

The Director General

Maisons-Alfort, 10 November 2011

OPINION

of the French Agency for Food, Environmental and Occupational Health & Safety

concerning the proposal for occupational exposure limits for chemicals

Assessment of health effects and methods for measuring workplace exposure for acrylamide [CAS no.: 79-06-1]

ANSES undertakes independent and pluralistic scientific expert assessments.

ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.

It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are made public.

This ANSES Opinion incorporates the expert appraisals conducted by AFSSET. ANSES became legally operational on 1 July 2010 following the promulgation of the Ministerial Order dated 8 January 2010 enacting its creation, and adopted the missions and knowledge of AFSSET and AFSSA.

On 12 June 2007, AFSSET received a solicited request from the French Directorate General for Labour to conduct the scientific expert appraisal work required for setting occupational exposure limits (OELs) for approximately twenty substances including acrylamide.

1. BACKGROUND AND PURPOSE OF THE REQUEST

Under a Circular¹, France has established an indicative 8h-OELV of 0.3 mg.m⁻³ (0.1 ppm) for acrylamide.

The European scientific committee in charge of undertaking the expert appraisal on occupational exposure limits for chemical agents (SCOEL) submitted an expert appraisal report on acrylamide twice consecutively for comments:

- a first report² recommended an 8-hour limit value of 0.01 mg.m⁻³ to prevent the neurotoxic effects of acrylamide;
- a revised document³, which considered acrylamide to be a non-threshold genotoxic substance, in which the SCOEL refrained from recommending any OELs.

¹ DRT Circular no. 95-4 of 12 January 1995 amending and supplementing the Circular of 19 July 1982 as amended, on the acceptable values for concentrations of certain hazardous substances in workplace atmospheres

² SCOEL/SUM/139 February 2008 for public consultation

³ SCOEL/SUM/139 May 2009 for public consultation

2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with the French standard NF X 50-110 "Quality in Expertise – General Requirements of Competence for Expert Appraisals (May 2003)".

The collective expert appraisal was undertaken by the Expert Committee on expert appraisal for recommending occupational exposure limits for chemical agents (OEL Committee). It appointed several rapporteurs (three experts from the OEL Committee and two officers from the Agency) to carry out the expert appraisal work.

The scientific aspects of this Opinion are based on the report entitled "Collective expert appraisal for setting occupational exposure limits for chemical agents" on the assessment of health effects and methods for measuring workplace exposure for acrylamide (June 2011, available in French only). This report was approved by the OEL Committee in its session of 10 June 2010 and was amended on 14 June 2011⁴.

3. ANALYSIS AND CONCLUSIONS OF THE EXPERT COMMITTEE

Considerations to be taken into account when setting OELs

In accordance with the conclusions of the collective expert appraisal report on the "**Assessment of health effects and methods for measuring workplace exposure for acrylamide**", the OEL Committee considers that acrylamide should be regarded by default as a non-threshold carcinogen for the following reasons:

- the European classification of the substance as a Category 2 carcinogen⁵ and the IARC classification of the substance as a Group 2A carcinogen⁶;
- the carcinogenic effects evidenced in several animal species;
- the numerous studies reporting mutagenic and/or genotoxic potential, which while low for acrylamide, is non-negligible for its primary metabolite glycidamide;
- the lack of a clearly explained mechanism of action.

The OEL Committee advises risk managers to refer to this assessment of additional individual risk of cancer for the setting of the 8-hour occupational exposure limit value of acrylamide.

⁴ After an error was detected in the formula for calculating excess risk, this report and the conclusions of the collective expert appraisal were amended on 14 June 2011 by the Expert Committee on expert appraisal for recommending occupational exposure limits for chemical agents to correct this calculation error.

⁵ Substances which should be regarded as carcinogenic to humans. Sufficient information is available to justify a strong presumption that human exposure to such substances can cause cancer

⁶ The agent (mixture) is probably carcinogenic to humans

To estimate the additional lifetime risk of cancer in humans in occupational conditions, the OEL Committee took the following into account:

- the identification of multi-site cancers (endocrine glands and other organs) in rats based on data taken from animal studies [Johnson *et al.* (1986) and Friedman *et al.* (1995)];
- the selection of testicular mesothelioma as the critical effect since it is the effect that has the most clearly established dose-response relationship and can be extrapolated to workers;
- the use of the benchmark dose method for making calculations to choose the model that is best suited to the available data on animals;
- the application of an allometric conversion factor to extrapolate animal data to humans;
- the extrapolation of oral exposure to inhalation based on the available information in the literature and international consensuses.

The following exposure scenario for workers was used: a lifetime of 75 years, with acrylamide exposure of 8 hours per day, 5 days per week and 48 weeks per year for 40 years.

Using an estimated BMDL (10%) for workers of 0.5 mg.m^{-3} as the starting point and considering linear extrapolation, the additional lifetime risk of cancer under conditions of occupational exposure is:

10^{-4} individual excess risk for 40 years of exposure to $4 \text{ }\mu\text{g.m}^{-3}$

10^{-5} individual excess risk for 40 years of exposure to $0.4 \text{ }\mu\text{g.m}^{-3}$

10^{-6} individual excess risk for 40 years of exposure to $0.04 \text{ }\mu\text{g.m}^{-3}$

These values are the reference values that the OEL Committee is recommending to risk managers for the setting of an OELV.

In comparison, even though it did not use precisely the same assumptions, the risk assessment undertaken by DECOS⁷ in 2006 led to the same result (10^{-4} individual excess risk for 40 years of exposure to $4 \text{ }\mu\text{g.m}^{-3}$).

Although the short-term effects of acrylamide exposure are numerous and have been described in several epidemiological studies (skin peeling on the palms, numbness of the limbs, fatigue, drowsiness, muscular weakness), the data were not deemed of sufficient quality to be able to recommend a short-term limit value (STEL) based on health considerations.

A "skin" notation should be assigned to prevent potential systemic effects. Indeed, there are quantitative data that indicate that skin exposure may substantially contribute to occupational exposure as compared to inhalation.

⁷ Dutch Expert Committee on Occupational Safety

Considerations to be taken into account when establishing a method for measuring exposure

Although three methods for measuring occupational exposure to acrylamide have been identified in the literature, the aerosol fraction sampled cannot be precisely determined due to the sublimation ability of this substance. Therefore, there are currently no validated measurement methods that are suitable for measuring occupational exposure levels in comparison with occupational exposure limit values.

The OEL Committee considers that the methods that are currently available should be improved in order to take into account the conventional fractions of acrylamide that is found both in vapour and aerosol form in workplace atmospheres.

4. THE AGENCY'S CONCLUSIONS AND RECOMMENDATIONS

In accordance with the conclusions of the Expert Committee on expert appraisal for recommending occupational exposure limits for chemical agents, ANSES recommends:

- **referring to this assessment of additional individual risks of cancer when setting the 8-hour occupational exposure limit value** for acrylamide;
- not exceeding, over a 15-minute period, a concentration equivalent to 5 times the 8h-OELV that will be established⁸ in order to limit exposure levels over short periods;
- assigning the **“skin” notation**.

Additional points

Further to this expert appraisal, ANSES considers that it is relevant to draw the attention of risk managers to the following points:

- like any risk assessment based on animal data, this assessment includes some uncertainties that are difficult to quantify:
 - uncertainties related to the model for the linear extrapolation of high doses (when effects have been observed) to low doses (actual exposure levels);
 - uncertainties related to the extrapolation of an effect (testicular mesothelioma) observed in animals (rats) to humans;
 - uncertainties related to the use of dose-response relationships established for oral exposure to predict those for inhalation;
 - uncertainties related to real exposure periods (use of an occupational scenario considering uninterrupted exposure to the indicated concentrations).
- several European countries have applied the recommendations of the ACGIH⁹ by establishing an 8h-OELV for acrylamide of 0.03 mg.m⁻³ (30 µg.m⁻³). When applying the linear model used in this expert appraisal, this value, which is currently recorded as the lowest in force, corresponds to an estimated individual excess risk of testicular mesothelioma of 2.10⁻³;
- although only a small number of measurements of acrylamide exposure were recorded from 2002 to 2008 in the INRS COLCHIC database, it should be noted that

⁸ For more details, refer to the collective expert appraisal report on setting occupational exposure limits for chemical agents of December 2008, on recommendations for occupational exposure limits intended to limit the size and number of exposure peaks over the working day (Part 1).

⁹ American Conference of Governmental Industrial Hygienists

these were primarily taken in the food processing industry, thus confirming that the high-temperature cooking of foods is a non-negligible source of both occupational and domestic exposure to acrylamide.

ANSES's conclusions

ANSES, by means of this collective expert appraisal, has provided several points that risk managers can use for the setting of occupational exposure limits for acrylamide.

ANSES would like to underline that:

- replacing carcinogenic substances with less harmful substances or processes should be a priority in the prevention of chemical risk;
- the ALARA¹⁰ principle should be applied in the presence of any substance that is considered a non-threshold carcinogen;

In addition, ANSES recommends:

- developing and improving current measurement methods for workplaces (particularly the INRS¹¹ Métropol method) so as to have a validated method for measuring occupational exposure levels in comparison with occupational exposure limit values;
- continuing this expert appraisal work by developing biological reference values for acrylamide in order to improve the prevention of chemical risk in the workplaces.

The Director General

Marc Mortureux

¹⁰ As Low As Reasonably Achievable

¹¹ Institut National de Recherche et de Sécurité (French National Research and Safety Institute)