Appendix B

Workshop on Federal Interagency Coordination of Neurotoxicity Research and Regulatory Programs

Federally sponsored activities in neurotoxicology are diverse and highly decentralized. They involve more than 15 different institutes, centers, and independent agencies, such as the Environmental Protection Agency (EPA) and the Consumer Product Safety Commission (CPSC), as well as agencies in several departments, including the Department of Health and Human Services (DHHS), the Department of Energy (DOE), the Department of Labor, and the Department of Defense (DoD). Coordination of neurotoxicity research and regulatory activities tends to be informal within agencies and more formal but less extensively developed between agencies. Notable exceptions at the interagency level have included the coordinating efforts of at least two Federal organizations-the Interagency Regulatory Liaison Group and, within DHHS, the Committee to Coordinate Environmental Health and Related Programs.

Results of research into the mechanisms of neurotoxicity must be made available rapidly to risk assessors and other officials at regulatory agencies. This need is magnified by current budgetary constraints, which provide a considerable impetus for improving coordination of Federal research and regulatory activities. Improved coordination of Federal neurotoxicological research could well benefit not only the regulatory sector, but also industry and consumers.

With such considerations in mind, representatives from more than a dozen Federal organizations were convened on May 23-24, 1989, at a workshop, 'Federal Interagency Coordination of Neurotoxicity Research and Regulatory Programs," sponsored jointly by the congressional Office of Technology Assessment (OTA) and EPA (l).

Overview of Federal Neurotoxicology Research Programs

Federal research in neurotoxicology spans the spectrum from basic to targeted. Coordination of Federal research and regulatory programs in neurotoxicology varies widely—with informal communication being the dominant means, particularly among basic researchers. Much of the data developed in Federal programs-but certainly not all of it—is being made accessible by publication, through on-line computer networks, or both. However, some information, including a great deal of data developed in the private sector and furnished to Federal regulatory agencies to support drug, pesticide, and other product marketing applications, is often unavailable except through cumbersome means, such as requests via the Freedom of Information Act. Still other data submitted to Federal agencies by companies in the private sector are considered proprietary and therefore confidential. The following section provides a brief overview of Federal research and regulatory activities in this area.

Department of Health and Human Services

The responsibility for overseeing neurotoxicology-related activities within DHHS falls to the Office of the Assistant Secretary for Health. The Committee to Coordinate Environmental Health and Related Programs operates within that office.

National Institutes of Health

Several Institutes within the National Institutes of Health (NIH) sponsor a great deal, perhaps the majority, of the U.S. basic research effort in neurotoxicology. Most NIH research is investigator-initiated, and the data produced are published in the scientific literature. The principal Institutes with such programs are the National Institute on Neurological Disorders and Stroke (NINDS), the National Institute of Environmental Health Sciences (NIEHS), the National Institute on Aging (NIA), and the recently created National Institute on Deafness and other Communication Disorders (NIDCD). These Institutes support a broad range of basic studies of the nervous system, including development of model systems for the etiology of neurological diseases, particularly chronic degenerative conditions.

Neurotoxicological research within NINDS is divided into two areas of interest: exogenously applied and endogenously occurring neurotoxic agents, The action of synthetic neurotoxicants may cause damage that mimics neurodegenerative diseases. For instance, the synthetic compound MPTP, sometimes formed during the illicit synthesis of a meperidine-like drug, destroys dopamine-producing cells of the central nervous system, making the drug a powerful tool for studying Parkinson's disease. Among endogenous toxins, the reactive forms of oxygen that can damage membranes through lipid peroxidation are now being studied as possible mediators of damage when cell protective mechanisms go awry.

NIEHS, which supports the most targeted of the several NIH-sponsored neurotoxicity research programs, is now taking a "broader look" at toxicology than it did when carcinogen testing dominated its activities. The Institute conducts and supports research to identify environmental agents that may cause adverse reproductive, neurological, and other effects on human health in addition to cancer. NIEHS oversees a substantial extramural grants program in the neurotoxicology field.

The National Toxicology Program within NIEHS conducts tests of selected chemicals, including suspected neurotoxic agents, and develops databases on them.

Although the selection of chemicals for testing receives a great deal of attention, the program ' 'shouldn't be driven purely by the [chemical] nomination-based process,' said one NIEHS official. Compounds are selected on the bases of extent of human exposure, quantity produced, adequacy of existing toxicological data, and regulatory and research agency concerns regarding potential adverse effects.

Although NIEHS, EPA, and the National Institute for Occupational Safety and Health (NIOSH) have overlapping research interests and can use similar research and testing technologies, there is little direct formal interaction between the agencies, according to an official from NIEHS. The executive committee that oversees the program is composed of directors or administrators from NIEHS, the National Cancer Institute, NIOSH, the Agency for Toxic Substances and Disease Registry (ATSDR), the Food and Drug Administration (FDA), CPSC, EPA, and the Occupational Safety and Health Administration; the program is reviewed by nongovernment scientists.

Because of its mandate, NIA supports researchers investigating the "special vulnerability of the aging nervous system to toxins, '' noted an official from NIA. As with programs in NINDS, the emphasis is on "the basic neurobiology of the problem. " The Institute also sponsors epidemiological studies to identify populations with chronic exposures to toxic substances, such as aging residents of rural areas, who maybe exposed to pesticides.

Alcohol, Drug Abuse, and Mental Health Administration

The National Institute on Drug Abuse (NIDA), which is part of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), sponsors research to study the neurotoxicological effects of addictive drugs as well as drugs being developed to treat or prevent drug abuse. Researchers at NIDA are trying to determine what areas of the brain are affected by such drugs and whether their effects are reversible. FDA and NIDA have an interagency agreement to develop and validate methods of assessing the neurotoxic actions of drugs that are currently being prescribed or considered for treatment of neuropsychiatric disorders. NIDA researchers are also seeking avenues for coordinating some of their efforts with officials of the Drug Enforcement Agency, but that "gap is difficult to bridge,' according to an official from NIDA. Cooperative agreements with other Federal agencies to develop and validate neurotoxicity screening tests and a neurotoxicity database should become priority activities, noted another NIDA official.

The National Institute of Mental Health (NIMH), another agency within ADAMHA, also sponsors research on therapeutic agents that can exert neurotoxic effects on brain function. NIMH researchers are helping to develop a neurophysiological battery of tests for evaluating central nervous system impairment, particularly among patients with AIDS. Because NIMH and NIDA interact closely with the pharmaceutical industry, some neurotoxicology data they obtain may be kept confidential because it is considered proprietary information.

Centers for Disease Control

The Centers for Disease Control (CDC) act as a sentinel protecting the public health. Currently, CDC is updating its regulations for setting lead safety standards and thus is reexamining the concentrations in the blood at which this potent neurotoxic agent exerts adverse effects.

NIOSH studies a broad range of products through both intramural and extramural programs. Specifically, NIOSH considers substances to which individuals may be exposed in the workplace, including field studies of farmworkers and others exposed to pesticides. In addition, Institute researchers conduct studies using various animal models. The primary concern of the NIOSH intramural program is methods assessment.

NIOSH is participating in the National Health and Nutrition Survey, which is organized under the auspices of the National Center for Health Statistics. During the course of this study, about 6,000 people will be given three tests from the neurobehavioral evaluation system in order to develop baseline data to assess future exposures to neurotoxic agents. NIOSH is also participating with the International Program on Chemical Safety and the World Health Organization (WHO) invalidation of a neurobehavioral screening battery for rodents.

Agency for Toxic Substances and Disease Registry

Under Superfund auspices, ATSDR carries out applied research on health effects of exposures to hazardous substances, including neurotoxic agents. ATSDR is "looking at data gaps," according to an official of the Agency. By law, the Agency must make a list of the 200 most toxic substances found at Superfund sites and help determine which of them maybe toxic in general as well as neurotoxic. Officials also expect to develop a standard battery of tests that could be used not only for broad testing of the population, but also for workers and other individuals at Superfund sites who might be exposed to mixtures of neurotoxic agents. In December 1988, the ATSDR cosponsored the Third International Symposium on Neurobehavioral Methods in Occupational and Environmental Health with WHO and the Pan American Health Organization. Discussions at the symposium have helped ATSDR officials develop a list of scientific priorities.

Food and Drug Administration

FDA evaluates the adverse effects of drugs on the nervous system through its general toxicological evaluations. Such testing is designed not only to detect drugs with adverse effects on the central nervous system, but also to evaluate psychoactive drugs, which generally act directly on the nervous system. Before a drug is approved for marketing, general toxicity is evaluated by a battery of studies, ranging from short-term acute tests in several species by different routes of administration to chronic dosing studies in two species exposed at three dose levels for up to 2 years. Behavior in test animals is monitored periodically, and abnormalities are recorded. Mating, fertility, developmental abnormalities, maternal behavior, and survival are among the endpoints that are evaluated. However, officials of some agencies voiced concern that FDA's general toxicological testing approach may miss some neurotoxicological effects. Many neurotoxicologists believe that specific neurotoxicological testing is necessary to detect some adverse effects.

Elsewhere in FDA, officials are concerned about pesticides, contaminants, and additives in the food supply and how they may affect individuals of different ages, on various diets, or with other risk factors. In addition, the National Center for Toxicological Research is developing models and trying to enhance current risk assessment methods in general, as it begins to examine neurotoxic agents specifically.

Department of Energy

DOE sponsors a relatively small program to study toxic chemicals. The Department is also interested in central nervous system disorders such as Alzheimer's disease. DOE researchers typically are interested in the underlying mechanisms of such diseases. Historically, their efforts have led to the development of complex instruments for examining central nervous system functions. DOE has also conducted evaluations of Federal agency carcinogen risk assessment procedures—an exercise that could prove helpful as many agencies try to develop consistent risk assessment procedures for analyzing neurotoxic substances.

Environmental Protection Agency

EPA faces a broad mandate under several statutes in regulating neurotoxic agents. Throughout the Agency, officials are refining risk assessment methods. Other efforts focus more directly on neurotoxic substances. For instance, the Agency maintains files on hundreds of pesticides, many of which are neurotoxic. EPA sponsors a sizable research program within the Office of Research and Development, which focuses on development of methods and applied research questions, including hazard identification and characterization.

EPA is currently revising and adapting guidelines for animal tests to screen organophosphorous pesticides for neurotoxic activity. The Agency has found evidence that pesticide residues in foods cause neurotoxic effects in children, and the identification and characterization of neurotoxic pesticides is a high priority for EPA officials. An EPA Scientific Advisory Panel recommended that routine testing of pesticides include observation for signs of neurobehavioral abnormality and neuropathology.

Under Superfund legislation, EPA officials are cooperating with their counterparts at ATSDR to study chemical mixtures at toxic waste sites, where individuals may be exposed to complex mixtures of chemicals that might act synergistically on the nervous system.

In 1986, EPA established an intra-agency work group to look at substances that act as reproductive and developmental toxicants. Testing guidelines for develop mental neurotoxicity are now being drafted. According to EPA scientists, animal models have consistently proved useful for predicting human response to neurotoxic agents.

Consumer Product Safety Commission

CPSC is beginning to develop neurotoxicity guidelines for manufacturers. The Commission program is directed at developing new regulations for products such as paint thinners and art materials that may have neurotoxicological effects under certain conditions of use. Appropriate labeling to warn of hazards, advise against hazardous uses or exposures, and provide first-aid instruction is required under statutes administered by CPSC.

Although the Commission develops guidelines and regulations rather than conducting research, staff members are identifying areas where scientific research would help them better fulfill their mandate. Development of test methods for identifying toxicants that cause neurological damage after chronic low-level exposures, identification of key species differences to aid in extrapolating animal test results to appropriate endpoints in humans, and development of a better understanding of the relationship between high- and low-dose neurotoxic effects are research areas of particular interest to CPSC officials.

Department of Labor

Although charged with setting neurotoxicity health and safety standards, the Occupational Safety and Health Administration (OSHA) conducts no research of its own. Instead, scientists at NIOSH and elsewhere supply OSHA with information needed to promulgate health standards. For example, to help in regulating neurotoxic agents, OSHA officials would like to see research conducted on subclinical effects of neurotoxic substances and at what exposure levels such effects remain reversible. OSHA would also like Federal agencies to standardize means for

conducting risk assessments, develop quantitative methods for expressing subtle behavioral changes, devise simple tests to measure toxic effects on individual workers, and publish a standardized list of neurotoxic substances.

OSHA health standards become legal documents intended to ensure that employees not suffer "material impairment of health or functional capacity, ' which the courts interpret to include subclinical effects. Thus, in setting standards, OSHA can act to prevent relatively mild and reversible forms of potentially serious diseases, such as those caused by a particular neurotoxic substance. "Material impairment" can also mean workplace exposures to chemicals that cause temporary narcosis, which can lead to accidents and injuries. The courts give OSHA considerable latitude in determining "significant risk" and the consequences of resetting exposure limits to particular chemicals.

Department of Defense

DoD has carried out extensive testing of protective drugs designed to counteract neurotoxic chemical agents. Its current program involves 26 laboratories, including support of research at laboratories within NIDA. To evaluate such drugs, DoD has developed a four-part procedure for extrapolating their effects to human performance in real-world situations, noted an official from DoD. DoD has developed sophisticated performance evaluation test batteries, risk identification procedures, a computer-based task-analysis procedure, and a real-world contingency analysis package, which provides information about the use and potential neurotoxic effects of antidotes for chemical warfare agents.

Workshop Discussion Groups

Identifying Testing Needs

Although there are processes prescribed by the National Testing Program (within ATSDR) and by the Interagency Testing Committee for nominating chemicals for neurotoxicity testing and evaluation, the discussion group concluded that the processes need revising. A major difficulty in conducting evaluations that lead to a chemical's nomination is the inadequate number of people with expertise in neurotoxicology. Having more appropriately trained experts would also help in educating regulators who select chemicals for such testing. The notion that neurotoxicity is a valid endpoint for evaluating chemicals needs general reinforcement.

Moreover, the scientific criteria for defining neurotoxicity, setting priorities, and selecting chemicals, including structure-activity relationships and comparisons of chemicals and chemical classes, also should be reevaluated and strengthened. For example, the volume of production and likely extent of human exposure to a particular chemical could be taken into account when deciding whether it should be nominated for testing, an official from NIEHS noted.

Thus, establishment of an independent advisory group of experienced individuals to better define neurotoxicity, to evaluate the nomination process, to review chemicals going through it, and to act as an information "resource" seems warranted, the discussion group concluded. If established, such an advisory group would not "sup plant' the regulatory agency, but would help 'sanction" the decisions the agency makes, an EPA official said.

A battery of standardized human neurotoxicity tests is needed, particularly for use in evaluating the effects of environmental exposures to potentially hazardous agents. Because several test batteries, such as the field performance battery used by DoD as well as another test battery developed by NIOSH, have been developed for testing humans exposed to suspected neurotoxic substances, it may be possible to adapt existing procedures into a more broadly applicable test battery.

''If you're going to do a particular test, at what level do you consider that some adverse health effect has occurred?" asked an official from ATSDR. "What you'd like is not only some tests, but indications for when to use them. . . .The whole idea. . . is to get the biggest bang for the Federal buck. " In that context the lack of resources for funding research and testing of suspected neurotoxic substances is a critical "rate-limiting" step.

Development and Use of Standardized Neurotoxicity Tests

Many neurotoxicity tests are now in use. The discussion group agreed that representatives from various agencies could form a coordinating group to compare the specific tests each agency is using and to evaluate strategies for developing new tests.

Some effort to coordinate research involving animal and human neurotoxicity testing is also needed. Improved efforts to obtain relevant information, such as pharmacokinetic data about a chemical's behavior in a particular species, are part of this overall task, an FDA official said.

Despite differences in statutory authority, other agencies besides EPA need to acknowledge critical arenas, such as developmental neurotoxicity, for evaluating chemicals and drugs, noted an official from EPA. However, any effort to move toward uniformity in testing becomes challenging because so much depends on the regulatory context in which a particular test will be used. EPA, for example, is expected to set and observe standards for tests that are mandated under several legislative acts—particularly the Toxic Substances Control Act-that are unique to the Agency. Working under quite different legislative mandates, NIDA and FDA have

developed specific, highly sophisticated tests for particular categories of neuropharmacological agents. Whatever the tests being performed, noted another EPA official, the interpretation of results is "very dependent on the expertise of your reviewers, " For example, without adequate training in neuropathology, agency reviewers might overlook telltale signs of neurotoxicity in a particular animal model test.

A practical consideration arising from mission and statutory differences among regulatory agencies is that the costs of testing commodity chemicals, for instance, rather than drugs ''can very often not be supported by the anticipated market, ' an EPA official pointed out. Nonetheless, sharing of adequately reviewed information among agencies could help individual agencies in making decisions about neurotoxic substances to fulfill their particular legislative mandates. Whether test methods should be standardized or merely codified remains an unresolved issue.

Coordination of Federal Research Programs

Neurotoxicity research is defined broadly because the definition is driven by individual investigators as well as legislatively mandated regulatory agencies. Existing mechanisms for coordinating such research, particularly its more basic components, are largely informal and often fragmented. The discussion group did not reach a consensus on whether a central coordinating mechanism would be useful or desirable.

In particular, several representatives of the basic research community thought that such a committee might be viewed as an advocacy body trying to obtain a larger share of resources for conducting neurotoxicity research instead of studies in other areas. Thus, their misgivings about a formal neurotoxicity research coordinating body are based on an underlying fear that a central committee might interfere with research freedom "through budget leverage. '

In addition, noted an official from NIH, although other Federal activities involving neurotoxicity may well benefit from coordination, research "would be the least important to coordinate. . . .We're trying to solve a nonproblem. " Informal exchanges of information now ensure that research interests and opportunities are shared fairly freely between various Institutes within NIH, he said. Moreover, that exchange of information occurs outside the formal budget process. Sometimes it involves efforts to minimize overlap, but it also permits a degree of research 'redundancy'—i.e., overlapping or even repetitive research by different investigators. (Such redundancy, when it occurs, is usually justified as a vital part of the self-correcting, confirmatory aspect of basic research.) There are plenty of "knowledge gaps" in the neuroscience, he said. "Instead of feeling redundant, we're working to fill the knowledge gaps. "

Representatives from agencies that are purely regulatory or that also conduct research to support their regulatory responsibilities see a need for more deliberate efforts to coordinate research. "We need to identify gaps in the research database available to the regulatory agencies, " said an official from EPA. "We need. . .to transfer information [when] trying to develop research strategies, added another EPA representative, "We want to test their validity with other agencies. "

Historically, basic research findings have had an enormous impact on setting neurotoxicity-related regulations, The current effort within CDC, for instance, to reevaluate safe blood levels for lead "arose from basic research findings about lead's neurotoxicity, ' an EPA official pointed out. "How can we [convey] basic information about how the nervous system responds to various insults . . . to [officials] to protect public health?" He and many other participants at the workshop agreed that such information could be evaluated and disseminated more effectively than current mechanisms allow. They also agreed that, by making basic researchers more aware of the scientific challenges facing regulatory agencies, the nature of some research undertakings may change in valuable ways. "We want NIH aware of problems facing regulatory agencies ., , to see if it can give a different emphasis to basic research," an EPA official noted.

Coordination of Testing and Monitoring Programs

Several Federal agencies, including, EPA, OSHA, NIOSH, FDA, and CPSC, have both passive and active neurotoxicity monitoring capabilities and interests. Data **developed during the conduct of such activities typically are stored by the agencies, Members of the discussion group concluded that sharing such information among agencies would be** useful-as would identifying key contact people at each agency and making agency-specific databases compatible with one another.

The handling of data is seen as a challenge. Agencies now have different criteria for evaluating such data. EPA, for example, stringently reviews data before entering them into the Integrated Risk Information System, an Agency official noted. "These data have status. [As] an agency policy. . . .1 would have to ask what status other kinds of shared data would have. ' The expected uses for a "centralized database. , . to a large extent might dictate what kind of data you would put in it" another EPA official said.

Officials face serious questions in evaluating neurotoxicity test schemes. The development and validation of new tests and test batteries are a central challenge.

Moreover, there is no agreed-on basis for moving from a tier-one to a tier-two battery of tests. A concise definition of "significant biological effect" is needed, as are consistent strategies for using test data when conducting risk assessments, The exchange of information, sometimes at the early stage of description in grant applications, might expedite development of useful procedures. In the same vein, it would be useful to track what compounds are being tested by which agencies so that interested parties could be kept informed about the status of particular suspect neurotoxic agents, even during the earliest stages of examination. Similarly, it would be useful to reexamine past neurotoxicology data, in part to gain a greater understanding of what test endpoints have proved particularly reliable.

Coordination of Risk Assessment and Regulatory Programs

Of the regulatory agencies represented at the workshop, EPA apparently has the most stringent guidelines for risk assessment. This stringency is dictated in part by EPA's need for consistency throughout its diverse programs and across its regional offices. For example, engineers at Superfund sites may be called on to make $20-million decisions, pointed out an EPA representative, In such circumstances, guidance and consistency are essential—to support the on-site decision if it is subsequently challenged in court.

Although other regulatory agencies may not have such formal guidelines, they often have special offices for addressing risk assessment, scientific, and policy issues. OSHA, for instance, has promulgated guidelines for carcinogens, according to an agency official. However, developing those guidelines "was time-consuming and not an effective process, ' this same official noted, adding that having consistent practices across agencies seems more important than publishing specific guidelines. Informally, many agencies follow a process outlined in the National Research Council document *Risk Assessment in the Federal Government: Managing the Process (2).* It distinguishes between risk assessment, which is considered principally a scientific evaluation process, and risk management, which involves political, economic, and other considerations, Efforts to coordinate neurotoxicity risk assessment ought to emphasize "science and. . . risk assessment and not . . . risk management" an EPA official recommended.

"I don't think you can make that kind of clean distinction,' another discussion group participant responded. "I don't think you can live with that kind of artificial situation. . . it's the sort of thing that gets us into trouble. And, noted another participant, "There is a basic political premise that is involved in that separation decision. If it works well for an agency under a set of circumstances, great. But I don't think it's universally clear that is the way to proceed. "

The discussion group considered whether universal guidelines for conducting risk assessments might exert untoward effects, such as restricting scientific judgments and, ultimately, impeding regulatory actions. "Standardized guidelines tend to stagnate the discipline," said an official from DOE. "Formalizing them too soon is not good. The important part of risk assessment is [holding] a social dialogue, focusing on a problem, and stimulating research." However, an official from EPA responded, "What you say is very nice if the agency doesn't have a lawsuit accusing [it] of not making a regulatory decision.

There was general agreement that careful thought must be exercised lest risk assessment concepts be introduced too early. Nonetheless, some principles of risk assessment may be applicable to neurotoxicity data from all regulatory agencies. Moreover, research issues common to most, if not all, regulatory agencies can be addressed in a coordinated fashion. "Looking at common research issues could certainly be a marked advantage,' the discussion group agreed. However, concern was voiced that other agencies feel "their input into what EPA is doing in risk assessment is. . . retrospective." Thus, there is a need for them to have input earlier in the process so as to have greater impact.

"Rather than adopt [guidelines] uniformly, we may want to see how a particular agency's guidelines work out . . . and then learn from each other's mistakes and successes, " suggested an official from FDA. "EPA and FDA may start at the same point trying to detect neurotoxic drugs or environmental agents, Later on, the FDA decision on setting a neurotoxic threshold for a drug will be different from [the standard] EPA sets for an environmental agent. "

The group was divided over how risk assessment procedures for evaluating suspected carcinogens stand up against procedures for evaluating putative neurotoxic substances. "In some ways, we know more in the area of neurotoxicity, ' an EPA official argued. "We know about variety, reversibility, as much or more about mechanisms. . . . [In neurotoxicity] somehow we are able to accept a certain level of risk. . . .It's not that cancer risk assessment is more developed, [but] we put an arbitrary structure on [it] largely in response to a political need. " Added an official from FDA, "The key is that we are better able to set a safe limit for a neurotoxicant than. . . for carcinogens.'

Sometimes the "politics of the situation require us to say, 'We don't know enough about what we're doing here',' said another EPA official. However, both EPA and FDA "have a long empirical track record of dealing

with neurotoxic agents, of establishing safe levels. . . .So we shouldn't confuse ourselves.

Such considerations also have an impact on "risk communication' '—that is, notifying individuals of the risk posed by particular substances. "That whole area is under great scrutiny within the cognitive psychology community, " noted a participant. Research "to explain a complex concept" and efforts to "develop a special language" could help in getting the public to understand risks more clearly.

Models for Coordinating Federal Neurotoxicity Efforts

There are several models for coordinating interagency neurotoxicity activities. The Interagency Regulatory Liaison Group was established more than a decade ago and seemed to work well until it became too difficult to manage, according to a DOE official. Moreover, with a change in administrations came a change in activities among regulatory agencies and a decreased emphasis on coordination among them.

Within DHHS, the Committee to Coordinate Environmental Health and Related Programs (CCEHRP) could coordinate neurotoxicity activities. The committee "is authorized to establish subcommittees and could readily accommodate interests in neurotoxicity among DHHS agencies with liaisons to agencies outside the Department. CCEHRP has a policy board and counsel that are research- and program-directed, according to a representative from DHHS. CCEHRP is also integrated vertically, meaning its membership includes researchers who work at the bench as well as high-level managers.

Historically, the Office of Science and Technology Policy (OSTP) within the Office of the President has functioned as an organizing body for cooperative activities to establish risk assessment principles for carcinogens. The OSTP Chemical Carcinogens Document published in the *Federal Register* on March 14, 1985, is widely accepted as a model achievement. Moreover, with OSTP leadership, representatives from academia, industry, and the Federal Government can work together in developing acceptable policies. A risk in calling on OSTP to undertake Federal coordination of neurotoxicity activities is that the issue could become too political. Thus, some workshop participants argued that the coordination of neurotoxicity activities to fulfill research and data needs might prove more workable if organized from "the bottom up. " Once successful, agency officials then are better positioned to convince management of particular policy options to implement.

Proposal

Toward the close of the workshop, participants agreed that an "Interagency Working Group on Neurotoxicology " should be formed.[1] The proposed working group, which would be dedicated to improving the Federal response to human health issues related to neurotoxicology, would include members from all Federal agencies and organizations having research, regulatory, or other pertinent interests in neurotoxicology. Such a forum for exchanging information could help minimize duplication of efforts. The working group could also help ensure that negative as well as positive findings are shared by individuals interested in neurotoxicology.

Although workshop participants limited their proposal to a sketch of what such an interagency working group should undertake, they did outline key areas where such a body could fill gaps and help to coordinate otherwise isolated efforts in research, testing, monitoring, risk assessment, regulation, and other areas. The working group also might develop a "conceptual framework. . .to identify long-range needs related to neurotoxicology, " suggested an official from EPA. It might also "encourage the Library of Medicine to participate in the establishment of a neurotoxicology database."

Appendix B References

1. This summary of the OTA/EPA workshop was prepared by Jeffrey Fox under contract No. L3-2630.O.
2. National Research Council, *Risk Assessment in the Federal Government: Managing the Process* (Washington, DC: National Academy Press, 1983).

[1]On Oct. 26,1989, the name was changed to the Interagency Committee on Neurotoxicology (ICON). The committee is adrninisteredthrough the Neurotoxicology Division of EPA's Health Effects Research Laboratory in Research Triangle Park, NC.

Federal Interagency Coordination of Neurotoxicity Research and Regulatory Programs

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