

The Director General

Maisons-Alfort, 16 June 2010

OPINION

of the French Agency for Environmental and Occupational Health Safety

"Assessment of the risks following occupational exposure to ethanol "

AFSSET's mission is to contribute to environmental and occupational health and safety and to assess the potential health risks.

It provides the competent authorities with full information on these risks, and with the expertise and technical support required for developing legislative and regulatory provisions and implementing risk management measures (Article L.1336-1 of France's Public Health Code).

In this context, AFSSET was asked on 9 February 2007 by the Directorate General for Health, the Directorate General for Risk Prevention and the Directorate General for Employment to evaluate the health risks of exposure to ethanol by inhalation and dermal exposure.

Presentation of the question

For each of these routes, AFSSET was asked to suggest appropriate measures to reduce any carcinogenic, mutagenic and reprotoxic risks that might be established and to consider the possibility of using substitutes for ethanol. The request specified that particular attention should be paid to reprotoxic risks for pregnant women of childbearing age.

AFSSET received an additional request on 16 May 2007 from the Directorate General for Health, the Directorate General for Risk Prevention and the Directorate General for Employment to assess the exposure of nursing professionals to alcohol-based hand sanitizers bearing in mind the volatility of ethanol.

This expert assessment addresses the first phase of the request relating to ethanol-related occupational risks, including in healthcare situations. An assessment of the risks to the general public will be carried out at a later date.

Context

In October 2006, the French National Research and Safety Institute (INRS) submitted a proposal for a standardised European classification of ethanol as a Category 1 or 2 (risk phrase R45¹) carcinogenic substance, a Category 2 (risk phrase R46²) mutagenic substance, and a Category 1 (risk phrases R60 and R61³) toxic substance likely to affect reproduction (and development).

It is hoped that the conclusions of the AFSSET risk assessment will clarify on the one hand the French position concerning the use of alcohol-based hand sanitizers, which is encouraged both by the World Health Organisation and by the French Ministry of Health (especially in health care institutions and as a measure for fighting pandemics), and on the other the relevance of discussing a standardised classification of ethanol at European level.

Organisation of the expert assessment

The expert assessment was carried out in a manner consistent with the French NF X 50-110 standard relating to "Quality in expert assessment – general requirements of competence for an expertise activity (May 2003)" with the intention of complying with the following points: competence, independence, transparency and traceability.

These issues fall within the remit of the committee of specialised experts (CES) on "Evaluation of risks related to chemical substances". AFSSET entrusted the appraisal to the work group "Evaluation of the risks of ethanol". The work was submitted periodically to the CES for consideration of both its methodological and scientific aspects and the conclusions were presented during the session held on 28 May 2009 and approved by the CES on "Evaluation of risks related to chemical substances".

This assessment has therefore been produced by a group of complementary experts.

The scientific aspects of this Opinion are based on the final report of this collective expert assessment on "Evaluation of ethanol-related risks to the working population", submitted in September 2009, as approved by the committee of specialised experts at its session of 28 May 2009.

Opinion (and recommendations where requested)

The results of the collective expert assessment indicate that:

- ▶ Concerning the evaluation of the effects of ethanol following exposure by inhalation or dermal exposure

The ethanol absorbed is found in the blood in proportions that vary depending on the route of exposure.

Numerous epidemiological and toxicological studies show that the consumption of alcoholic beverages increases the risk of cancer. Harmful effects on reproduction and development, the liver and the central and peripheral nervous system have also been observed.

These effects can be observed after ingestion of 10 g of ethanol per day (i.e. the equivalent of one glass of wine), which leads to a high level of blood ethanol concentration (ethanolaemia peak).

No ethanolaemia peak is observed following inhalation. Exposure at very high atmospheric concentrations of ethanol would be necessary, which is not the case in occupational exposure situations. It is therefore not possible to observe the toxic effects found in people who have recently ingested alcoholic beverages following occupational exposure by inhalation.

¹ R45: "May cause cancer"

² R46: "May cause genetically inherited damage"

³ R60: "May impair fertility"; R61: "May harm the unborn child"

Furthermore, the few studies that have been carried out on animals concerning the absorption of ethanol by inhalation do not show any effect on reproduction or development.

The amount of ethanol passing through the skin may be considered as negligible (even during the use of alcohol-based hand sanitizers). Indeed, on healthy skin, about 1% of the dose of ethanol initially placed on the surface actually penetrates the skin barrier. The amount is thus negligible when compared to pulmonary absorption, which is estimated at 60%.

In the current state of knowledge, the toxic effects of ethanol, related to chronic exposure by inhalation or dermal exposure, have not been documented in humans.

- ▶ Concerning the characterisation of occupational exposure to ethanol (and particularly the modes and intensity of this exposure)

In the absence of a job exposure matrix, exposure in the workplace was characterised on the basis of bibliographic research and analysis of the data contained in the SEPIA and COLCHIC databases maintained by the INRS. This information was completed by a sectorial study carried out by the National Union of Alcohol-Distillers Groups (UNGDA), a questionnaire survey carried out jointly by AFSSET and UNGDA, and the results of the SUMER survey (2003).

According to all the data thus collected, ethanol is found in a large number of products likely to be used in professional situations. Paints, varnishes and inks, alcohol-based sanitary products and biofuels are among those with the largest documented tonnages.

It is thought that occupational exposure related to the inhalation of ethanol concerns more than 650,000 people in France (in the agricultural, industrial and healthcare environments).

The intensity of occupational exposure is currently evaluated by measuring atmospheric concentrations of ethanol. Whether estimated or measured, these fall mostly between 95 mg.m⁻³ and 300 mg.m⁻³. A wide range of occupations is concerned. The mean values of the measurements taken in occupational sectors covered by France's general health insurance system are 51 mg.m⁻³, taken over 8 hours, and 547 mg.m⁻³ over 15 minutes⁴.

The data contained in the INRS COLCHIC database suggests that about 2600 employees covered by the general health insurance system are exposed to levels higher than the Time Weighted Average (TWA) for ethanol (1900 mg.m⁻³, over 8 hours) during a working day. Some occupational situations exceed the Short Term Exposure Limit (STEL) for ethanol (9500 mg.m⁻³ over 15 minutes) in the industrial distillation sector.

Concerning workers in the agricultural sector, exposure occurs occasionally and seasonally. Jobs such as filling, topping up or emptying containers of wine or spirits are particularly concerned. In certain specific jobs such as cleaning maceration tanks, atmospheric concentrations of ethanol can exceed the MEL for ethanol, set at 9500 mg.m⁻³ over 15 minutes and intended to protect workers from the possible effects of peak exposure levels.

Concerning health care professionals, exposure occurs daily, especially because of the use of alcohol-based sanitary products. Current data show that it is not possible to find any significant increase in ethanolæmia in employees using these products.

⁴ Source of the data: COLCHIC database

Furthermore, the experts chose to estimate ethanol levels after the use of alcohol-based sanitary products and exposure in the winemaking and distillery sector, after a working day, by modelling⁵. The results obtained indicate that estimated ethanol levels of occupational origin are of the same order of magnitude as endogenous ethanolaemia⁶ (endogenous ethanolaemia levels are between 0 and 35 mg.L⁻¹ with a mean value of 1.1 mg.L⁻¹).

- ▶ Concerning the evaluation of health risks

Whereas:

- there is no documentation about the consequences of chronic exposure to ethanol in humans by inhalation or dermal exposure;
- no animal studies concerning the absorption of ethanol by inhalation have established any effects on reproduction or development;
- there are no animal studies evaluating carcinogenic effects following the absorption of ethanol by inhalation and dermal exposure;
- the extrapolation of data obtained for ingestion to inhalation or dermal exposure is not judged to be pertinent (particularly regarding differences in toxicokinetic profiles);

... it is not possible to achieve a quantitative risk assessment for long term exposure by inhalation or dermal exposure. With regard to the current state of available knowledge and the modelling carried out, the expert assessment was unable to establish a health risk specifically related to exposure by inhalation or dermal exposure in the work environment.

- ▶ Concerning the identification of occupational risks associated with ethanol and appropriate measures to reduce these risks

In companies, the ethanol-related risks that are best known and treated most seriously are fire and the consumption of alcoholic beverages.

Indeed, the fact that ethanol is currently classified and labelled as an inflammable substance means that the evaluation of the risks of ethanol in the work environment mainly leads to setting up preventive measures against the risk of fire (such as limiting loss of ethanol by evaporation or spillage in application of the ATEX and SEVESO Directives). It should be noted that when these measures are implemented they also contribute to limiting atmospheric concentrations of ethanol and, as a consequence, the exposure levels of workers.

- ▶ Concerning the possibilities of substitution

With the exception of certain industrial sectors (such as the production of alcoholic beverages, the cosmetics industry, the food flavours and fragrances industry, etc), it is technically possible to find substitutes for ethanol in most products for professional use. The wide variety of

⁵ The following five scenarios were considered:

- rubbing the hands 42 times with an alcohol-based solution, over a period of eight hours, interrupted by a one-hour lunch break,
- rubbing the hands 42 times with alcohol at 60°, over a period of eight hours, interrupted by a one-hour lunch break,
- a working day spent cleaning a vinification tank (*décuvage*), interrupted by a one-hour lunch break
- a working day in a wine cellar spent topping up vinification barrels (*ouillage*), interrupted by a one-hour lunch break
- a working day filling barrels with alcohol at 40° (*entonnage*), interrupted by a one-hour lunch break

⁶ Quite apart from the absorption of alcoholic beverages, small quantities of ethanol are synthesised by the body during the process of breaking down sugars contained in food.

substitute products matches the numerous properties of ethanol. However, it should be remembered that industrialists already massively use ethanol (which has no toxicity labelling) to replace certain substances identified as being dangerous to health.

In the light of these results, AFSSET concludes that:

Neurotoxic, carcinogenic or reprotoxic effects of ethanol have been very well documented for ingestion. Symptoms of inebriation, related to acute occupational exposure to high concentrations of ethanol vapour, cannot be excluded. They are listed as an occupational disease.

However, the ethanol hazard described in this expert assessment should be taken into account when classifying and labelling it.

It would thus be beneficial to take into account the negative effects related to ethanol (carcinogenic, mutagenic and reprotoxic) for the prevention of occupational hazards, by raising awareness of danger in the workplace, beyond the risk related to the chemical/ **physical** properties of ethanol. It would furnish greater leverage for the application of preventive measures in the workplace such as the evaluation of exposure levels at different posts, limiting exposure and the use of protective equipment.

It could result in the enforcement of more specific measures to inform workers about the reprotoxic effects and the possibility of temporarily changing jobs during pregnancy (measures that have already been implemented in some companies).

AFSSET recommends:

- that the pertinence of the occupational exposure limit values for ethanol be re-examined in the light of the scientific knowledge acquired since 1982, particularly as concerns the neurotoxic effects (acute toxicity);
- that classification of the dangers of ethanol be updated in accordance with procedures currently in force;
- undertaking individual measurement campaigns among the producers of raw ethanol and in the winemaking sector in order to characterise exposure levels in these sectors;
- performing experimental studies for a precise evaluation of the chronic risks of low doses of ethanol and the mechanisms of action;
- encouraging the study of the mechanisms leading to the presence of endogenous ethanolaemia, in order to improve assessment of ethanol-related risks.

Finally, AFSSET wishes to emphasise that:

- the inflammable nature of ethanol already obliges companies to apply risk prevention measures in the workplace that are applicable to dangerous chemical agents and particularly to implement technical and organisational measures to limit exposure to a minimum (see Article R.4412-11 of France's Labour Law);
- in the light of the data currently available and in the absence of proven occupational risk, there is no justification for systematically replacing ethanol with substitute products in the workplace;
- the implementation of the REACH Directive should lead to more complete knowledge of exposure to ethanol.

Signed in four copies,

The Director-General

Martin GUESPEREAU