DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333

JUN 27 2002

Paul H. Dugard, Ph.D.
Director of Scientific Programs
Halogenated Solvents Industry Alliance, Inc.
2001 L Street, N.W.
Suite 506A
Washington, D.C. 20036

Dear Dr. Dugard:

I am responding to your June 21 letter in which you enclosed two originals of the Agreement to be signed between the Agency for Toxic Substances and Disease Registry (ATSDR) and the Halogenated Solvents Industry Alliance Inc. (HSIA). The Agreement covers studies on trichloroethylene and tetrachloroethylene that HSIA will conduct to fill ATSDR's remaining priority data needs for these substances. I am pleased to inform you that ATSDR has signed the Agreement and a fully executed original is enclosed in this letter. We believe that the document represents a step forward in filling ATSDR's critical research needs via HSIA's voluntary research efforts. Please proceed with the submission of the study protocols as indicated in your letter.

We look forward to continuing collaboration with HSIA to address ATSDR's priority data needs for volatile organic compounds. Please call me at (404) 498-0160 or e-mail me at CDerosa@cdc.gov if you have any questions.

Sincerely yours,

Christopher T. De Rosa

Christopher T. De Rosa, Ph.D.
Director, Division of Toxicology

Enclosure

cc:
Henry Falk
Peter McCumiskey
Robert Spengler
William Cibulas
Yee-Wan Stevens
Charles Auer
W. Caffey Norman

AGREEMENT BETWEEN THE AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY AND THE HALOGENATED SOLVENTS INDUSTRY ALLIANCE, INC. FOR TESTING AND MODELING TO MEET PRIORITY DATA NEEDS

I. INTRODUCTION

As part of its implementation of Section 104(i)(5) of the Comprehensive Environmental Response, Compensation and Liability Act of 1980 (CERCLA) as amended by the Superfund Amendments and Reauthorization Act of 1986 (SARA), 42 U.S.C. § 9604(i)(5), the Agency for Toxic Substances and Disease Registry (ATSDR) enters into this Agreement with the Halogenated Solvents Industry Alliance, Inc. (HSIA). This Agreement is intended to satisfy priority data needs identified for trichloroethylene ("tri") and tetrachloroethylene ("perc") by ATSDR.

This Agreement is also intended to develop data that will satisfy commitments made by HSIA in connection with the Voluntary Children's Chemical Evaluation Program (VCCEP) announced by the Environmental Protection Agency (EPA) in 2000. 65 Fed. Reg. 81700-708 (Dec 26, 2000). EPA requested manufacturers of 23 pilot chemicals to volunteer to sponsor them in Tier I of the VCCEP program. Tri and perc manufacturers, through HSIA, agreed to sponsor tri and perc in Tier I of the VCCEP pilot in a letter of commitment to EPA dated June 22, 2001. This correspondence is available in the EPA OPPTS docket 00247D.

In its commitment letter, HSIA agreed to prepare and submit to EPA hazard, exposure, risk, and data needs assessments and prepare peer consultation documents for tri and perc. HSIA indicated that these will be prepared and submitted in a timely fashion following completion of the toxicity testing and acceptance of the test results by ATSDR. In this way, results from the ATSDR testing program will feed back into consideration of data needs for the VCCEP and may avert overlap in testing requirements between the two initiatives.

II. CHEMICALS SUBJECT TO AGREEMENT

This Agreement covers testing and data development for the chemical substances trichloroethylene (CAS No. 79-01-6) and tetrachloroethylene (CAS No. 127-18-4).

III. PURPOSE OF THE TESTING PROGRAM

The purpose of the testing program specified in this Agreement is to supplement available information in order to further characterize the potential for subchronic toxicity, neurotoxicity, immunotoxicity, developmental toxicity, reproductive toxicity, and developmental neurotoxicity effects of tri and perc. One component of this testing program will develop or refine pharmacokinetic and mechanistic (PK/MECH) data directed at characterizing the mode of action of tri and perc. Such information, along with data from health effects studies, will be used to inform route-to-route extrapolations as specified in Table 1 of this Agreement.

ATSDR believes that the PK/MECH studies designed to construct quantitative dosimetric characterization of the disposition and relevant response mechanisms with regard to tri and perc, in conjunction with the studies and route-to-route extrapolation reporting that are specified in Table 1, will generate high quality test data that will be adequate to meet its priority data needs for tri and perc. To ensure data quality, ATSDR has adopted procedures for conducting voluntary research, 57 Fed. Reg. 54160 (Nov. 16, 1992), that will apply to development of data under this Agreement. These procedures require that ATSDR and HSIA sign a memorandum of understanding (MOU) prior to initiation of research projects.

Pursuant to these procedures, HSIA will submit to ATSDR for each study identified in Table 1 a study plan that includes test protocols and a schedule with deadlines for initiation and completion of each test and submission of interim and final reports. The test protocols will be reviewed by an ATSDR-appointed peer-review panel. Consistent with CERCLA § 104(i)(13), the peer review panel will consist of no fewer than three nor more than seven peer reviewers who (a) are selected by the Administrator of ATSDR; (b) are disinterested scientific experts; (c) have a reputation for scientific objectivity; and (d) lack institutional ties with any person involved in the conduct of the study under review.

If the study plan is approved by ATSDR following review of the protocol by the peer reviewers, HSIA and ATSDR will proceed to enter into an MOU for the study. Each MOU will meet the content requirements specified at 57 Fed. Reg. 54162, including without limitation deadlines for initiation and completion of each test and submission of interim and final reports.

IV. MODIFICATION AND BREACH

If for reasons beyond its control HSIA is unable to submit a study plan by the date identified in Table 1, it shall notify ATSDR in writing of the need for modification of Table 1 and the reasons supporting such modification. ATSDR shall respond in writing to the proposed modifications within 2 to 6 weeks either: (i) approving the modifications as proposed, (ii) approving the modifications as revised by ATSDR, or (iii) disapproving the modifications entirely. If ATSDR does not approve the modifications as proposed, HSIA will have 2 weeks within which to: (i) accept ATSDR's decision and proceed in accordance therewith, (ii) request that ATSDR reconsider its decision, or (iii) withdraw from this Agreement. ATSR will respond to a request for reconsideration within 2 weeks.

If HSIA submits a request for modification of Table 1 to ATSDR, the time schedule established for submission of a study plan shall be extended by the length of time required by ATSDR and HSIA to respond to and approve the modifications.

Failure by HSIA to submit a study plan by the date identified in Table 1 (as it may be modified) shall constitute a breach of this Agreement. In the event of a breach, ATSDR will not impose any claim to damages, but at the Agency's discretion may terminate this Agreement.

V. EFFECTIVE DATE

This Agreement shall be effective July 1, 2002.

VI. SIGNATURES

Agency for Toxic Substances and Disease Registry

Date: 6/27/02 By: Christopher T. DeRosa

Christopher T. De Rosa, Ph.D.
Director
Division of Toxicology

Halogenated Solvents Industry Alliance, Inc.

Date: June 21, 2002 By: _____

Paul H. Dugard, Ph.D., Dip RCPath (tox)
Director of Scientific Programs

TABLE 1

TESTING SCHEDULE

TRICHLOROETHYLENE

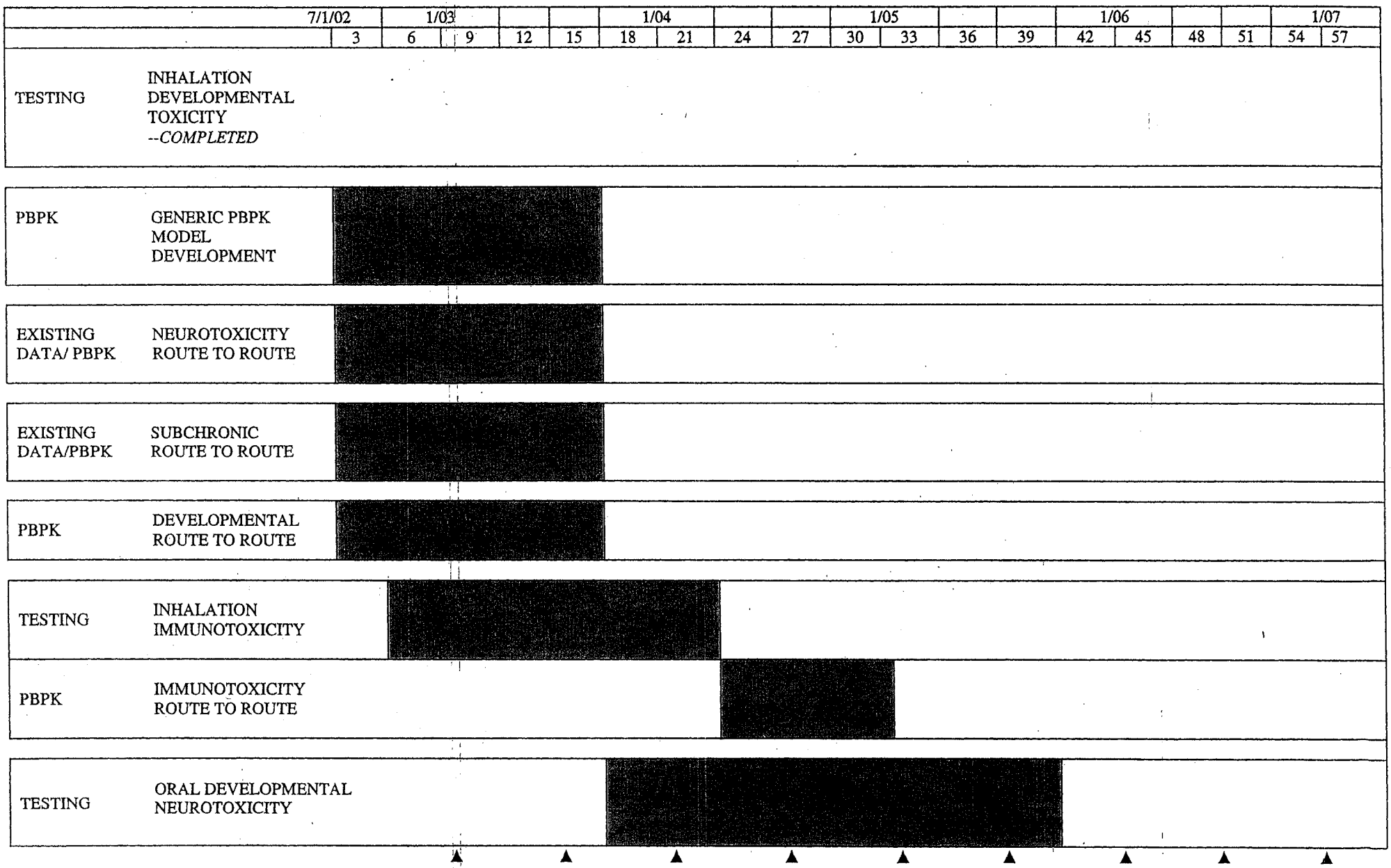
Test	Submission of Protocol (month/year)	
Developmental toxicity (rat)		
- Testing by inhalation route	Study Complete	
Generic PBPK model development	7/2002	✓
Neurotoxicity		
- PBPK extrapolation of extant data	7/2002	✓
Subchronic toxicity		
- PBPK extrapolation of extant data	7/2002	✓
Developmental toxicity (rat)		
- PBPK route-to-route extrapolation	7/2002	✓
Immunotoxicity (rat)		
- Testing by inhalation route	10/2002	✓
Developmental neurotoxicity (rat)		
- Testing by oral route	10/2003	
Immunotoxicity (rat)		
- PBPK route-to-route extrapolation	4/2004	

TESTING SCHEDULE

PERCHLOROETHYLENE

Test	Submission of Protocol (month/year)
Developmental toxicity (rat)	
- Testing by inhalation route	7/2002
Generic PBPK model development	10/2002
Neurotoxicity	
- PBPK extrapolation of extant data	10/2002
Subchronic toxicity	
- PBPK extrapolation of extant data	10/2002
Reproductive toxicity	
- PBPK extrapolation of extant data	10/2002
Immunotoxicity (rat)	
- Testing by inhalation route	7/2003
Developmental toxicity (rat)	
- PBPK route-to-route extrapolation	1/2004
Developmental neurotoxicity (rat)	
- Testing by oral route	7/2004
Immunotoxicity (rat)	
- PBPK route-to-route extrapolation	1/2005

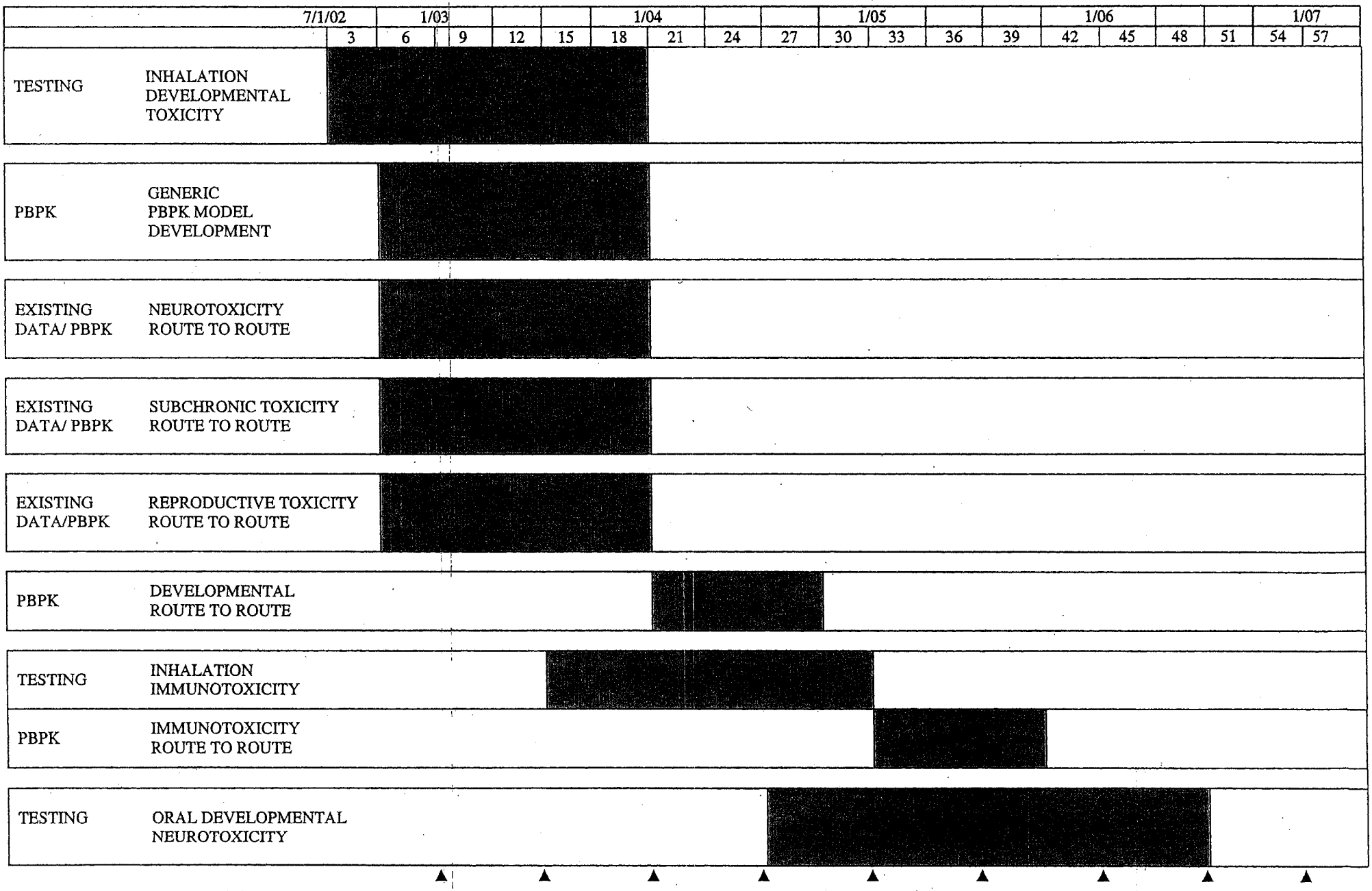
Proposed Schedule for Toxicity Testing and PBPK Modeling Activities for Trichloroethylene



Deadlines for submission of protocols coincide with the beginning of shaded areas. Expected timing of start and completion of testing and submission of reports is indicated by shaded areas.

Progress reports marked by arrows will be provided every six months to ATSDR after initiation of testing and will cover all categories.

Proposed Schedule for Toxicity Testing and PBPK Modeling Activities for Perchloroethylene



Deadlines for submission of protocols coincide with the beginning of shaded areas. Expected timing of start and completion of testing and submission of reports is indicated by shaded areas.

Progress reports marked by arrows will be provided every six months to ATSDR after initiation of testing and will cover all categories.

Doc 3603583

PPG Industries, Inc. One PPG Place Pittsburgh, Pennsylvania 15272

James A. Barter, Ph.D.
Global Director, Environmental Health Sciences & Toxicology
Environment, Health & Safety

Phone: 412-434-2801
Fax: 412-434-2014
E-mail: barter@ppg.com

March 21, 2005

Charles M. Auer
Director, Office of Pollution Prevention and Toxics
7401M
USEPA Headquarters
Ariel Ross Building
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Dear Director Auer:

It is PPG's understanding that the Agency, in cooperation with the Agency for Toxic Substances and Disease Registry (ATSDR), is developing a proposed TSCA Test Rule for chloroethane (CAS 75-00-3), also commonly referred to as ethyl chloride. PPG has additional information on several topics germane to the Agency's efforts in developing the proposed Test Rule that we are willing to provide to the Agency. As you may recall, PPG has an established track record of voluntarily participating in key Agency initiatives, e.g. (i) sponsorship of a number of chemicals in the EPA and ICCA High Production Volume (HPV) Chemical initiatives, (ii) participation in Enforceable Consent Agreements for certain chemicals under the proposed Hazardous Air Pollutants rule, (iii) participation in the pilot phase of the Pollution Prevention (P2) initiative and subsequent execution of an XL Project on the use of P2 assessments for new product evaluations, and (iv) participation in the Agency's Sustainable Futures initiative. Additionally, as a member of the Halogenated Solvents Industry Alliance, PPG has entered into several Memoranda of Understanding (MOU) with ATSDR to address ATSDR identified data needs. PPG is willing to work with the Agency to provide information on chloroethane that should be helpful to the Agency in its determination of the need for a Test Rule on chloroethane.

Specifically, we recently provided additional ***hazard*** information on chloroethane, i.e. information on chemical properties and toxicity endpoints (see below). In addition to this hazard information already provided, PPG is also able now to provide updated information to the Agency concerning current ***production volumes*** and ***end uses*** of

chloroethane. In the past when large volumes of tetraethyl lead were produced in the US, there were several US manufacturers of chloroethane. In the more recent past, PPG and Dow were the only US chloroethane producers. However, Dow stopped US production of this chemical in the mid-1990s, and PPG is now the only US manufacturer. Therefore, PPG is in a unique position to provide the best information available on current production volume and end use patterns for chloroethane. In recent years there have been significant changes in both of these areas that have resulted in significant reductions in the amount of ***chloroethane emissions***.

Hazard Information: Through contacts with Dr. James Holder at his poster presentations at past Society of Toxicology meetings, we were aware that Dr. Holder was preparing an EPA document on health effects of chloroethane. Dr. Holder was also aware that an industry group was conducting a similar project as part of industry's sponsorship of the chemical in a HPV program. We have supplied Dr. Holder with an electronic copy of the *Hazard Assessment Dossier for Chloroethane (CAS No. 75-00-3),* submitted by the Chloroethane Producers Consortium to USEPA OPPTS in 2003 for the Agency's use in its role as the sponsoring country for this chemical in the ICCA High Production Volume (HPV) Initiative. After review of this document, Dr. Holder stated there was a considerable amount of information on various toxicity endpoints that was previously unavailable to the Agency and is of value in the Agency's review of chloroethane. He also requested copies of the original reports for some of the studies, and we are in the process of attempting to provide those to him from the member companies of our consortium.

Review of the extensive body of existing hazard information shows that chloroethane is a material that appears to exhibit toxicity only at high concentrations, i.e. at concentrations in the thousands of ppm level. There has been considerable potential human exposure to chloroethane over the last 60 or more years due to its past use as an anesthetic for tonsillectomies and as a topically applied local anesthetic for sport injuries. Additionally, there has been considerable potential occupational exposure due to its use as a foam-blowing agent. Despite these extensive human exposures, there are no reports of significant human health effects in the literature.

Production Volume Information: Historical production volume data from 1955 to 1995 are available from the Chemical Economics Handbook (see attached copy of the pertinent section from this reference) and are shown in Figure 1. The peak US production of chloroethane was during the 1960s and 1970s, when total annual production exceeded 675 million pounds. However, from 1980 to 1990 production volume decreased to 149 million pounds and has subsequently declined further. These decreases in total US production to present levels are primarily due to changes in end uses, i.e. discontinuation of chloroethane use as a raw material in the manufacture of the gasoline additive tetraethyl lead and more recently by replacement of the chloroethane as a blowing agent in the production of synthetic foam. Figure 1 also shows PPG's US production of chloroethane from 1996 to present. PPG's present production of chloroethane is about 65

million pounds per year. This production is sold primarily in the US, although some material is exported. The production volume is estimated by PPG to decrease further over the next five years.

End Use Patterns Information: As mentioned above, in recent years two previous end uses of chloroethane (i.e. manufacture of tetraethyl lead and use as a foam blowing agent) have largely been eliminated. The current end uses of chloroethane are presented in Table 1. These data show that nearly all of the chloroethane produced for the current US markets goes into consumptive uses, i.e. uses where the chloroethane is a feedstock used to produce different end product chemicals. Only a small volume goes into emissive uses such as foam blowing (2%).

Chloroethane Emissions Information: Data on environmental emissions of chloroethane are available from the Toxic Release Inventory databases as well as from derivative information sources, e.g. the National Library of Medicine website http://toxmap.nlm.nih.gov/toxmap/releases/navigate.do.

Based on the most current publicly available TRI data (2002), there were 46 facilities that reported on-site releases of chloroethane totaling approximately 775,000 lbs. Based on the present production volume range of about 65 million lbs/yr, total emissions of 775,000 lbs represent slightly over 1% of the manufactured volume.

The 2002 TRI data show a significant reduction in chloroethane emissions from earlier time periods, i.e. the 775,000 lbs of emissions in 2002 are only approximately 15% of the >5,000,000 lbs. of emissions annually released in the earlier years of the TRI reporting (late 1980s) through the mid-1990s. For comparison purposes, TRI data from 1989 can be used as representative of emissions during that earlier period. Figure 2 illustrates the significant reduction in emissions that have been achieved over the years, i.e. from 5,200,000 lbs in 1989 to 775,000 lbs in 2002. In fact, the ***total*** 2002 emissions from all 46 sites (775,000 lbs) are comparable to the amount of emissions from some ***individual*** sites (700,000 to >1,000,000 lbs) in the TRI reports from the late 1980's.These significant emission reductions are likely attributable to (i) changes in end uses, (ii) substitution of other materials for chloroethane in most foam blowing applications, and (iii) more efficient emission controls at facilities.

In 2002, the highest emitting individual site reported releases of 470,600 lbs (approximately 60% of the total chloroethane emissions for all sites), whereas the other 45 sites combined accounted for the remaining 375,000 lbs (approximately 40%). With the exception of the highest emitting site, all of the sites reported emissions of 100,000 lbs or less per year in 2002, with the majority of sites (26/46) reporting emissions of <1,000 lbs/year, i.e. less that 3 lbs/day. Table 2 shows a stratified comparison of the number of sites reporting chloroethane emissions in various emission ranges in 1989 vs. 2002. These data clearly demonstrate that the number of facilities emitting large amounts of chloroethane has been significantly reduced over the time span and that the majority of facilities are emitting less than 1,000 lbs/yr in 2002.

Based on the above information, it is apparent that the present production volume of about 65 million pounds is greatly reduced from past peaks and that end uses of chloroethane are significantly different in 2005 than they were in the past. Most of the material produced now goes into consumptive uses and only a small percentage goes into emissive uses. As a result of these changes, the emissions of chloroethane into the environment have been greatly reduced from past eras, as corroborated by the fact that the total chloroethane emissions represent only about 1% of the current production volume. The emissions in 2002 were from a number of sources and were of a magnitude that they would not represent either a general or substantial human exposure that would warrant proposal of a Test Rule to develop additional data under the Toxic Substances Control Act. We believe that the emissions in 2005 are likely to reflect a continuing decline.

Proposed Test Rule: As PPG understands, EPA may propose a test rule for a chemical substance based upon the criteria set out in Section 4 (a) of the Toxic Substances Control Act (TSCA). EPA can make either a finding under TSCA section 4(a)(1)(A)(i), referred to here as an "A" Finding or under TSCA section 4 (a)(1)(B)(i), referred to here as a "B" Finding. In addition, EPA must also find that there is insufficient data or experience upon which EPA can reasonably determine the effects of this chemical on health or the environment.

PPG believes that the available information concerning the current production, use and emission of chloroethane does not indicate a level of concern that requires EPA to make either "A" or "B" findings warranting development of a Test Rule.

With regard to a possible "A" finding, i.e. the finding "may present an unreasonable risk of injury to health or the environment," EPA is to consider both the toxicity and exposure in determining risk. The extensive existing toxicology database has established that chloroethane is a virtually non-toxic material that shows effects only with exposures at extremely high concentrations. In fact, the material has a past history of extensive human use as an anesthetic, both general and topical. The documented low toxicity of chloroethane combined with the existing data on emissions do not provide a sufficient basis for concluding that the levels of exposure to the population could constitute an "unreasonable risk" to health or the environment.

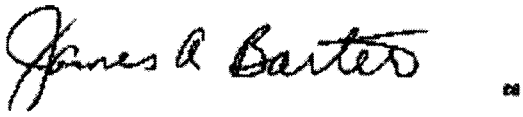
With regard to a possible "B" finding, i.e. the "substantial quantities or substantial human exposure" finding, EPA may consider a substance's production volume and potential for human or environmental exposure. Although the present production volume of 65 million pounds exceeds the Agency's "substantial production" criteria, the majority of the material is now utilized in consumptive rather than emissive uses. This fact becomes important in reaching conclusions concerning the potential for human or environmental exposure. The Agency has established criteria for making a "B" finding when a chemical had been released to the environment in quantities equal to at least 10% of total production or one million pounds, whichever is lower. As summarized above, the most

current publicly available EPA TRI data establish that 775,000 pounds of chloroethane (1% of production volume) was released into the environment in 2002. Neither of these measures reaches or exceeds the Agency's criteria for making a "B" finding.

Summary: PPG respectfully submits that the currently available information on the toxicity of chloroethane, historical human exposures, including its extensive medical uses, changes in end uses and substantial reduction in production volumes and emissions, provides EPA with sufficient information from which it can reasonably determine that chloroethane does not present an unreasonable risk of injury to health or the environment. For these reasons, PPG believes that consideration of currently available information on chloroethane, including the new information provided in this communication, provides sufficient data and experience with chloroethane to support a finding by EPA that development of a Test Rule is not warranted.

Should you have any questions or if we can be of further assistance, please do not hesitate to contact me.

Yours truly,



James A. Barter, Ph.D., DABT

Attachments:

Caruso, R. CEH Data Summary: Ethyl Chloride – United States. Chemical Economics Handbook – SRI International, April 1997.

Figure 1. US Cholorethane Production Volume – 1995 to present.

Table 1. US Chloroethane End Uses in 2004

Table 2. Stratified Comparison of Chloroethane Site Emissions: Year1989 vs. 2002.

Figure 2. Comparison of Total Chloroethane Emissions: Year 1989 vs. 2000.

cc: Oscar Hernandez, USEPA - OPPT
Greg Schweer, USEPA - OPPT
James Holder, USEPA - NCEA
Chris DeRosa, ATSDR

Note: The entire file can be reviewed in OIRA/Records Management, 202.395.6880