



May 2, 2007

Sent via Email shane@niehs.nih.gov
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NTP Liaison and Scientific Review Office
NIEHS/NIH
P.O. Box 12233, MD A3-01
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Re: Public comments to NTP Draft Report TR 522 (Propargyl Alcohol)

Dear Dr. Shane:

International Specialty Products has reviewed the draft NTP Technical Report on the Toxicology and Carcinogenesis Studies of Propargyl Alcohol in F344/N Rats and B6C3F1 Mice. Below are our comments

Genetic Toxicity

1. Bacterial mutagenicity studies in strain TA 100 showed an increase in revertants in all three experiments. However, the increase was not large and only one experiment slightly exceeded a 2-fold increase. In addition, in one experiment, there was not a dose response relationship as a lower number of revertants were observed at a higher concentration that did not exhibit toxicity. According to current guidelines (OECD 473), statistical significance should not be the only indicator for a positive response. No historical data was available for comparison. If one considers the biological relevance of the results, it seems more appropriate to consider these effects equivocal.
2. The micronucleus study was considered to be equivocal in females based on a statistical trend test. No differences were noted when each concentration was compared to the controls values. Based on the data presented, the number of micronuclei in some of the treatment groups was below that observed in the controls. Unfortunately, NTP does not have a historical database which would have been useful to compare the micronucleus in the treatment groups. According to current guidelines (OECD 474), statistical significance is only one of the criteria that can be used to evaluate a positive response. No statistical significance was observed in males. The conclusion in the technical report is different than that listed on NTP's testing status page which reports propargyl alcohol to be negative in the micronucleus study in both males and females. Please consider changing the conclusion for the micronucleus study in the technical report to "negative".

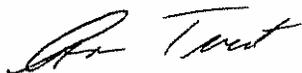
Carcinogenicity

1. The Harderian gland adenomas in male mice did not exhibit a dose response relationship and were within the historical range (3-10) with the exception of the high dose group which had 11 animals with this adenoma. Please consider changing this finding from "equivocal" to "not treatment related".
2. The draft report concludes propargyl alcohol exhibits some evidence of carcinogenic activity in male rats based on increases in respiratory epithelial adenomas in the nose and an increase in mononuclear cell leukemia. Only the high dose group exhibited

leukemia above historical control values. However, this is a common finding in male rats, the staging for this cancer was comparable to controls and a dose dependent decreased latency period was not observed. Please consider changing the conclusion to from “some evidence” to “equivocal evidence”.

Thank you again for the opportunity to comment on the draft report. Please let me know if any of my comments need clarification. You can reach me at 973-628-3924 (email atveit@ispcorp.com).

Sincerely,

A handwritten signature in black ink, appearing to read "Ann Tveit". The signature is fluid and cursive, with the first name "Ann" and last name "Tveit" clearly distinguishable.

Ann Tveit, Ph.D, DABT
Senior Toxicologist
Product Stewardship Department