



Gezondheidsraad  
Health Council of the Netherlands

**Reactie Gezondheidsraad op  
commentaar openbaar concept  
*1,2-Dichloorethaan***

**Response Health Council  
to comments draft report  
*1,2-Dichloroethane***

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# 1 Reactie op commentaar EDC/ Respons to comments EDC

Op 27 augustus 2019 heeft de Gezondheidsraad per brief gereageerd op het commentaar van het *Industry Consortium for EDC* op het openbare concept van het advies *1,2-Dichloorethaan*. De reactie staat hieronder, in het Engels.

*On August 27, 2019, the Health Council sent a letter to the Industry Consortium for EDC in response to the comments on the draft report on 1,2-Dichloroethane. The response is cited below, in the same language as the original comments.*

'Thank you for accepting the invitation to comment on the draft report *1,2-Dichloroethane*, which was published for public review in June 2018 by the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council of the Netherlands. The DECOS highly appreciates your comments, which enabled the committee to modify and improve its report. On behalf of the President of the Health Council, I send you a reply.

In an enclosed position paper, the EDC consortium objected to the Committee's overall assessment and use of a stochastic approach for the cancer risk assessment of 1,2-dichloroethane. The EDC consortium argued that there is no evidence that 1,2-dichloroethane is an *in vivo* mutagen, and provided a (sponsored) study on the mode of action of the 1,2-dichloroethane-induced mammary tumours in rats. The Committee has considered the EDC consortium's review and reassessed the genotoxicity and carcinogenicity data on 1,2-dichloroethane. Furthermore, the Committee requested the advice of the Subcommittee on the Classification of Carcinogenic Substances on the mode of action of 1,2-dichloroethane. The recommendation of the subcommittee has been added as an annex to the final report.

The reassessment has not changed the conclusion of the Committee on the genotoxic mode of action. Overall, based on positive findings in *in vitro* mutagenicity assays and chromosomal aberration tests, positive results in *in vivo* indicator test, limited data on mutagenicity *in vivo* and limited data on a specific mode of action, the Committee considers 1,2-dichloroethane a (low-potency) stochastic genotoxic carcinogen. For such substances, the Committee applies a non-threshold approach. Details of the considerations on the genotoxic mode of action of the Committee can be found in the final report.

The final advisory report *1,2-Dichloroethane* was published on August 27<sup>th</sup>, 2019. It can be found on the website of the Health Council. Also your comment and this letter by the DECOS can be found on the website. The comments and the response of the Committee are publicly available.'

## 2 Reactie op commentaar Shin-Etsu PVC B.V./ Respons to comments Shin-Etsu PVC B.V.

Op 27 augustus 2019 heeft de Gezondheidsraad per brief gereageerd op het commentaar van Shin-Etsu PVC B.V. op het openbare concept van het advies *1,2-Dichloorethaan*. De reactie staat hieronder.

*On August 27<sup>th</sup>, 2019, the Health Council sent a letter to Shin-Etsu PVC B.V. in respons to the comments on the draft report on 1,2-Dichloroethane. The respons is cited below, in the same language as the original comments (Dutch).*

'Hartelijk dank voor uw belangstelling voor het conceptadvies over 1,2-dichloorethaan, opgesteld door de Commissie Gezondheid en beroepsmatige blootstelling aan stoffen (GBBS) van de Gezondheidsraad en in juli 2018 beschikbaar gesteld voor openbare consultatie. Op 11 januari 2019 stuurde u een beschouwing van mevrouw A. Gennissen, bedrijfsarts bij Shin-Etsu. De Commissie GBBS stelt dit commentaar op prijs omdat dit bijdraagt aan de kwaliteit van het advies. Namens de voorzitter van de Gezondheidsraad geef ik u in deze brief een reactie.

Gennissen vraagt of bij de lineaire extrapolatie vanuit een hogere concentratie, de vlakke dosis-responsrelatie bij lagere concentraties voldoende wordt meegewogen. Er lijkt namelijk volgens haar sprake te zijn van metabole verzadiging van de oxidatieve cytochroom P450 systeem, waardoor verzadiging optreedt.

De Commissie acht het plausibel dat verzadiging een rol speelt bij de vlakke dosis-responsecurve die gezien wordt. De vlakke curve wordt meegewogen omdat er pas bij een relatief hoge concentratie een 10% toename in tumorincidentie wordt afgeleid. Desalniettemin beaamt de commissie dat de lineaire extrapolatie een conservatieve benadering is. De commissie gaat er vanuit dat carcinogene effecten ook bij lagere concentraties kunnen optreden, hoewel deze bij laag-potente carcinogenen niet goed zijn vast te stellen. Ook ontbreken gegevens over de blootstelling-responsrelatie van genotoxische effecten bij deze lage concentraties. De commissie gaat daarom niet verder in op kwantitatieve aspecten met betrekking tot mogelijk metabole verzadiging en blijft bij haar vaste werkwijze.

De Gezondheidsraad heeft het advies *1,2-Dichloroethane* op 27 januari 2019 gepubliceerd en beschikbaar gesteld via haar website. Op de website vindt u ook uw commentaar en de reactie hierop van de Gezondheidsraad. De reacties en antwoorden zijn openbaar en voor iedereen in te zien.'

### 3 Reactie op commentaar BOHS/ Respons to comments BOHS

Op 27 augustus 2019 heeft de Gezondheidsraad per brief gereageerd op het commentaar van twee experts van BOHS op het openbare concept van het advies 1,2-Dichloorethaan. De reactie staat hieronder, in het Engels.

*On August 27<sup>th</sup>, 2019, the Health Council sent a letter to BOHS in response to the comments of two BOHS-experts on the draft report on 1,2-Dichloroethane. The response is cited below, in the same language as the original comments.*

'In July 2016, the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council of the Netherlands published a draft report on the recommendation of an occupational exposure limit of 1,2-dichloroethane. The British Occupational Hygiene Society (BOHS) submitted comments of two of its members on the report. Since a draft report on 1,2-dichloroethane was released by the Scientific Committee on Occupational Exposure Limits (SCOEL) in parallel, it was decided to withdraw the report by the DECOS to be able to include findings of the SCOEL later on. In July 2018, an updated version of the draft report was released for public consultation. This updated draft report contained no critical changes concerning the scientific content. The Committee has taken the comments sent by BOHS into account when finalising the updated report on 1,2-dichloroethane. On behalf of the President of the Health Council, I send you a reply.

Dr. Cherrie commented on the quantitative hazard assessment, for which the DECOS used the number of mammary gland adenocarcinomas observed in a mouse carcinogenicity study by Nagano et al. (2006). He noted that 'the justification for this study is rather weak'. In the subsequent paragraphs Dr. Cherrie outlined several limitations of the exposure-response relationship that were observed.

The Committee uses data from the type of tumour that occurs at the lowest exposure concentration (or the tumour type with the highest increase in incidence). It considers the mammary gland adenocarcinoma relevant for humans, although the Committee agrees that the observed relationship is relatively weak. However, also in rats an increased incidence in mammary gland adenocarcinomas was observed, though at a higher 1,2-dichloroethane exposure level. The Committee considers this finding in rats supportive for selecting mammary gland adenocarcinoma as starting point.

In the second part of his commentary, Dr. Cherrie provided information on current 1,2-dichloroethane exposure levels and the number of people exposed, and concluded that 'it is still unlikely that any of them would have a cancer associated with their exposure'. The Committee notes that its task is to recommend health-based recommended values, regardless of the actual exposures.

Mr. Jones made textual suggestions leading to several adaptations in the report.'

## 4 Reactie op commentaar NIOSH/ Respons to comments NIOSH

Op 27 augustus 2019 heeft de Gezondheidsraad per brief gereageerd op het commentaar van NIOSH op het openbare concept van het advies *1,2-Dichloorethaan*. De reactie staat hieronder, in het Engels.

*On August 27<sup>th</sup>, 2019, the Health Council sent a letter to NIOSH in response to the comments on the draft report on 1,2-Dichloroethane. The response is cited below, in the same language as the original comments.*

'Thank you and your colleague Mrs Forester for accepting the invitation to comment on the draft report *1,2-Dichloroethane*, which was published for public review in June 2018 by the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council of the Netherlands. The DECOS highly appreciates your comment, which enabled the committee to modify and improve its report. On behalf of the President of the Health Council, I send you a reply.

The Committee is pleased that NIOSH supports the outline and conclusions of the report. The final advisory report *1,2-Dichloroethane* was published on August 27<sup>th</sup>, 2019. It can be found on the website of the Health Council. Also your comments and the response by the DECOS can be found on the website. The comments and replies are publicly available.'