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Gezondheidsraad
Health Council of the Netherlands

Date:	10 June 2020	Your ref:	Your e-mail, February 4th 2020	Our ref:	1671523/EvV/iv/543
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Subject: Comments on draft report Tretinoin

Dear dr. Olgun,

Thank you for accepting the invitation to comment on the draft report Tretinoin, that the Health Council published for public review in November 2019. The Council's Subcommittee on the Classification of Substances Toxic to Reproduction is pleased that you support the recommended classification and labelling, and appreciates the thorough review of the report. The suggestions you made to improve the report have been very helpful.

The Committee has changed the name of the document, as suggested, and renamed it 'All-trans retinoic acid'. The Committee limited the assessment to this substance and did not focus on retinoic acids, because the Ministry of Social Affairs and Employment requested the Health Council to assess all-trans retinoic acid. The contents and wording were changed accordingly.
A comment regarding several summaries of developmental animal studies was that they were incomplete as to purpose and design. These studies have not been described more thoroughly, because only the information considered relevant for classification purposes was selected. A sentence to explain this has been inserted at the beginning of section 2.4.2.
Another comment of a general nature regards the repetitive character of statements about maternal toxicity in the animal studies and the suggestion to delete them. The Committee considers the results of maternal toxicity analysis crucial to correct interpretation of teratogenicity findings (cf. EU regulation 1272/2008 and the additional considerations described in Chapter 1). However, the repetitive statements have been deleted and replaced by an explanation at the beginning of section 2.4. Unless mentioned otherwise, maternal toxicity data have not been included in the papers.
One of the references proposed for inclusion was added. The other references suggested are reviews. The Committee bases classification and labelling of substances for reproductive toxicity on primary publications. Therefore, the reviews were only used as a source of missed references relevant for this purpose, if any. None were found.
Furthermore, your remarks led to a variety of improvements throughout the report. Some of the wording has been left unchanged, however, because it has been taken from the EU regulation. An example is 'effects on or via lactation'.

The final advisory report *All-trans retinoic acid* was published on the website of the Health Council (www.healthcouncil.nl) on June 10, 2020. This letter and your comments can also be found there.

Best regards,

P.W. van Vliet, Ph.D.
Scientific Secretary