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Guidance for Testing Closed System Intermediates for the HPV Challenge Program

The HPV Challenge Program's approach to testing of intermediates is modeled on the SIDS program adopted by the OECD[1]. The SIDS program allows for a reduced set of testing for chemicals that qualify as closed system intermediates. The special treatment of closed system intermediates in the SIDS program is the only major instance where exposure considerations can impact the battery of tests performed for a specific chemical. The definitions, reduced testing requirements, and information required to substantiate a reduced slate of testing in the HPV Challenge are the same as in the SIDS program. The SIDS treatment of closed system intermediates is described in Section 3.6 of the SIDS manual which is titled : "Testing of Chemicals with Limited Exposure Potential". The "SIDS Manual: Screening Information Data Set Manual of the OECD Program on the Cooperative Investigation of High Production Volume Chemicals", July 1997 is available by electronic link from www.epa.gov/chemrtk/volchall.htm.

It is important to note that the list of 2,800 chemicals that are the focus of the HPV Challenge was derived from chemicals reported in the 1990 reporting cycle of the TSCA Inventory Update Rule (IUR). Chemicals that are "non-isolated intermediates" are not subject to IUR reporting and therefore only chemicals that are isolated are included in the HPV Challenge. Accordingly, this guidance applies only to HPV Challenge chemicals (which by virtue of their reporting under IUR are isolated chemicals) that also qualify as closed system intermediates as described below.

EPA encourages companies to review testing needs for all HPV chemicals, including closed system intermediates, and commit to testing where data gaps exist. **Claims for reduced testing needs for closed system intermediates must be documented in the Test Plan sponsors prepare for the chemical in question**.

Definition of Closed System Intermediates

Any chemical which is intended to undergo a further deliberate reaction to produce another industrial substance is considered an **intermediate.** In the context of the HPV Challenge, the

[1]There is one aspect of the HPV Challenge that is quite different from the OECD SIDS Program. In the SIDS Program "intermediates currently have a lower priority in the context of the SIDS work and, consequently, the choice of these chemicals by Sponsor countries is discouraged." In the HPV Challenge, this distinction is not made and all chemicals are considered of equal importance.

following types of **intermediates**[2] which are **contained in closed systems** and therefore have a limited potential for exposure can be identified:

a) isolated intermediates which are stored in controlled on-site facilities; and

b) isolated intermediates with controlled transport, i.e. to a limited number of locations within the same company or second parties which use the chemical in a controlled way as an intermediate with a well-known technology.

The definitions of these two types of intermediates are the same as those included in the SIDS Manual.

To be eligible for this provision, it is necessary to establish that **all** sites in the United States manufacture and handle the chemical in a manner consistent with the definition of closed-system intermediate. If this is not the case, the full SIDS battery of testing is required.

Reduced Testing Requirements

For closed system intermediates a reduced test plan package reflecting the information needed to evaluate the hazards in case of an accident is considered the appropriate level of testing for screening purposes. This is because exposures resulting from chemical accidents are likely to be of relatively short versus chronic duration. The reduced testing consists of the Screening Information Data Set (SIDS) minus the tests for repeated dose toxicity and reproductive toxicity, but including a developmental toxicity test.

If the intermediate is stored onsite or transported to other sites (that is, intermediates in categories a) and b) mentioned above), HPV Challenge participants should consider, on a case-by-case basis, whether to also test for the repeated dose and reproductive toxicity endpoints. For example, production and storage at, or transport to, numerous sites for ultimate reaction may warrant full testing, even though the chemical is a closed system intermediate.

Substantiation of Closed System Intermediate Status

When a claim for reduced testing is made based on considerations of a chemical's "closed-system intermediate" status, further information will need to be provided to support that claim in the Test Plan, including the number of sites, process description, monitoring data, presence in

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[2]OECD SIDS procedures also address non-isolated intermediates, i.e. those chemicals whose life-cycle is restricted to the reaction vessel and its specific equipment. In the U.S., non-isolated intermediates are not subject to TSCA IUR reporting requirements and thus such provisions need not be included in the U.S. HPV Challenge Program. The language appears in OECD's SIDS manual because other OECD member countries include non-isolated intermediates in their programs.

products, and transport. The information needed consists of responses to the attached list of questions which is excerpted from the SIDS manual. As mentioned above, this information must cover all sites manufacturing, processing, or using the chemical in the U. S. The OECD procedure for closed system intermediates requires the reporting of information regarding the presence of the intermediate in end products. In the OECD SIDS program, the information provided that substantiates that a chemical is "not present" in end products is evaluated. EPA has clarified this element below to request information from sponsors in Test Plans that substantiates that a chemical is **not present above trace concentrations** as an impurity.

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The following is excerpted from "SIDS Manual: Screening Information Data Set Manual of the OECD Program on the Cooperative Investigation of High Production Volume Chemicals", July 1997. **EPA clarifications, explanations or embellishments of the data sought by OECD are shown in italics**.

Annex

Information Requirements Supporting Exemption Claims for Reduced SIDS Testing Based on Exposure Considerations

1. Information on sites

A. Number of sites

B. Basis for "closed process" conclusion at each site:

1) process description in enough detail to clarify the basis for claiming that the process is closed;

[This should consist of a narrative and a process flow diagram covering major unit operations used at all steps from manufacture through any storage, ,further reaction to consume the chemical, or preparation for transfer to other site(s). The narrative should identify any points of release or wastes for which items B. 2 and B. 3, below, must be addressed, that is, evidence that the chemical is not present in such wastes or releases. Sponsor companies should attempt to provide information that is in sufficient detail to support the closed system intermediate claim but at the same time avoid the inclusion of confidential business information]

2) if available, monitoring data showing no detection in any media, including the limits of detection;

3) if monitoring data are not available, a statement that no monitoring has taken place and the basis for believing, in the absence of data, that the chemical has not been released and that exposure does not occur.

[Note: Distinguishing between no data and no detection is important.]

C. Data on "presence in distributed product" or, in the absence of data, the basis for believing it is not present *at levels above trace concentrations*.

II. **Information on transport**

If transport also occurs, then in addition to the above, the following should be provided:

- Mode of transport (e.g. water, truck, rail, pipeline)
- Volume (annual)
- Types of consignments (e.g. bulk or drums)
- Controls during transport and transfer at dispatching and receiving sites (placards, labels. etc.)

III. Supporting evidence from a data search showing that the chemical is not present in other end-products

[This item is intended to provide further indication that the chemical is not otherwise present in end products or is present only in trace concentrations. For example, a company seeking this exemption may claim that its operations involve a specific chemical only as a closed system intermediate but if an examination of product literature or similar information shows that the chemical is present in some end products above trace concentrations or as an intentional component (i.e., not an impurity) the closed system intermediate claim would be invalid. The sponsor should discuss this aspect to support the basis for the claim]