federal register

Friday
January 15, 1999

Part VI

Department of Health and Human Services

Agency for Toxic Substances and Disease Registry

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

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Toxic Substances and Disease Registry

[ATSDR–140]

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 provides the status of ATSDR's Superfund-mandated Substance-Specific Applied Research Program (SSARP), which was last updated in a **Federal Register** notice in 1996 (61 FR 14420). Authorized by the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA, also known as the Superfund statute), 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 frequently found at waste sites 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 Priority List of Hazardous Substances (62 FR 61332, November 17, 1997), 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.

On July 30, 1997, priority data needs for 12 additional hazardous substances frequently found at waste sites were determined and announced in the **Federal Register** (62 FR 40820). The 12 substances, each of which is included in ATSDR's Priority List of 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.

To date, 124 priority data needs have been identified for the first set of 38 hazardous substances, and 64 priority data needs have been identified for the second set of 12 hazardous substances. ATSDR fills these data needs through regulatory mechanisms (test rules), private-sector voluntarism, and the direct use of CERCLA funds. Additional data needs are being addressed through an interagency agreement with the National Toxicology Program (NTP), by ATSDR's Great Lakes Human Health Effects Research Program, and other agency programs. To date, 79 priority data needs associated with the first set of 38 priority substances (Table 1), and 23 priority data needs associated with the second set of 12 priority substances (Table 2) are being addressed via these mechanisms.

Table 1 also shows the progress ATSDR has made in filling research needs for the first set of 38 hazardous substances. On the basis of criteria developed by ATSDR, 14 priority data needs and 2 data needs have been filled, 26 priority data needs have been reclassified as data needs, and 2 additional priority data needs and 1 data need are considered conditionally filled pending ATSDR peer review of the final reports.

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 identified in this Notice by indicating their interest through submission of a letter of intent to ATSDR (see **ADDRESSES** section of this Notice). A Tri-Agency Superfund Applied Research Committee (TASARC) composed of scientists from ATSDR, NTP, and the Environmental Protection Agency (EPA), will review all proposed voluntary research efforts.

DATES: ATSDR provides updates on the status of its Substance-Specific Applied Research Program approximately every 3 years. ATSDR considers the voluntary research effort to be important to the continuing implementation of the SSARP. Therefore, the agency strongly encourages private-sector organizations to volunteer at any time to conduct research to fill data needs until ATSDR announces that other research mechanisms are in place to address those specific data needs.

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, NE., Mailstop E–29, Atlanta, Georgia 30333. Information about pertinent ongoing or completed research that may fill priority data needs cited in this Notice should be similarly addressed.

FOR FURTHER INFORMATION CONTACT: Dr. William Cibulas, Chief, Research Implementation Branch, Division of Toxicology, ATSDR, 1600 Clifton Road, NE., 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).

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 information necessary to improve the database to conduct comprehensive public health assessments of populations living near hazardous waste sites. We anticipate that the information will enable the agency to establish linkages between levels of contaminants in the environment and levels in human tissue and organs associated with adverse health effects. Once such links have been established, strategies to mitigate potentially harmful exposures can be developed. 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 information base for addressing a broader range of data needs.

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 hazardous substances (57 FR 54150). Since 1992, the total number of priority

data needs for the 38 substances has increased from 117 to 124 because the database was reevaluated (Table 1). The 7 additional priority data needs consist of 5 substances now considered as candidates for subregistries of exposed persons (determined by the ATSDR Division of Health Studies; the priority data needs for nickel, PCBs, toluene, and zinc were added in 1996, and that for beryllium was added in 1998), and 2 new priority data needs for trichloroethylene.

Regarding the 2 additional priority data needs for trichloroethylene, the need for intermediate-duration oral exposure data resulted from the withdrawal of the corresponding minimal risk level (MRL, a health guidance value) from the 1997 ATSDR updated Toxicological Profile for Trichloroethylene (Table 1). The other new priority data need for trichloroethylene is for a 1-species developmental toxicity study with emphasis on developmental neurotoxicity. Recent reports in humans, together with findings in animals, suggest that developmental effects may be the most sensitive end point for trichloroethylene.

Therefore, the proposed study may provide more definitive information on dose-response relationships for these effects and more fully characterize the potential for adverse health outcome in the developing fetus.

Two additional changes from the 1992 list of priority data needs have been made for tetrachloroethylene. The priority data need for chronic-duration oral exposure data has been replaced by the need for intermediate-duration oral exposure data because of the withdrawal of the intermediate-duration oral MRL from the 1997 ATSDR updated Toxicological Profile for Tetrachloroethylene (Table 1). ATSDR considers it is more appropriate to obtain intermediate-duration data before assigning priority to the conduct of chronic-duration studies. With regard to the priority to obtain developmental toxicity data, the use of 1-species (instead of the previously recommended 2-species) in the study is now considered adequate based on reevaluation of the database.

Table 1 also includes 3 PCB research needs that are not considered ''priority'' but were filled via voluntary research (see PDN ID#s 7G, 7H, and 7I).

On July 30, 1997, 77 priority data needs for 12 additional priority hazardous substances were determined and announced in the **Federal Register** (62 FR 40820). At that time, the 77 priority data needs included the need to evaluate existing data on concentrations of all 12 substances in environmental media at hazardous waste sites. The agency continues to recognize the need to collect, evaluate, and interpret such data, but no longer considers these ''priority.'' This is because a substantial amount of this information has already been collected through individual state programs and the EPA's CERCLA activities. Further, an ongoing effort at the agency is to evaluate the extant information from these programs to better characterize the need for additional site-specific information. Finally, during a recent reevaluation of potential candidates for subregistries of exposed persons conducted by ATSDR, manganese was removed from the candidate pool; consequently, this priority data need was reclassified as a data need. Therefore, the current total number of priority data needs associated with the second set of 12 priority substances is now 64 (Table 2).

CERCLA section 104(i)(5)(D) 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 the direct use of CERCLA funds.

The TASARC, composed of scientists from ATSDR, NTP, and EPA has been set up to:

(1) Advise ATSDR on the assignment of priorities for mechanisms to address data needs;

(2) Coordinate knowledge of research activities to avoid duplication of research in other programs and under other authorities;

(3) Advise ATSDR on issues of science related to substance-specific data needs; and

(4) Maintain a scheduled forum that provides an overall review of the ATSDR SSARP.

TASARC has met eight times since the initiation of the SSARP. It has guided referral of data needs to EPA and the associated development of test rules through TSCA. In addition, it has endorsed the proposals of several private-sector organizations to conduct voluntary research. Furthermore, TASARC has become a forum for other federal agencies to bring forth their research agenda. For example, it has coordinated research efforts on hazardous pollutants with the Office of Air and Radiation, EPA. TASARC has developed testing guidelines for immunotoxicity; and it has endorsed the use of decision support methodologies such as physiologically based pharmacokinetic (PBPK) modeling and benchmark-dose modeling, where appropriate.

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, 79 priority data needs associated with the first set of 38 priority substances (Table 1), and 23 priority data needs associated with the second set of 12 priority substances (Table 2) are being addressed via these mechanisms.

Criteria for Evaluating Status of Priority Data Needs

To update the activities covered under the SSARP, criteria for evaluating the status of the priority data needs were developed. Based on these criteria and the review of the current literature, a priority data need may be filled, reclassified as a data need, or unchanged. Further, during the literature review, new studies may be identified suggesting other effects of concern, such as those related to endocrine disruptors and children's health, which have not been included in the original list of priority data needs. In such cases, additional data needs or priority data needs may be added to the research agenda.

The criteria for evaluating the status of the priority data needs are described below.

General Criteria

1. A priority data need is filled:

- If a study, specifically designed to address a priority data need and conducted via any of the ATSDR implementation mechanisms, has been completed and published in a peer-reviewed journal, or has been accepted by ATSDR based on the recommendations of the agency's peer reviewers, or
- If an updated ATSDR toxicological profile or other recent review document contains relevant new (peer reviewed and publicly available) studies since the finalization of the priority data needs document; and it is generally agreed that a priority data need no longer exists.

Note: Priority data needs documents that describe ATSDR's rationale for prioritizing research needs for each substance in Tables 1 and 2 are available. See **ADDRESSES** section of this Notice.

2. A priority data need is reclassified as a data need:

- If an updated ATSDR toxicological profile or other recent review document contains relevant new (peer reviewed and publicly available) studies since the finalization of the priority data needs document; however, in the data needs section of the toxicological profile, a need for additional data to fully characterize the end point is still identified, or
- If a study addressing a priority data need has been reviewed by members of the Tri-Agency Superfund Applied Research Committee and it is agreed that a data need still exists although it is no longer a priority (See priority data need ''Evaluation of the environmental fate of cyanide in soil'' in Table 1), or
- For any substance whose overall rank on the ATSDR Priority List of Hazardous Substances falls below 275.

3. A priority data need is unchanged:

- If no mechanism or information has been identified to address the priority data need, or
- If the ATSDR toxicological profile has not been updated since the finalization of the priority data needs document (Exception: See Section ''Specific Criteria'' for the priority data need ''Exposure levels in humans''), or
- If the priority data need is included in the ATSDR test rule under development, or
- If ongoing discussions between ATSDR and a private-sector organization indicate that the priority data need is a candidate to be addressed via the voluntary research program, or
- If a study, specifically designed to address a priority data need and conducted via any of the ATSDR implementation mechanisms, is ongoing.

Specific Criteria

1. Priority data need, ''Inhalation and/or oral dose-response data for acute, intermediate, and/or chronic duration.''

These priority data needs are filled if minimal risk levels (MRLs) have been derived in the updated ATSDR toxicological profile since the finalization of the priority data needs document. However, in certain cases where the database (from which an MRL is derived) is sparse, a data need may still be identified in the toxicological profile to increase the confidence in the MRL.

2. Priority data need, ''Exposure levels in humans.''

This priority data need is considered filled if there are reference range data (e.g., National Health and Nutrition Examination Survey [NHANES]) or generally agreed upon background population levels *AND* if there are current and adequate biomonitoring data for exposed populations associated with health effects (from published or ongoing studies).

This priority data need is reclassified as a data need if only *one* of the following 2 criteria is met: (1) There are reference range data or generally agreed upon background population levels *OR* (2) if there are current and adequate biomonitoring data for exposed populations associated with health effects (from published or ongoing studies).

3. Priority data need ''Mechanism of toxic action.''

This priority data need is considered filled if there is scientific consensus indicating that the mechanism(s) of toxic action is well characterized.

This priority data need is reclassified as a data need if an updated toxicological profile contains relevant new (peer reviewed and publicly available) studies since the finalization of the priority data needs document; however, the database may not be sufficient to achieve scientific consensus on the mechanism of toxic action.

Based on the above criteria, the status of the research needs for the first set of 38 priority substances was evaluated (Table 1). To date, 14 priority data needs and 2 data needs have been filled, 26 priority data needs have been reclassified as data needs, and 2 additional priority data needs (Table 1, vinyl chloride, PDN ID #4B and 4E) and 1 data need (Table 1, PCBs, PDN ID #7H) are considered conditionally filled pending ATSDR peer review of the final reports.

Update of Activities in the SSARP

An update of the activities associated with the mechanisms for implementing the ATSDR Substance-Specific Applied Research Program (SSARP) is discussed below.

A. TSCA/FIFRA

In developing and implementing the SSARP, ATSDR, NTP, and EPA identified priority data needs for substances on the TSCA inventory of mutual interest to the federal programs. These data needs are being addressed through a program of toxicologic testing under TSCA according to established procedures and guidelines. 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. Currently, an EPA/ATSDR test rule, under development, includes 7 ATSDR substances, i.e., benzene, chloroethane, cyanide (including hydrogen cyanide and sodium cyanide), methylene chloride, tetrachloroethylene, trichloroethylene, and toluene, and addresses 15 priority data needs (Table 3). The test rule was reviewed by ATSDR and is undergoing EPA final review. It will be available for public comment in the near future.

TASARC has established an interagency task force on metals and has recently conducted a survey to assess federal agencies' needs for testing metals. Currently, the task force has agreed to examine at least 7 metals included in the ATSDR's SSARP (arsenic, beryllium, chromium, manganese, mercury, nickel, and selenium, associated with 22 priority data needs) (Table 3). The EPA will solicit testing proposals for these metals and pursue test rule development for these metals at a later date.

B. Private-Sector Voluntarism

As part of the SSARP, on February 7, 1992, ATSDR announced a set of proposed procedures for conducting voluntary research (57 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 specific priority data needs.

ATSDR currently has memoranda of understanding (MOUs) in place with the General Electric Company (GE), the Halogenated Solvents Industry Alliance (HSIA), and the Chemical Manufacturers Association (CMA) (Table 3). Through the voluntary research efforts of these organizations, 12 research needs for two classes of substances (polychlorinated biphenyl compounds [PCBs] and volatile organic compounds, including methylene chloride, tetrachloroethylene, trichloroethylene, and vinyl chloride) are being addressed (Table 3).

Recently, the agency received a study protocol from the Counselors for Management, Inc., on behalf of a spectrum of the zinc industry which is considering to conduct research to address ATSDR's priority data needs for zinc. This represents the first study proposed by a private-sector organization to address priority data needs for a metal. Voluntary research covered under the three existing MOUs is described next.

General Electric Company

In 1995, ATSDR entered into an MOU with GE. This marked the first time a private-sector organization had volunteered to conduct research to address data needs identified in ATSDR's SSARP. The MOU with GE covers two studies on PCBs: (1) ''An assessment of the chronic toxicity and oncogenicity of Aroclors 1016, 1242, 1254, and 1260 administered in diet to rats,'' including ''PCB congener analyses,'' and (2) ''Metabolite detection as a tool for determining naturally occurring aerobic PCB biodegradation.'' While the above studies do not address ATSDR's *priority* data needs for PCBs, they do address other agency research needs for these substances.

The agency accepted the final report for the first study (chronic toxicity and oncogenicity) in October 1997. The study provided an in-depth understanding of the relative toxicity of the prevalent commercial mixtures of PCBs (Aroclor 1016, Aroclor 1242, Aroclor 1254, and Aroclor 1260) after long-term exposures. The investigators found exposure-related toxicity for all four Aroclors. Furthermore, the study includes characterization of PCB composition, tissue accumulation, and correlations with tumorigenicity in chronically dosed rats. With regard to the second GE study (aerobic PCB biodegradation), also covered under the MOU, the final report is being evaluated by ATSDR's peer reviewers. The acceptance of the final report will be based on the recommendations of the reviewers and GE's satisfactory response to the reviewers' comments.

Halogenated Solvents Industry Alliance (HSIA)

In 1995, ATSDR entered into an MOU with HSIA covering studies to address three priority toxicity data needs for methylene chloride. The studies, ''Addressing priority data needs for methylene chloride with physiologically based pharmacokinetic modeling,'' evaluated acute- and subchronic-duration toxicity via oral exposures and developmental toxicity via oral exposure. The data were obtained by using physiologically based pharmacokinetic modeling.

The final report for these studies, the first one to be completed under the voluntary research program, was accepted by the agency in February 1997. The HSIA studies indicated that adverse health effects on the central nervous system, liver, and the development of newborns may occur if people drink water containing high concentrations of methylene chloride (565 to 6,170 milligrams methylene chloride per liter of water). These amounts are much larger than what most people are exposed to in the environment. However, these amounts approach levels found at industrial sites and in waste waters (ATSDR's Toxicological Profile for Methylene Chloride, 1993). HSIA has also proposed to conduct an immunotoxicity assessment for methylene chloride via inhalation exposure. The agency expects to receive a study protocol from HSIA for peer review in the near future.

In addition, ATSDR and HSIA are continuing negotiation to expand the existing MOU to include research on trichloroethylene and tetrachloroethylene.

Chemical Manufacturers Association (CMA)

In 1996, ATSDR entered into an MOU with CMA covering two studies, ''Vinyl chloride: Combined inhalation two-generation reproduction and developmental toxicity study in CD rats.'' Recently, the ATSDR peer review of the final report on the developmental toxicity study was completed. The final report for the reproductive toxicity study is undergoing ATSDR peer review. Acceptance of the final reports is based on the reviewers' recommendations and CMA's satisfactory response to the reviewers' comments.

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. 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 purpose of this cooperative agreement is to address substance-specific data needs for priority hazardous substances identified by ATSDR. In addition, this agreement strengthens the environmental health research opportunities for scientists and students at MHPF member institutions and enhances existing disciplinary capacities to conduct research in toxicology and environmental health.

In the first 5-year project period that concluded during FY 1997, 9 priority data needs for 21 priority hazardous substances and 22 data needs for these and other substances were addressed. The MHPF has developed a report, ''Environmental Health and Toxicology Research Program: Meeting Environmental Health Challenges Through Research, Education, and Service,'' that describes the research findings and other successes from the first 5 years of the program. New research initiated in the second 5-year project period includes studies to address 10 additional priority data needs for chlordane, 1,2-dibromo-3-chloropropane, di-n-butyl phthalate, lead, manganese, the polycyclic aromatic hydrocarbons (PAHs), and zinc, and another 8 data needs.

To date, the MHPF activities have resulted in the publication of 21 manuscripts in peer-reviewed journals. Findings from this program were presented at a symposium held in April 1997, in New Orleans. Also, these and other research findings from the program were featured in a special session during the 1998 annual meeting of the Society of Toxicology in Seattle. The institutions receiving awards and their respective research projects are listed in Table 3.

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, various environmental and industrial groups, and ATSDR to improve its 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) was filled (Table 1). Research efforts to address reproductive toxicity data needs for chlordane, endrin, and heptachlor, the bioavailability of PCBs in soil, and dose-response data for di-n-butyl phthalate are also ongoing (Table 3).

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, PBPK modeling, and functional toxicity testing. The ATSDR-supported NTP studies in these areas are ongoing.

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.

In support of the Great Lakes Critical Programs Act of 1990, ATSDR announced in FY 1992 the availability of $2 million for a grant program to conduct research on the potential for short-and long-term adverse health effects from consumption of contaminated fish from the Great Lakes basin. Research undertaken through this program is intended to build on and amplify the results of past and ongoing fish consumption research in the Great Lakes basin. The ATSDR-supported research projects focus on known high-risk populations to further define the human health consequences of exposure to persistent toxic substances (PTSs) identified in the Great Lakes basin. These at-risk populations include sport anglers, Native Americans, pregnant women, fetuses and nursing infants of mothers who consume contaminated Great Lakes fish, infants and children, the elderly, and the urban poor.

To date, the research activities of the ATSDR Great Lakes research program have resulted in 22 manuscripts in peer-reviewed journals. An additional 13 manuscripts have been accepted for publication and will soon be in press. Research findings from this program have been presented at 8 international conferences and various scientific meetings and symposia.

Currently, 13 priority data needs and 1 data need for 24 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 3.

F. Other ATSDR Programs

In its role as a public health agency addressing environmental health, ATSDR may collect human data to validate substance-specific exposure and toxicity findings. The need for additional information on levels of contaminants in humans has been identified and remains as a priority data need for 37 of the first set of 38 priority substances (Table 1). Similarly, this priority data need has been identified for all 12 of the second set of 12 priority substances. 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 50 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 1994 document, ''National Exposure Registry: Policies and Procedures Manual (Revised),'' Agency for Toxic Substances and Disease Registry, Public Health Service, U.S. Department of Health and Human Services, Atlanta, Georgia, NTIS Publication No. PB95–154571. To date, of the first set of 38 priority substances in the SSARP, ATSDR has selected benzene, chromium, and trichloroethylene as primary contaminants to establish subregistries in the National Exposure Registry. However, aldrin/dieldrin, beryllium, carbon tetrachloride, chloroethane, chloroform, cyanide, p,p'-DDT, DDE, DDD, di(2-ethylhexyl)phthalate, mercury, methylene chloride, nickel, PAHs, PCBs, selenium, tetrachloroethylene, toluene, vinyl chloride, and zinc remain in the candidate pool and therefore continue to be classified as priority data needs. They will be considered for selection as primary contaminants during each selection process (Table 1). Arsenic, cadmium, and lead are not considered to be in the pool of candidate substances for an exposure registry at this time, and therefore, are not considered priority data needs. This decision will be reevaluated as more information on the chemicals and exposure sites become available.

Regarding the second set of 12 priority substances, all of them were included in the candidate pool for establishment of exposure subregistries (i.e., priority data needs, published in the 1996 **Federal Register** Notice [61 FR 14430]). However, during a recent reevaluation of the database, manganese was removed from the candidate pool, and therefore, this priority data need for manganese has been reclassified as a data need, and is not included in Table 2.

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 provide an update on the status of this research program every three years.

Dated: January 11, 1999.

Georgi Jones,

Director, Office of Policy and External Affairs, Agency for Toxic Substances and Disease Registry.

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Table 1

Substance-Specific Priority Data Needs (PDNs) for First Set of 38 Priority Hazardous Substances

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
Lead	1A	Mechanistic studies on the neurotoxic effects of lead	MHPF	Data need	Multiple new studies (11 published MHPF studies + more than 10 new relevant published studies and at least 3 ongoing studies in the updated toxicological profile [(August 1997]) potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	1B	Analytical methods for tissue levels		Data need	Two relevant ongoing studies in the updated toxicological profile (August 1997) potentially address the PDN.
	1C	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	MHPF G. Lakes	Filled	Referent population blood and urine lead levels are available (NHANES III, Paschal et al. 1998), and at least 19 ATSDR studies that evaluated blood lead levels and potential adverse health effects are available.
Arsenic	2A	Comparative toxicokinetic studies to determine if an appropriate animal species can be identified	EPA		
	2B	Half-lives in surface water, groundwater	EPA		
	2C	Bioavailability from soil	EPA		
	2D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes	Data need	Background level data are available in toxicological profile (April 1993), and at least 7 ATSDR studies that evaluated urine arsenic levels and potential adverse health effects are available. This PDN may be further reclassified as "filled" during the ongoing development of the updated toxicological profile.

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
Mercury	3A	Multigeneration reproductive toxicity study via oral exposure	MHPF		
	3B	Dose-response data in animals for chronic-duration oral exposure	EPA		
	3C	Immunotoxicology battery of tests via oral exposure	EPA		
	3D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes	Filled	Background levels data are available in the updated toxicological profile (August 1997), and multiple studies that evaluated blood, urine, and hair mercury levels and potential adverse health effects are available (5 ATSDR studies+ at least 8 ongoing studies of the Great Lakes research program).
	3E	Potential candidate for subregistry of exposed persons	ATSDR		
Vinyl Chloride	4A	Dose-response data in animals for acute-duration inhalation exposure		Filled	An MRL was derived since the finalization of the PDN document.
	4B	Multigeneration reproductive toxicity study via inhalation	Vol Res	Filled[4] pending agency review	The Chemical Manufacturers Association conducted a study to address this PDN.
	4C	Dose-response data in animals for chronic-duration inhalation exposure			
	4D	Mitigation of vinyl chloride-induced toxicity			
	4E	2-Species developmental toxicity study via inhalation	Vol Res	Filled[5] pending agency review	The Chemical Manufacturers Association conducted a study to address this PDN.

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[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	ATSDR		
Benzene	5A	Dose-response data in animals for acute- and intermediate-duration oral exposure. The subchronic study should include an extended reproductive organ histopathology.	EPA		
	5B	2-Species developmental toxicity study via oral exposure	MHPF		
	5C	Neurotoxicology battery of tests via oral exposure	EPA		
	5D	Epidemiologic studies on the health effects of benzene (Special emphasis end points include immunotoxicity.)			
	5E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Reference range concentrations are available (Ashley et al. 1992, 1994, Needham et al. 1995), and at least one ATSDR study that evaluated blood benzene levels and potential adverse health effects is available.
Cadmium	6A	Analytical methods for biological tissues and fluids and environmental media		Data need	At least 8 new relevant studies in the updated toxicological profile [(September 1997]) potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	6B	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes	Filled	Referent population urine cadmium levels are available (NHANES III), and at least 9 ATSDR studies that evaluated blood and urine cadmium levels and potential adverse health effects are available.
PCBs	7A	Dose-response data in animals for acute- and intermediate-duration oral exposures	G. Lakes		
	7B	Biodegradation of PCBs in water; bioavailability of PCBs in air, water, and soil	NTP[6]		
	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 end points include immunotoxicity, gastrointestinal toxicity, liver toxicity, kidney toxicity, thyroid toxicity, and reproductive/developmental toxicity.)	G. Lakes	Data need	At least 2 new relevant published studies in the updated toxicological profile (September 1997) and at least 5 ongoing studies in the Great Lakes research program potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	7E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes	Filled	Background levels data are available (updated toxicological profile, September 1997, and Needham et al. 1996), and multiple studies that evaluated blood and breast milk PCB levels and potential adverse health effects are available (at least 6 ATSDR studies + at least 8 ongoing studies in the Great Lakes research program).
	7F	Potential candidate for subregistry of exposed persons	ATSDR		

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	7G[7]	Chronic toxicity and oncogenicity via oral exposure	Vol Res	Filled	The General Electric Company study addressing this data need was accepted by ATSDR upon the recommendations of the ATSDR peer reviewers.
	7H[7]	Aerobic PCB biodegradation in sediment	Vol Res	Filled[8] pending agency review	The study was conducted by the General Electric Company.
	7I[7]	PCB congener analysis	Vol Res G. Lakes	Filled	The General Electric Company study addressing this data need was accepted by ATSDR upon the recommendations of the ATSDR peer reviewers.
Chloroform	8A	Dose-response data in animals for intermediate-duration oral exposure		Filled	An MRL was derived in the updated toxicological profile (September 1997).
	8B	Epidemiologic studies on the health effects of chloroform (Special emphasis end points 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		Data need	Reference range concentrations in blood are available (Ashley et al. 1992, 1994, and Needham et al. 1995).
	8D	Potential candidate for subregistry of exposed persons	ATSDR		
PAHs	9A	Dose-response data in animals for intermediate-duration oral exposures. The subchronic study should include extended reproductive organ histopathology and immunopathology.	MHPF	Filled	MRLs for 4 PAHs were derived in the updated toxicological profile (August 1995).

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	9B	2-Species developmental toxicity study via inhalation or oral exposure	MHPF		
	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		Data need	At least 12 new relevant studies in the updated toxicological profile (August 1995) potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	9D	Dose-response data in animals for acute- and intermediate-duration inhalation exposures. The subchronic study should include extended reproductive organ histopathology and immunopathology.	MHPF		
	9E	Epidemiologic studies on the health effects of PAHs (Special emphasis end points include cancer, dermal, hemolymphatic,and hepatic toxicity.)		Data need	At least 3 new relevant studies in the updated toxicological profile (August 1995) potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	9F	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes		
	9G	Potential candidate for subregistry of exposed persons	ATSDR		
Trichloro-ethylene	10A	Dose-response data in animals for acute-duration oral exposure		Filled	An MRL was derived in the updated toxicological profile (September 1997).
	10B	Neurotoxicology battery of tests via the oral route	EPA MHPF		

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	10C	Immunotoxicology battery of tests via the oral route	EPA Vol Res		
	10D	Epidemiologic studies on the health effects of trichloroethylene (Special emphasis end points include cancer, hepatotoxicity, renal toxicity, developmental toxicity, and neurotoxicity.)		Data need	At least 6 new relevant studies and 1 ongoing study in the updated toxicological profile (September 1997) potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	10E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Reference range concentrations in blood are available (Ashley et al. 1992, 1994, Needham et al. 1995).
	10F[9]	Dose-response data in animals for intermediate-duration oral exposure	EPA		
	10G[10]	1-Species developmental toxicity study via oral exposure	EPA Vol Res		
DDT	11A	Dose-response data in animals for chronic-duration oral exposure			
	11B	Comparative toxicokinetic study (across routes/species)			
	11C	Bioavailability and bioaccumulation from soil			
	11D	Epidemiologic studies on the health effects of DDT, DDD, and DDE (Special emphasis end points include immunotoxicity, and reproductive and developmental toxicity.)	G. Lakes	Data need	At least 6 new relevant studies in the updated toxicological profile (May 1994) and 5 ongoing studies in the Great Lakes research program potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	11E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes		
	11F	Potential candidate for subregistry of exposed persons	ATSDR		
Chromium	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	EPA		
	12B	Multigeneration reproductive toxicity study via oral exposure to chromium (III) and (VI)	EPA		
	12C	Immunotoxicology battery of tests following oral exposure to chromium (III) and (VI)	EPA		
	12D	2-Species developmental toxicity study via oral exposure to chromium (III) and (VI)	EPA		
	12E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes	Data need	Reference range concentrations in urine are available (Paschal et al. 1998). Also, at least 2 ATSDR studies that evaluated urine chromium levels and potential adverse health effects are available. This PDN may be further reclassified as "filled" during the ongoing development of the updated toxicological profile.
Tetrachloro-ethylene	13A	Dose-response data in animals for acute-duration oral exposure, including neuropathology and demeanor, and immunopathology		Filled	An MRL was derived in the updated toxicological profile (September 1997).

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	13B	Multigeneration reproductive toxicity study via oral exposure	Vol Res	Data need	The Halogenated Solvents Industry Alliance, Inc.'s inhalation study was accepted by ATSDR and included in the updated toxicological profile (September 1997) upon the recommendations of the ATSDR peer reviewers. The oral data may potentially be obtained from the inhalation data by physiologically based pharmacokinetic (PBPK) modeling.
	13C[11]	Dose-response data in animals for intermediate-duration oral exposure, including neuropathology and demeanor, and immunopathology	EPA Vol Res		The Halogenated Solvents Industry Alliance, Inc. intends to obtain oral data for neurotoxicity by PBPK modeling, and to conduct an immunotoxicology study.
	13D[12]	1-Species developmental toxicity study via oral exposure	EPA Vol Res		
	13E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Reference range concentrations in blood are available (Ashley et al. 1992, 1994, Needham et al. 1995).
	13F	Potential candidate for subregistry of exposed persons	ATSDR		
Aldrin/ Dieldrin	14A	Dose-response data in animals for intermediate-duration oral exposure			
	14B	Bioavailability from soil			
	14C	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes		
	14D	Potential candidate for subregistry of exposed persons	ATSDR		

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
Cyanide	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 end points.	EPA		
	15B	2-Species developmental toxicity study via oral exposure	EPA		
	15C	Evaluation of the environmental fate of cyanide in soil		Data need	A study addressing the PDN was submitted by industry to the Environmental Protection Agency (EPA) in response to EPA's solicitation for proposals for test rule making. Scientists from EPA and ATSDR reviewed the study and considered a data need still exists, although it is no longer a priority. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	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	ATSDR		
Carbon Tetrachloride	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	Filled	NTP dose-finding study and one new study in the updated toxicological profile (May 1994) addressed the PDN. Also, no additional studies for this exposure route were identified in the data needs section of the updated toxicological profile.

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	16C	Half-life in soil		Data need	One new study in the updated toxicological profile (May 1994) potentially addresses the PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	16D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Reference range concentrations in blood are available (Ashley et al. 1992, 1994, Needham et al. 1995).
	16E	Potential candidate for subregistry of exposed persons	ATSDR		
Beryllium	17A	Dose-response data in animals for acute- and intermediate-duration inhalation exposures. The subchronic study should include extended reproductive organ histopathology.	EPA		
	17B	2-Species developmental toxicity study via inhalation exposure	EPA		
	17C	Environmental fate in air; factors affecting bioavailability in air	EPA		
	17D	Analytical methods to determine environmental speciation			
	17E	Immunotoxicology battery of tests following oral exposure	EPA		
	17F	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Reference range concentrations in urine are available (Paschal et al. 1998).
	17G[13]	Potential candidate for subregistry of exposed persons	ATSDR		

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
Toluene	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.	EPA	Filled	MRLs for acute and intermediate exposure durations were derived in the updated toxicological profile (May 1994).
	18B	Comparative toxicokinetic studies (Characterization of absorption, distribution, and excretion via oral exposure)			
	18C	Neurotoxicology battery of tests via oral exposure	EPA MHPF		
	18D	Mechanism of toluene-induced neurotoxicity		Data need	At least 15 new relevant studies in the updated toxicological profile (May 1994) potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	18E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Reference range concentrations in blood are available (Ashley et al. 1992, 1994, Needham et al. 1995).
	18F	Potential candidate for subregistry of exposed persons	ATSDR		
Nickel	19A	Epidemiologic studies on the health effects of nickel (Special emphasis end points include reproductive toxicity.)		Data need	At least 2 new relevant studies in the updated toxicological profile (September 1997) potentially address this PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.
	19B	2-Species developmental toxicity study via the oral route	EPA	Data need	In the updated toxicological profile (September 1997), a new study confirming the results of 2 previous studies potentially addresses the PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	19C	Dose-response data in animals for acute- and intermediate-duration oral exposures	EPA		
	19D	Neurotoxicology battery of tests via oral exposure	EPA		
	19E	Bioavailability of nickel from soil	EPA		
	19F	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	G. Lakes		
	19G	Potential candidate for subregistry of exposed persons	ATSDR		
Methylene Chloride	20A	Dose-response data in animals for acute- and intermediate-duration oral exposure. The subchronic study should include extended reproductive organ histopathology, neuropathology and demeanor, and immunopathology.	EPA Vol Res	Filled	ATSDR accepted the Halogenated Solvents Industry Alliance, Inc.'s study addressing this PDN upon the recommendations of the ATSDR peer reviewers.
	20B	2-Species developmental toxicity study via the oral route	EPA Vol Res	Filled	ATSDR accepted the Halogenated Solvents Industry Alliance, Inc.'s study addressing this PDN upon the recommendations of the ATSDR peer reviewers.
	20C	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Reference range concentrations in blood are available (Ashley et al. 1992, 1994, Needham et al. 1995).
	20D	Potential candidate for subregistry of exposed persons	ATSDR		

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
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.	MHPF		
	21B	Multigeneration reproductive toxicity study via oral exposure	MHPF		
	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	Vol Res		
	21E	Potential candidate for subregistry of exposed persons	ATSDR		
DEHP	22A	Epidemiologic studies on the health effects of DEHP (Special emphasis end points 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.		Filled	MRLs for acute and intermediate exposure durations were derived in the updated toxicological profile (April 1993).
	22C	Multigeneration reproductive toxicity study via oral exposure		Data need	At least 3 new relevant studies in the updated toxicological profile (April 1993) potentially address the PDN. This PDN may be further reclassified as "filled" during future reevaluation of the database.

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
	22D	Comparative toxicokinetic studies (Studies designed to examine how primates metabolize and distribute DEHP as compared with rodents via oral exposure)			
	22E	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers			
	22F	Potential candidate for subregistry of exposed persons	ATSDR		
Selenium	23A	Dose-response data in animals for acute-duration oral exposure	EPA		
	23B	Immunotoxicology battery of tests via oral exposure	EPA		
	23C	Epidemiologic studies on the health effects of selenium (Special emphasis end points include cancer, reproductive and developmental toxicity, hepatotoxicity, and adverse skin effects.)			
	23D	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers		Data need	Referent population serum selenium levels are known (NHANES).
	23E	Potential candidate for subregistry of exposed persons	ATSDR		

Substance	PDN ID	PDN description	Program[1]	Status change[2]	Rationale for status change[3]
Chloroethane	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.	EPA		
	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	ATSDR		

[1]Programs addressing data needs. ATSDR=ATSDR's Division of Health Studies; EPA=Environmental Protection Agency-TSCA/FIFRA testing; G. Lakes=Great Lakes Human Health Effects Research Program; MHPF=Minority Health Professions Foundation schools; NTP=National Toxicology Program; Vol Res=Voluntary research.

[2] PDN may be *reclassified as a data need* or considered *filled* based on reevaluation of the database using criteria developed by ATSDR.

[3] Ashley et al. 1992=Ashley DL, Bonin MA, Cardinali FL, et al. Anal Chem (1992) 64:1021-1029; Ashley et al. 1994=Ashley DL, Bonin MA, Cardinali FL et al., Clin Chem (1994) 40/7:1401-1404; ATSDR studies=Studies conducted by ATSDR's Division of Health Studies; MHPF=Minority Health Professions Foundation schools; MRL=Minimal Risk Level; Needham et al. 1995=Needham LL, Hill RH Jr, Ashley DL, Pirkle JL, and Sampson EJ. Environ Health Perspect 103(Suppl 3):89-94 (1995); Needham et al. 1996=Needham LL, Patterson DG Jr, Burse VW, Paschal DC, Turner WE, and Hill VW Jr. Toxicol Ind Health (1996)12:507-513; NHANES III= The Third National Health and Nutrition Examination Survey, conducted by the National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, GA; NTP=National Toxicology Program; Paschal et al. 1998=Paschal DC, Ting BC, Morrow JC, et al. (1998) Environ Res, Section A 76: 53-59; Toxicological profile=ATSDR's toxicological profiles for the agency's priority hazardous substances.

[4] This PDN will be considered *filled* pending peer review of final report and satisfactory response to the reviewers' comments by the Chemical Manufacturers Association.

[5] The final report was peer reviewed. This PDN will be considered *filled* pending satisfactory response to the reviewers' comments by the Chemical Manufacturers Association.

(6) NTP is addressing bioavailability of PCBs in soil only.

(7) Not a priority data need.

(8) Final report under ATSDR peer review. This data need will be considered *filled* pending peer review of final report and satisfactory response to the reviewers' comments by the General Electric Company.

(9) New priority data need resulting from withdrawal of intermediate oral MRL from ATSDR's *Toxicological Profile for Trichloroethylene*.

(10) New priority data need. Study to be conducted with special emphasis on developmental neurotoxicity.

(11) New priority data need resulting from withdrawal of intermediate oral MRL from ATSDR's *Toxicological Profile for Tetrachloroethylene*.

(12) Study to be conducted with special emphasis on developmental neurotoxicity.

(13) New priority data need. Beryllium has been included in the pool of candidate substances for subregistry development since the publication of the **Federal Register** notice on April 1, 1996 (61 FR 14420).

Table 2
Substance-Specific Priority Data Needs (PDN) for Second Set of 12 Priority Hazardous Substances

Substance		PDN ID	Priority Data Need	Program[1]
Hexachlorobutadiene	Exposure	25A	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
		25B	Environmental fate studies that determine the extent to which hexachlorobutadiene volatilizes from soil, and studies that determine the reactions and rates which drive degradation in soil	
		25C	Bioavailability studies in soil and plants	
		25D	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	25E	Dose-response data in animals for acute-duration exposure via the oral route	
Chlordane	Exposure	26A	Exposure levels in humans living near hazardous waste sites and other populations potentially exposed to chlordane	
		26B	Bioavailability studies following ingestion of contaminated media	
		26C	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	26D	Oral multigenerational studies to evaluate reproductive toxicity	MHPF NTP

Hexachlorocyclohexane α Hexachlorocyclohexane β Hexachlorocyclohexane δ Hexachlorocyclohexane γ	Exposure	27A	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
		27B	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	27C	Dose-response data for chronic-duration oral exposure	
		27D	Mechanistic studies on the neurotoxicity, hepatotoxicity, reproductive toxicity, and immunotoxicity of hexachlorocyclohexane	
Heptachlor Heptachlor epoxide	Exposure	28A	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
		28B	Bioavailability from contaminated air, water, and soil and bioaccumulation potential	
		28C	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	28D	Dose-response animal data for acute- and intermediate-duration oral exposures, including immunopathology	
		28E	Multigeneration reproductive toxicity studies via the oral route of exposure	NTP
		28F	2-Species developmental toxicity studies via the oral route of exposure	
Di-n-butyl phthalate	Exposure	29A	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
		29B	Environmental fate of di-n-butyl phthalate in environmental media	
		29C	Bioavailability in contaminated environmental media near hazardous waste sites	
		29D	Potential candidate for subregistry of exposed persons	ATSDR

	Toxicity	29E	Dose-response data in animals for acute-duration exposure via the oral route	NTP
		29F	Dose-response data in animals for chronic-duration exposure via the oral route	
		29G	Carcinogenicity studies via oral exposure	
		29H	In vivo genotoxicity studies	MHPF
		29I	Immunotoxicology studies via oral exposure	MHPF
		29J	Neurotoxicity studies via oral exposure	MHPF
Toxaphene	Exposure	30A	Exposure levels in humans living in areas near hazardous waste sites with toxaphene and in those individuals with the potential to ingest it	
		30B	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	30C	Identify the long-term health consequences of exposure to environmental toxaphene via oral exposure	
		30D	Conduct additional chronic animal immunotoxicity studies via the oral route of exposure	
		30E	Conduct additional chronic animal neurotoxicity studies via the oral route of exposure	
Endosulfan Endosulfan α Endosulfan β Endosulfan sulfate	Exposure	31A	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
		31B	Data on the bioavailability of endosulfan from soil	
		31C	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	31D	Acute-duration oral exposure studies	
		31E	Sensitive end point neurologic data on the effects of oral endosulfan exposure	

Disulfoton	Exposure	32A	Exposure levels of disulfoton in tissues/fluids for populations living near hazardous waste sites and other populations, such as exposed workers	
		32B	Disulfoton should be considered as a potential candidate for a subregistry of exposed persons.	ATSDR
	Toxicity	32C	Immunotoxicology testing battery following oral exposure.	
Endrin Endrin aldehyde	Exposure	33A	Exposure levels for endrin and its degradation products in humans living near hazardous waste sites	
		33B	Accurately describe the environmental fate of endrin, including environmental breakdown products and rates, media half-lives, and chemical and physical properties of the breakdown products that help predict mobility and volatility	
		33C	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	33D	Dose-response animal data for acute oral exposure to endrin	
		33E	Multigeneration reproductive toxicity studies via oral exposure to endrin	NTP
		33F	Accurately describe the toxicokinetics of endrin and its degradation products and identify the animal species to be used as the most appropriate model for human exposure	

Manganese	Exposure	34A	Exposure levels in humans living near hazardous waste sites and other populations, such as exposed workers	
		34B	Relative bioavailability of different manganese compounds and bioavailability of manganese from soil	EPA
	Toxicity	34C	Dose-response data for acute- and intermediate-duration oral exposures (the subchronic study should include reproductive histopathology and an evaluation of immunologic parameters including manganese effects on plaque-forming cells (SRBC), surface markers (D4:D8 ratio), and delayed hypersensitivity reactions)	MHPF EPA
		34D	Toxicokinetic studies on animals to investigate uptake and absorption, relative uptake of differing manganese compounds, metabolism of manganese, and interaction of manganese with other substances following oral exposure	MHPF EPA
		34E	Epidemiological studies on the health effects of manganese (Special emphasis end points include neurologic, reproductive, developmental, immunologic, and cancer.)	
Methoxychlor	Exposure	35A	Exposure levels of methoxychlor and primary metabolites in humans living near hazardous waste sites and in those individuals with the potential to ingest it	
		35B	Evaluate the fate, transport, and levels of the degradation products of methoxychlor in soil	
		35C	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	35D	Evaluate neurologic effects after long-term, low-level oral exposure	

1,2-dibromo-3-chloropropane	Exposure	36A	Exposure levels in humans living near hazardous waste sites and other exposed populations, such as exposed workers	
		36B	Potential candidate for subregistry of exposed persons	ATSDR
	Toxicity	36C	Dose-response data in animals for acute-duration exposure via the oral route (including reproductive organ histopathology)	
		36D	Dose-response data in animals for chronic-duration exposure via the oral route (including reproductive organ histopathology)	
		36E	Two-species developmental toxicity study via oral exposure	
		36F	Immunotoxicology testing battery via oral exposure	MHPF
		36G	Neurotoxicology testing battery via oral exposure	MHPF

(1) Programs addressing priority data needs. ATSDR= ATSDR's Division of Health Studies; MHPF=Minority Health Professions Foundation schools; NTP=National Toxicology Program.

Table 3
Groups Addressing ATSDR Priority Data Needs (PDNs)

ATSDR Program	Firm, Institution, Agency, or Consortium	Substance	PDN ID
Voluntarism	Chemical Manufacturers Association	Vinyl Chloride	4B, 4E
	General Electric Company	PCBs	7G[1], 7H[1], 7I[1]
	Halogenated Solvents Industry Alliance, Inc.	Trichloroethylene	10C, 10G
		Tetrachloroethylene	13B, 13C, 13D
		Methylene chloride	20A, 20B
	Counselors for Management, Inc.[2]	Zinc	21D
Minority Health Professions Foundation Schools	Florida A & M University	Lead	1A
	The King/Drew Medical Center of the Charles R. Drew University of Medicine and Science	Lead	1C
	Meharry Medical College	PAHs	9A, 9B, 9D
	Morehouse School of Medicine	Lead	1C
	Texas Southern University	Lead	1A
		Trichloroethylene	10B
		Toluene	18C
		Di-n-butyl phthalate	29H, 29I, 29J
		1,2-dibromo-3-chloropropane	36F, 36G
	Tuskegee University	Mercury	3A
		Zinc	21A, 21B
		Chlordane	26D
	Xavier University	Benzene	5B
		Zinc	21A
		Manganese	34C, 34D

ATSDR Program	Firm, Institution, Agency, or Consortium	Substance	PDN ID
Great Lakes Human Health Effects Research Program	Michigan State University	Lead	1C
		Mercury	3D
		PCBs	7E, 7I
		DDT/DDE	11D, 11E
	New York State Health Department	Lead	1C
		Mercury	3D
		PCBs	7E, 7I
		DDT/DDE	11E
	State University of New York at Buffalo	Lead	1C
		Mercury	3D
		PCBs	7D, 7E, 7I
		DDT/DDE	11D, 11E
		Aldrin/Dieldrin	14C
	State University of New York at Oswego	Lead	1C
		Mercury	3D
		PCBs	7D, 7E, 7I
		DDT/DDE	11D, 11E
	University of Illinois at Chicago	Lead	1C
		Mercury	3D
		PCBs	7D, 7E, 7I
		DDT/DDE	11D, 11E
	University of Illinois at Urbana-Champaign	Lead	1C
		Mercury	3D
		PCBs	7D, 7E, 7I
	University of Wisconsin - Milwaukee	Lead	1C
		Mercury	3D
		PCBs	7A, 7D, 7E, 7I
	Wisconsin Department of Health and Social Services--5 State Consortium	Lead	1C
		Mercury	3D

ATSDR Program	Firm, Institution, Agency, or Consortium	Substance	PDN ID
		Arsenic	2D
		Cadmium	6B
		PCBs	7E, 7I,
		PAHs	9F
		DDT/DDE	11D, 11E
		Chromium	12E
		Nickel	19F
Environmental Protection Agency TSCA/ FIFRA	ATSDR Test Rule	Benzene	5A, 5C
		Trichloroethylene	10B, 10C, 10F, 10G
		Tetrachloroethylene	13C, 13D
		Cyanide	15A, 15B
		Toluene	18A, 18C
		Methylene chloride	20A, 20B
		Chloroethane	24A
	Metals Testing Task Force (TASARC)	Arsenic	2A, 2B, 2C
		Mercury	3B, 3C
		Chromium	12A, 12B, 12C, 12D
		Beryllium	17A, 17B, 17C, 17E
		Nickel	19B, 19C, 19D, 19E
		Selenium	23A, 23B
		Manganese	34B, 34C, 34D
National Toxicology Program	National Institute of Environmental Health Sciences	PCBs	7B
		Carbon Tetrachloride	16B
		Chlordane	26D
		Heptachlor	28E
		Di-n-butyl phthalate	29E
		Endrin	33E

(1) Not priority data needs.
(2) To date, no MOU has been signed.

[FR Doc. 99–971 Filed 1–14–99; 8:45 am]
BILLING CODE 4163–70–C