

All-trans retinoic acid

Evaluation of the effects on reproduction, recommendation for classification

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Executive summary

Health Council of the Netherlands



At the request of the Minister of Social Affairs and Employment, the Health Council of the Netherlands evaluated the effects of all-trans retinoic acid on reproduction. This advisory report has been drafted by the Subcommittee on the Classification of Reproduction Toxic Substances of the Dutch Expert Committee on Occupational Safety (DECOS) of the Health Council. The Health Council has a permanent task in assessing the hazard of substances to which man can be exposed occupationally. More information about this task can be found at www.gezondheidsraad.nl.

Use of all-trans retinoic acid

All-trans retinoic acid occurs naturally in the body and plays a crucial role in cellular processes during embryogenesis. It is produced as a result of vitamin A metabolism. Due to its cell-activating properties, all-trans retinoic acid – also known as tretinoin – is widely used in

therapeutic creams for skin disorders, as well as in ‘anti-aging’ creams. Other uses are the treatment of acute promyelocytic leukemia and other forms of cancer (experimental approaches). Workers can be occupationally exposed to all-trans retinoic acid in the pharmaceutical industry, in pharmacies or in hospitals.

Classification according to strength of evidence for toxic effect

For assessing the effects on reproduction, the Committee evaluates the effects on male and female fertility and on the development of the offspring. Moreover, the Committee considers the effects of a substance on lactation and on the offspring via lactation.

If data indicating hazardous properties are available, the Committee recommends classification in a category based on the strength of the evidence. Based on

that proposal, the minister of Social Affairs and Employment can decide whether to classify the substance as toxic to reproduction.

The classification is performed according to EU-regulation (EC) 1272/2008.

Recommendations to the minister

Based on the available scientific data, the Committee recommends to classify all-trans retinoic acid for effects on offspring development only. There are insufficient data for classification with regard to effects on paternal and maternal fertility and effects on or via lactation.

The Committee’s classification proposal for all-trans retinoic acid:

- For fertility, the Committee recommends not classifying all-trans retinoic acid due to a lack of appropriate data.
- For developmental toxicity, the Committee recommends classifying all-trans retinoic acid



in category 1B (*presumed human reproductive toxicant*) and to label it H360D (*may damage the unborn child*).

- For effects on or via lactation, the Committee recommends not labelling all-trans retinoic acid due to a lack of appropriate data.



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Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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