

201-14412



NCIC HPV
Sent by: Mary-Beth
Weaver

04/17/2003 09:28 AM

To: NCIC HPV, moran.matthew@epa.gov
CC:

Subject: ChemRTK HPV Challenge Program Submission - CASRN 3296-90-0 -
Revised Test Plan and Robust Summaries



James McBriarty <McBriartyJ@ameribrom.dsbg.com> on 04/17/2003 03:44:09
AM

To: "oppt.ncic@epamail.epa.gov" <oppt.ncic@epamail.epa.gov>, "hvp.chemrtk@epa.gov"
<hvp.chemrtk@epamail.epa.gov>
cc: "rdenison@environmentaldefense.org" <rdenison@environmentaldefense.org>, "jessicas@peta.org"
<jessicas@peta.org>, Oscar Hernandez/DC/USEPA/US@EPA

Subject: ChemRTK HPV Challenge Program Submission - CASRN 3296-90-0 - Revised Test Plan and Robust
Summaries

Attached are electronic copies of the
* Submission letter (1 file)
* Revised Test Plan (1 file)
* Robust Summaries (28 files) - Some revised or corrected

For the HPV Chemical Challenge Program chemical 1,3-Propanediol,
2,2-bis(bromomethyl)-, CAS No. 3296-90-0.

There are therefore 30 files attached, all in MSWord (*.doc) format. This
letter was dispatched today via Certified Mail ID No. 7002 0860 0006 1941
1731.

If you have any questions or cannot access the files, please contact me.

Best Regards,

James P. McBriarty, CIH
Director of Regulatory Affairs
AmeriBrom, Inc.
2115 Linwood Ave.
Fort Lee, NJ 07024-5004
Phone: -t-1 (201) 242-6572
Fax: +1 (201) 242-6561
E-mail: McBriartyJ@AmeriBrom.DSBG.com

<<Submission Letter 2003 0416.doc>> <<Revised Test Plan 2003 0416.doc>>
<<01.0 Physchem Melting Point.doc>> <<03.0 Physchem Vapour pressure.doc>>
<<04.0 Physchem Partition coefficient.doc>> <<04.1 Physchem Partition
coefficient.doc>> <<04.2 Physchem Partition coefficient.doc>> <<05.0
Physchem Water Solubility.doc>> <<05.1 Physchem Water Solubility.doc>>
<<06.0 Photodegradation.doc>> <<09.0 Environ Biodegradation.doc>> <<13.1
Human Health (Acute oral tox).doc>> <<13.2 Human Health (Acute oral
tox).doc>> <<13.3 Human Health (Skin Irritation).doc>> <<13.4 Human Health
(Eye Irritation).doc>> <<14.1 Human Health (Mouse Micronucleus).doc>>
<<14.2 Human Health (Mouse Micronucleus).doc>> <<14.3 Human Health (Mouse
Micronucleus).doc>> <<15.1 Human Health (Ames test).doc>> <<15.2 Human
Health (Ames test).doc>> <<15.3 Human Health (Ames test).doc>> <<15.4
Human Health (Ames test).doc>> <<15.5 Human Health (Chromosomal
aberrations).doc>> <<15.6 Human Health (Sister chromatid exchanges).doc>>
<<15.7 Human Health (Ames test).doc>> <<15.8 Human Health (Ames test).doc>>
<<16.1 Human Health (Repeat dose 2 yr).doc>> <<16.2 Human Health (Repeat
dose 13 wk).doc>> <<16.3 Human Health (Repeat dose 2 yr).doc>> <<17

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Human Health (Reproductive toxicity).doc>>

This inbound mail was checked by DSBG
mail sweeping system .

- Submission Letter 2003 0416.doc 
- Revised Test Plan 2003 0416.doc 
- 01.0 Physchem Melting Point.doc 
- 03.0 Physchem Vapour pressure.doc 
- 04.0 Physchem Partition coefficient.doc 
- 04. 1 Physchem Partition coefficient.doc 
- 04.2 Physchem Partition coefficient.doc 
- 05.0 Physchem Water Solubility.doc 
- 05.1 Physchem Water Solubility.doc 
- 06.0 Photodegradation.doc 
- 09.0 Environ Biodegradation.doc 
- 13.1 Human Health (Acute oral tox).doc 
- 13.2 Human Health (Acute oral tox).doc 
- 13.3 Human Health (Skin Irritation).doc 
- 13.4 Human Health (Eye Irritation).doc 
- 14.1 Human Health (Mouse Micronucleus).doc 
- 14.2 Human Health (Mouse Micronucleus).doc 
- 14.3 Human Health (Mouse Micronucleus).doc 
- 15.1 Human Health (Ames test).doc 
- 15.2 Human Health (Ames test).doc 
- 15.3 Human Health (Ames test).doc 
- 15.4 Human Health (Ames test).doc 
- 15.5 Human Health (Chromosomal aberrations).doc 
- 15.6 Human Health (Sister chromatid exchanges).doc 
- 15.7 Human Health (Ames test).doc 
- 15.8 Human Health (Ames test).doc 
- 16.1 Human Health (Repeat dose 2 yr).doc 
- 16.2 Human Health (Repeat dose 13 wk).doc 
- 16.3 Human Health (Repeat dose 2 yr).doc 
- 17 Human Health (Reproductive toxicity).doc 

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AmeriBrom, Inc.

2115 Linwood Avenue, Fort Lee, NJ 07024-5004

Tel: (201) 242-6560 Fax: (201) 242-6561 Info@AmeriBrom.dsbg.com

Sent via Certified Mail

April 16, 2003

Christie Todd Whitman, Administrator
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Re: Chemical Right-to Know HPV Challenge Program Submission
2,2-Bis(bromomethyl)-1,3-propanediol (CAS No. 3296-90-o)

Dear Ms. Whitman:

In March 2003, AmeriBrom, inc. received comments on the proposed Test Plan and supporting Robust Summaries for 2,2-Bis(bromomethyl)-1,3-propanediol (CAS No. 3296-90-o) that were submitted to EPA on October 24, 2002 under the HPV Challenge Program. AmeriBrom also received comments from Environmental Defense (ED) and People for the Ethical Treatment of Animals (PETA).

In the interests of sharing comments and communicating our intent with interested stakeholders, AmeriBrom is providing, via carbon copy, a single response to those parties who provided comments.

General Comments

ED suggested that the Test Plan should clearly state whether the chemical is an additive or reactive flame retardant

Response:

The chemical is a reactive flame retardant and the Test Plan has been modified to include this information.

ED suggested that the term 'flame retardant' is more appropriate than 'fire retardant' since products containing this chemical will still burn, but less rapidly than those that do not contain a retardant.

Response:

We agree with the suggested change and have altered the Test Plan accordingly.

Physicochemical properties and Environmental Fate

Vapor pressure: EPA states that the vapor pressure needs to be determined experimentally, as the calculated value is higher than the acceptable limit described in OECD TG 104.

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Response:

AmeriBrom will measure the vapor pressure of 2,2-Bis(bromomethyl)-1,3-propanediol experimentally using OECD Guideline 104. The Test Plan has been altered accordingly.

Octanol-Water Partition Coefficient: EPA recommends adding the additional data it has located as well as the EPIWIN estimate to the robust summary.

Response:

AmeriBrom has incorporated this data into the robust summaries for the octanol-water partition coefficient.

Photodegradation: EPA highlighted an error in the Test Plan, where it was stated that the Mackay level III Fugacity model would be used to estimate photodegradation.

Response:

An AOPWIN estimate has been run and a robust summary for this estimate has been added to the Test Plan. The Test Plan has been amended to reflect that a photodegradation study will not be run.

Biodegradation: EPA asked for information on temperature, dosing procedure, sampling frequency, controls and analytical methods to be added, if available, to the robust summary.

Response:

None of the information requested is available; therefore the robust summary will remain as written.

Ecotoxicity

Acute fish toxicity: EPA agreed with the original Test Plan that a test for acute toxicity to fish should be conducted. PETA disagreed with this and suggested several *in vitro* alternatives.

Response:

AmeriBrom does not feel that it is appropriate to use an *in vitro* alternative to the acute fish toxicity study unless EPA has approved its use. Since this is not the case at present, AmeriBrom plans to proceed with the OECD 203 acute fish toxicity test.

Health Effects

Acute toxicity: EPA requested that the percentage of CAS No. 32960-90-0 present in the test substance used in the acute toxicity studies be added to the robust summaries.

Response:

This information is not available for studies 13.2, 13.3 or 13.4. The robust summaries for these studies have been amended to make this clear. Study 13.1 already contains the purity of the test substance.

Genetic toxicity: EPA requested clarification in the robust summaries of the dosage information for study 14.3 and requested the purity of the test substance for studies 15.4, 15.5 and 15.6

Response:

The robust summary for Study 14.3 has been revised to include the actual dose received in mg/kg bw and to clarify that the doses listed were in ppm rather than mg/kg bw. The test substance purity for studies 15.4, 15.5 and 15.6 has now been included in the robust summaries.

Repeated dose toxicity: EPA requested that the post exposure observation period be added to the robust summary for Study 16.1.

Response:

The robust summary for Study 16.1 has been revised to show that there was a 91/92 week post exposure observation period for the stop-exposure group animals.

Developmental toxicity: EPA agreed with the original Test Plan proposal that a test for developmental toxicity should be performed. PETA disagreed with the proposed testing and have argued that conducting a study focused simply on the developmental toxicity of this compound will provide no further information that will affect the regulation and control of this chemical.

Response:

AmeriBrom has further reviewed the available data on the effects on reproduction and offspring development provided by the NTP continuous breeding study in the mouse. In summary these results show:

- 1. At the higher dose levels there are effects upon bodyweight and morphological changes in the kidney.***
- 2. An effect on fertility as indicated by reduction in the number of litters produced***
- 3. An effect on live litter size and offspring bodyweight.***
- 4. No observations of gross developmental effects in offspring.***
- 5. Reproductive/developmental effects were seen at dose levels that were toxic to the adult.***

The observation of no gross developmental effects in offspring, not related to lack of weight gain or survival, at dose levels that were toxic to the adult and a clear NOEL suggests that there may be no serious developmental toxicity risk associated with exposure to the test material below the threshold of adult toxicity.

Given that this substance has also been shown to induce lesions in both sexes in several repeat dose studies, controlling exposures to reduce the risk of a carcinogenic effect should provide an adequate margin of safety to protect against subtle developmental effects.

AmeriBrom believes that the elements of the continuous breeding protocol are sufficient to provide a reasonable screening level assessment of the hazard to reproduction and offspring development and therefore considers that sufficient screening level information is available for this endpoint. Therefore no developmental toxicity test is proposed at this time. The Test Plan has been amended to reflect this.

If you have any questions, please do not hesitate to contact me [Phone: +1 (201) 242-6572; <mailto:mc Briartyj@ameribrom.dsb g.com>].

Sincerely,

James P. McBriarty, CIH
Director of Regulatory Affairs

cc: Richard Denison, Environmental Defense
Jessica Sandler, People for the Ethical Treatment of Animals
Oscar Hernandez, US EPA OPPT RAD