

EPA Comments on Chemical RTK HPV Challenge Submission: 1-Naphthol

Summary of EPA Comments

The sponsor, Bayer CropScience LP, submitted a test plan and robust summaries to EPA for 1-naphthol (CAS No. 90-15-3), dated July 28, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on October 16, 2003.

EPA has reviewed this submission and reached the following conclusions:

1. Physicochemical Properties. The data for melting point, boiling point, and partition coefficient are adequate for the purposes of the HPV Challenge Program. However, the submitter needs to verify the vapor pressure value provided and provide additional information on water solubility or conduct testing.
2. Environmental Fate. The data are adequate for the purposes of the HPV Challenge Program.
3. Health Effects. The acute, repeated-dose, and developmental toxicity data are adequate for the purposes of the HPV Challenge Program. EPA reserves judgment on the genetic toxicity data pending the receipt of adequate robust summaries. The submitter also needs to provide a robust summary of the reproductive effects seen in the 13-week rat gavage study if the reproductive organ tissues were examined histologically, because the reproductive toxicity study submitted is inadequate.
4. Ecological Effects. The acute and chronic toxicity data for fish and invertebrates are adequate for the purposes of the HPV Challenge Program. The acute toxicity data for algae are inadequate. Testing is recommended for this endpoint.

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

EPA Comments on The 1-Naphthol Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for melting point, boiling point, and partition coefficient are adequate for the purposes of the HPV Challenge Program.

Vapor pressure. The submitted value of 36 hPa (27 mmHg) at 25 °C is not consistent with data located by EPA: 1 mm Hg at 94 °C, 10-760 mmHg at 141.5-282.5 °C, and 1.7 mmHg at 100 °C (Jordan 1954; Lewis 1999; Terres et al. 1955). Also, EPA estimated vapor pressures ranging from 0.000274 to 0.010 mm Hg at 25 °C (MPBPWIN v1.40; McEntee 1987) using values measured at elevated temperatures. The submitter needs to provide measured vapor pressure data following OECD TG 104 or resolve this inconsistency.

Water solubility. The submitted assessments of “insoluble” and “not soluble” from handbook and manufacturer sources (CIRS SpA, no date; Lide 1999-2000) are not adequate. However, EPA located water solubility data ranging from 300 mg/L at 25 °C to 3,099 mg/L at 50 °C in handbooks and BEILSTEIN (Booth 1991; Hassett et al. 1980; Korenman 1983; Korenman et al. 1980, 1981; Rouse et al. 1995; Talukder and Kates 1995). The submitter needs to include the above information in the robust summary or test for water solubility following OECD TG 105.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted data for all endpoints are adequate for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data for acute, repeated-dose, and developmental toxicity are adequate for the purposes of the HPV Challenge Program.

Genetic Toxicity. EPA reserves judgment on the data submitted for mutagenicity (in bacteria) and chromosomal aberration (*in vivo* micronucleus assays in rodents) pending receipt of adequate robust summaries.

Reproductive Toxicity. The submitted two-generation dermal study is not adequate because the test material is a hair-dye formulation containing 99.5% undefined substances and only 0.5% 1-naphthol. However, no additional testing is needed if adequate data on reproductive organ histopathology are available from the 13-week rat gavage study. If the reproductive organs were examined in the 13-week study, the sponsor needs to provide a separate robust summary that discusses the reproductive (organ) effects from this study.

Ecological Effects (fish, invertebrates, and algae)

The acute algal toxicity study was not conducted according to accepted guidelines with regard to study duration (20 days). In addition, it could not be determined if the test concentrations were measured. EPA recommends that an acute algal toxicity test be conducted with a duration of 72 hours (OECD TG 201) or 96 hours (preferred; OPPTS TG 850.5400) using measured concentrations under a closed system.

Specific Comments on the Robust Summaries

Health Effects

Most of the robust summaries, especially those for supporting studies, do not provide sufficient detail.

Acute Toxicity. The robust summary for an acute oral (gavage) toxicity study in mice does not indicate whether body weights were monitored. Four additional summaries report similar acute oral LD₅₀ values in rats, but none include sufficient detail to adequately evaluate each study. Robust summaries of inhalation and dermal studies either lack sufficient detail or the studies did not follow OECD Guidelines.

Repeated-Dose Toxicity. The robust summary for the 13-week rat gavage study does not report the gavage vehicle, the magnitude of body weight changes, organs weighed and examined for histopathology, and hematological, clinical chemistry, and urinalysis parameters examined.

Genetic Toxicity. Robust summaries for three negative reverse mutation assays in *Salmonella typhimurium* (2, 5, or 7 strains) do not report test concentrations, the number of replicates, the source of the metabolic activation system, the use of positive controls, the cytotoxic concentrations, and the criteria for determining positive results.

Robust summaries for two negative micronucleus assays—in rats exposed by oral gavage or in mice exposed by intraperitoneal injection—do not indicate group sizes, whether positive controls were used, tissue examined (peripheral blood or bone marrow), number of cells examined, clinical signs of toxicity (if observed), and the criteria for a positive result. Neither summary provides enough information to demonstrate that methods were consistent with OECD TG 474.

Developmental Toxicity. The robust summary for a developmental toxicity study in rats exposed by gavage on gestation days 7-17 does not indicate the magnitude of the body weight changes in high-dose dams.

Followup Activity

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

References

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