American Chemistry Council

BY FAX

May 18, 2006

Dr. Donald R. Arbuckle
Acting Administrator
Office of Information and Regulatory Affairs
Office of Management and Budget
725 17th Street, NW
Washington, DC 20503
Fax: 202-395-3047

RE: EPA TSCA Section 4 Test Rule based on ATSDR's Substance-Specific Priority Data Needs

Dear Dr. Arbuckle:

The American Chemistry Council would like to request an opportunity to meet with your office to discuss concerns we have about a TSCA Section 4 Test Rule the Environmental Protection Agency (EPA) is developing requiring specific toxicity tests for certain chemicals based on the Agency for Toxic Substances and Disease Registry's (ATSDR) Substance-Specific Priority Data Needs. In the most recent ATSDR Federal Register Notice describing Substance-Specific Priority Data Needs (70 Fed. Reg. 73749, Dec. 13, 2005), several chemicals are listed, including a number of which are in the EPA's Voluntary Children's Chemical Evaluation Program (VCCEP) pilot program. Further, some of the toxicity tests described in the ATDSR Substance-Specific Priority Data Needs correspond to the exact tests embodied in the EPA's VCCEP.

One of the most important aspects of the EPA VCCEP pilot is the Data Needs evaluation and decision. Through the VCCEP program, EPA and stakeholders have come to recognize that a data gap is not necessarily a data need. In the context of the VCCEP *data gaps* are any areas in which information is lacking, and *data needs* are those data gaps for which additional information is required before the potential risk to children can be adequately characterized. EPA has endorsed the approach of using quantitative estimates of risk to assist in determining whether a "data gap" is actually a "data need." In several of the EPA's formal Data Needs Decisions for VCCEP chemicals, the Agency has determined that "data gaps" with respect to specific toxicity tests, including some specific tests which fall into the VCCEP Tier 2 or Tier 3 categories, are not actual "data needs." The VCCEP model has shown that the absence of one or more toxicity tests does not mean that there is a data need for collection of such information. Instead, VCCEP has shown that when exposure information is integrated with hazard information, it is both feasible and scientifically supportable to conclude that risk has been adequately characterized, even if the database is lacking in one or more specific toxicity tests.

In short, the Data Needs evaluation of VCCEP will address whether or not specific testing information is actually needed for substances in that program. We are concerned, therefore, that issuance of this TSCA Section 4 Test Rule, for toxicity tests of substances currently involved in the VCCEP pilot, would effectively negate the Agency's and Administration's commitment to VCCEP.

We look forward to the opportunity to meet with OIRA and EPA to discuss our concerns. We will contact you in the next day or so to schedule a meeting. In the meantime, if you have any question, please contact me by phone at 703/741-5210 or by e-mail at Rick_Becker@americanchemistry.com.

Sincerely,

Rick Becker, Ph.D., DABT
Senior Director
ACC Health, Product & Science Policy Team

modifications might be made which would make the VCCEP run more efficiently and the recommendations coming out of the pilot program evaluation will be used to improve the subsequent implementation of the VCCEP.

D. What Toxicity Studies Will Be Collected by the VCCEP and Will the Studies Be Divided into Tiers?

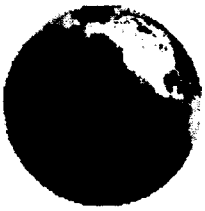
The toxicity studies EPA would collect for the VCCEP are the studies listed in Unit II.F. These are the studies EPA believes are appropriate to be included in a core toxicology data set to evaluate the toxicity of chemicals to which children have a significant potential for exposure. These are also the studies the SAP agreed with EPA regarding their inclusion in such a program. The SAP supported the application of this battery of tests as a single tier (Ref. 33). However, during stakeholder discussions, EPA frequently heard comments from various individuals that several of the studies in the test battery should be initiated only after lower level (e.g., HPV Challenge Program) tests and exposure information indicate additional cause for concern. In order to meet the needs of as many of the stakeholders as possible and to ensure the participation of industry sponsors in a voluntary program, testing tiers have been incorporated in the VCCEP. Also, many of the chemicals selected for this voluntary program are sponsored in the HPV Challenge Program and the health effects studies conducted in that Program will satisfy the Tier 1 test requirements of the VCCEP, thereby allowing a resource-saving integration of the VCCEP and the HPV Challenge Program. Table 3 of this unit indicates how the test battery will be divided among three tiers and lists the appropriate guideline for conducting each test.

TABLE 3.—THREE TIERS OF VCCEP TESTS

Tier	Test	Test Guideline
1[1]	Acute oral toxicity (up/down) OR Acute inhalation toxicity	OECD 425 or ASTM E1163–98 OECD 403 or 40 CFR 799.9130
	In vitro gene mutation: Bacterial reverse mutation assay	OECD 471, 870.5100, or 40 CFR 799.9510
	Combined repeated dose toxicity with reproductive and developmental toxicity screens OR Repeated dose oral toxicity AND Reproductive toxicity (1-generation)	OECD 422 OECD 407 OECD 415/421
	In vitro chromosomal aberrations OR *In vivo* chromosomal aberrations OR *In vivo* mammalian erythrocyte micronucleus	OECD 473, 870.5375, or 40 CFR 799.9537 OECD 475, 870.5385, or 40 CFR 799.9538 OECD 474, 870.5395, or 40 CFR 799.9539
2	90-Day subchronic toxicity in rodents	870.3100 (oral), 870.3250 (dermal), 870.3465 (inhalation), or 40 CFR 799.9346 (inhalation)
	Reproduction and fertility effects	870.3800 or 40 CFR 799.9380
	Prenatal developmental toxicity (two species)	870.3700 or 40 CFR 799.9370
	In vivo mammalian bone marrow chromosomal aberrations, OR *In vivo* mammalian erythrocyte micronucleus (triggered off results from *in vitro* mammalian chromosomal aberration test if conducted in Tier 1)	OECD 475, 870.5385, or 40 CFR 799.9538 OECD 474, 870.5395, or 40 CFR 799.9539
	Immunotoxicity	870.7800 or 40 CFR 799.9780
	Metabolism and pharmacokinetics	870.7485 or 40 CFR 799.9748
3	Carcinogenicity OR chronic toxicity/carcinogenicity	870.4200 or 40 CFR 799.9420 870.4300
	Neurotoxicity screening battery	870.6200 or 40 CFR 799.9620
	Developmental neurotoxicity	870.6300 or 40 CFR 799.9630

[1] The tests and test guidelines in Tier 1 are the same as those in the HPV Challenge Program. For example, under the HPV Challenge Program, EPA encourages persons required to conduct testing for chromosomal damage to use the *in vitro* Mammalian Chromosome Aberration Test to generate the needed data unless known chemical properties (e.g., physical/chemical properties, chemical class characteristics) preclude its use. As another example, if not superseded by a higher tier study, EPA recommends the use of the Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test. See HPV Challenge Program web site at http://www.epa.gov/chemrtk/.

For chemicals which are in both the HPV Challenge Program and the VCCEP, sponsors should consider conducting appropriate upper tier VCCEP test(s) instead of the screening studies (such as OECD 422 or OECD 407 and 415/421 studies) included in the HPV Challenge Program to avoid conducting the lower tier studies unnecessarily. For example, if a chemical which was included in the HPV Challenge Program as well as the VCCEP lacked repeated dose testing data, it would be prudent for the sponsor to conduct a 90-day subchronic study to meet the needs of the VCCEP versus the recommended studies under the HPV Challenge program (OECD 422 or 407). Similarly, although the OECD 422 and 415/421 evaluate certain developmental and reproductive endpoints, they do not provide as full



TERA

Toxicology Excellence for Risk Assessment

a nonprofit corporation dedicated to the best use of toxicity data for risk values

TERA Home
About *TERA*
TERA News
Programs
ITER Database
TERA Tools
Links
Contact *TERA*
GSA Contracts
Search TERA

Toxicology Excellence for Risk Assessment (*TERA*)

2300 Montana Avenue, Suite 409, Cincinnati OH 45211
Phone: 513-542-7475
Fax: 513-542-7487

Email: *TERA@TERA.org*

VCCEP Peer Consultation Pilot Chemicals

Peer Home News Meeting Reports Current Meetings General Information \

Listed below are the chemicals in the Voluntary Children's Chemical Evaluation Program (VCCEP) pilot. The peer consultation meeting date is indicated for tho chemicals which have undergone a peer consultation (or if a meeting has been scheduled). Information on the sponsors for each VCCEP pilot chemical is foun EPA's VCCEP website.

Acetone - November 2003
Benzene - June 15-16, 2006
Decabromodiphenyl Ether - April 2003
n-Dodecane, Undecane, Decane (n-Alkanes) - September 2004
p-Dichlorobenzene - not yet scheduled, anticipated to occur in 2007
p-Dioxane - not yet scheduled
Ethylbenzene - not yet scheduled, anticipated to occur in 2007
Ethylene Dichloride - not yet scheduled
Methyl Ethyl Ketone - February 2004
Octabromodiphenyl Ether - June 2003
Pentabromodiphenyl Ether - June 2003
a-Pinene - not yet scheduled, anticipated to occur in 2007
Tetrachloroethylene - not yet scheduled, anticipated to occur in 2008
Toluene - November 7-8, 2006
Trichloroethylene - not yet scheduled, anticipated to occur in 2008
Vinylidene Chloride - January 2003
m-Xylene, o-Xylene, p-Xylene, and mixed-Xylenes- December, 2005

ATSDR Department of Health and Human Services
Agency for Toxic Substances & Disease Registry

ATSDR's Substance-Specific Priority Data Needs

Being Filled via EPA/ATSDR Test Rule and/or Voluntary Research Program (file size 76k)

Substances	PDN Description	Status [1]	
Benzene	• Dose-response data in animals for acute[2]- and intermediate[3]-duration oral exposure. The intermediate-duration study should include an extended reproductive organ histopathology • Prenatal developmental toxicity study via oral exposure • Neurotoxicology battery of tests via oral exposure	EPA/ATSDR test rule	VCCEP
Chloroethane	• Dose-response data in animals for acute- and intermediate-duration oral exposures. The intermediate-duration study should include an evaluation of immune and nervous system tissues, and extended reproductive organ histopathology • Dose-response data in animals for chronic[4] inhalation exposures. The study should include an evaluation of nervous system tissues	EPA/ATSDR test rule	
Cyanide (Hydrogen cyanide and sodium cyanide)	• Dose-response data in animals for acute- and intermediate-duration exposures via inhalation. The intermediate-duration study should include extended reproductive organ histopathology and evaluation of neurobehavioral and neuropathological end points • Prenatal developmental toxicity study via oral exposure	EPA/ATSDR test rule	
Methylene chloride	• Neurotoxicity testing via oral exposure	EPA/ATSDR test rule	
Tetrachloroethylene	• Multigeneration reproductive toxicity study via oral exposure • Dose-response data in animals for intermediate-duration oral exposure, including neuropathology, and immunopathology • Prenatal developmental toxicity study via oral exposure • Developmental neurotoxicity study via oral exposure	EPA/ATSDR test rule and Voluntary Research	VCCEP
Toluene	• Neurotoxicology battery of tests via oral exposure	EPA/ATSDR test rule	VCCEP

[1] EPA/ATSDR test rule: The priority data need is included in the EPA/ATSDR test rule which is under review at EPA. In the implementation of the Substance-Specific Applied Research Programs, ATSDR and the U.S. Environmental Protection Agency identified a subset of priority data needs for substances of mutual interest to the federal programs. These priority data needs are being addressed through a program of toxicological testing under the Toxic Substances Control Act according to established procedures and guidelines.

Voluntary Research: ATSDR encourages industry groups to volunteer to conduct studies to fill priority data needs at no expense to the Agency. The industry groups' study protocols and final reports are subjected to ATSDR's external peer review before the Agency's acceptance of the study results. In some instances, the studies conducted under voluntary research will also fill priority data needs included in the EPA/ATSDR test rule.

[2] Acute-duration exposure =14 days or less.

(3) Intermediate-duration exposure = 15-364 days.

(4) Chronic-duration exposure = 365 days or more.

This page was updated on 03/29/2006