



201-15148

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March 25, 2004

Administrator

U.S. Environmental Protection Agency

P.O. Box 1473

Merrifield, VA 22116

Attn: Chemical Right-to-Know Program

RE: HPV Chemical Challenge Program

Response to Comments

AR-201-14390

p-nitrophenol

CAS No. 100-02-7

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We are pleased to provide the Agency our responses to comments received from EPA and other stakeholders on our referenced HPV Chemical Challenge submission for p-nitrophenol, CAS No. 100-02-7, which you will find attached. We are forwarding responses to the specific comments, along with a revised Test Plan and Robust Summary package.

Thank you for your consideration. Please contact me directly should there be any question related to this submission.

Sincerely,

Regards,

Donald A. Lederer, CHMM

Product Stewardship Manager

Response to Comments on HPV Challenge Submission

4-Nitrophenol CAS Number 100-02-7

Solutia Inc.
March 25, 2004

EPA Comments

Specific Comments on the Test Plan

COMMENT 1: *Boiling point.* The boiling point for 4-nitrophenol is given as >279 C in Table 2 on page 9; however, according to handbook sources this value reflects decomposition (Verschuren, K. 2001. Handbook of environmental data on organic chemicals, 4th ed. New York, NY: John Wiley & Sons, p. 1636). The submitter needs to state that this is a decomposition temperature.

RESPONSE: Decomposition was indicated and the reference was brought up to date since the current Handbook of Chemistry and Physics does not list a boiling or decomposition point for PNP.

COMMENT 2: *Vapor pressure.* The submitter obtained a calculated vapor pressure of 0.0067 hPa (0.0050 mmHg) at 20 C from HSDB 2002. However, the value for PNP from Schwarzenbach et al. (1988) was misreported in the HSDB. The value 0.0050 mmHg corresponds to the vapor pressure at 20 C for the subcooled liquid of 2,4-dinitrophenol.

Schwarzenbach *et al.* also reported extrapolated vapor pressures for 4-nitrophenol at 20 C of 1.10×10^{-6} atm (8.33×10^{-4} mmHg) for the subcooled liquid, and 1.29×10^{-7} atm (9.79×10^{-5} mmHg) for the solid. The value for solid 4-nitrophenol can satisfy the endpoint in this case.

RESPONSE: Thank you for the excellent analysis. The vapor pressure has been reported over a range of values from different sources but the extrapolated Schwarzenbach value that you cite for solid material is probably the most accurate and appropriate. We have used the recommended value.

We would like to point out that the U.S. EPA has "Air Toxics" information on their website giving the following: "The vapor pressure for 4-nitrophenol is 0.0003 mm Hg at 30 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.91."
<http://www.epa.gov/ttn/atw/hlthef/nitrophe.html>

The correspondence of the EPA 30°C value (0.0003 mm) to the Schwarzenbach 20° value (0.0000974 mm) is actually quite close if the Antoine equation is used for extrapolation between the two temperatures.

COMMENT 3: *Photodegradation.* The submitter provided values of 5.7 days (pH 5), 6.7 days (pH 7), and 13.7 days (pH 9) (Hustert et al. 1981). The submitter indicates that these values compare favorably with an AOPWIN estimated value of 2.48 days based on a 12-hr day and 1.5×10^6 OH/cm³. This comparison is in error. The data in Hustert et al. (1981) are for direct photolysis in aqueous solution by sunlight. The estimations from AOPWIN provide half-lives for the reactions of vapor phase 4-nitrophenol with photochemically generated hydroxyl radicals. The submitter needs to address this error.

RESPONSE: This section was modified to show the relative contributions of direct and indirect photolysis on PNP. The direct reaction of PNP in aqueous media with sunlight is expected to be an important consideration in the fate of PNP since it has such low volatility.

COMMENT 4: *Stability in water.* While EPA agrees that this chemical is stable to hydrolysis, the submitter needs to include this information in a robust summary. Furthermore, the submitter needs to indicate that 4-nitro-phenol does degrade in water upon exposure to sunlight, referencing the relevant data presented in the photodegradation section.

RESPONSE: The direct photodegradation information and reference were added.

COMMENT 5: *Biodegradation.* The submitter needs to provide a detailed description of each test including the OECD Screening test, and resolve other issues identified under the comments on the robust summaries.

RESPONSE:

This has been done. See response to “Comment 12”

COMMENT 6: *Fugacity.* The submitter used an incorrect vapor pressure in the input parameters. The correct value for 4-nitrophenol is 9.79×10^{-5} mmHg (see vapor pressure section, above). The submitter's Henry's law constant is not consistent with the experimental value cited in the PHYSPROP database, 4.15×10^{-10} atm-m³/mole (Parsons et al. 1971). The submitter used half-lives in air, water, soil, and sediment that were very short, and did not explain why these were used. The submitter needs to address these vapor pressure, Henry's law constant, and half-life input issues.

RESPONSE: The correct values for the physical constants were used in a revised modeling exercise. The half-lives were revised based on the information that PNP is

clearly inherently biodegradable using revised conservative estimates considered representative of environmental conditions. The model was also run assuming release only to water as this is considered the most likely industrial situation. The information in the test plan was also modified accordingly.

COMMENT 7: *Repeated-dose toxicity.* The submitter needs to include in the robust summaries the 18-month chronic toxicity study in mice (NTP, 1994) discussed in the test plan.

RESPONSE:

A robust summary of this study has been added. As this is beyond the scope of the HPV screening and as it is a publicly available document, only a brief overview of the study design and results have been included in the robust summary.

COMMENT 8: *Genetic toxicity (gene mutation).* The submitter needs to provide separate robust summaries for the *Drosophila* sex-linked recessive lethal assay (NTP, 1994) and the NTP's CHO-HGPRT forward mutation assay (Oberly et al, 1990), which are discussed as supporting data in the test plan.

RESPONSE:

These reports have been included in the robust summary of the Ames test as supporting studies with results and full references. We believe it is outside the scope of the HPV program guidelines to provide robust summaries for all supporting studies, especially those that are readily available in the open literature.

COMMENT 9: *Genetic toxicity (chromosomal aberration).* The submitter needs to provide the SCE assay as a separate robust summary.

RESPONSE:

This report has been included in the robust summary of the chromosome aberration study as a supporting study with results and full references and a description of the major findings. We believe it is outside the scope of the HPV program guidelines to provide robust summaries for all supporting studies, especially those that are readily available in the open literature.

COMMENT 10: *Developmental toxicity.* The submitter needs to discuss the developmental toxicity criteria for the submitted 2-generation reproductive toxicity study. Since the study was conducted with much lower doses than those recommended by the OECD guidelines for the dermal route, and did not elicit any maternal toxicity at the

highest dose tested, the submitter needs to provide information on the selection of doses and exposure route.

The test plan and Tables 1 and 5 in the test plan need to specifically address the developmental toxicity endpoint.

RESPONSE:

An oral developmental toxicity in rats that shows clear maternal toxicity was inadvertently omitted from the initial submission. This study has been added as a separated robust summary. Administration by the oral route allowed a maternally toxic dose to be investigated relative to effects on the conceptus. In this study, high-dose pregnant dams showed both reductions in body weight and body weight gain without any adverse effects on fetal parameters. Although this study has some deficiencies, it serves as the adequate developmental toxicity screening study required by the HPV program.

Information about this study has also been incorporated into the Test Plan in Table 1 and Table 5, and into a new section in the mammalian toxicity part of the plan.

Specific Comments on the Robust Summaries

COMMENT 11: Generic Comments: Some of the definitive values (e.g., EC50/LC50 and NOAELs/LOAELs) were reported as greater than or equal to () in the respective fields. The submitter needs to remove the greater than (>) sign.

RESPONSE:

The “greater than” indication has been removed from the LOAELs and NOAELs

COMMENT 12: *Biodegradation.* (a) The submitter indicates that it used five OECD guideline 301 methods. However, the only tests that seem to follow OECD Guideline 301 are the Sturm test (301 B), the OECD Screen test (301 E), and the Closed Bottle test (301 D). This point needs clarification. (b) The Zahn-Wellens test is OECD Guideline 302 B for determining inherent biodegradability, not ready biodegradation as indicated in the robust summary. (c) The submitter needs to indicate clearly and accurately which tests provide inherent biodegradation results and which provide ready biodegradation results, rather than categorize them all as ready biodegradation. (d) The degradation time periods for the MITI test, the AFNOR test, and the Sturm test are missing.

RESPONSE:

A table of the biodegradation results giving the appropriate classification and some experimental details has been added to the test plan. The table provides a high degree of clarity about the individual tests but the question of the classification of PNP as readily

biodegradable cannot be unequivocally resolved. Discussion about this issue is included in the test plan.

The robust summary has been broken up into multiple robust summaries reflecting the various types of studies and outcomes. Because the article did not give a high-degree of detail about the conduct of each study, the guideline designation is left off where it cannot be assigned.

COMMENT 13: *Algae*. The submitter needs to provide the test concentrations used in the algal study.

RESPONSE:

The paper did not specifically give the concentrations used for each substance tested. Based on the dilution method given in the paper, the relevant concentrations of PNP in the concentration range of inhibition were calculated and added to the robust summary.

Environmental Defense Comments

COMMENT 14: The robust summary contains only a 2-generation reproductive study on NP administered via the dermal route. No developmental toxicity studies were reported. Since dermally-administered NP is not acutely toxic and no information was provided on the systemic levels of NP following dermal administration, the reproductive/developmental dataset is inadequate for screening level purposes. We do note that no histological alterations of reproductive organs were detected in the oral or inhalation repeat dose studies, so a new reproductive toxicity study is not needed. However, an oral or inhalation developmental toxicity study is warranted, as data on this endpoint are not available.

RESPONSE:

We appreciate your thoughtful comments and have added a definitive oral developmental toxicity study that we found subsequent to the initial submission. The combination of the repeated-dose data and the developmental toxicity study indicate lack of reproductive toxicity potential. This conclusion is supported and supplemented by the dermal 2-generation study.

Animal Protection Organizations Comments

No responses necessary