DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institute of Environmental Health Sciences, National Toxicology Program; Request for Comments on Substances Nominated to the National Toxicology Program (NTP) for Toxicological Studies and on the Testing Recommendations Made by the NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC); Solicitation of Information on Nominated Substances

Summary

The National Toxicology Program (NTP) routinely solicits, accepts and reviews for consideration nominations for toxicological studies to be undertaken by the Program on substances of potential human health concern. Nominations are received from Federal agencies, industry, the public, and other interested parties and undergo several levels of review before toxicological studies are designed and implemented. The NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC) serves as the first level of review for NTP nominations. At the December 13, 1999 meeting of the ICCEC, 12 new nominations were reviewed and testing recommendations made. As part of an effort to inform the public and to obtain input about the selection of chemicals for evaluation, the NTP routinely seeks public comment on (1) substances nominated to the Program for toxicological studies and (2) the testing recommendations made by the ICCEC. This announcement outlines briefly the process for nomination and selection of substances for NTP study, presents the testing recommendations made by the ICCEC at the December 13, 1999 meeting, requests comment on those nominations and recommendations, and solicits the submission of additional information for consideration by the NTP in its subsequent evaluation of the nominations.

Background

1. Nomination and Selection of Substances for NTP Studies

The nomination and selection for study of chemicals and agents with the highest potential for adversely impacting public health are essential to the success of the NTP's testing program. The nomination process is open and nominations are solicited from academia, Federal and State regulatory and health agencies, industry, and labor unions, as well as from environmental groups and the general public. Particular assistance is sought for the nomination of studies to be undertaken by the NTP that permit the testing of hypotheses to enhance the predictive ability of future NTP studies, address mechanisms of toxicity, or fill significant gaps in the knowledge of the toxicity of chemicals or classes of chemicals. Substances selected for study generally fall into two broad overlapping categories: (1) Those substances of greatest concern for public or occupational health and (2) chemicals for which toxicological data is needed to reduce uncertainty in risk assessment by aiding species-to-species extrapolation and understanding dose-response relationships. Substances may be studied for a variety of health-related effects, including but not limited to, reproductive and developmental toxicity, genotoxicity, immunotoxicity, metabolism and disposition, as well as carcinogenicity. The possible public health consequences of exposure remain the over-riding factor in the decision to study a particular chemical or agent. Selections for government testing are based on the principle that responsible manufacturers will evaluate their own chemicals or agents for health and environmental effects as mandated by Congress under legislative authorities. Increased efforts continue to be focused on: (1) Improving the quality of the nominations of chemicals, environmental agents, or issues for study so that public health and regulatory needs are addressed; (2) broadening the base and diversity of nominating organizations and individuals; and (3) increasing nominations for studying toxicological endpoints in addition to carcinogenesis.

II. Review Process for Substances Nominated for NTP Studies

Nominations are first reviewed by a multi-disciplinary NIEHS committee to determine whether the nominated agent has undergone adequate toxicological testing or has been previously considered by the NTP. For nominations not eliminated from consideration or deferred at this stage, the available literature is examined in detail to prepare Toxicological Summaries that describe and summarize relevant information for each nominated substance. Included in each Toxicological Summary are information on chemical and physical properties, production levels, use, human exposure, regulatory status, toxicological effects, and rationale for the nomination. The Toxicological Summaries are distributed to the NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC), which is composed of representatives from the Agency for Toxic Substances and Disease Registry, Consumer Product Safety Commission, Department of Defense, Environmental Protection Agency, Food and Drug Administration's National Center for Toxicological Research, Occupational Safety and Health Administration, National Cancer Institute, National Institute of Environmental Health Sciences, National Institute for Occupational Safety and Health, and the National Library of Medicine. ICCEC members are assigned as reviewers for each substance after consideration of the nature of its uses and exposure so that, to the extent possible, appropriate regulatory concerns will be addressed. Members are requested to identify their agency's interests, if any, in the chemical and to provide any relevant information from their respective agencies regarding the nominated chemicals or structurally related substances. During the evaluation process, the NTP works actively with regulatory agencies and interested parties to supplement the information about nominated substances and to ensure that the nomination and selection process meets regulatory and public health needs.

At its meeting to consider the nominated substances, the ICCEC makes testing recommendations including testing priorities and also may make recommendations for studies in addition to those requested by the nominator. Summaries of the ICCEC recommendations and any public comments received on these nominations are then presented to the NTP Board of Scientific Counselors (the Program's external scientific advisory committee) for review and comment in an open public session. The ICCEC's recommendations, NTP Board of Scientific Counselors' recommendations, and public comments are incorporated into recommendations that are then submitted to the NTP Executive Committee, the Federal interagency policy oversight body. For each substance nominated for the various types of studies, the NTP Executive Committee reviews and approves action to move forward to test, defer testing, or remove from testing consideration, and recommends testing priorities. The selection of a substance by the Executive Committee does not automatically commit the NTP to its evaluation. The priority of the nominations and the proposed studies are assessed during the nomination and

selection process and reassessed during the study design process. During any of these stages, a chemical or study may be withdrawn if applicable research data or higher priority studies are identified, or if a study proves impractical. A broad range of regulatory and toxicological concerns is addressed during the nomination and selection process through the participation of representatives from Federal agencies concerned with public health issues. In addition, representatives from non-government organizations including academia, industry, labor, and public interest sit on the NTP Board of Scientific Counselors, and thus have input into chemical selection decisions.

Nominated Substances and ICCEC Review

At its meeting on December 13, 1999, the ICCEC reviewed 12 nominations for NTP studies. For six of these nominations, metabolism, toxicity, or carcinogenicity studies were recommended. No studies were recommended at this time for two nominations, and a testing recommendation for four chemicals was deferred pending receipt of (1) additional data from other organizations on related studies completed, anticipated, or in progress or (2) information on production, exposure, and use patterns. The nominated substances with CAS numbers, nomination source, types of studies recommended, study rationale, and other information are given in the attached tables.

Request for Comment

Interested parties are encouraged to provide comments or supplementary information on the nominated substances and recommendations that appear in this announcement. The Program would welcome receiving toxicology and carcinogenesis information from completed, ongoing, or planned studies, as well as information on current production levels, human exposure, use patterns, or environmental occurrence for any of the substances listed in the attached tables. To provide comments or information, please contact Dr. William Eastin at the address given below within 60 days of the publication date of this announcement. Persons submitting comments or additional information are asked to include their name, affiliation, mailing address, phone, fax, e-mail and sponsoring organization (if any) with the submission. An electronic copy of this announcement as well as further information on the NTP and the NTP Chemical Nomination and Selection Process can be accessed through the NTP web site. The URL for the NTP homepage is http://ntp-server.niehs.nih.gov.

Contact may be made by mail to Dr. William Eastin, NIEHS/NTP, P. O. Box 12233, Research Triangle Park, North Carolina 27709; by telephone at (919) 541–7941; by FAX at (919) 558–7057; or by email at eastin@niehs.nih.gov.

Dated: February 17, 2000.

Samuel H. Wilson,

Deputy Director, National Institute of Environmental Health Sciences.

Attachment—Substances Nominated to the NTP for Study and Testing Recommendations Made by the ICCEC on December 13, 1999

TABLE 1.—SUBSTANCES RECOMMENDED FOR TESTING

Substance [CAS No.]	Nominated by	ICCEC recommendations	Study rationale; other information
1-Bromopropane [106–94–5] and 2-Bromopropane [75–26–3].	OSHA NIOSH	*1-Bromopropane* —carcinogenicity —reproductive and developmental toxicity —toxicokinetics —mechanistic studies —neurotoxicity —genotoxicity —exposure studies in workers 2-Bromopropane —subchronic toxicity	Reported increasing production and use in many industrial applications as an alternative to ozone depleting substances; available data from limited repeat dose studies indicate toxicity to multiple organ systems. 2-Bromopropane is a contaminant in reagent grade 1-Bromopropane with known reproductive toxicity.
Chitosan [9012–76–4]	NCI	—mechanistic studies to evaluate vitamin E and mineral depletion	Significant human exposure through use as a dietary supplement and other commercial applications; potential for toxicity from interference with dietary fat absorption.
DNA-based products	FDA	—establish joint NIEHS/FDA program to evaluate long-term toxicity in anticipation of regulatory needs	Rapidly growing market for DNA-based therapeutic agents and a lack of adequate mechanisms and methodologies for evaluating safety.
Juglone [481–39–0]	NCI	—mechanistic studies —metabolism studies —mouse lymphoma assay —mammalian mutagenicity —carcinogenicity testing pending results of preliminary studies	Potential human exposure resulting from use of walnut-based products as dietary supplements and natural dyes and stains; suspicion of carcinogenicity based on quinone structure.
Potassium ferricyanide [13746–66–2]	NCI.	—genotoxicity —subchronic toxicity	Potential consumer and worker exposure resulting from use in photographic processing; suspicion of toxicity based on potential for redox cycling; inadequate toxicity information available.
Radio frequency radiation emissions of wireless communication devices.	FDA	—establish interagency program to design studies assessing cancer and non-cancer health effects to fulfill regulatory needs	Widespread consumer and worker exposure; available data is inadequate to properly assess safety.

TABLE 2.—SUBSTANCES FOR WHICH NO TESTING IS RECOMMENDED AT THIS TIME

Substance [CAS No.]	Nominated by	Nominated for	Rationale for not testing
Cafestol [469–83–0] and Kahweol [6894–43–5].	Private individual	—toxicity and carcinogenicity testing.	Anti-carcinogenic effects demonstrated in animal studies; limited data indicate low potential for toxicity; other natural products with higher potential for toxicity and human exposure exist; ongoing research efforts as opposed to new testing may provide basis for determining relevance of metabolic modulatory effects to chronic toxicity.
Plumbagin [481–42–5].	NCI	—mechanistic studies —metabolism studies —mouse lymphoma assay —mammalian mutagenicity —carcinogenicity	Structurally similar to Juglone which is selected for study; low magnitude and/or prevalence of human exposure; adequate evidence of acute and reproductive toxicity.

TABLE 3.—SUBSTANCES FOR WHICH A TESTING RECOMMENDATION IS DEFERRED PENDING RECEIPT AND CONSIDERATION OF ADDITIONAL INFORMATION

Substance [CAS No.]	Nominated by	Nominated for	Additional information needed
Ethylenebis (tetrabromophthalimide) [32588–76–4].	NIEHS	—toxicity and carcinogenicity testing	Ongoing and planned industry testing efforts; better characterization of uses and potential human exposures.
Terpinolene [586–62–9]	NIEHS	—toxicity and carcinogenicity testing	Ongoing and planned industry testing efforts; better characterization of uses and potential human exposures; study results for structurally related compounds.
Tetrabromophthalic anhydride [632–79–1].	NIEHS	—toxicity and carcinogenicity testing	Ongoing and planned industry testing efforts; better characterization of uses and potential human exposures.
Texanol benzyl phthalate [16883–83–3] or [32333–99–6].	NIEHS	—toxicity and carcinogenicity testing	Ongoing and planned industry testing efforts; better characterization of uses and potential human exposures.

[FR Doc. 00–4964 Filed 3–1–00; 8:45 am]
BILLING CODE 4140–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Substance Abuse and Mental Health Services Administration

Fiscal Year (FY) 2000 Funding Opportunities

AGENCY: Substance Abuse and Mental Health Services Administration, HHS.

ACTION: Notice of funding availability.

SUMMARY: The Substance Abuse and Mental Health Services Administration (SAMHSA) Center for Mental Health Services (CMHS) announces the availability of FY 2000 funds for grants for the following activity. This activity is discussed in more detail under Section 3 of this notice. This notice is not a complete description of the activity; potential applicants *must* obtain a copy of Parts I and II of the Program Announcement (PA) before preparing an application. Part I is entitled Community Action Grants for Service Systems Change (PA00–003). Part II is entitled General Policies and Procedures Applicable to all SAMHSA Applications for Discretionary Grants and Cooperative Agreements.

Activity	Application deadline	Estimated funds available, FY 2000	Estimated Number of awards	Project period
Community Action Grants for Service Systems Change.	4/19/00* recurring submission dates of May 10 and September 10 thereafter for Phase I & II.	$3 million, phase I $1.5 million, phase II.	20–30, phase I .... 10–20, phase II ...	1 year. 1 year.

*Only Phase II applications will be received on April 19, 2000. Thereafter, the schedule provided above will be in effect for Phase II applications starting with the next receipt date of September 10, 2000.

There are two addenda to PA00–003: American Indian and Alaska Native Youth Priority Initiative, Phase I; and Hispanic Priority Initiative, Phase I.

The American Indian and Alaska Native (AI/AN) Youth Priority Initiative addendum provides funds to support the adoption of exemplary practices related to the delivery and organization of services for AI/AN Youth with serious emotional and substance abuse problems. $450,000 in FY 2000 is available to support 5 to 10 awards under this initiative. Federally recognized tribal governments, tribal organizations, and urban Indian organizations as defined by the Indian Self Determination Act and the Indian Health Care Improvement Act are eligible. The terms ''Indian,'' '' tribal,'' ''AI/AN,'' and ''Native American'' include Alaska Native organizations. The receipt date for Phase I applications under this initiative is May 10, 2000.