infants, asthmatics) are at risk from the substance, the population at risk will only be a fraction of the exposed population.

The workgroup adopted some principles for dealing with these problems and to provide a consistent approach to exposure assessment.

- All available concentration/exposed population data pairs should be used. Substances with more than one data pair had all the available data pairs carried forward into the next steps of the work group's methodology (scoring and ranking).

- o If a concentration or an exposed population can be estimated only within a range, the range will be converted to a single number by taking the geometric mean.

- o A concentration and its corresponding exposed population should be generated under consistent ground rules.

- o Exposure estimates across the different substances should exhibit a similar degree of conservatism. Excessively conservative estimates should either be revised, or they will mentally be scaled down in the final ranking stage.

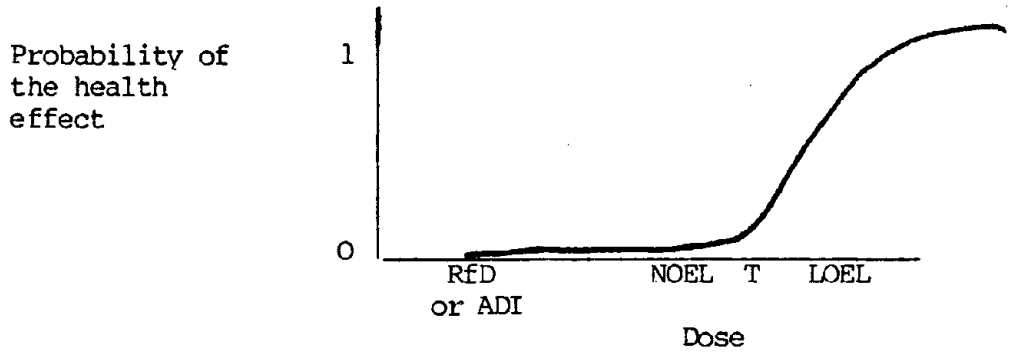
- o The population estimated should be the population at risk for the particular effect. For example, if the risk applies only to infants, then the estimate should be of the infant population.

The workgroup did not, however, rework and revise all the exposure estimates to comply with these principles. For the most part the general direction and magnitude of any error in an exposure estimate could be guessed at, and if this error was not likely to be large enough to affect the work group's conclusions, the estimate was left alone. The work group ultimately converted the estimated population exposed to a substance into a score from 1 to 4. One point of change in the score represented a difference in exposed population of two orders of magnitude. Thus, it was not likely to matter if an estimated exposure varied from the actual by a factor of 2, 5, or even 10. Most of the problems in exposure estimates seemed to be within this range, and the work group thus believed most of the population estimates to be sufficiently accurate for the purposes of this project.

6. Potency

The work group was interested in developing a mathematical representation of the potency of a substance in inducing its adverse health effects. Potency is generally the relationship between the dose of a substance and the likelihood that the dose will produce the health effect. A dose-response function for a substance is a representation of its potency. A typical dose-response function for a non-carcinogenic effect is shown in Figure A-2 below.

Figure A-2: Typical Dose-Response Function for Non-Carcinogen



Most non-carcinogenic dose-response functions are thought to involve a threshold (T on the graph). The threshold is the minimum level of dose that is necessary

before there is any significant probability of the health effect occurring. Or alternatively, the threshold is the highest level of dose for which there is no probability of the health effect occurring. Noncarcinogenic health effects that are thought not to involve thresholds include mutagenicity and in some cases teratogenicity.

Research on responses to different doses of a substance will yield data on the highest dose at which no effect has been observed (the "No observed effect level" or NOEL) and the lowest dose at which some effect has been observed (the "Lowest observed effect level" or LOEL). These two levels presumably bracket the threshold level. When regulating a substance and establishing a level of dose that is safe, EPA typically applies uncertainty factors to the NOEL. The Acceptable Daily Intake (ADI) or the Reference Dose (RfD) of a substance is the NOEL divided by an uncertainty factor ranging usually from 10 to 1,000. The magnitude of the uncertainty factor is related to the degree of confidence we have in our knowledge about the health effects of the substance in question. If we are dealing with a well-studied chemical with results from humans we can be reasonably confident of where the threshold is. We can set the RfD only slightly below the LOEL (using a small uncertainty factor of 10 or so) and still be confident that the RfD really is a safe level. But if we are dealing with a poorly understood chemical, with only experimental evidence from an animal study, we cannot be very sure of where the threshold is. In this case, we must use a larger uncertainty factor (1,000 or so) and set the RfD well below the LOEL in order to have the same level of confidence that the RfD represents a level that really is safe.

Although the work group might have liked to use real dose-response functions to represent the potency of the selected substances, acquiring the data would have been very difficult. Whereas a LOEL, NOEL, ADI or RfD is easily available for many substances, the dose-response functions themselves are not. In some cases they could be estimated by reviewing the original studies, but this would have been very time consuming. In EPA practice, dose-response functions are rarely used to assess risks of non-carcinogenic effects. Instead, a margin of safety (MOS) approach is employed by many programs. For most programs, the MOS is the RfD divided by the dose of the chemical actually received. If the MOS is low, the dose is at levels near the RfD and the exposure may be of regulatory concern; if the MOS is high the problem is minimal.

The work group decided to use an inverse MOS approach to reflect potency. The MOS approach is generally used in cases where low doses may be high enough to threaten to cause a problem. The work group inverted this concept to provide a notion of how large a problem there is when doses are high. A ratio which the work group termed the "individual exposure ratio" was calculated as the concentration at which exposure occurs divided by the RfD. The more a concentration level is above the RfD, the higher this ratio becomes. The individual exposure ratio correlates roughly with the probability that an individual encountering the substance at a given concentration will suffer the health effect. At concentrations near the RfD we expect little likelihood of the effect; the ratio signifies this with a value near 1. At concentrations far above the RfD, the likelihood of the health effect will be much greater, and the ratio signifies this with values that are much higher. A few points relating to the individual exposure ratio should be noted:

- The concentration and the RfD must be expressed in similar units so that the ratio is dimensionless. This can be done either by convert-

ing the concentration to an equivalent dose (by using standard uptake assumptions) and dividing by a RfD in traditional units of mg/kg/day, or by leaving the concentration as is but expressing the RfD in concentration terms.

- The work group decided that there was negligible risk at levels below the RfD (i.e., when the ratio was less than one). The work group thus did not consider any substances in exposure settings where concentrations were less than RfDs.

- In order to calculate this individual exposure ratio, RfDs were needed for all substances selected to represent the 31 problems. Approved ADIs or RfDs are available for only some of the substances of concern, so the workgroup had to generate a large number of unofficial RfDs. This was done in the traditional way by applying uncertainty factors to LOELs or NOELs in the experimental literature.

- The work group debated whether to use the RfD, NOEL, or LOEL in the denominator of the individual exposure ratio. The decision to use the RfD was made for two reasons: to be consistent with general EPA practice in focusing on RfDs when making risk management decisions, and to base the ratio on a level we know presents negligible risks. (If the denominator were the NOEL or the LOEL, an ambient exposure below that level -a ratio of less than one -- might nevertheless be above the threshold and be unsafe.)

  The choice of RfD rather than NOEL or LOEL perhaps has an important influence on the eventual rankings of the problem areas. The NOEL is converted to an RfD by dividing by an uncertainty factor, the magnitude of which depends basically on how poorly understood the health effects of the substance are. For well-understood chemicals such as certain criteria air pollutants the uncertainty factors are small. For more unusual chemicals such as many pesticides, the uncertainty factors are much larger. In general, the RfDs for criteria air pollutants are slightly lower than their NOELs, while the RfDs for pesticides are far lower than their NOELs. A pesticide exposure at the NOEL for that pesticide will tend to get an individual exposure ratio score 10 or 100 times higher than a criteria air pollutant will get for an exposure at its NOEL. If NOELs or LOELs were used as the denominator, the workgroup's estimated "potency" for chemicals such as pesticides would be reduced sharply, while the estimated potency for chemicals like criteria air pollutants would be reduced only minimally.

The work group realizes that there are some major conceptual problems in representing potency or the probability of an effect at some exposure level through this individual exposure ratio. First, the real probability of an effect can actually range only between zero and one. But our individual exposure ratio can range from zero to extremely large. Whereas a real dose-response function will asymptotically approach a probability of effect of one as the dose increases, our individual exposure ratio continues to grow indefinitely. Secondly, using our ratio implicitly assumes an identical shape to the dose-response function for every substance. We implicitly assume that at a dose of twice the RfD for a chemical there will be the same probability of an effect no matter what the chemical. This clearly is not true; at least in part because

of the differential uncertainty factors intervening between the RfD and the LOEL for different chemicals. We also implicitly assume for all substances that a dose of ten times the ADI is twice as bad as a dose of five times the RfD. There is no reason, in reality, that dose-response functions have to exhibit these properties. Real dose-response functions may have very different shapes and slopes for different chemicals.

Despite these problems, the work group believes that for the purposes of this project the "individual exposure ratio" is a reasonable and practical representation of the potency of a substance, or of the likelihood of an effect resulting from exposure to the substance at a given ambient level. The individual exposure ratio is not a precise measure of potency, but the two are roughly correlated.

7. Combining Data on Endpoints, Exposure and Potency

At this point, the work group had accumulated data for representative substances on:

- The driving health endpoint expected from exposure to the substance, and the severity of that endpoint. The severity of the endpoint was expressed by a score ranging from 1 to 7.

- The amount of exposure to the substance. This was expressed as the population exposed to a given concentration of the substance.

- The potency of the substance in causing the adverse health effect for exposures at the given concentration. This was expressed by an "individual exposure ratio" derived by dividing the dose at ambient concentrations by the RfD for the substance (or by using the equivalent concentrations).

These data were organized into a large matrix, in the format of Figure A-3.

A subgroup of the work group recommended a procedure for converting the data in this matrix into a basis for assessing risks from particular substances. The subgroup suggested multiplying the individual exposure ratio (akin to individual risk) by the exposed population to derive a "population exposure ratio" (akin to population risk or number of cases), as in Column 9 of the matrix. This population risk would then be multiplied by the severity index in order to convert cases of disparate health effects into common terms. The severity-weighted number of cases (Column 10 of the matrix) would then provide the overall score for assessing the non-cancer risk from a particular substance within a problem area.

When the work group as a whole met to begin ranking the 31 problems, they found in practice that they did not like this highly quantitative approach the subgroup had developed. Three problems arose:

1. For some substances, there was not a complete set of data available on the severity score, the exposed population and the individual exposure ratio. For substances missing some of this data, an overall score could not be calculated.

FIGURE A-3 SUMMARY DATA ON ENDPOINTS, EXPOSURE, AND POTENCY

(1) Problem Area	(2) Chemical	(3) Population Number	(4) Exposure Concentration	(5) RfD or ADI	(6) Effects	(7)	(8) Individ. Exp. Ratio (4)/(5)	(9) Pop. Exp. Ratio (3) x (8)	(10) Overall Score (9) x (7)
					Nature	Score			

2. In concept the overall score represented something like the nationwide number of severity-weighted cases. Many members of the work group felt that this score overemphasized population risk, and that individual risk should be an equally important determinant of the final ranking. A problem area which caused very high risks for the small number of exposed individuals should perhaps be scored as high even if population risks from this problem were small.

   This conceptual problem with the scoring process the subgroup had tentatively designed was exacerbated by a mathematical problem. The variance across substances in the severity score was small (scores ranged from 1 to 7). The variance in the individual exposure ratios was much larger, with scores ranging across about three orders of magnitude. But the variance in the exposed population numbers was huge, with the range covering about seven orders of magnitude. The result, when severity, individual exposure ratio and population were multiplied together to determine the overall score, was that the overall score depended most heavily on the exposed population. In statistical terms, the variance in the overall score was determined largely by the variance in population. Mathematically, the other factors didn't matter much in determining the overall score.

3. Perhaps most importantly, the work group did not feel that the level of precision implied by these mathematical operations and by the quantitative overall score matched the degree of confidence the work group had in the data. The severity index represented only the rough judgment of the endpoints subcommittee. The individual exposure ratio was subject to all of the theoretical misgivings discussed in the potency section. The exposed population figures were known in most cases to be shaky; generated by a variety of incompatible techniques and frequently biased by differing degrees of conservatism.

The work group responded to these problems by turning to a much less precisely quantitative scoring scheme. The three factors -- severity index, individual exposure ratio, and exposed population -- were turned into three scores for each substance, with each score ranging from 1 to 4:

- o A severity score. The severity index was converted to a score as follows:

Severity score	Severity index from endpoints group
1	1-2
2	3-4
3	5-6
4	7

- o A ratio score. The individual exposure ratio was converted to a score as follows:

Ratio score	Individual exposure ratio
1	1 - 10
2	10 - 100
3	100 - 1,000
4	>1,000

- o A population score. The exposed population was converted to a score as follows:

Population score	Number of people exposed
1	<1,000
2	1,000 - 100,000
3	100,000 - 10,000,000
4	>10,000,000

Converting the data on individual substances into these scores solved many of the work group's problems. First, where data were missing, the work group felt reasonably confident in its ability to assign an appropriate score between 1 and 4 to fill the gap. Secondly, with severity, exposed population and individual risk now represented by scores ranging equally from 1 to 4, much of the statistical domination of the final ranking by population could be avoided. The influence of population was also diluted somewhat by requiring a two order of magnitude increase in order to gain a point in the population score, while only a one order of magnitude increase was needed to gain a point in the ratio score. Also, the three scores could be combined in various different ways intended to emphasize or deemphasize the importance of any of the factors. Finally, the work group felt that the 1 through 4 score signified about the right level of precision in the data that had been generated. For example, although the absolute number of people exposed to a substance at a given concentration might easily have been mis-estimated by a factor of two or five, the work group felt it unlikely that a mis-estimate was by two orders of magnitude, the amount necessary to produce a change in the population score.

A few more issues had to be resolved before the work group had a full set of scores for all the representative substances in all problem areas.

First, some programs were able to produce data on incidence of adverse health effects rather than data on concentrations and exposed populations. For example, the drinking water program could produce data on the number of reported cases of giardiasis and legionnaire's disease, but had no data on typical concentrations of or exposures to these microbial contaminants. Similarly, data were available on mortality and morbidity from accidental chemical releases, and on the number of pesticide poisonings attributable to different agents. In these areas again it would have been extremely difficult to estimate typical concentrations and exposed populations.

In these cases, the incidence data were converted to a population score and a ratio score in order to be consistent with the remainder of the data. The population at risk of suffering the health effect measured by incidence was estimated roughly and scored using the 1-4 population score. A ratio score was then calculated as follows:

$$\text{Average individual risk where data are on incidence} = \frac{\text{annual incidence}}{\text{estimated population at risk}}$$

Ratio Score	Avg. Individual Risk	Individual Exposure Ratio
1	<1.00E-06	1 - 10
2	1.00E-06 - 1.00E-04	10 - 100
3	1.00E-04 - 1.00E-02	100 - 1,000
4	>1.00E-02	>1,000

For comparison, the individual exposure ratios that would result in the same scores if data were available on concentrations are shown also.

In effect, we broke apart the incidence data into a population score to represent the size of the population at risk, and into a ratio score to reflect the degree of risk faced by an individual in that population. In one respect, this process is unusual. Incidents of harm are what we really care about in this entire project. Our basic methodology is designed to take data on the components of harm (exposure concentrations; population exposed; likelihood of harm at those concentrations) and implicitly combine them. The paradox is that when we have fairly good data on incidence, our methodology requires us to break that data apart into some probably poorer estimates of exposure and likelihood of harm, in order to be able to describe that environmental problem in terms consistent with all the others. Nevertheless, the bulk of our data on chemicals was in the form of exposed populations, ambient concentrations and likelihood of harm rather than on incidence, and the work group believed that that a consistent ranking scheme demanded that all the data be converted into one format.

The final step taken in scoring was to develop scores for the problem areas for which we had inadequate data on representative substances. It had not been possible to produce data sets on exposure concentrations and exposed populations for substances representing several of the 31 environmental problems. For problem areas like this, the work group scored the entire problem area rather than individual representative substances. A representative of the cognizant program described the problem area to the work group, and the work group as a whole then scored the problem area. For inactive hazardous waste sites (problem area # 17) for example, the work group thought that perhaps several million people could be exposed to potentially harmful levels of toxic chemicals in drinking water or air around such sites. But we did not think this number was likely to be as high as 10 million people, so we gave inactive hazardous waste sites a 3 for a population score. A similar sort of process was used to give inactive hazardous waste sites a severity score and a ratio score. The problem areas that were scored in this way as a whole, without scoring specific representative substances, included sludge, accidental releases and all the waste site categories (active and inactive hazardous, municipal and industrial non-hazardous industrial, and mining). In some of these cases, the work group decided to score the problem as a whole despite having some data on representative substances. (The particularly attentive reader may note that Table A-1 thus lists some substances that were ultimately not scored. For example, although we had data on sulfuric acid, hydrochloric acid, etc. involved in accidental releases, we chose to score the accidental release problem area directly rather than scoring its representative substances.)

For certain problem areas, the work group lacked the information needed to estimate scores for specific factors (i.e., population, health endpoint and individual exposure ratio). Instead, the work group discussed what was known about the problem with representatives from the relevant program office

and agreed upon an overall ranking of high, medium or low. This approach was used for direct discharges to surface water (industrial), indirect discharges to surface water (POTWs), non-point source discharges to surface water, estuaries, wetlands and releases from storage tanks.

The final scores developed by the work group for the representative substances and the problems scored as a whole are shown in Table A-6.

8. Producing the Final Ranking

The work group had produced a set of scores that generally represented the exposed population, individual risk and the severity of the health endpoint for each representative substance or problem area. Two steps remained before producing a final ranking:

- o For problem areas represented by multiple substances, deciding how to combine the scores on individual substances to produce scores for the problem as a whole.

- o Deciding how to combine the three scores for a problem area into a single ranking for the problem area.

The work group decided to look at some options on the second issue first. The group was most concerned that they did not want to make a judgment that either population risk or individual risk was more important. If the ranking for a problem area would differ substantially depending on whether individual or population risk were emphasized, the work group wanted to display two sets of rankings. To test the importance of this issue, the work group developed a concept called a scatter plot. The scatter plot would graph the individual risk of each substance or a problem area against the population risk of this substance or problem area. If most of the points in the scatter plot are on or near the diagonal for which individual and population risk were equal, the issue of what sort of risk to focus on is not terribly important. But if most of the points are off this diagonal (i.e., if individual risk for a substance or problem area usually does not look much like population risk for that substance or problem area), the issue is an important one.

Thus, work group developed the matrix shown in Figure A-4. On the horizontal axis is the population score given to the substance or problem area. On the vertical axis is a representation of the severity of individual risk associated with the substance or problem area (called the "individual score," developed by adding the severity score and the ratio score, dividing by two, and rounding upward). Most of the substances and problem areas are either on the diagonal where the population score and the individual score are equal or in adjacent boxes (where one score differs from the other by 1). Relatively few substances and problem areas have scores differing by 2 or more. The work group concluded that the individual risk vs. population risk issue was not likely to be critical in practice.

More interesting conclusions can be drawn from the matrix. The items that rank the highest (scores of 4,4; 4,3; or 3,4) are associated with accidental releases (Problem 21), air and radiation (Problems 1, 2, 4, 5, and 6), drinking water (Problem 15) and consumer exposures (Problem 30). More items are given high population scores than are given high individual scores. The work group interpreted this observation as consistent with the fact that EPA generally deals with broad exposure environmental problems, and not so much with narrow

TABLE A-6 SCORES AND ACTUAL NUMBERS FOR ALL ENVIRONMENTAL PROBLEM AREAS

Problem Area	Substance or Problem Area		Population Exposed	Pop. Score a	Driving Health Endpoint	Endpoint Score b	Individual exposure ratio or Incidence/population *	Ratio Score c
1	Lead(children)		2.68E+03	2	learning disabilities	3	1.70E+00	1
1	Carbon monoxide		3.23E+06	3	aggravation of angina	3	4.80E+00	1
1	Sulfur dioxide		2.75E+05	3	aggravation of asthma	2	2.50E+01	2
1	Particulate matter(elderly, diseased)-Acute		3.00E+06	3	premature mortality	4	2.50E+01	2
1	Particulate matter - Chronic		1.20E+07	4	respiratory symptoms	2	2.60E+01	2
1	Acid Aerosols	>	1.00E+07	4	increased mortality	4	1.00E+02	3
1	Ozone - Acute		1.08E+08	4	increased resp. infections	2	1.00E+02	3
1	Ozone - Chronic		2.37E+08	4	lung structure changes	3	2.92E+02	3
2	Benzene		1.36E+07	4	bone marrow hypoplasia	3	1.20E+01	2
2	Carbon tetrachloride		8.50E+06	3	jaundice	2	1.00E+01	2
2	Chlorine		2.31E+05	3	pulmonary edema	3	1.70E+02	3
2	Chromium		2.70E+06	3	bronchitis	2	3.00E+00	1
2	Formaldehyde		1.70E+08	4	pulmonary irritation	2	1.33E+04	4
2	Hydrogen sulfide		9.90E+05	3	pulmonary irritation	2	2.32E+02	3
3	Other air pollutants				Group consensus -- dropped			
4	Radon (indoor air only)**			4		4		1
5-a	Benzene		1.14E+08	4	bone marrow hypoplasia	3	3.16E+00	1
5-b	Benzene		6.75E+07	4	bone marrow hypoplasia	3	3.16E+01	2
5-c	Benzene		4.50E+06	3	bone marrow hypoplasia	3	3.16E+02	3
5-a	Carbon tetrachloride		4.76E+07	4	jaundice	2	3.17E+00	1
5-b	Carbon tetrachloride		8.60E+06	3	jaundice	2	3.17E+01	2
5-c	Carbon tetrachloride		2.40E+06	3	jaundice	2	3.17E+02	3
5	Environmental tobacco smoke(adults)	>	1.00E+07	4	inc. mort. from heart disease	4	3.70E+01	2
5	Environ.tobac. smoke(infants & children)	>	1.00E+07	4	hosp. for bronchitis/pneumonia	3	2.25E+01	2
5-a	Formaldehyde		1.00E+08	4	pulmonary irritation	2	1.20E+02	3
5-b	Formaldehyde		6.00E+06	3	pulmonary irritation	2	9.75E+02	3
5	Nitrogen dioxide - Acute		3.00E+06	3	lung function changes	2	2.00E+01	2
5	Nitrogen dioxide - Chronic	>	1.00E+07	4	lung injury/structure changes	3	1.14E+01	2
5-a	Xylene		1.76E+07	4	teratogenicity	4	3.16E+00	1
5-b	Xylene		2.40E+06	3	teratogenicity	4	3.16E+01	2
6	Radiation - occupational		1.95E+06	3	mutagen. (hereditary disorders)	4	1.65E-05 *	2
6	Radiation - consumer		2.38E+08	4	mutagen. (hereditary disorders)	4	6.50E-07 *	1
7	UV Radiation/Ozone depletion **			4	cataracts	3		1
8	Carbon dioxide and global warming				Group consensus -- dropped			
9	Direct indus. disch. to surf. water				Group consensus -- low rating; but no specific scores			
10	Indirect disch. to surf. water(incl. POTWs)				Group consensus -- medium rating; but no specific scores			
11	Nonpoint source discharges to surface water				Group consensus -- medium rating; but no specific scores			
12	Sludge **			1		1		1
13	Discharges to estuaries, coastal waters, oceans				Group consensus -- medium rating; but no specific scores			
14	Discharges to wetlands				Group consensus -- low rating; but no specific scores			
15	Lead (children)		1.67E+07	4	learning disabilities	3	2.11E+00	1
15	Legionella **			3	Legionnaires' disease	3		2
15	Nitrate (infants)		1.50E+04	2	methemoglobinemia	3	1.00E+00	1
15	Pathogens (Giardia/Viruses)**			4		2		3
15	Chlorine disinfectants		1.50E+08	4	hepatotoxicity	2 **		1 **
16	Active hazardous waste sites**			1		2		1
17	Inactive hazardous waste sites**			3		2		1
18	Municipal non-hazardous waste sites**			4		2		1
19	Industrial non-hazardous waste sites**			3		2		2
20	Mining waste**			2		1		1

TABLE A-6 (CONTINUED)

Problem Area	Substance or Problem Area	Population Exposed	Pop. Score a	Health Endpoint	Endpoint Score b	Individual exposure ratio or Incidence/population *	Ratio Score c
21	Accidental releases - Toxics (mortality)**	1.50E+06	3	death	4	8.00E-04*	3
21	Accidental releases - Toxics (morbidity)**	1.50E+06	3	injuries	3	2.70E-02*	4
22	Accidental releases -- oil spills			Group consensus -- dropped			
23	Releases from storage tanks			Group consensus -- low rating; but no specific scores			
24	Other groundwater contamination			Group consensus -- dropped			
25	Aldicarb**		3	AcHE inhibition	3		1
25	Diazinon**		4	AcHE inhibition	3		1
25	EPN**		3	AcHE inhibition	3		2
26	Dinoseb - males**		2		3		3
26	Dinoseb - females**		1		4		3
26	Paraquat**	2.50E+05	3	fibrosis	3	4.00E-04 *	3
26	Ethyl parathion**		2	AcHE inhibition	3		4
27	Pesticides (Ground/Surface water) -- carbamates**		3	AcHE inhibition	3		1
27	Pesticides (Indoor Air) -- cyclodienes**		4	increased liver weight	2		1
28	New toxic chemicals			No information available			
29	Biotechnology			No information available			
30	2-Ethoxyethanol	2.00E+05	3	teratogenicity	4	3.20E+00	1
30	Methylene chloride	2.50E+07	4	liver histopath. alterations	2	8.81E+02	3
30	Formaldehyde	1.00E+06	3	sensory irritation	1	2.10E+03	4
31	2-Ethoxyethanol	4.50E+05	3	teratogenicity	4	1.26E+00	1
31-a	Methylene chloride	2.70E+05	3	liver histopath. alterations	2	4.00E+02	3
31-b	Methylene chloride	3.00E+04	2	liver histopath. alterations	2	4.76E+03	4
31	Perchloroethylene**		3	renal/liver histopath. changes	2		4
31	Formaldehyde	1.10E+06	3	sensory irritation	1	3.20E+03	4

* Incidence/Population = number of cases / number of people exposed; calculated when the number of cases were available and no Individual Exposure Ratio was available.

** Group consensus.

TABLE A-6 (CONTINUED)

a Pop. Score derived as follows:

Score	Number of people exposed
1	< 1,000
2	1,000 - 100,000
3	100,000 - 10,000,000
4	> 10,000,000

b Health Endpoint Score derived as follows:

Score	Score given by Endpoints Group
1	1 - 2
2	3 - 4
3	5 - 6
4	7

c Ratio Score derived as follows:

Score	Ind. Exp. Ratio	# cases / # people exposed*
1	1 - 10	< 1.00E-06
2	10 - 100	1.00E-06 - 1.00E-04
3	100 - 1000	1.00E-04 - 1.00E-02
4	> 1000	> 1.00E-02

* Incidence/Population = number of cases / number of people exposed; calculated when only the number of cases were available and no Individual Exposure Ratio was available.

F_GURE A-4 MATRIX OF INDIVIDUAL SCORES AND POPULATION SCORES FOR ALL ENVIRONMENTAL PROBLEM AREAS

	1	2	3	4
4	26 Dinoseb - females	26 Ethyl parathion	21 Accidental releases - Toxics (mortality) 21 Accidental releases - Toxics (morbidity)	1 Acid Aerosols
3		26 Dinoseb - males 31 Methylene chloride-b	1 Particulate matter - Acute 2 Chlorine 2 Hydrogen sulfide 5 Benzene-c 5 Carbon tetrachloride-c 5 Formaldehyde-b 5 Xylene-b 6 Radiation - occupational 15 Legionella 25 EPN 26 Paraquat 30,31 2-Ethoxyethanol 31 Methylene chloride-a 31 Perchloroethylene 30,31 Formaldehyde	1 Ozone - Acute 1 Ozone - Chronic 2 Benzene 2 Formaldehyde 4 Radon (indoor air only) 5 Benzene-b 5 Environmental tobacco smoke (adults) 5 Environmental tobacco smoke (children) 5 Formaldehyde-a 5 Nitrogen dioxide - Chronic 5 Xylene-a 6 Radiation - consumer 15 Pathogens (Giardia/Viruses) 30 Methylene chloride
2	16 Active hazardous waste sites	1 Lead 15 Nitrate (infants)	1 Carbon monoxide 1 Sulfur dioxide 2 Carbon tetrachloride 2 Chromium 5 Carbon tetrachloride-b 5 Nitrogen dioxide - Acute 17 Inactive hazardous waste sites 19 Industrial non-hazardous waste sites 25 Aldicarb 27 Pesticides (Ground/Surface Water)	1 Particulate Matter - Chronic 5 Benzene-a 5 Carbon tetrachloride-a 7 UV Radiation/Ozone depletion 15 Lead (children) 15 Chlorine disinfectants 18 Municipal non-hazardous waste sites 25 Diazinon 27 Pesticides (Indoor air)
1	12 Sludge	20 Mining waste		

POPULATION SCORE

* INDIVIDUAL SCORE was calculated by adding the Health Endpoint Score (Table A-6) and the Individual Exposure Ratio Score (Table A-6), and dividing that sum by 2. All values were rounded upwards.

a,b,c - See Table A-6 for exposure distribution.

high risk exposures to small subgroups such as OSHA might be concerned with.

The work group had hoped that the matrix would show clear trends for all representative substances within a problem area. If, for example, all the criteria air pollutants ranked quite high (4,4; 4,3; 3,4; or 3,3), then the work group could easily rank criteria air pollutants as a whole very high. Such was not the case, however. Disaggregated matrices concentrating on particular areas (air and radiation, water, waste, pesticides and toxics) show a few trends, but present no obvious conclusions. The work group had to return to the question of how to aggregate scores for individual representative substances into scores for a whole problem area.

A few members of the workgroup convened to perform various mathematical operations on the scores, with the aim of producing different rankings of the 31 problem areas that resulted under different mathematical ground rules. The different approaches included:

- Different ways for aggregating population, endpoint and ratio scores into a total score for a problem area or substance. Methods were used that weighted the three scores equally or that weighted one or another factor more heavily.

- Different ways of aggregating scores (population score, endpoint score and ratio score) for substances into scores for whole problem areas. Three different methods were used:

    1. Select the substance with the highest total score to represent the problem. The rationale was that no problem should get a lower score than any single component of the problem.

    2. Represent the problem by the highest population score for any substance, and with the average endpoint and ratio scores for all the substances.

    3. Represent the problem by the average population, endpoint and ratio scores for all the substances.

Different combinations of these approaches were pursued, and resulting mathematical rankings of the problem areas were shown to the entire workgroup. In general, as suggested by the analysis, shifting the weights among population and individual risk made relatively little difference to the final results. The process for aggregating multiple substances had slightly more effect on the ultimate mathematical ranking, but again there was substantial stability to whether a particular problem area ranked at the top, in the middle, or low. Table A-7 shows a few of the alternative mathematical rankings that came from varying the aggregation process.

The work group adopted these mathematical rankings as the starting point for its final ranking of problem areas. A problem area was grouped by whether it generally showed up high in the mathematical rankings, medium, or low. The qualitative logic for such a ranking was then reviewed for each problem area. Substantial discussion ensued on the following problem areas:

- The initially high rankings for indoor radon and radiation/not radon. Data supporting these rankings came from modeled incidence of mutagenic

TABLE A-7 COMPARISON OF RANKING RESULTS BY METHODS A.1, A.2, AND A.3

Problem Area No.	Problem Area	A.1*	Problem Area No.	Problem Area	A.2**	Problem Area No.	Problem Area	A.3***
1	Criteria air pollutants	11.0	21	Accidental releases - Toxics	10.0	21	Accidental releases - Toxics	10.0
21	Accidental releases - Toxics	10.0	6	Radiation - other than radon	9.5	6	Radiation - other than radon	9.0
5	Indoor air pollution - other than radon	10.0	26	Application of pesticides	9.5	4	Radon (indoor air only)	9.0
2	Hazardous/toxic air pollutants	10.0	30	Consumer product expsoure	9.0	5	Application of pesticides	8.5
15	Drinking water	9.0	4	Radon (indoor air only)	9.0	26	Indoor air pollution - other than radon	8.4
31	Worker exposure to chemicals	9.0	1	Criteria air pollutants	9.0	1	Criteria air pollutants	8.4
26	Application of pesticides	9.0	5	Indoor air pollution - other than radon	8.9	30	Consumer product expsoure	8.3
4	Radon (indoor air only)	9.0	2	Hazardous/toxic air pollutants	8.8	31	Worker exposure to chemicals	8.2
6	Radiation - other than radon	9.0	31	Worker exposure to chemicals	8.4	2	Hazardous/toxic air pollutants	8.2
30	Consumer product expsoure	9.0	25	Pesticides residues on food	8.3	7	UV Radiation/Ozone depletion	8.0
7	UV Radiation/Ozone depletion	8.0	15	Drinking water	8.2	25	Pesticides residues on food	7.7
25	Pesticides residues on food	8.0	7	UV Radiation/Ozone depletion	8.0	15	Drinking water	7.6
19	Industrial non-hazardous waste sites	7.0	27	Other pesticide risks	7.5	18	Municipal non-hazardous waste sites	7.0
18	Municipal non-hazardous waste sites	7.0	19	Industrial non-hazardous waste sites	7.0	19	Industrial non-hazardous waste sites	7.0
27	Other pesticide risks	7.0	18	Municipal non-hazardous waste sites	7.0	27	Other pesticide risks	7.0
17	Inactive hazardous waste sites	6.0	17	Inactive hazardous waste sites	6.0	17	Inactive hazardous waste sites	6.0
20	Mining waste	4.0	20	Mining waste	4.0	20	Mining waste	4.0
16	Active hazardous waste sites	4.0	16	Active hazardous waste sites	4.0	16	Active hazardous waste sites	4.0
12	Sludge	3.0	12	Sludge	3.0	12	Sludge	3.0

*A.1 Population Score + Endpoint Score + Ratio Score = Total Score.
When multiple chemicals exist for a Problem Area the one with the highest Total Score was selected.

**A.2 Highest Population Score + Average Endpoint Score + Average Ratio Score = A.2

***A.3 Average Population Score + Average Endpoint Score + Average Ratio Score = A.3

and teratogenic effects. The work group was concerned about the uncertainty of these estimates, and also believed that these effects of radiation are very close to cancer effects and perhaps should more properly be included with cancer risks. Accordingly, the rankings for the two radiation problem areas were downgraded to medium risk.

- The high ranking for indoor air pollution. This was due primarily to environmental tobacco smoke, and substantial discussion took place about whether the risk and exposure estimates here were believable. The work group eventually decided they were persuasive.

- The high ranking given to drinking water. Data were cited on levels of disinfection byproducts widely found in drinking water and the possible health effects from them. Recent findings on lead were also discussed. It was suggested that there may be no threshold for cardiovascular effects associated with exposure to lead. In addition, the group discussed the more certain data on learning disabilities in children, the driving endpoint used for lead. Some concern was expressed that the scores for lead did not accurately reflect the seriousness of it as a problem. However, the high risk ranking for drinking water seemed clear, and the lead scores were not revised.

- No ranking given to new toxic chemicals. Various approaches and rationales were discussed in an attempt to rank this problem area. Arguments were made that it should rank low because: the new chemical review program catches many of the potentially harmful chemicals, new chemicals often replace riskier existing chemicals, and most new chemicals are low volume specialty chemicals not resulting in any widespread exposure. An argument was made that it might rank high because unanticipated adverse effects are often discovered long after a chemical has been put in commerce. Ultimately, the work group decided it could not develop a satisfactory approach to analyzing the effects of new chemicals and ranking them as a problem area.

- Detailed consideration was given to the relative rankings among five water-related problem areas: direct point source dischargers, indirect point sources, non-point sources, discharges to estuaries, and discharges to wetlands. Representatives of the Office of Marine and Estuarine Protection and the Office of Water Regulations and Standards were asked to join the work group and present relevant data. The work group eventually concluded that the most significant non-cancer risk in this area was from consumption of contaminated fish and shellfish, with pathogens being the primary contaminants of concern and metals and pesticides of slightly lesser importance. POTWs (defined as constituting the "indirect point source" problem area) and non-point sources are the major contributors of these contaminants, with direct industrial dischargers far less significant. The estuaries and the wetlands problem areas were distinguished from each other on the basis of the much greater amount of fish and shellfish taken from estuaries and marine waters than from wetlands. Ultimately, all five of these water-related problem areas were ranked on the basis of this group consensus rather than through the scoring process.

- The work group reviewed the areas ranked as low risk, and asked if anyone had a rationale for any of them entailing substantial risks. No one did.

Two final issues discussed by the work group during the ranking process were the treatment of uncertainty and the question of how the percentage of the problem captured by the selected substances should affect the ranking.

The discussion of uncertainty was prompted by the rankings of radiation problems. Some work group members felt that a problem should be ranked lower if the data available for ranking it are qualitatively weak. The highest rankings should be given only to problems that seem to entail a large amount of risk and that we are confident about. Others argued that the non-cancer group had been asked to give its best guess about the relative risks across problem areas, and that a best guess should be simply that -- whatever we can say about a problem area given existing information, whether that information is good or bad. Ultimately the work group agreed that the quality of available data had two aspects to it: bias and imprecision. To the extent that the workgroup felt some data were biased and there was reason to believe that a problem was really larger than the data indicated or really smaller than the data indicated, this judgment should be reflected in the rankings. Qualitative corrections for biased estimates were appropriate; in fact the work group had been making them frequently in the process of assigning scores. But qualitative corrections should not be made for imprecision when there is no suggestion of bias. The work group agreed to note the problem areas where rankings were more and less confident, but the ranking itself was not to be affected by the judgment about precision.

The work group also considered the question of how to deal with problem areas where the ranking had been based on substances representing a small proportion of the total problem. The work group spent some time developing estimates of the proportion of the problem captured by the representative substances; how should they use the estimates? The argument that was ultimately persuasive was this. The problems that had been ranked as high risk had an average total score about two points higher than the average total score for those that had been ranked as medium risk. Similarly, medium risk problems had an average total score about two points higher than low risk problems. Because of the highly logarithmic nature of the point scoring system, a two point score difference entailed more than a two order of magnitude difference in the data underlying the scores. It thus seemed appropriate to move a problem up in the ranking (in effect to give its score two more points) only if the entire problem was about two or more orders of magnitude larger than the portion of the problem covered by the selected substances. Four of these "tip of the iceberg" type problem areas -- hazardous air pollutants, pesticide residues on food, worker exposure, and consumer exposures -- ranked in either the high or medium categories, depending on the particular mathematical ranking process chosen. The work group decided to give all four a final ranking of high, combining judgments that substances in these problem areas ranked fairly high and that the substances studied represented a small fraction of the total problems.

The final rankings of problem areas by the work group are in Tables 2-1 and 2-2 in Chapter 2.