DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Centers for Disease Control and Prevention
National Institute for Occupational
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The Health Council of the Netherlands
Attn: Ms. J.M. Rijnkels
PO Box 16052
2500 BB The Hague
The Netherlands

Dear Ms. J.M. Rijnkels:

Thank you for the opportunity to review the draft report on *Tetrahydrofuran* prepared by the Subcommittee on the Classification of Carcinogenic Substances of the Dutch Expert Committee on Occupational Safety (DECOS).

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,

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

1 Enclosure

NIOSH Comments on Tetrahydrofuran by Steven Reynolds, Health Effects Laboratory Division, NIOSH, 1095 Willowdale Rd., Morgantown, WV 26505-2888

Tetrahydrofuran is used as a medium for various hydride reactions; in the synthesis of other chemical compounds; in the manufacture of articles for packaging, transporting and storing foods; as a solvent for dyes and lacquers; and as a chemical intermediate in polymerization solvent for fat oils, unvulcanised rubber, resins, and plastics.

1) The review used data that were retrieved from online databases Medline, Toxline, and Chemical abstracts with the last online search performed in June 2012. No IARC-monograph for tetrahydrofuran was available. An additional August 2012 online search using PubMed revealed no additional relevant data for tetrahydrofuran regarding carcinogenicity or genotoxicity.

2) The critical studies were presented in sufficient detail to support the conclusions regarding the characterization of risk.

3) The presentation of the available information is sufficiently concise and does not need to be condensed.

4) The report accurately described the limitations of the critical studies which were presented.

5) According to the judgment of the committee, the available data are insufficient to evaluate the carcinogenic properties of tetrahydrofuran. In general, given the available data on tetrahydrofuran, this is an appropriate conclusion. However, given that there was a statistically significantly higher increase of hepatocellular adenomas and carcinomas in the livers of the highest dose group of female B6C3F1 mice, the committee's literature review might wish to note that furfural, a precursor used in the synthesis of tetrahydrofuran, was deemed carcinogenic [Natl Toxicol Program Tech Rep Ser. 1990 Mar; 382:1-201; NTP Toxicology and Carcinogenesis Studies of Furfural (CAS No. 98-01-1) in F344/N Rats and B6C3F1 Mice (Gavage Studies); SH Reynolds et al., Activated oncogenes in B6C3F1 mouse liver tumors: implications for risk assessment. Science. 1987 Sep 11;237 (4820):1309-1316].

Also, in Section 4.1.1, line 12 – "doses of 10.000, 40,000, or 125,000 ppm" should probably read "doses of 10,000, 40,000, or 125,000 ppm" and Section 5.1, line 8, "Tetrahydrofuran did not induces..." should read ""Tetrahydrofuran did not induce..."