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Ms. Lisa Jackson
U.S. Environmental Protection Agency
Ben Franklin Post Office
P.O. Box 862
Washington, DC 20044
Attn: Chemical Right-to-Know Program

Subject:
Submission of Revised Test Plan and Robust Summaries for 1,2-dimethyl-4-nitrobenzene (CAS No. 99-51-4) under the HPV Challenge Program, AR 201, via electronic submission to oppt.ncic@epa.gov and chem.rtk@epa.gov

Date.
October 14, 2009

Contact:
Jane Staveley

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919-544-4535

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jane.staveley@arcadis-us.com

Our ref:
RN006166.0001

Dear Administrator Jackson:

On November 29, 2006, ARCADIS (on behalf of BASF Corporation) submitted a test plan and robust summaries under the HPV Challenge Program for 1,2-dimethyl-4-nitrobenzene (CAS No. 99-51-4). On June 22, 2009, the U.S. EPA posted comments on this submission.

In response to EPA's comments, we are submitting a revised test plan and robust summaries for the above-referenced substance and supporting analogs.

EPA found that existing data were adequate for the purposes of the HPV Challenge Program for Physical/Chemical Properties and for Health Effects. EPA also found that the existing data were adequate for Environmental Fate, but requested an enhancement of the biodegradation discussion. Regarding Ecological Effects, EPA requested that deficiencies in the robust summaries be addressed.

We have made changes to the test plan and robust summaries in response to EPA comments and present the following discussion:

Test Plan:

Biodegradation: EPA requested discussion in the text and tables of the 28-day study cited in the robust summary for the analogue 3-nitrotoluene, showing <10% degradation. The test plan has been revised to include this information.

No other specific revisions to the test plan were needed.

Robust Summaries

Health Effects

Repeated-dose toxicity:
A 28-day repeat dose study in the German language was included in the robust summaries originally submitted for the analogue 2,4-dimethyl-1-nitrobenzene. A brief summary of the study results was provided in English; however, EPA has requested additional study information to be presented in English. This information was not available to the sponsor as the data owner is BG Chemie.

Genotoxicity:
Two Ames assays for the sponsored chemical were missing important study information. One of the studies is in a peer-reviewed journal; however, it is in Japanese. Study information for the other study is located on the National Toxicology Program's Database Search Application; therefore, additional information was located and added about the methodology and results of this study.

EPA commented that there are 10 *in vitro* gene mutation studies for the analogue 2,4-dimethyl-1-nitrobenzene; however, they were missing nearly all study information. After additional review of these robust summaries, four of the studies appear to be duplicates. The remaining six studies are originally from five sources, two of which are the same sources described in the paragraph immediately above. Of the remaining three references, one is a peer-reviewed journal. The other two are owned by BG Chemie and Hoechst AG and were not available to the sponsor. Where data were available, the robust summaries were revised. An *in vivo* cytogenetics assay in the robust summaries for this analogue was missing important study information; the data owner is BG Chemie and thus the study was not available to the sponsor.

Reproductive toxicity:
Regarding the robust summaries for the analogue 2-nitrotoluene (ECB 2000 IUCLID Dataset), EPA commented that the reported histopathological observations of reproductive organs were inadequate in the summary of a 13-week NTP study in rats and mice. These details can be found at

http://ntp.niehs.nih.gov/ntp/htdocs/ST_rpts/tox023.pdf. Since this substance was an analogue, the existing IUCLID dataset created by the ECB was not updated to include these details as part of this submission.

Health Effects: Summary

Since EPA has accepted the previously submitted robust summaries in fulfillment of the health effects endpoints, changes to the robust summaries for the three nitrotoluene isomers were not made. Additional study details for health effects endpoints were added, where the sponsor was able to obtain the information, to the robust summaries for the sponsored chemical, 1,2-dimethyl-4-nitrobenzene and for the analogue, 2,4-dimethyl-1-nitrobenzene.

Ecological Effects

EPA commented that the available data for the sponsored chemical and its analogue, 2,4-dimethyl-1-nitrobenzene, are sufficient to characterize these endpoints pending the following revisions to the supporting robust summaries.

For fish toxicity, a 96-hour acute study with *Brachydanio rerio*, cited in the ECB 2000 IUCLID Dataset, was used for 2,4-dimethyl-1-nitrobenzene. EPA commented on deficiencies in the reported study methodology and results. The study owner is Hoechst AG; this information was thus unavailable to the sponsor. Although EPA did not comment on the fish toxicity study for the sponsored chemical, ARCADIS did revise this robust summary to include additional details from the cited reference.

For aquatic invertebrates, a 48-hour *Daphnia magna* study for the sponsored chemical was included in the submitted robust summaries and test plan. EPA commented that this study lacked most methodological details. ARCADIS was able to add details based upon the cited methodology (Dutch standard NEN 6501, 1980) and other published literature. For the supporting analogue 2,4-dimethyl-1-nitrobenzene, the same deficiencies were noted in another 48-hour *Daphnia magna* test obtained from the 2000 IUCLID Dataset. The study owner is Hoecsht AG; this information was unavailable to the sponsor.

For algae, EPA commented that a 96-hour study testing the sponsored chemical with *Chlorella pyrenoidosa* was lacking most methodological details. ARCADIS was able to add details based upon the cited methodology (OECD 201, 1984) and other published literature.

Ecological Effects: Summary

Details were added, where available, to the robust summaries for the sponsored chemical, 1,2-dimethyl-4-nitrobenzene and for the analogue, 2,4-dimethyl-1-nitrobenzene

On behalf of BASF Corporation, ARCADIS therefore submits the enclosed revised test plan and robust summaries which we believe are responsive to EPA's comments and are adequate for the purposes of the HPV Challenge Program. The documents are being submitted in electronic format (Adobe Acrobat pdf files). In addition, we are submitting two revised IUCLID export files for inclusion in HPVIS. If you have difficulty with the electronic submission or require additional information, please contact me, as BASF's representative, by phone (919-544-4535) or e-mail (jane.staveley@arcadis-us.com).

Sincerely,

ARCADIS

Jane Staveley
Principal Environmental Scientist

Attachments:

- Test Plan for 1,2-dimethyl-4-nitrobenzene, prepared by ARCADIS (pdf)
- Robust Summaries – 1,2-dimethyl-4-nitrobenzene (CAS No. 99-51-4), prepared by ARCADIS (pdf)
- IUCLID (Version 4) Export file – 1,2-dimethyl-4-nitrobenzene (99-51-4.exp), prepared by ARCADIS
- Robust Summaries – 2,4-dimethyl-1-nitrobenzene (CAS No. 89-87-2), prepared by ARCADIS (pdf)
- IUCLID (Version 4) Export file – 2,4-dimethyl-1-nitrobenzene, prepared by ARCADIS (89-87-2.exp), prepared by ARCADIS
- Robust Summaries – 2-nitrotoluene, IUCLID dataset created by European Commission, European Chemicals Bureau (pdf)

- Test Plan for m-Nitrotoluene, prepared by American Chemistry Council, Monocyclic Aromatic Amines and Nitroaromatics Panel (pdf)
- Condensed Robust Summaries, 3-nitrotoluene, prepared by American Chemistry Council, Monocyclic Aromatic Amines and Nitroaromatics Panel (pdf)
- SIDS Initial Assessment Report for SIAM 17 for 4-nitrotoluene, UNEP Publications (pdf)

Copies:
Dr. Ralph Parod, BASF
Dr. David Cortes, BASF
Mr. Mark Townsend, US EPA