
Gezondheidsraad

Health Council of the Netherlands



Mr. W. Cremers
Manager Coal Chemicals Sector Group
European Chemical Industry Council
Avenue E. van Nieuwenhuysse 4
B-1160 Brussels
Belgium

Subject : Comment on the draft report *Naphthalene*
Your references : Letter dated, August 7, 2012
Our reference : I 1315/SV/fs/246-X17
Enclosure(s) : 1
Date : December 7, 2012

Dear Mr. Cremers,

Thank you for your interest in the draft report on the carcinogenic classification of naphthalene, which was made public in May 2012 by the Subcommittee on the Classification of Carcinogenic Substances of the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council. The subcommittee has taken notice of your comments, and has included several recent reviews on the mode of action of naphthalene and human relevance in the finalisation of the report (Bogen et al. 2008; Grieco et al., 2008; Magee et al., 2010; Piccirillo et al., 2012; Rhomberg et al., 2010).

For its evaluation, the subcommittee appreciates the use of mechanistic data. For naphthalene, such data on the carcinogenicity of naphthalene are available and have recently been evaluated. The most extensive evaluation has been provided by Rhomberg et al., who have discussed each identified key event in the development of cancer in rats and mice after naphthalene exposure, i.e. metabolism, cytotoxicity, inflammation, genotoxicity and ultimately, tumour formation. Importantly, the available information has been discussed in context of the existing inconsistencies and remaining uncertainties concerning the risk for humans.

The subcommittee values the use of mechanistic data in the case of naphthalene, and concurs with the weight-of-evidence approach as proposed by Rhomberg et al. Based on the presented thorough analyses of the available mechanistic information, the subcommittee considers it unlikely that upon naphthalene exposure, reactive metabolites are formed in humans to a degree that leads to cytotoxicity and subsequent carcinogenicity. Therefore, the subcommittee considers the mode of carcinogenic action of naphthalene in rodents not relevant for humans.

P.O. Box 16052
NL-2500 BB The Hague
E-mail: sr.vink@gr.nl
Telephone +31 (70) 340 5508

Visiting Address
Parnassusplein 5
NL-2511 BX The Hague
The Netherlands
www.gr.nl



Subject : Comment on the draft report *Naphthalene*
Our reference : I 1315/SV/fs/246-X17
Enclosure(s) : 1
Date : December 7, 2012

The subcommittee has therefore decided to reconsider its recommendation, and concludes that the available animal data on naphthalene do not provide sufficient evidence of carcinogenicity in humans. As the available human data are not sufficient to draw conclusions on the carcinogenicity of naphthalene in humans, the subcommittee classifies naphthalene in category 3¹ (insufficient data to evaluate the carcinogenicity of naphthalene).

The final version was published in December 2012. Enclosed you will find copy of it.

Yours sincerely,

Mr. S.R. Vink, PhD
Scientific secretary

¹ According to the classification system of the Health Council.

Gezondheidsraad

Health Council of the Netherlands



Mrs. Anne P. LeHuray, PhD
Naphthalene Council, Inc.
2308 Mount Vernon Avenue, Suite 134
Alexandria, VA 22301
USA

Subject : Comment on the draft report *Naphthalene*
Your references : Letter dated, August 31, 2012
Our reference : I 1335/SV/fs/246-Y17
Enclosure(s) : 1
Date : December 7, 2012

Dear Dr. LeHuray,

Thank you for your interest in the draft report on the carcinogenic classification of naphthalene, which was made public in May 2012 by the Subcommittee on the Classification of Carcinogenic Substances of the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council. The subcommittee has taken notice of your comments, and has included several recent reviews on the mode of action of naphthalene and human relevance in the finalisation of the report (Bogen et al. 2008; Grieco et al., 2008; Magee et al., 2010; Piccirillo et al., 2012; Rhomberg et al., 2010).

For its evaluation, the subcommittee appreciates the use of mechanistic data. For naphthalene, such data on the carcinogenicity of naphthalene are available and have recently been evaluated. The most extensive evaluation has been provided by Rhomberg et al., who have discussed each identified key event in the development of cancer in rats and mice after naphthalene exposure, i.e. metabolism, cytotoxicity, inflammation, genotoxicity and ultimately, tumour formation. Importantly, the available information has been discussed in context of the existing inconsistencies and remaining uncertainties concerning the risk for humans.

The subcommittee values the use of mechanistic data in the case of naphthalene, and concurs with the weight-of-evidence approach as proposed by Rhomberg et al. Based on the presented thorough analyses of the available mechanistic information, the subcommittee considers it unlikely that upon naphthalene exposure, reactive metabolites are formed in humans to a degree that leads to cytotoxicity and subsequent carcinogenicity. Therefore, the subcommittee considers the mode of carcinogenic action of naphthalene in rodents not relevant for humans.

Gezondheidsraad

Health Council of the Netherlands



Subject : Comment on the draft report *Naphthalene*
Our reference : I 1335/SV/fs/246-Y17
Enclosure(s) : 1
Date : December 7, 2012

The subcommittee has therefore decided to reconsider its recommendation, and concludes that the available animal data on naphthalene does not provide sufficient evidence of carcinogenicity in humans. As the available human data are not sufficient to draw conclusions on the carcinogenicity of naphthalene in humans, the subcommittee classifies naphthalene in category 3¹ (insufficient data to evaluate the carcinogenicity of naphthalene).

The final version was published in December 2012. Enclosed you will find copy of it.

Yours sincerely,

Mr. S.R. Vink, PhD
Scientific secretary

¹ According to the classification system of the Health Council.