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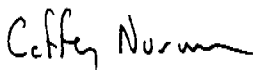
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April 3, 1996

MEMORANDUM FOR VINYL CHLORIDE PANEL

Re: ATSDR Voluntary Research Program

Attached is a notice published earlier this week by the Agency for Toxic Substances and Disease Registry (ATSDR) to update the status of its voluntary research program. The notice reports that the acute inhalation toxicity study of vinyl chloride has been determined no longer to be a data need. It notes that CMA submitted a protocol to address the priority data needs for reproductive and developmental toxicity studies of vinyl chloride by inhalation, and states that ATSDR expects to enter a Memorandum of Understanding with CMA for this study in the near future.


W. Caffey Norman, III

Attachment

CMA 113302

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency For Toxic Substances and Disease Registry

[ATSDR-106]

Update on the Status of the Superfund Substance-Specific Applied Research Program

AGENCY: Agency for Toxic Substances and Disease Registry (ATSDR), Department of Health and Human Services (HHS).

ACTION: Notice.

SUMMARY: This Notice is an update on the status of ATSDR's continuing effort to implement the Substance-Specific Applied Research Program (SSARP). Authorized by the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (Superfund) or CERCLA, as amended by the Superfund Amendments and Reauthorization Act of 1986 (SARA) (42 U.S.C. 9604 (i)), this research program was initiated on October 17, 1991. At that time, a list of priority data needs for 38 priority hazardous substances was announced in the Federal Register (56 FR 52178). The list was subsequently revised based on public comments and published in final form on November 16, 1992 (57 FR 54150).

The 38 substances, each of which is found on ATSDR's List of Priority Hazardous Substances, are aldrin/dieldrin, arsenic, benzene, beryllium, cadmium, carbon tetrachloride, chloroethane, chloroform, chromium, cyanide, p,p'-DDT, DDE, DDD, di(2-ethylhexyl) phthalate, lead, mercury, methylene chloride, nickel, polychlorinated biphenyl compounds (PCBs), polycyclic aromatic hydrocarbons (PAHs—includes 15 substances), selenium, tetrachloroethylene, toluene, trichloroethylene, vinyl chloride, and zinc (56 FR 52166, October 17, 1991).

Priority data needs for 12 additional priority hazardous substances were recently identified and are also being announced in a Federal Register Notice. The 12 substances, each of which is included in ATSDR's List of Priority Hazardous Substances, are chlordane, 1,2-dibromo-3-chloropropane, di-n-butyl phthalate, disulfoton, endrin (includes endrin aldehyde), endosulfan (alpha-, beta-, and endosulfan sulfate), heptachlor (includes heptachlor epoxide), hexachlorobutadiene, hexachlorocyclohexane (alpha-, beta-, delta- and gamma-), manganese, methoxychlor, and toxaphene.

This Notice also serves as a continuous call for voluntary research proposals. Private-sector organizations may volunteer to conduct research to address specific priority data needs by indicating their interest through submission of a research proposal to ATSDR (see ADDRESSES section of this Notice). A Tri-Agency Superfund Applied Research Committee (TASARC) comprised of scientists from ATSDR, the National Toxicology Program (NTP), and the Environmental Protection Agency (EPA) will review all proposed voluntary research efforts.

DATES: ATSDR considers the voluntary research effort to be important to the continuing development of the SSARP. Therefore, the agency strongly encourages private-sector organizations to volunteer at any time to conduct research to address identified data needs unless ATSDR announces that research has already been initiated for that specific data need.

ADDRESSES: Private-sector organizations interested in volunteering to conduct research may write to Dr. William Cibulas, Chief, Research Implementation Branch, Division of Toxicology, ATSDR, 1600 Clifton Road, N.E., Mailstop E-29, Atlanta, Georgia 30333.

FOR FURTHER INFORMATION CONTACT: Dr. William Cibulas, Chief, Research Implementation Branch, Division of Toxicology, ATSDR, 1600 Clifton Road, N.E., Mailstop E-29, Atlanta, Georgia 30333, telephone 404-639-6306.

SUPPLEMENTARY INFORMATION:

Background

CERCLA as amended by SARA (42 U.S.C. 9604(i)) requires that ATSDR (1) jointly with the EPA, develop and prioritize a list of hazardous substances found at National Priorities List (NPL) sites, (2) prepare toxicological profiles for these substances, and (3) assure the initiation of a research program to address identified data needs associated with the substances. Before starting such a program, ATSDR will consider recommendations of the Interagency Testing Committee on the type of research that should be done. This committee was established under section 4(e) of the Toxic Substances Control Act of 1976 (TSCA).

On October 17, 1991, ATSDR announced the identification of the priority data needs for 38 priority hazardous substances (56 FR 52178), requested public comments, and invited private-sector organizations to volunteer to conduct research to address specific priority data needs. On November 16, 1992, the agency

published a revised list of 117 priority data needs for these priority hazardous substances (57 FR 54150).

The major goals of the ATSDR SSARP are (1) to address the substance-specific information needs of the public and scientific community, and (2) to supply necessary information to improve the database to conduct comprehensive public health assessments of populations living near hazardous waste sites. This program will also provide data that can be generalized to other substances or areas of science, including risk assessment of chemicals, thus creating a scientific base for addressing a broader range of data needs.

In section 104(i)(5)(D), CERCLA states that it is the sense of Congress that the costs for conducting this research program be borne by the manufacturers and processors of the hazardous substances under TSCA and by registrants under the Federal Insecticide, Fungicide, and Rodenticide Act of 1972 (FIFRA), or by cost recovery from responsible parties under CERCLA. To execute this statutory intent, ATSDR developed a plan whereby parts of the SSARP are being conducted via regulatory mechanisms (TSCA/FIFRA), private-sector voluntarism, and through the direct use of CERCLA funds.

The TASARC, comprised of scientists from ATSDR, NTP, and the EPA has been set up:

- (1) To advise on the assignment of priorities on mechanisms for addressing data needs;
- (2) To coordinate knowledge of research activities to avoid duplication of research in other programs and under other authorities;
- (3) To advise on issues of science related to substance-specific data needs; and
- (4) To maintain a scheduled forum that provides an overall review of the ATSDR SSARP.

The TASARC has met six times since the SSARP began. This Notice is an update on the status of ATSDR's efforts to implement the SSARP, focusing on ongoing activities relevant to test-rule development under TSCA/FIFRA, private-sector voluntarism, and the direct use of CERCLA funds.

Additional data needs are being addressed through an interagency agreement with NTP, by ATSDR's Great Lakes Human Health Effects Research Program, and other agency programs. To date, a total of 63 research needs associated with 38 ATSDR priority hazardous substances (including 15 polycyclic aromatic hydrocarbons) are being addressed via these mechanisms (Table 1).

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ATSDR believes that these priority data needs will remain on the agency's list until ongoing studies to address them have been completed, peer-reviewed, and accepted by ATSDR. However, priority data needs could be deleted from the list (Table 1) if upon re-evaluation of the existing database, the agency determines that additional studies are no longer needed. Three recent examples follow. ATSDR, in consultation with the TASARC, re-evaluated the database for acute inhalation toxicity for vinyl chloride and determined no additional data are needed at this time (Table 1). With regard to the priority data need for oral developmental toxicity studies for tetrachloroethylene (PERC), ATSDR recently re-evaluated the database during the update of the toxicological profile for this substance. ATSDR concluded that the database was sufficient to derive a minimal risk level (MRL) for acute oral exposure based on a developmental toxicity study. Although ATSDR believes that additional developmental data would be useful to more fully characterize the effects and increase the confidence level of the MRL, the agency now believes that this data is more appropriately classified as a *data need* rather than a *priority data need*. Therefore, this priority data need has also been deleted from the list (Table 1). Similarly, the *priority data need* for additional acute oral studies for trichloroethylene has been reclassified as a *data need* and thus deleted from the list (Table 1) because an MRL was derived during the updating of the toxicological profile. Conversely, additional priority data needs could be included in the ATSDR list based on assessment by agency programs (See Section F, "Other ATSDR Programs," which discusses exposure subregistries).

A. TSCA/FIFRA

In developing and implementing the Substance-Specific Applied Research Program, ATSDR, NTP, and EPA have established procedures to identify priority data needs of mutual interest to Federal programs. These data needs are being addressed through a program of toxicologic testing under TSCA. This research will be conducted according to established TSCA procedures and guidelines. Generally, this testing will address more than one Federal program's need. Following review and endorsement by the TASARC oversight committee during fiscal year (FY) 1993, of the 117 priority data needs for 38 substances, approximately 60 priority data needs were referred to the EPA under TSCA/FIFRA authorities.

During 1994, EPA added 11 ATSDR substances (and associated 28 priority data needs) to its master testing list, the first step in test-rule development under TSCA, Section 4 (59 FR 11434, March 10, 1994). On September 30, 1994, EPA published a Federal Register Notice soliciting testing proposals from industry to address the priority data needs identified for ATSDR's priority hazardous substances (59 FR 49934). Although no manufacturers or processors of these substances came forward with testing proposals, several industry groups responded by submitting proposals to address some of the data needs via ATSDR's voluntary research program described in detail in Section B, "Private-Sector Voluntarism." The priority data needs currently being addressed by TSCA/FIFRA are listed in Table 2.

ATSDR shared its priority data needs for these substances with other Federal agencies and programs. On several occasions when ATSDR identified priority data needs for oral exposure, other agencies needed inhalation data. In response, ATSDR is considering proposals to conduct inhalation studies in conjunction with physiologically based pharmacokinetic (PBPK) studies in lieu of oral bioassays. ATSDR expects that inhalation data derived from these studies can be used with PBPK modeling to address its oral toxicity data needs.

Table 2 includes the priority data needs for three metals, i.e., beryllium, chromium and mercury. However, the specific forms of the metals to be tested are yet to be determined. The TASARC has established a workgroup to address this issue. The workgroup will also consider the needs of other Federal agencies and EPA programs. The EPA will solicit testing proposals for these three metals at a later date.

B. Private-Sector Voluntarism

As part of the SSARP, on February 7, 1992, ATSDR initially announced a set of proposed procedures for conducting voluntary research (56 FR 4758). Revisions based on public comments were published on November 16, 1992 (57 FR 54160). Private-sector organizations were encouraged to volunteer to conduct research to address these specific priority data needs.

ATSDR has been pursuing voluntary research interests with three private-sector organizations: the General Electric Company (GE), the Halogenated Solvents Industry Alliance (HSIA), and the Chemical Manufacturers Association (CMA). Preliminary discussions are being held with a fourth organization, the Shell Oil Company. Through the

voluntary research efforts of these organizations, data needs for two classes of substances (PCB compounds and volatile organic compounds) are being addressed (Table 2). To date, two memoranda of understanding (MOU) have been signed by ATSDR and the interested parties. A third MOU is under development.

General Electric Company (GE)

On February 8, 1995, ATSDR entered into an MOU with GE. This was the first time a private-sector organization volunteered to conduct research to address ATSDR's data needs identified in its SSARP. The MOU with GE covers the following three studies on PCBs:

- * Project 1, "An assessment of the chronic toxicity and oncogenicity of Aroclor-1016, Aroclor-1242, Aroclor-1254, and Aroclor-1260 administered in diet to rats," was initiated on February 8, 1993.
- * Project 2, "Metabolite detection as a tool for the determination of naturally occurring aerobic PCB biodegradation," was initiated on January 2, 1995.
- * Project 3, "PCB congener analyses," was initiated on February 8, 1993.

While the above studies do not address ATSDR's *priority data needs* for PCBs, the three projects will address some of the agency's data needs for these substances. Specifically, although ATSDR has identified bioassays via the inhalation and dermal routes as data needs for PCBs, agency scientists believe information gained via GE's oral bioassay (Project 1) is pertinent to understanding the toxicity of PCBs. Furthermore, first-pass metabolism does not appear to play a key role for these substances. Therefore, toxicity information to be obtained from the GE oral bioassay is expected to be relevant to the inhalation and dermal routes.

ATSDR has identified PCB degradation in sediment as a data need. Additional environmental fate information is needed to estimate exposure to PCBs under various conditions of environmental release in order to plan and conduct follow-up exposure and health studies. Therefore, Project 2 will address ATSDR's data need for the environmental fate of PCBs.

Although ATSDR has not identified PCB congener analyses (Project 3) as a data need, agency scientists believe that the toxicokinetics data (using selected tissues from Project 1) may provide important knowledge about the correlation of health effects with relevant PCB congeners.

Halogenated Solvents Industry Alliance (HSIA)

On April 4, 1995, ATSDR entered into an MOU with HSIA covering studies to address three ATSDR priority toxicity data needs for methylene chloride. The studies consist of acute- and subchronic-duration, and developmental toxicity via oral exposure. The data will be obtained by using PBPK modeling. These studies were initiated on May 23, 1995.

HSIA has also proposed to conduct a 28-day immunopathology assessment for methylene chloride at low-dose exposure, a priority data need identified by ATSDR. The agency expects to receive a study protocol from HSIA for peer review in the near future.

Currently, HSIA and ATSDR continue to discuss voluntary research efforts for trichloroethylene (TCE) and tetrachloroethylene (PERC).

With regard to TCE, ATSDR has recently reclassified the *priority data need* for acute oral data to a *data need*, (see Background section of this Notice). The agency is continuing its discussion with HSIA to assess the possibility of conducting a study or utilizing benchmark dose modeling to address this data need. As for immunopathology data, HSIA proposed to first review the existing data for TCE. If the data are inadequate and the methylene chloride immunopathology study mentioned above has provided meaningful information, HSIA would then conduct a similar study for TCE.

Regarding the priority data needs for PERC, HSIA plans to obtain the oral neurotoxicity data called for by the agency by PBPK modeling. The database to be used for modeling will include the HSIA-sponsored inhalation neurotoxicity study recently approved by EPA. EPA and ATSDR scientists recently reviewed and accepted the HSIA-sponsored reproductive toxicity study of PERC via inhalation. HSIA proposed to address ATSDR's priority data need for oral reproductive data using PBPK modeling. As for ATSDR's priority data need for immunopathology data, HSIA would follow the same procedures as for TCE (described above).

Finally, with regard to ATSDR's data need for oral developmental toxicity studies for PERC (see Background section of this Notice), ATSDR is continuing its discussion with HSIA to obtain this data via PBPK modeling once the EPA-required inhalation developmental toxicity study has been completed.

Chemical Manufacturers Association (CMA)

During FY 1995, the CMA submitted a study protocol addressing two ATSDR priority data needs for vinyl chloride, specifically, inhalation reproductive and developmental toxicity studies in rats.

ATSDR accepted the study protocol as a candidate for voluntary research based on ATSDR peer reviews and CMA's satisfactory response to the peer reviewers' comments. ATSDR expects to finalize an MOU with CMA covering this study in the near future.

EPA no longer requires inhalation neurological data for vinyl chloride as originally stated in its solicitation Notice (59 FR 49934, September 30, 1994). Its decision is based on a recent reevaluation of the database.

C. CERCLA-Funded Research (Minority Health Professions Foundation Research Program)

During FY 1992, ATSDR announced a \$4 million cooperative agreement program with the Minority Health Professions Foundation (MHPF) to support substance-specific investigations. This cooperative venture is supported by the direct use of CERCLA funds. About \$4 million was allocated annually for FYs 1993 to 1995 to continue this research program that ends in September 1997.

Currently, 9 priority data needs for 21 priority hazardous substances (including 15 PAHs) in the SSARP are being addressed by the MHPF institutions through this program. Also, the MHPF research program will address 13 other substance-specific data needs identified in the ATSDR toxicological profiles concerning exposures and related health effects. To date, more than 20 abstracts have been presented at scientific meetings, 4 manuscripts have been published in peer-reviewed journals, and 7 manuscripts are in preparation. The institutions receiving awards and their respective research projects are listed in Table 2.

A not-for-profit 501(c)(3) organization, the MHPF comprises 11 minority health professions schools. Its primary mission is to research the health problems that disproportionately affect poor and minority citizens. The purposes of the ATSDR-MHPF cooperative agreement are (1) to initiate research to address ATSDR-identified data needs for priority hazardous substances, and (2) to enhance existing disciplinary capacities to conduct research in environmental health at MHPF member institutions.

The areas of research at MHPF institutions include those related to

broad areas of toxicology and environmental health science. Some MHPF members are conducting health studies of minority groups exposed to ATSDR's priority hazardous substances.

D. National Toxicology Program (NTP)

ATSDR maintains an interagency agreement (IAG) with NTP to conduct toxicologic testing of substances identified at NPL sites. The studies determine levels of exposure that present a significant risk to humans of acute, subchronic, and chronic health effects. Often these studies include an assessment of the substance's ability to cause cancer, reproductive toxicity, and birth defects. The results of these studies are used by regulatory agencies such as the Food and Drug Administration and EPA, various environmental and industrial groups, and ATSDR to improve the ability to conduct public health assessments at NPL sites.

Under this agreement, one toxicity priority data need identified in the SSARP (immunotoxicology study of carbon tetrachloride) is being addressed.

An area of ongoing research by the NTP is to study the bioavailability of PCBs in soil, a priority data need for ATSDR. Therefore, NTP research may also potentially address this ATSDR priority data need.

During FY 1993, the existing IAG was modified to include toxicity studies of ATSDR's priority hazardous substances via application of structure-activity relationship (SAR) techniques and PBPK modeling. NTP indicated future plans for SAR modeling for reproductive and immunologic endpoints. ATSDR is continuing to work closely with NTP as the agency has identified many reproductive and immunologic data needs for the 38 priority hazardous substances. As discussed in Section A, "TSCA/FIFRA," ATSDR will consider using PBPK modeling to address data needs when models are well developed and validated. Therefore, ATSDR will continue to work closely with NTP in its efforts to refine the models.

E. Great Lakes Human Health Effects Research Program

Some of the priority data needs identified in the SSARP have been independently identified as research needs through the ATSDR Great Lakes Human Health Effects Research Program, a separate research program. To date, 12 priority data needs for 19 priority hazardous substances (including 15 PAHs) identified in the SSARP are being addressed through this program. The institutions receiving

awards and their respective studies are listed in Table 2.

The Great Lakes Critical Programs Act of 1990 mandated that EPA, in consultation with ATSDR, prepare a report that assesses the adverse effects of pollutants in the Great Lakes system on the health of individuals in the Great Lakes states. This report was recently transmitted to the Congress by the EPA Administrator.

In support of this directive, ATSDR received funds to carry out research. The ATSDR-supported research projects focus on at-risk populations to further define the human health consequences of exposure to persistently toxic substances in the Great Lakes basin. The research activities include but are not limited to the following:

- (1) Characterizing exposure and determining the profiles and levels of Great Lakes contaminants in biologic tissues and fluids in at-risk populations;
- (2) Identifying sensitive and specific human reproductive/developmental endpoints and correlating them to exposure to Great Lakes contaminants;
- (3) Determining the short- and long-term risk(s) of adverse health effects in progeny whose parents were exposed to Great Lakes contaminants;
- (4) Investigating the feasibility of establishing registries and surveillance cohorts in the Great Lakes region; and
- (5) Establishing a chemical mixtures database with emphasis on tissue and blood levels in order to identify new cohorts, conduct surveillance and health effects studies, and establish registries and surveillance cohorts.

During FY 1992, ATSDR announced a \$2 million grant program to conduct research on the impact on people's health from eating contaminated fish from the Great Lakes region. On September 30, 1992, ATSDR announced 9 awards under this program.

In FY 1993, about \$3 million was allocated to support the continuation of the research projects conducted at the 9 institutions originally funded during FY

1992. In addition, ATSDR awarded one new grant to the Michigan Department of Public Health to design, establish, and operate a professionally creditable, interlaboratory quality assurance/quality control program for the ATSDR Great Lakes Human Health Effects Research Program. Additional funding of \$3 million and \$4 million for FYs 1994 and 1995, respectively, was allocated to continue support of the 10 research projects.

During FY 1994, ATSDR held a Great Lakes Research Symposium in Detroit, Michigan. The proceedings of the symposium will be published in the *Journal of Toxicology and Industrial Health* in the near future.

Other ATSDR Programs

In its role as a public health agency addressing environmental health, when appropriate, ATSDR may collect human data to validate substance-specific exposure and toxicity findings.

Information on levels of contaminants in humans has been identified and remains as a priority data need for 37 of the 38 priority substances (Table 1). ATSDR will obtain this information through exposure and health effects studies, and through establishing and using substance-specific subregistries of people within the agency's National Exposure Registry who have potentially been exposed to these substances.

The list of 38 priority hazardous substances in the SSARP was forwarded to ATSDR's Exposure and Disease Registry Branch (EDRB), Division of Health Studies, for consideration as potential candidates for subregistries of exposed persons, based on criteria described in its 1988 document, "Policies and Procedures for Establishing a National Registry of Persons Exposed to Hazardous Substances."

To date, ATSDR has selected benzene, chromium, and trichloroethylene as primary contaminants to establish subregistries in the National Exposure

Registry. However, aldrin/dieldrin, carbon tetrachloride, chloroethane, chloroform, cyanide, p,p'-DDT, DDE, DDD, di(2-ethylhexyl)phthalate, mercury, methylene chloride, PAHs, selenium, tetrachloroethylene, and vinyl chloride remain in the candidate pool. They will be considered for selection as primary contaminants during each selection process (Table 1).

Since the publication of the ATSDR March 10, 1994, Federal Register Notice (59 FR 11434), EDRB has re-evaluated the databases and included nickel, PCBs, toluene, and zinc in the candidate pool for consideration during each selection process (Table 1). However, arsenic, beryllium, cadmium, and lead are not considered to be in the pool of candidate substances for an exposure registry at this time. This decision will be re-evaluated as more information on the chemicals and exposure sites become available.

Finally, the need to collect, evaluate, and interpret environmental data from contaminated media around hazardous waste sites remains a priority data need for all 38 priority hazardous substances by ATSDR. However, agency scientists realize that a substantial amount of this information has already been collected through individual State programs and the EPA's CERCLA activities; therefore, ATSDR will evaluate the extant information from these programs to characterize better the need for additional site-specific information.

The results of the research conducted via the SSARP will be used for public health assessments and to reassess ATSDR's substance-specific priority data needs. The agency expects to re-evaluate the priority data needs for priority hazardous substances every three years.

Dated: March 28, 1996.

Claire V. Broome,

Deputy Administrator, Agency for Toxic Substances and Disease Registry.

TABLE 1.—SUBSTANCE-SPECIFIC PRIORITY DATA NEEDS (PDN) CURRENTLY BEING ADDRESSED UNDER ATSDR'S APPLIED RESEARCH PROGRAMS

Substance	PDN ID	PDN description	Programs (1)
Lead	1A	Mechanistic studies on the neurotoxic effects of lead	M
	1B	Analytical methods for tissue levels.	
	1C	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	M, G
Arsenic	2A	Comparative toxicokinetic studies to determine if an appropriate animal species can be identified ...	
	2B	Half-lives in surface water, groundwater.	
	2C	Bioavailability from soil.	
	2D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
Mercury	3A	Multigeneration reproductive toxicity study via oral exposure	M, G
	3B	Dose-response data in animals for chronic-duration oral exposure	E

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TABLE 1.—SUBSTANCE-SPECIFIC PRIORITY DATA NEEDS (PDN) CURRENTLY BEING ADDRESSED UNDER ATSDR'S APPLIED RESEARCH PROGRAMS—Continued

Substance	PDN ID	PDN description	Programs ⁽¹⁾
Vinyl Chloride	3C	Immunotoxicology battery of tests via oral exposure	E
	3D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	G
	3E	Potential candidate for subregistry of exposed persons	A, G
	4A	Dose-response data in animals for acute-duration inhalation exposure	O ⁽²⁾
	4B	Multigeneration reproductive toxicity study via inhalation	V ⁽³⁾
	4C	Dose-response data in animals for chronic-duration inhalation exposure.	
	4D	Mitigation of vinyl chloride-induced toxicity.	
Benzene	4E	2-species developmental toxicity study via inhalation	V ⁽³⁾
	4F	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	4G	Potential candidate for subregistry of exposed persons	A
	5A	Dose-response data in animals for acute- and intermediate-duration oral exposure. The subchronic study should include an extended reproductive organ histopathology.	E
	5B	2-species developmental toxicity study via oral exposure	M
	5C	Neurotoxicology battery of tests via oral exposure	E
	5D	Epidemiologic studies on the health effects of benzene (Special emphasis endpoints include immunotoxicity).	
Cadmium	5E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	6A	Analytical methods for biological tissues and fluids and environmental media.	
	6B	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
PCBs	7A	Dose-response data in animals for acute- and intermediate-duration oral exposures	G
	7B	Biodegradation of PCBs in water; bioavailability of PCBs in air, water and soil	
	7C	Dose-response data in animals for acute- and intermediate-duration inhalation exposures. The subchronic study should include extended reproductive organ histopathology	
	7D	Epidemiologic studies on the health effects of PCBs (Special emphasis endpoints include immunotoxicity, gastrointestinal toxicity, liver, kidney, thyroid toxicity, reproductive/developmental toxicity).	G
	7E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	G
	7F	Potential candidate for subregistry of exposed persons	A ⁽¹⁾
	7G ⁽⁴⁾	Chronic toxicity and oncogenicity via oral exposure	V
Chloroform	7H ⁽⁵⁾	Aerobic PCB biodegradation in sediment	V
	7I ⁽⁶⁾	PCB congener analysis	V
	8A	Dose-response data in animals for intermediate-duration oral exposure.	
	8B	Epidemiologic studies on the health effects of chloroform (Special emphasis endpoints include cancer, neurotoxicity, reproductive and developmental toxicity, hepatotoxicity, and renal toxicity)	
	8C	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
	8D	Potential candidate for subregistry of exposed persons	A
	9A	Dose-response data in animals for intermediate duration oral exposures. The subchronic study should include extended reproductive organ histopathology and immunopathology.	M
PAHs	9B	2-Species developmental toxicity study via inhalation or oral exposure	
	9C	Mechanistic studies on PAHs, on how mixtures of PAHs can influence the ultimate activation of PAHs, and on how PAHs affect rapidly proliferating tissues	
	9D	Dose-response data in animals for acute- and intermediate-duration inhalation exposures. The subchronic study should include extended reproductive organ histopathology and immunopathology.	M
	9E	Epidemiologic studies on the health effects of PAHs (Special emphasis endpoints include cancer, dermal, hemolymphatic, and hepatic).	G
	9F	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	G
	9G	Potential candidate for subregistry of exposed persons	A
	10A	Dose-response data in animals for acute- duration oral exposure.	O ⁽²⁾
Trichloro-ethylene	10B	Neurotoxicology battery of tests via the oral route	M
	10C	Immunotoxicology battery of tests via the oral route	V ⁽⁴⁾
	10D	Epidemiologic studies on the health effects of trichloroethylene (Special emphasis endpoints include cancer, hepatotoxicity, renal toxicity, developmental toxicity, and neurotoxicity).	
	10E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	11A	Dose-response data in animals for chronic-duration oral exposure.	
	11B	Comparative toxicokinetic study (across routes/species).	
	11C	Bioavailability and bioaccumulation from soil.	
DDT	11D	Epidemiologic studies on the health effects of DDT, DDD and DDE (Special emphasis endpoints include immunotoxicity, reproductive and developmental toxicity).	G
	11E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	G

TABLE 1.—SUBSTANCE-SPECIFIC PRIORITY DATA NEEDS (PDN) CURRENTLY BEING ADDRESSED UNDER ATSDR'S APPLIED RESEARCH PROGRAMS—Continued

Substance	PDN ID	PDN description	Programs ⁽¹⁾
Chromium	11F	Potential candidate for subregistry of exposed persons	A, G
	12A	Dose-response data in animals for acute-duration exposure to chromium (VI) and (III) via oral exposure and for intermediate-duration exposure to chromium (VI) via oral exposure.	E
	12B	Multigeneration reproductive toxicity study via oral exposure to chromium (III) and (VI)	E
	12C	Immunotoxicology battery of tests following oral exposure to chromium (III) and (VI)	E
	12D	2-Species developmental toxicity study via oral exposure to chromium (III) and (VI)	
Tetrachloro-ethylene.	12E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	13A	Dose-response data in animals for acute-duration oral exposure, including neuropathology and demeanor, and immunopathology.	V(4,5)
	13B	Multigeneration reproductive toxicity study via oral exposure	V(4,5)
	13C	Dose-response data in animals for chronic-duration oral exposure, including neuropathology and demeanor, and immunopathology	
	13D	2-Species developmental toxicity study via oral exposure	O(2)
Aldrin/Dieldrin ...	13E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	13F	Potential candidate for subregistry of exposed persons	A
	14A	Dose-response data in animals for intermediate-duration oral exposure.	
	14B	Bioavailability from soil.	
Cyanide	14C	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	14D	Potential candidate for subregistry of exposed persons	A
	15A	Dose-response data in animals for acute- and intermediate-duration exposures via inhalation. The subchronic study should include extended reproductive organ histopathology and evaluation of neurobehavioral and neuropathological endpoints.	E
	15B	2-Species developmental toxicity study via oral exposure	E
	15C	Evaluation of the environmental fate of cyanide in soil	E
Carbon Tetra-chloride.	15D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	15E	Potential candidate for subregistry of exposed persons	A
	16A	Dose-response data in animals for chronic oral exposure. The study should include extended reproductive organ and nervous tissue (and demeanor) histopathology.	
	16B	Immunotoxicology battery of tests via oral exposure.	NTP
	16C	Half-life in soil.	
Beryllium	16D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	16E	Potential candidate for subregistry of exposed persons	A
	17A	Dose-response data in animals for acute- and intermediate-duration inhalation exposures. The subchronic study should include extended reproductive organ histopathology.	E
	17B	2-Species developmental toxicity study via inhalation exposure	E
	17C	Environmental fate in air; factors affecting bioavailability in air	E
Toluene	17D	Analytical methods to determine environmental speciation.	
	17E	Immunotoxicology battery of tests following oral exposure	E
	17F	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	18A	Dose-response data in animals for acute- and intermediate-duration oral exposures. The subchronic study should include an extended histopathologic evaluation of the immune system.	E
	18B	Comparative toxicokinetic studies (Characterization of absorption, distribution, and excretion via oral exposure).	E
Nickel	18C	Neurotoxicology battery of tests via oral exposure.	M
	18D	Mechanism of toluene-induced neurotoxicity.	
	18E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	18F	Potential candidate for subregistry of exposed persons	A(3)
	19A	Epidemiologic studies on the health effects of nickel (Special emphasis endpoints include reproductive toxicity).	
Methylene Chloride.	19B	2-Species developmental toxicity study via the oral route.	
	19C	Dose-response data in animals for acute- and intermediate-duration oral exposures.	
	19D	Neurotoxicology battery of tests via oral exposure.	
	19E	Bioavailability of nickel from soil.	
	19F	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	19G	Potential candidate for subregistry of exposed persons	A(3)
	20A	Dose-response data in animals for acute- and intermediate-duration oral exposure. The sub-chronic study should include extended reproductive organ histopathology, neuropathology and demeanor, and immunopathology.	V(5,6)
	20B	2-Species developmental toxicity study via the oral route	V(5)
	20C	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	20D	Potential candidate for subregistry of exposed persons	A

TABLE 1.—SUBSTANCE-SPECIFIC PRIORITY DATA NEEDS (PDN) CURRENTLY BEING ADDRESSED UNDER ATSDR'S APPLIED RESEARCH PROGRAMS—Continued

Substance	PDN ID	PDN description	Programs ⁽¹⁾
Zinc	21A	Dose-response data in animals for acute- and intermediate-duration oral exposures. The subchronic study should include an extended histopathologic evaluation of the immunologic and neurologic systems.	M
	21B	Multigeneration reproductive toxicity study via oral exposure.	
	21C	Carcinogenicity testing (2-year bioassay) via oral exposure.	
	21D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
DEHP	21E	Potential candidate for subregistry of exposed persons.	A ⁽³⁾
	22A	Epidemiologic studies on the health effects of DEHP (Special emphasis endpoints include cancer).	
	22B	Dose-response data in animals for acute- and intermediate-duration oral exposures. The subchronic study should include an extended histopathologic evaluation of the immunologic and neurologic systems.	
	22C	Multigeneration reproductive toxicity study via oral exposure.	
	22D	Comparative toxicokinetic studies (Studies designed to examine how primates metabolize and distribute DEHP as compared to rodents via oral exposure).	E
	22E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
Selenium	22F	Potential candidate for subregistry of exposed persons	A
	23A	Dose-response data in animals for acute-duration oral exposure.	
	23B	Immunotoxicology battery of tests via oral exposure.	
	23C	Epidemiologic studies on the health effects of selenium (Special emphasis endpoints include cancer, reproductive and developmental toxicity, hepatotoxicity and adverse skin effects).	
Chloroethane	23D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers.	
	23E	Potential candidate for subregistry of exposed persons	A
	24A	Dose-response data in animals for acute- and intermediate-duration oral exposures. The subchronic study should include an evaluation of immune and nervous system tissues, and extended reproductive organ histopathology.	E
	24B	Dose-response data in animals for chronic inhalation exposures. The study should include an evaluation of nervous system tissues.	
	24C	Potential candidate for subregistry of exposed persons	A

¹ ATSDR programs for addressing data needs. A=ATSDR Division of Health Studies; E=Environmental Protection Agency-TSCA/FIFRA testing; G=Great Lakes Human Health Research Program; M=Minority Health Professions Foundation Schools; NTP=National Toxicology Program; V=Voluntary research; O=Other.

² No longer considered a priority data need based on recent evaluation of the database by ATSDR.

³ These substances have been included in the pool of candidate substances for subregistry development since the publication of the FEDERAL REGISTER notice on March 10, 1994 (59 FR 11434).

⁴ Potentially to be addressed by ATSDR's Voluntary Research Program.

⁵ Data to be obtained by PBPK modeling.

⁶ Initiation of immunopathology study pending submission and peer review of study protocol.

⁷ Data to be obtained from a combined 2-generation reproduction and developmental toxicity study in rats.

⁸ Not a priority data need.

TABLE 2.—GROUPS ADDRESSING ATSDR PRIORITY DATA NEEDS (PDN)

ATSDR Program	Firm, institution, agency, or Consortium	Substance	PDN ID
Voluntarism	Chemical Manufacturers Association	Vinyl Chloride	4B, 4E
	General Electric Company	PCBs	7G, 7H, 7I
	Halogenated Solvents Industry Alliance	Trichloroethylene	10C
		Tetrachloroethylene	13A, 13B
Minority Health Professions Foundation Schools.		Methylene chloride	20A, 20B
		Lead	1A
	Florida A & M University		
	The King/Drew Medical Center of the Charles R. Drew University of Medicine and Science.	Lead	1C
	Meharry Medical College	PAHs	9A, 9D
	Morehouse School of Medicine	Lead	1C
	Texas Southern University	Lead	1A
		Trichloroethylene	10B
		Toluene	18C
	Tuskegee University	Mercury	3A
		Zinc	21A
	Xavier University	Benzene	5B
Great Lakes Human Health Research Program.		Zinc	21A
	Michigan State University	Lead	1C
		Mercury	3D
		PCBs	7F

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TABLE 2.—GROUPS ADDRESSING ATSDR PRIORITY DATA NEEDS (PDN)—Continued

ATSDR Program	Firm, institution, agency, or Consortium	Substance	PDN ID
TSCA/FIFRA	New York State Health Department	DDT	11D, 11E
		Lead	1C
		Mercury	3D
	State University of New York at Buffalo	PCBs	7F
		Lead	1C
		Mercury	3D
	State University of New York at Oswego	PCBs	7E, 7F
		DDT	11D, 11E
		Lead	1C
	University of Illinois at Chicago	Mercury	3A, 3D
		PCBs	7E, 7F
		DDT	11D, 11E
	University of Illinois at Urbana-Champaign	Lead	1C
		Mercury	3D
		PCBs	7E, 7F
	University of Wisconsin—Superior	Lead	1C
		Mercury	3D
		PCBs	7A, 7E, 7F
	Wisconsin Department of Health and Social Services	Lead	1C
		Mercury	3D, 3E
		PCBs	7F
	Environmental Protection Agency	PAHs	9E, 9F
		DDT	11D, 11E, 11F
		Mercury	3B
	National Institute of Environmental Health Sciences	Mercury	3C
		Benzene	5A
		Benzene	5C
		Chromium	12A
		Chromium	12B
		Chromium	12C
		Cyanide	15A
		Cyanide	15B
		Cyanide	15C
		Beryllium	17A
		Beryllium	17B
		Beryllium	17C
		Beryllium	17E
		Toluene	18A
		Toluene	18B
National Toxicology Program	National Institute of Environmental Health Sciences	DEHP	22D
		Chloroethane	24A
		Carbon Tetrachloride	16B

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