

National Toxicology Program

Web site: http://cerhr.niehs.nih.gov/news/fr8_19_02.html

Notice of a Meeting of the NTP Board of Scientific Counselors

CCEC Recommendations for Substances Nominated for Future NTP Studies

Information about substances nominated to the NTP for toxicology and carcinogenesis studies and the ICCEC's recommendations was published in the Federal Register on June 12, 2002 (Vol. 67, No. 113, p. 40329-33). This notice is available on the web (<http://ntp-server.niehs.nih.gov/htdocs/Liason/ICCECFinal02JuneFR.html>) along with supporting documents for each nomination (<http://ntp-server.niehs.nih.gov/htdocs/liason/BkgrSum02June.html>) or by contacting the NTP Executive Secretary (contact information below).

This meeting provides an additional opportunity for the public to provide comment on these nominations and study recommendations to the Board and NTP staff. Comments submitted to the NTP in response to the June 2002 Federal Register notice are under consideration and do not need to be resubmitted or readdressed.

Substances recommended for study:

- Abrasive blasting agents - 5 different industrial materials used as alternatives to sand
- 5-Amino-o-cresol - permanent hair dye ingredient
- tert-Butyl hydroperoxide - high production volume industrial catalyst
- Chloramine-T and p-Toluenesulfonamide - active ingredient and metabolite of therapeutant used in aquaculture to control bacterial infections
- Cobalt metal dust - important industrial material linked to lung problems in workers
- Ephedrine alkaloid dietary supplements - widely used in herbal dietary supplements with numerous reports of adverse effects
- Ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-(Iso-E-Super) - high-production-volume fragrance material
- Hexafluorosilicic acid and Sodium hexafluorosilicate - primary agents used to fluoridate public drinking water system
- Ketamine hydrochloride - approved anesthetic drug that causes brain lesions in developing rats
- Mercury, ((o-carboxyphenyl)thio)ethyl-, sodium salt (Thimerosal) - organomercuryl-based preservative used in vaccines and other biological products
- Nitrogen trifluoride - cleaning and etching agent in the semiconductor industry
- Sodium metasilicate - industrial cleaning agent
- Turpentine - high-production-volume industrial solvent and raw material
- Welding fumes - variable composition mixture responsible for respiratory and other adverse effects in exposed workers

BELOW IS RELEVANT EXCERPT FROM FED. REG. (NOTE: IN ORIGINAL, NOMINATION IS IN A TABLE WITH COLUMNS WHICH IS REPRODUCED IN DIFFERENT FORMAT BELOW FOR SILICOFLUORIDES ONLY)

[Federal Register: June 12, 2002 (Vol. 67, No. 113)] [Notices] [Pages 40329 - 40333]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Toxicology Program

Announcement of and Request for Public Comments on Substances Nominated to the National Toxicology Program (NTP) for Toxicological Studies and on Study Recommendations Made by the NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC)

Summary

The NTP continuously solicits and accepts nominations for toxicological studies to be undertaken by the program. Nominations of substances of potential human health concern are received from Federal agencies, the public, and other interested parties. These nominations undergo several levels of review before selections for testing are made and toxicological studies are designed and implemented. Evaluation by the NTP ICCEC is the initial external review step in the NTP's formal selection process for NTP study nominations. On April 17, 2002 the ICCEC met to review 19 new nominations and make study recommendations. This announcement (1) provides brief background information regarding the substances nominated to NTP for study, (2) presents the ICCEC's study recommendations from its April 17, 2002 meeting, (3) solicits public comment on the nominations themselves and on the study recommendations by the ICCEC, and (4) requests the submission of additional relevant information for consideration by the NTP in its continued evaluation of these nominations.

Review of Study Nominations

At its meeting on April 17, 2002, the ICCEC reviewed 19 new nominations for NTP studies. For 14 of these nominations, one or more types of toxicological studies were recommended, and for 5 nominations, no studies were recommended at this time. The nominated substances with CAS numbers, nomination source, nomination rationale, specific study recommendations, and other pertinent information are given in the attached tables.

Evaluation by the NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC) is the initial external review step in the NTP's formal selection process for NTP study nominations. The ICCEC is composed of representatives from the Agency for Toxic Substances and Disease Registry, U.S. Consumer Product Safety Commission, Department of Defense, U.S. Environmental Protection Agency, U.S. Food and Drug Administration's National Center for Toxicological Research, National Cancer Institute, National Center for Environmental Health, National Institute of Environmental Health Sciences, National Institute for Occupational Safety and Health, National Library of Medicine, and the Occupational Safety and Health Administration. The ICCEC meets once or twice annually to evaluate groups of new study nominations and to make recommendations with respect to both specific types of studies and testing priorities.

Request for Public Comments

Interested parties are invited to submit comments or supplementary information on the nominated substances and study recommendations that appear in the attached tables. The NTP welcomes toxicology

and carcinogenesis information from completed, ongoing, or planned studies, as well as information on current production levels, use patterns, human exposure, environmental occurrence, or public health concerns for any of the nominated substances. The NTP is also interested in identifying appropriate new animal models for mechanistic based research, including transgenic or knockout mice, and welcomes comments regarding the use of specific animal models to address scientific questions relevant to the nominated substances and studies under consideration. All information received will be considered by the NTP in its continued review of these nominations. Comments or information should be sent to Dr. Scott Masten by August 12, 2002. Persons responding to this request should include their name, affiliation, mailing address, phone, fax, e-mail address and sponsoring organization (if any) with the submission. Written submissions will be made available electronically on the NTP's web site as they are received.

An electronic copy of this announcement, internet links to electronic versions of supporting documents for each nomination, and further information on the NTP and the NTP Chemical Nomination and Selection Process can be accessed through the NTP web site: <http://ntp-server.niehs.nih.gov>.

Send comments or information to Dr. Scott A. Masten, Office of Chemical Nomination and Selection, NIEHS/NTP, P. O. Box 12233, MD A3-07, Research Triangle Park, North Carolina 27709; telephone: (919) 541-5710; FAX: (919) 541-3647; email: masten@niehs.nih.gov.

Background

The NTP actively seeks to identify and select for study chemicals and other agents for which sufficient information is not available to adequately evaluate potential human health hazards. The NTP accomplishes this goal through a formal open nomination and selection process. Substances considered appropriate for study generally fall into two broad yet overlapping categories: (1) those substances of greatest concern for public health based on the extent of human exposure and/or suspicion of toxicity; and (2) substances for which toxicological data gaps exist and additional studies would aid in assessing potential human health risks, e.g. by facilitating cross-species extrapolation or evaluating dose-response relationships. Input is also solicited regarding the nomination of studies 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 classes of chemical, biological, or physical substances. Substances may be studied to evaluate a variety of health-related effects, including but not limited to reproductive and developmental toxicity, genotoxicity, immunotoxicity, neurotoxicity, metabolism and disposition, and carcinogenicity. In reviewing and selecting nominated substances, the NTP also considers legislative mandates that require responsible private sector commercial organizations to evaluate their products for health and environmental effects. The possible human health consequences of anticipated or known human exposure, however, remain the overriding factor in the NTP's decision to study a particular substance.

The review and selection of substances nominated for study is a multi-step process. A broad range of concerns are addressed during this process through the participation of representatives from the National Institute of Environmental Health Sciences, other Federal agencies, the NTP Board of Scientific Counselors - an external scientific advisory body, the NTP Executive Committee - the NTP Federal interagency policy body, and the public. This process is described in further detail in a March 2, 2000 Federal Register announcement (Volume 65, Number 42, pages 11329-11331). This multi-step evaluative process provides the NTP with direction and guidance to ensure that its testing program addresses toxicological concerns relative to all areas of public health, and furthermore, that there is balance among the types of substances selected for study (e.g., industrial chemicals, consumer products, therapeutic agents). As such, it should be recognized that at any given time, the new study nominations under consideration do not necessarily reflect

the overall balance of substances historically or currently being evaluated by the NTP in its testing program. For further information on NTP toxicology studies (previous or in progress) visit the NTP web site at <http://ntp-server.niehs.nih.gov>.

Dated: June 5, 2002

Samuel Wilson, M.D.
Deputy Director
National Toxicology Program

[Billing Code 4140-01-P]

Attachment Substances Nominated to the NTP for Toxicological Studies and Recommendations Made by the ICCEC on April 17, 2002

Table 1. -- Substances Recommended for Study

Substance [CAS No.] Hexafluorosilicic acid [16961-83-4] and Sodium hexafluorosilicate [16893-85-9]

Nominated by: Private Individuals (multiple nominations)

Nominated for: Chemical characterization- Toxicological characterization including chronic toxicity, carcinogenicity, neurotoxicity, and toxicokineticsl -Mechanistic studies related to cholinesterase inhibition and lead bioavailability

Rationale for Nomination: Primary agents used to fluoridate public drinking water systems;lack of toxicity information; assumed complete dissociation to free fluoride under normal conditions of use not supported by experimental evidence

ICCEC Recommendations: - Chemical characterization studies to assess chemical fate under aqueous conditions -Toxicological studies may be considered when results of chemical characterization studies are available for review.