

Comments on the public review draft 'acetaldehyde' prepared by a subcommittee of the DECOS, the Health Council

Van: David Coggon [<mailto:dnmc@mrc.soton.ac.uk>]

Verzonden: donderdag 19 juni 2014 8:46

Aan: Schaap, F.S. (Femke)

Onderwerp: Re: Draft document Acetaldehyde

Femke

Thank you for sending me the draft report on acetaldehyde. I have a few comments.

Page 11, lines 5-6. It is unclear what is meant by "retained for 45 to 70% in human subjects".

Page 11, line 7. Given that acetaldehyde is formed endogenously, it would be helpful to know whether the levels of acetaldehyde that were found after single inhalation exposure were higher than in unexposed control animals. Is it possible to say "increased acetaldehyde was found"

Page 11, line 20. There must be some data on metabolism in humans as we know the main route of metabolism (section 6.3.1), and I am surprised that no reliable quantitative data are available. Would such information not have been collected to support registration of the drug, disulfiram?

Page 11, lines 28-9. Half-time values in which tissues?

I hope that this is helpful.

Best wishes

David



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July 16, 2014

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 re-review the draft report on *Acetaldehyde* prepared by the Subcommittee on the Classification of Carcinogenic Substances of the Dutch Expert Committee on Occupational Safety (DECOS). Comments are enclosed that were prepared by Qiang Ma who had previously reviewed the document.

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,

A handwritten signature in black ink, appearing to read "T. Lentz".

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

1 Enclosure

Comment on DECOS Document "Acetaldehyde: Re-evaluation of the Carcinogenicity and Genotoxicity" by Qiang Ma, NIOSH/HELD, 1095 Willowdale Rd., Morgantown, WV 26506-2888

The Re-evaluation is a revision of the Evaluation of 2012 by DECOS. The Re-evaluation was based on published data reviewed in the IARC monograph and data from the European Chemicals Agency (ECHA) as well as several relevant online databases on acetaldehyde with a focus on the compound alone. IARC classified acetaldehyde as Group 2B "possibly carcinogenic to humans" agent in 1999 and concluded that acetaldehyde in association with alcohol consumption is carcinogenic to humans (Group 1) in 2012. The Re-evaluation concluded that acetaldehyde is presumed to be carcinogenic to humans (category 1B) and is a germ cell mutagen in category 1B with a stochastic genotoxic mechanism of action. This conclusion is in agreement with the IARC classification of the compound on carcinogenicity with additional evaluations of genotoxicity and mechanism of action. The review is logical, evidence-based, and clearly written.

On page 37, lines 12 to 14, and on page 38, lines 2 to 5, it was stated "that in none of the studies on genetic polymorphism and alcohol-related cancer risk, direct evidence was found that acetaldehyde had caused cancer, although the indirect data are suggestive for this." However, genetic polymorphism studies, as well as alcohol consumption-cancer relationship studies, are generally taken as "association studies" that provide evidence to support or negate an association with cancer incidence or severity; but the studies do not, in general, provide "direct evidence" to establish a causal relationship with cancer. This sentence potentially causes confusion in this regard.