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## Request for advice

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Date of request: March 13, 2001. Reference: ARBO/AMIL/01 14479.

Dear sir,

Various studies indicate that there is a link between working with (aromatic) solvents and reduced fertility. A report to that effect emerged in 1999, resulting in some media consternation as well as questions in parliament. In my answers to these questions (TK 1326, 1998-1999), I indicated that I would ask the Health Council for an advisory report on this problem.

### **Background**

In 1999, the publication of a Dutch study generated concern about the possible harmful effects on fertility and on employees' children of occupational exposure to organic (aromatic) solvents. This study<sup>\*</sup> showed that there was a correlation, in men attending fertility clinics with fertility problems, between the quality of sperm and working with certain organic (aromatic) solvents.

In addition to the study in question, the last decade has also seen international research into the link between working with solvents and reduced fertility, particularly in men. For the time being, the available data does not seem to result in a clear picture. Positive findings in one study are contradicted by negative results in another. Virtually all the studies concern exposure to complex mixtures of substances.

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\* Occupationally Related Exposures and Male Reproductive Function, E. Tielemans, University of Utrecht, 1999.

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There is a shortage of concrete data showing that individual solvents can affect fertility. Recently, your Council's Committee for Compounds Toxic to Reproduction initiated, pursuant to the reports referred to above and at my request, individual assessments of a number of solvents in widespread use. The purpose of these assessments was to determine the toxic effects of the solvents on reproduction (the substances in question were toluene, xylene, styrene, trichloroethylene and tetrachloroethylene) on the basis of the European Union criteria. However, it proved awkward to classify the solvents according to compound on the basis of human data since exposure mainly involves mixtures of these solvents.

The epidemiological reports of possible detrimental effects on fertility as a result of exposure to organic solvents should, as such, be taken seriously. However, combining these reports with toxicological data about individual substances does not, for the time being, point in any definite direction. I would like the Health Council to provide an assessment of the consistencies and inconsistencies in the scientific data and to provide an overview of the gaps and uncertainties it finds in the field in question. If the Health Council finds that there is cause for concern about the link between occupational exposure to solvents and damage to fertility, this could be a reason for extending the current strategy for the reduction of occupational exposure to organic solvents – which is based on the neurotoxic effects of these compounds – to include the risk relating to damage to fertility. As you are aware, the Ministry of Social Affairs and Employment has been engaged in an active approach to the prevention of organic psychosyndrome (OPS) for a number of years now. This occupational disease is caused by occupational exposure to organic solvents. In the context of this prevention policy, sectors in which solvents are used and in which there is a high risk of OPS are now subject to statutory requirements in order to reduce exposure to solvents. The aim of limiting peak exposures in response to your recent advisory report on this issue<sup>\*</sup> fits in with this strategy. A request for an advisory report on this subject has now been submitted to the Social and Economic Council.

The policy of the Ministry of Social Affairs and Employment therefore focuses on the avoiding as far as possible the presence of harmful concentrations of solvents in the workplace. Your advisory report will make it clear whether this strategy is adequate to deal with any existing or suspected threat to fertility from organic solvents or whether additional policy measures are required. An example of the latter is the reevaluation, where necessary, of existing standards for organic solvents which do not include data about the possible toxic effects on reproduction.

### **Request**

I therefore request your Council to formulate answers to the following questions:

- 1 What is the view of the Health Council with respect to the 'power' of the epidemiological link between damage to fertility and occupational exposure to solvents on the basis of the existing scientific literature?

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\* Peak exposures to organic solvents, Health Council, 1999/12.

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- 2 If the Health Council considers an epidemiological link of this kind to be plausible, can this link be explained on the basis of the mechanism of action of the compounds in question? In other words, does the Council find a *causal* link plausible?
- 3 If an epidemiological or causal link is plausible, is it possible to state with some degree of certainty when a link of this kind is present or absent in the case of specific organic solvents (or groups of solvents)?
- 4 What are the uncertainties/gaps in scientific knowledge in the answers to questions 1 to 3?
- 5 In the opinion of the Health Council, what kinds and levels of precautions should these uncertainties result in, given the observed effects? I am thinking in particular of your opinion with respect to the level of protection provided by existing limit values from the point of view of effects on fertility as well as possible gaps in the prevailing system for the classification of individual compounds as toxic for reproduction. This latter issue should be considered in the light of the fact that, in practice, exposure almost exclusively involves mixtures of solvents.

Yours faithfully,

The State Secretary of Social Affairs and Employment,

(signed)

J.F.Hoogervorst

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Date of request: March 21, 2005. Reference: ARBO/P&G/2005/17432.

Dear Prof. Knottnerus,

In March 2001, I sent you a letter (ARBO/AMIL01 14479) containing a request for advice with respect to the issue of solvents and fertility.

Recent epidemiological studies\* have produced data which strongly suggests that exposure to solvents has additional effects, namely physical and mental abnormalities in painters' offspring. The classification (with regard to reproduction toxicity) of some solvents also pointed in this direction, a finding that was supported by epidemiological studies. I would appreciate it if you would incorporate these effects in the above-mentioned advisory report that is to be dealt with by your council, employing the same five questions that were put forward in connection with the relationship with fertility.

Additional questions:

- researchers have estimated that the average level of exposure is below current MAC values. Do current MAC values offer sufficient protection against effects on offspring? Is there any new information that sheds a different light on the established MAC value? Could continuous low-level exposure account for the observed effects?
- are the identified effects related to peak exposure, as indicated on several occasions by the same researchers with regard to exposure to inhaled anaesthetics?

As previously stated, I would appreciate it if this request for advice could be dealt with as a matter of great urgency. Please send me details of the projected delivery date of this advisory report.

Yours sincerely,  
the State Secretary of Social Affairs and Employment  
(signed)  
(H.A.L. van Hoof)

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\* Press conference on February 23, 2005, Study by Hooiveld and Roeleveld, Radboud University Nijmegen Medical Centre. Data presented on that occasion. Study report not available, submitted for publication

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