

June 13, 2001

LuAnn Maloney
FMC Corporation
Agricultural Products Group
1735 Market Street
Philadelphia, PA 19103

Dear Ms. Maloney:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on FMC's submission to the RTK HPV Challenge Program of the robust summaries and test plans for two single chemicals, 3-chloro-2-methylpropene (Methallyl chloride, CAS No. 563473) and 2,3-dihydro-2,2-dimethyl-7-benzofuranol (CAS No. 1563388), posted on EPA's ChemRTK Web site on February 13, 2001. I commend FMC for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Chemical RTK HPV Challenge Program website EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

Methallyl chloride comments

As outlined in the Comments, we suggest that special procedures be followed for the planned ecotoxicity testing and that the assumption and data inputs to the fugacity model be included with the report for that endpoint. FMC also needs to supply information missing from certain health robust summaries.

FMC summarized an acute oral toxicity study conducted with a 10% solution of the test material. Aspects of the study are unclear. The Company needs to explain why the diluted substance was tested and how the results can be applied to the undiluted material.

Finally, because 13-week repeated-dose rat and mouse studies are available for methallyl chloride, EPA recommends that FMC consider conducting the planned reproduction/developmental toxicity study according to OECD Test Guideline 421: Reproduction/Developmental Toxicity Screening Test instead of Guideline 422: Repeated dose/Reproductive/Developmental Toxicity study,.

Because FMC proposes to perform reproduction/developmental toxicity testing, I emphasize that, as pointed out in my letter to FMC dated March 7, 2001, in order to conform to the intent of EPA's October 14, 1999, letter (<http://www.epa.gov/chemrtk/ceoltr2.htm>), animal testing for SIDS endpoints on individual chemicals shall be deferred until November, 2001.

2,3-Dihydro-2,2-dimethyl-7-benzofuranol comments

As explained in the comments, the submitted test data summaries for ecological effects could not be adequately evaluated because many required robust summary data elements are missing; this information needs to be supplied. The Company also needs to better define the chemical identity of test substances.

The proposed acute dermal toxicity test is not necessary because acute dermal toxicity testing is not an element of the U.S. HPV Challenge Program. There also appear to be existing data on repeat dose toxicity and developmental toxicity not identified in the submission that, depending on the adequacy of the studies, might alter the proposed test plan.

FMC proposes to perform an *in vivo* study for chromosomal effects. In order to conform to the intent of EPA's October 14, 1999, letter to sponsors, which encourages the use of *in vitro* genotoxicity tests unless known chemical properties preclude their use, we ask FMC to elaborate why it considers *in vivo* testing necessary in this case. As stated above for methallyl chloride, animal testing for SIDS endpoints for individual chemicals shall be deferred until November, 2001.

As with other submissions where the available data are either inadequate or insufficiently documented, these cases will remain open until adequate documentation is in hand.

EPA will post this letter and the attached Comments on the Chemical RTK web site within the next few days. As noted in the comments, we ask that FMC advise the Agency, within 60 days of the posting on the Chemical RTK website, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-260-3470. Submit general questions about the HPV Challenge Program through the Chemical RTK web site comment button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsc-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Attachment

cc: W. Sanders
C. Auer
M. E. Weber
A. Abramson

EPA Comments on Chemical RTK HPV Challenge Submission: Methallyl chloride

SUMMARY OF EPA COMMENTS

The sponsor, FMC Corporation, submitted a Test Plan and Robust Summaries to EPA dated December 28, 2000, for 3-Chloro-2-methyl-propene (Methallyl chloride, CAS No. 563-47-3). EPA posted the submission on the ChemRTK HPV Challenge Web site on February 13, 2001. FMC later supplied clarifications to the test plan, which have replaced the original posting.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical and Environmental Fate Data. EPA agrees with the submitter's test plan for these endpoints.
2. Health Endpoints. (a) The Sponsor summarized an acute oral toxicity study conducted with a 10% solution of the test material. EPA requests additional information on the acute oral toxicity of methallyl chloride (see Test Plan and Robust Summary comment sections); (b) the sponsor may consider conducting the planned reproduction/developmental toxicity study according to OECD Test Guideline 421: Reproduction/Developmental Toxicity Screening Test instead of Guideline 422: Repeated dose/Reproductive/Developmental Toxicity study, because 13-week repeated dose rat and mouse studies are available; and (c) the *in vivo* genotoxicity robust summary needs to be enhanced.
3. Ecotoxicity. The sponsor's proposal to conduct all three basic tests is acceptable. EPA suggests that, to address volatility concerns, all testing be done with measured concentrations in a closed system with no head space.

EPA is requesting that the Sponsor advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE METHALLYL CHLORIDE CHALLENGE SUBMISSION

Test Plan

The test plan consists of a table that lists the availability of studies and identified those tests required under the SIDS program.

Chemistry (melting point, boiling point, vapor pressure, water solubility, and partition coefficient).

The sponsor's approach is acceptable for these endpoints.

Fate (photodegradation, stability in water, biodegradation, and transport/distribution).

Adequate data are available for photodegradation. The sponsor's plan for addressing the remaining endpoints is acceptable.

When developing the fugacity model, the sponsor needs to provide the assumption and data inputs to the model (see Guidance for Robust Summary preparation). Furthermore, in order to develop the fugacity model, EPA recommends using the EQC Level III model from the Canadian Environment Modeling Centre at Trent University, which allows full control of data inputs. This model can be found at the following Web address: <http://www.trentu.ca/academic/aminss/envmodel/>.

Health Effects (acute toxicity, repeat dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Three acute toxicity studies were summarized. The inhalation and dermal studies (both adequate) used undiluted test material, whereas the oral study used a 10% solution. EPA questions the potential usefulness of the reported acute oral toxicity values for hazard evaluation (see Robust Summary comments below).

EPA agrees that a reproductive/developmental screening test needs to be conducted because no such data are available. However, instead of conducting a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Screening Test (OECD Guideline 422), the sponsor should consider a Reproduction/Developmental Screening Test (Guideline 421) because 13-week repeated dose studies in rats and mice are available.

Ecological Effects (fish, invertebrate and algal toxicity).

The sponsor's proposal to conduct all three basic tests is acceptable. It would be helpful to identify in the test plan the test guidelines to be used. Because of this substance's volatility, EPA suggests that all testing be done with measured concentrations in a closed system with no head space. Testing should follow the Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (OECD, June 2000-available on the OECD website at <http://www.oecd.org/ehs/test/monos.htm>).

SPECIFIC COMMENTS ON ROBUST SUMMARIES

Health Effects

Acute toxicity. The submitter needs to provide an explanation for an acute oral toxicity study being conducted with a 10% solution and elaborate how the latter may be used to characterize acute toxicity for the subject chemical. It is likely that the undiluted test material will be more toxic; the available data in the reported repeat dose studies - as well as information in IUCLID - support this concern.

Genetic Toxicity *In Vivo*. Study No. 15. Data in a table format would be useful. Although the study is acceptable for the HPV Challenge Program, the robust summary needs to be enhanced with the following information to allow an independent assessment: (1) whether a positive control was used and its response; and (2) the PCE/NCE ratio.

Repeated Dose Toxicity. Studies No. 19 and 21. Information such as an OECD or EPA guideline citation is lacking on the method and the study design. In addition, information on a dose range-finding study, if available, would help in understanding why there was such high mortality.

The sponsor needs to submit the missing information.

Ecotoxicity Studies

Robust summaries for two acute toxicity tests in fish (goldfish and golden orfe) and one acute toxicity test in daphnia are provided. The information presented in the Robust Summaries was taken from secondary sources and does not offer any experimental details. As the sponsor considers the studies inadequate and plans to conduct testing for all three endpoints, these summaries need not be updated.

Followup Activity

EPA requests that the Sponsor advise the Agency within 60 days of any modifications to its submission.