MEMORANDUM OF UNDERSTANDING FOR VOLUNTARY RESEARCH PROGRAM

Under Section 104(i)(5) of CERCLA

An agreement between

AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY
Division of Toxicology
Research Implementation Branch

and

HALOGENATED SOLVENTS INDUSTRY ALLIANCE, INC.

February 27, 1995

Duplicate Copy
1249

SL 108326

Table of Contents

I. PURPOSE

This Memorandum of Understanding (MOU) is entered into by the Agency for Toxic Substances and Disease Registry (ATSDR) and the private sector organization(s) identified in Paragraph II below (hereinafter referred to as "HSIA") in order to implement 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). These Congressional acts direct ATSDR to assure the initiation of a program of research designed to determine the health effects of hazardous substances for which adequate health effects information is not available. In order to facilitate the discharge of ATSDR's responsibilities under Section 104(i)(5) of CERCLA, and in recognition of the fact that HSIA represents manufacturers and/or processors, or registrants of the hazardous substance(s) that is the subject of this MOU, ATSDR and HSIA hereby agree as follows:

II. IDENTIFICATION OF THE PRIVATE SECTOR PARTIES TO THIS MEMORANDUM OF UNDERSTANDING

The following trade association is a party to this MOU and shall be responsible for ensuring that the obligations and undertakings of its member companies under this MOU are discharged and carried out as provided herein:

Halogenated Solvents Industry Alliance, Inc.
2001 L Street, N.W., Suite 506A
Washington, D.C. 20036

III. IDENTIFICATION OF THE SUBSTANCE(S) SUBJECT TO RESEARCH REQUIREMENTS UNDER THIS MEMORANDUM OF UNDERSTANDING

The chemical substance(s) that is the subject of this MOU is methylene chloride (CAS No. 75-09-2).

IV. IDENTIFICATION OF THE EFFECTS OR CHARACTERISTICS FOR WHICH RESEARCH IS TO BE CONDUCTED

The health effects, environmental fate or other characteristics for which research is to be conducted by HSIA under this MOU are listed below:

Acute toxicity -- Oral [Fodor and Winneke (1971); Stewart *et al.* (1972); Winneke (1974); Cherry *et al.* (1983)]

Subchronic toxicity -- Oral [Haun *et al.* (1972); reagent grade (*i.e.*, > 99.9% pure)]

Developmental toxicity -- Oral [Schwetz *et al.* (1975); 97.86% pure]

This research will be conducted using physiologically-based pharmacokinetic modeling. It is intended to satisfy the priority data needs for methylene chloride identified by ATSDR and referred to the Environmental Protection Agency, as described at 59 Fed. Reg. 49937 (Sept. 30, 1994).

ATSDR believes that the proposed research agenda addresses the Agency's priority data needs for methylene chloride as follows:

- ATSDR has identified developmental toxicity studies via oral exposure as a priority data need for methylene chloride.

- ATSDR has identified a priority data need for acute-duration oral studies to determine target organs and establish dose-response relationships. HSIA's proposal to use physiologically-based pharmacokinetic modeling to predict central nervous system effects following oral exposure should provide critical information for a potential target organ.

- HSIA's proposal to obtain oral data for liver effects for subchronic duration will partially address ATSDR's priority data need for subchronic-duration oral studies that also include special emphasis on immunopathology, neuropathology and demeanor.

V. IDENTIFICATION OF STUDY PLANS AND TESTING PROTOCOLS AGREED TO BY ATSDR AND HSIA PRIOR TO SIGNING OF MOU

The research to be conducted on methylene chloride pursuant to this MOU is described in the study protocol *Addressing Priority Data Needs for Methylene Chloride with Physiologically-Based Pharmacokinetic Modeling* that was agreed to by ATSDR and HSIA (Attachment 1 to this MOU). HSIA agrees to sponsor and fund the performance of the research identified in Attachment 1 in accordance with the guidelines and schedules established pursuant to the protocol.

VI. SUBMISSION OF STUDY PLANS AND ESTABLISHMENT OF SCHEDULE FOR INITIATION OF RESEARCH AND SUBMISSION OF INTERIM AND FINAL REPORT

A. Prior to signing of this MOU HSIA shall have submitted to ATSDR the protocol for each test that is to be conducted pursuant to this MOU (see Attachment 1).

B. Prior to entering into this MOU, the study plan including all testing protocols and guidelines shall have been

reviewed by an ATSDR appointed peer review panel. Consistent with CERCLA section 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.

C. The study shall be initiated within 8 weeks of the date on which ATSDR and HSIA have signed this MOU. Written notification of the starting date of the test will be submitted to ATSDR by HSIA. The study shall be completed within 10 weeks of the initiation of the study.

D. Unless modified pursuant to Paragraph VII, a final draft report shall be submitted to ATSDR within 10 weeks of the end of the study for ATSDR's peer review, consistent with CERCLA section 104(i)(13). Following acceptance by ATSDR, upon recommendation by the peer review panel, HSIA will submit a final report of the study to ATSDR within 10 weeks. Final reports will not be accepted if the data are designated Confidential Business Information (CBI) or otherwise restricted from public disclosure with the exception of personally identifiable information on study subjects.

E. Unless modified pursuant to Paragraph VII, interim progress reports on each testing program conducted pursuant to a study plan approved by ATSDR under this MOU shall be submitted to ATSDR within 6 months after the initiation of testing, and thereafter, within 6 months after the submission of each previous interim report. If the study is scheduled to be completed in one year, an interim brief letter addressing the status of the research must be submitted to ATSDR within 6 months of the initiation of the study.

VII. MODIFICATION OF STUDY PLANS, GUIDELINES, AND SCHEDULES

A. If HSIA seeks to modify a study plan, guidelines, or schedules that have been approved by ATSDR pursuant to this MOU, HSIA shall notify ATSDR in writing of the proposed modifications and the reasons therefor. 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 the MOU. ATSDR will respond to a request for reconsideration within 2 weeks.

B. If HSIA submits a request for modification to ATSDR pursuant to Paragraph VII. A., the time schedule established for completion of these tests shall be extended by the length of time required by ATSDR and HSIA to respond to and approve the modifications.

VIII. OBSERVANCE OF GOOD LABORATORY PRACTICES

All research agreed to in this MOU shall be conducted in accordance with the Good Laboratory Practice (GLP) standards codified in 40 C.F.R. Part 792, Subparts B, C, D, E, F, G, J, and L, to the extent that such GLP standards apply. Should Good Epidemiology Practices ("e.g., Guidelines for Good Epidemiology Practices for Occupational and Environmental Epidemiologic Research"--The Chemical Manufacturers Association's Epidemiology Task Group, Journal of Occupational Medicine, Volume 33, 1221-1229, 1991) be relevant to a research project, those Practices should be affixed to the study plan.

IX. INSPECTIONS

HSIA shall ensure that an authorized employee or duly designated representative of ATSDR is permitted, at reasonable times and in a reasonable manner, to (i) inspect any research or testing

facility that is conducting research pursuant to this MOU, and (ii) inspect (and, in the case of records, copy) any records and specimens required to be maintained in connection with research performed pursuant to this MOU.

X. PAYMENT OF COST AND EXPENSES

HSIA agrees to pay all costs, direct and indirect, associated with the research programs. ATSDR will assume responsibility for administrative costs including the cost of peer review as part of its overall program.

XI. EVENTS CONSTITUTING A BREACH OF THIS MEMORANDUM OF UNDERSTANDING

Failure by HSIA to:

i) initiate any test agreed to in any approved study plan by the date established pursuant to the study plan;

ii) adhere to GLP's or established test procedures to the extent that these standards apply;

iii) submit any interim report required under this MOU by the date established pursuant to this MOU; or

iv) submit any final report which receives ATSDR's approval following the peer reviewers' recommendations

shall constitute a breach of this MOU. In the event of a breach, ATSDR will not impose any claim to damages, but at the Agency's discretion may terminate the MOU.

Since this MOU is entered into voluntarily by both parties, termination by ATSDR is not considered reviewable agency action pursuant to the Administrative Procedures Act or any other applicable federal law, and there will be no appeal process beyond that set out in the agreement or otherwise mutually agreed to by the parties.

SL 108333

XII. FINAL REPORT - SUBMISSION AND PUBLICATION OF DATA

All data and reports submitted to ATSDR pursuant to this MOU shall be sent to ATSDR, in duplicate, at the address indicated in Paragraph XIV below. Acceptance of the final report is contingent upon approval by ATSDR following the peer review panel's recommendations, consistent with CERCLA peer review requirements. HSIA maintains all rights to publication of data results, however all results of research conducted pursuant to this MOU and all supporting data associated with the final research report will be made available by ATSDR to the public as part of its implementation of Section 104(i)(5) of CERCLA. The final report will not be accepted if the data are designed Confidential Business Information (CBI) or otherwise restricted from public disclosure with the exception of personally identifiable information on study subjects.

XIII. STATUTORY COMPLIANCE

Nothing in this MOU shall be construed to delay or otherwise affect or impair the authority of the President, the Administrator of ATSDR, or the Administrator of EPA to exercise any authority of the President, the Administrator of ATSDR, or the Administrator of EPA under any other provision of law, including TSCA and FIFRA, or the response and abatement authorities of CERCLA.

XIV. ADDRESSES

Any notifications, reports, or other written statements required to be submitted or sent to a party to this MOU shall be sent by certified mail to the parties at the following addresses:

Agency for Toxic Substances and Disease Registry
Division of Toxicology, Research Implementation Branch
Mail Stop E-29
1600 Clifton Road, N.E.
Atlanta, GA 30333

Attention: Dr. William Cibulas

Halogenated Solvents Industry Alliance, Inc.
2001 L Street, N.W., Suite 506A
Washington, D.C. 20036

Attention: Dr. Peter Voytek

XV. SIGNATURES

Agency for Toxic Substances and Disease Registry

Date: 4-4-95

By: _____

Halogenated Solvents Industry Alliance, Inc.

Date: 2/27/95

By: _____

SL 108335