



Centers for Disease Control and Prevention
National Institute for Occupational
Safety and Health
1090 Tusculum Avenue
Cincinnati OH 45226-1998

December 29, 2015

The Health Council of the Netherlands
Attn: Mrs. T.M.M. Coenen
PO Box 16052
NL-2500 BB The Hague
the Netherlands

Dear Mrs. Coenen:

Thank you for the opportunity to review the draft report on *4-Vinylcyclohexene diepoxide* prepared by the Subcommittee on Classification of Carcinogenic Substances of the Dutch Expert Committee on Occupational Safety (DECOS). Comments are enclosed that were prepared by Steven Reynolds, Research Pharmacologist, NIOSH/Health Effects Laboratory Division (HELD), 1095 Willowdale Rd., Morgantown, WV 26505-2888.

If you have any questions regarding the comments, please contact me at 513-533-8260 (telephone) or by Email at tbl7@cdc.gov.

Sincerely yours,

Co-Jutt Botson for Thomas J. Lentz
29 Dec 2015

Thomas J. Lentz, Ph.D., M.P.H.
Branch Chief
Document Development Branch
Education and Information Division

1 Enclosure

Review on DECOS draft document 4 –Vinylcyclohexene diepoxide
By: Steven Reynolds, Research Pharmacologist,
NIOSH/Health Effects Laboratory (HELD),
1095 Willowdale Road, Morgantown, WV 26505

SECTION & PARAGRAPH	COMMENT
General Comments	<p>Data for this draft were obtained from the online databases Medline, Toxline, Chemical Abstracts, and RTECS covering the period to September 2015 using 4 - Vinylcyclohexene diepoxide as keywords in combination with keywords representative for carcinogenesis and mutagenesis. A December 10, 2015 search using Ovid MEDLINE with “4 – Vinylcyclohexene diepoxide, germ cell and mutagenicity” as keywords provided no additional relevant information other than what is currently contained within the report. All critical studies relevant to germ cell mutagenicity of 4-Vinylcyclohexene diepoxide seem to have been included in the report.</p> <p>The critical studies are presented in sufficient detail to support the conclusions regarding the germ cell mutagenicity of 4 - Vinylcyclohexene diepoxide.</p> <p>The presentation of the material is sufficiently concise.</p> <p>The limitations of the critical studies were discussed.</p> <p>There are no obvious alternative interpretations regarding the overall assessment of 4 - Vinylcyclohexene diepoxide germ cell mutagenicity.</p>
Specific Comments	
Pg. 18 (Conclusion)	<p>“4 – Vinylcyclohexene diepoxide caused an increase in Chinese hamster ovary cells with chromosome aberrations...” might possibly be better stated as “4 – Vinylcyclohexene diepoxide caused an increase in chromosome aberrations in Chinese hamster ovary cells ...”</p>

<p>Pg. 20 (5.3 Summary)</p>	<p>“ ...in the presence and absence of metabolic activation and in mammalian cells (mouse lymphoma study, tk locus) in the absence of metabolic activation and in mammalian cells (mouse lymphoma study, tk locus) in the absence of metabolic activation” is either redundant or was actually supposed to indicate both “in the absence of metabolic activation and in the presence of metabolic activation”. There is also no period at the end of that sentence in the review so it is difficult to determine what the sentence was supposed to convey.</p>
<p>Pg. 29 (6.1 Non-human information)</p>	<p>”...at the application site as did normal mice in the two-your mouse study by the NTP.” Should read “...at the application site as did normal mice in the two-year mouse study by the NTP.”</p>
<p>Pg. 30 (6.5 Comparison with criteria)</p>	<p>“.. shows genotoxic properties in bacterial and mammalian cells in vitro and DNA adducts in vitro and vivo.” should be “..genotoxic properties in bacterial and mammalian cells in vitro and DNA adducts in vitro and in vivo.”</p>