ENVIROMENTAL PROTECTION AGENCY


1,2-Ethylene Dichloride; Completion of EPA Program Review

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA issued a testing consent order that incorporated an enforceable consent agreement (ECA) for 1,2-Ethylene Dichloride (EDC) in June 2003, using authorities under section 4 of the Toxic Substances Control Act (TSCA). The companies subject to the ECA agreed to conduct toxicity testing in a tiered testing program that included development of pharmacokinetics and mechanistic data and a computational dosimetry model for route-to-route extrapolations. The testing program was designed to satisfy the toxicological data needs for EDC identified in a TSCA section 4 proposed test rule for a number of hazardous air pollutant chemicals. The modeling is intended to allow toxicological studies conducted using oral exposures to be interpreted so that they could also be used to predict the effects of inhalation exposures. This notice announces the completion of the program review component of the ECA for EDC. This notice also states EPA’s findings and conclusion regarding the adequacy of the derived models to perform satisfactory route-to-route extrapolations, responds to comments on the Tier I Program Review Testing, and establishes revised deadlines for completion of Tier II testing and computational route-to-route dosimetry modeling for extrapolations listed under Tier II of the ECA for EDC.

FOR FURTHER INFORMATION CONTACT: For general information contact: Colby Lintner, Regulatory Coordinator, Environmental Assistance Division (7406M), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 200 Independence Ave., NW., Washington, DC 20460–0001; telephone number: (202) 554–1404; e-mail address: TSCA-Hotline@epa.gov.

For technical information contact: John Schaeffer, Chemical Control Division (7405M), Office Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: (202) 564–8173; e-mail address: schaeffer.john@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

This action is directed to the public in general, and may be of particular interest to those persons who are or may be required to conduct testing of chemical substances under TSCA. Since other entities may also be interested, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the applicability of this action to a particular entity, consult the technical person listed under FOR FURTHER INFORMATION CONTACT.

B. How Can I Get Copies of this Document and Other Related Information?

1. Docket. EPA has established a docket for this action under docket identification (ID) number EPA–HQ–OPPT–2003–0010. All documents in the docket are listed in the docket index available at http://www.regulations.gov. Although listed in the index, some information is not publicly available, e.g., Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, will be publicly available only in hard copy. Publicly available docket materials are available electronically at http://www.regulations.gov, or if only available in hard copy, at the OPPT Docket. The OPPT Docket is located in the EPA Docket Center (EPA/DC) at Rm. 3334, EPA West Bldg., 1301 Constitution Ave., NW., Washington, DC. The EPA/DC Public Reading Room hours of operation are 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding Federal holidays. The telephone number of the EPA/DC Public Reading Room is (202) 566–1744, and the telephone number for the OPPT Docket is (202) 566–0280. Docket visitors are required to show photographic identification pass through a metal detector, and sign the EPA visitor log. All visitor bags are processed through an X-ray machine and subject to search. Visitors will be provided an EPA/DC badge that must be visible at all times in the building and returned upon departure.

2. Electronic access. You may access this Federal Register document electronically through the EPA Internet under the “Federal Register” listings at http://www.epa.gov/fedregstr.


5. E-mail. You may e-mail comments to linkert.andy@epa.gov.

6. Postal Mail. You may send comments to Lintner, Andy, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone: (202) 564–8173; e-mail address: linkert.andy@epa.gov.
II. Background

A. What is the EPA Program Review for EDC?

In the Federal Register of September 5, 2006 (71 FR 52329) (FRL–8088–3), EPA announced that it was conducting the program review component of the ECA for the EDC alternative testing program, and solicited public comment on data received under the Tier I Program Review testing segment of the ECA for EDC (CAS No. 07–06–3). Comments were to inform EPA's decision on whether or not additional data and/or model development are needed before Tier II testing and computational route-to-route dosimetry modeling extrapolations could proceed for the Tier II endpoints listed in the ECA for EDC. Details of the testing program for EDC are available in the ECA and in the Federal Register of June 3, 2003 (68 FR 33125) (FRL–7300–6), in which EPA announced that it had entered into an ECA and issued a testing consent order for EDC. The ECA for EDC was developed in response to EPA's consent order for EDC. The ECA for EDC (CAS No. 107–06–2), in the Federal Register of September 5, 2006 (71 FR 52329). That notice, as well as the final study reports, can be accessed in the docket (EPA–HQ–OPPT–2003–0010) as explained in Unit I.B.

As specified in the ECA, the EPA program review is required before the Tier II Testing segment is undertaken. In the Federal Register of September 5, 2006 (71 FR 52329), EPA announced that it was conducting the program review component of the ECA for EDC, and solicited public comment on data received under the Tier I Program Review Testing segment of the ECA. Comments were to inform EPA's decision on whether or not additional data and/or model development were needed before Tier II Testing and computational route-to-route dosimetry extrapolations can proceed for the Tier II endpoints listed in the ECA for EDC.

B. What were the Public Comments on the Tier I Program Review Testing for EDC?

EPA received two public comments in response to its solicitation for comments on the Tier I Program Review Testing. Comments from People for the Ethical Treatment of Animals (PETA) were on behalf of themselves and the following organizations: The Physicians’ Committee for Responsible Medicine, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. PETA expressed support for the use of PBPK modeling to limit additional animal testing through the use of route-to-route extrapolation to existing studies. However, PETA also stated that they disagreed that additional Tier II tests (i.e., for reproductive effect or subchronic neurotoxicity) are needed; contending that existing studies for these effects are adequate. EPA disagrees, and its basis for requiring this additional testing is discussed in previous Federal Register documents, cited in Unit II.A.

C. What are the Conclusions of the EPA Tier I Program Review Testing for EDC?

The companies have completed the Tier I and Tier I Program Review testing segments of the ECA for EDC. The companies have also examined additional PBPK models and other available information in order to more fully update the model developed by D’Souza et al., 1987, 1988; as specified in the ECA agreement. The results of this work, the updated model, and model simulations have been discussed with EPA (Refs. 3 through 6) and have also been recently published as a peer-reviewed article in the scientific literature (Ref. 7). It is EPA’s conclusion that the PBPK model developed by the test sponsors under the EDC ECA is acceptable for route-to-route extrapolations and that Tier II testing and extrapolation reporting can proceed as per the schedule set forth below (Ref. 8). Specifically, EPA concludes that:

1. The PK/MECH data report and Tier I toxicity studies have been conducted in accordance with the protocols and specifications as described in Appendix C of the ECA.

2. The available study records are sufficient to allow an evaluation of the quality of the studies performed.

3. The EDC PBPK model is appropriately chemical-specific, and suitably based on the current understanding of the kinetics of EDC.

4. The species, dose level, exposure regimens, and vehicles used are relevant for the toxicity data that are the object of the Tier II extrapolations.

5. The Tier I Program Review PK/MECH data, along with additional data, show that periodicity was demonstrated and that the various data sets bearing on the issue of periodicity can be properly
interpreted and managed in the studies that support the model.

6. Refinements of the model related to absorption, tissue distribution, and metabolism were accomplished, or suitably explained, including the role of extrahepatic metabolism as it impacts the model dose metrics and route-to-route extrapolation; appreciably improving prior PBPK models of EDC.

It is EPA’s decision that the HAP Task Force can proceed with the Tier II Testing under the schedule set forth in Table 1. of this Federal Register document.

**TABLE 1.—REQUIRED TESTING, TEST STANDARDS, AND REPORTING REQUIREMENTS FOR EDC**

<table>
<thead>
<tr>
<th>Testing segment</th>
<th>Required testing</th>
<th>Test standard</th>
<th>Deadline for final report* (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier II testing and/or extrapolation reporting</td>
<td>Subchronic toxicity route-to-route extrapolation of dose-response (oral Tier II testing to inhalation) of a study reported by Daniel, et al., (1994)</td>
<td>ECA appendix C.2 and C.6</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Subchronic neurotoxicity (oral)</td>
<td>40 CFR 799.9620 (as annotated in ECA appendix D.2)</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Subchronic neurotoxicity route-to-route extrapolation of dose-response (oral Tier II testing to inhalation)</td>
<td>ECA appendix C.3 and C.6</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Reproductive toxicity (oral)</td>
<td>40 CFR 799.9380 (as annotated in ECA appendix D.3)</td>
<td>25</td>
</tr>
</tbody>
</table>

*Number of months after the date of publication of this Federal Register document, which announces that EPA has concluded the EPA Program Review, when the final report is due. In addition, every 6 months from the effective date of the Order until the end of the ECA testing program, interim reports describing the status of all testing to be performed under this ECA must be submitted by the Companies to EPA.

**III. References**


**List of Subjects**

Environmental protection, 1,2-Ethylene Dichloride, EDC, Hazardous chemicals.