

COLLECTIVE EXPERT APPRAISAL: **SUMMARY AND CONCLUSIONS**

Regarding the “expert appraisal for recommending occupational exposure limits for chemical agents”

Assessment of health effects and methods for the measurement of exposure levels in workplace atmospheres for

Hexavalent chromium compounds

This document summarises and presents the work of the Expert Committee.

Presentation of the issue

On 12 June 2007, the French Agency for Environmental and Occupational Health Safety (AFSSET) received a formal request from the French Directorate General of Labour to conduct an expert appraisal with the aim of determining occupational exposure limit values for chromium VI compounds.

Background

In December 2004, the European Scientific Committee on Occupational Exposure Limits to Chemical Agents (SCOEL) published a report in which it concluded that hexavalent chromium compounds cause the following effects: irritation by inhalation, skin and respiratory sensitisation, nephrotoxicity and lung cancer.

The SCOEL focused its analysis on the carcinogenic effect, which was considered to be the most significant, and for which large quantities of human data are available.

To establish a dose-response relationship, the SCOEL used a meta-analysis (Steenland *et al.*, 1996) grouping 10 epidemiological studies in workers exposed to different hexavalent chromium compounds. The excess risk calculations from a linear no-threshold model gave the following cancer risks: from 5 to 28 additional lung cancer cases in a population of 1000 workers, for an occupational exposure of 50 µg of chromium VI/m³.

The General Directorate of Labour asked AFSSET to consider the SCOEL report and propose exposure limit values in occupational environments for hexavalent chromium compounds.

Organisation of the expert appraisal

AFSSET commissioned the Expert Committee (CES) on *expert appraisal for setting exposure limits for chemical agents in occupational environments* (OEL Committee), to investigate this formal request. The Committee then mandated four rapporteurs (three experts from the OEL Committee and an AFSSET officer) to conduct this expert appraisal.

The summary report on the health effects of hexavalent chromium compounds results from the work of several rapporteurs appointed by virtue of the skills required to investigate a dossier on a no-threshold effect carcinogenic substance in accordance with the OEL Committee's methodology. The rapporteurs reassessed the referenced source articles whenever they considered it necessary, or whenever the Committee requested it. The choice of a risk assessment model, as well as of all the epidemiological studies, was carefully reviewed.

The methodological and scientific aspects of the rapporteurs' work was regularly submitted to the CES. The reports produced reflect the additional comments and information provided by the other CES members.

This expert appraisal was therefore conducted by a group of experts with complementary skills. It was carried out in accordance with the French standard NF X 50-110 "Quality in Expertise Activities" to ensure compliance with the following points: competence, independence, transparency, and traceability.

Description of the method

1- For the assessment of health effects:

Analysis of the literature led to the conclusion that chromium VI and its compounds are genotoxic and mutagenic, and lead to carcinogenic effects.

The selected critical effect by inhalation is pulmonary tract cancer. Derivatives of chromium VI are substances for which there is no threshold of toxicity.

A no-threshold effect approach was used; the abundance of data in humans allowed various scientific teams and reference bodies to calculate the excess health risks for this critical effect in the occupational environment.

The OEL Committee selected the Painesville (Gibb *et al.*, 2000) and Baltimore (Luippold *et al.*, 2003) cohorts, because it considered them to be the ones with the best exposure data, and with the most specific for exposure to chromium VI. As is customary in any calculation of excess risk from epidemiological data, it discussed the limits of the extrapolations and particularly the uncertainties related to the actual exposure of workers, the models, the existence of a threshold, or the shape of the dose-response curve. The influence of factors such as smoking, age or the "healthy worker" effect, was also discussed, as well as the possibility of extrapolating the risk calculations based on a cohort of US workers in the chromium industry, to workers in other industry sectors.

2 - For the evaluation of methods for measuring exposure levels in the workplace

The summary report is based on a metrology data collection sheet, which lists and classifies the existing measurement methods available up to January 2009. The list of the main sources consulted is given in the corresponding report.

The OEL Committee adopted the following reports:

- the summary report assessing the health effects, at its meeting held on 18 June 2009,

- the summary report on methods for measuring exposure levels in the workplace, at the meeting held on 18 June 2009.

The OEL Committee adopted the summary and the conclusions of the collective expert appraisal on 17 September 2009.

Conclusions of the collective expert appraisal

The OEL Committee does not recommend the establishment of different occupational values according to the type and in particular the solubility of chromium VI components. A single value, valid for all chromium VI derivatives, should be considered. The health risk assessment proposed below therefore applies to all types of chromium VI.

To the extent that, according to the currently available data, it does not seem possible to identify any health effect thresholds (particularly with regard to the proven carcinogenicity in humans of hexavalent chromium derivatives), the OEL Committee considers that the toxicity of these derivatives occurs through a non-threshold mechanism of action, with lung cancer being selected as the critical effect.

Given that the available data on carcinogenicity are sufficient to derive a dose-response relationship at low doses and associate them with excess risks, the Committee has chosen not to recommend occupational exposure limit values for hexavalent chromium derivatives, but to assess the additional individual risk of death by lung cancer.

The excess risk calculation from the upper interval from the OSHA estimate, obtained from the Gibb cohort of workers, has been used for the following reasons:

- The estimates made from these calculations are considered solid, since they were verified by the NIOSH and the chromium industry, and gave substantially the same results.
- Smoking data were taken into account in order to minimise the influence of this confounding factor.
- The reference population chosen to apply this model was the Baltimore cohort, using the best and most specific exposure data in relation to exposure to chromium VI and its derivatives;
- The study of the Gibb cohort at the origin of the risk calculations was financed by public funds (US EPA), and the many measurements allowed the establishment of a job-exposure matrix.
- the exposure scenario is the one typically considered in calculating risk for the occupational population (8 hours a day, 5 days a week, 240 days a year, for 45 years, from the age of 20 to 65, with cumulative exposure) and the results are expressed as "whole life" risk.

The linear model (excess relative risk) was chosen as it best fits the data. The Committee conducted a linear extrapolation passing through the origin by considering, as a starting point, a concentration of $1\mu\text{g CrVI}/\text{m}^3$ associated with a risk of 10 additional cases of cancer for 1000 workers, by approximation of the OSHA results on the Gibb cohort. The following results were obtained:

- $0.1\mu\text{g CrVI}/\text{m}^3$ for an individual excess risk of death from lung cancer of 10^{-3}
- $0.01\mu\text{g CrVI}/\text{m}^3$ for an individual excess risk of death from lung cancer of 10^{-4}

The OEL Committee considered it more prudent not to give an estimate for lower exposure levels, since approximations made to express the individual excess risks at 10^{-5} and 10^{-6} are too large in relation to the original calculations.

However, the OEL Committee stresses that when an adjustment is made to the exposure durations, these values are consistent with those given by various organisations such as the OEHHA, the WHO or the US EPA for exposure in the general population.

No studies have established a threshold effect for acute exposure to chromium VI derivatives. However, some data in the literature report respiratory irritation as from $1.3 \mu\text{g CrVI/m}^3$ and nasal perforations after repeated exposure to peaks of chromic acid (concentration equivalent to $10 \mu\text{g CrVI/m}^3$). The short-term exposure value should be determined not only in line with the selected OELV, but also taking into account the effects mentioned above.

The "skin" notation must be retained because, for some chromium VI derivatives, quantitative elements allowed the calculation of a contribution by the dermal route of well over 10% for exposure levels corresponding to the limit value recommended by the NIOSH during the drafting of the report (REL-TWA= $1 \mu\text{g/m}^3$) and at the highest risk level calculated by the CES: 10^{-3} . Furthermore, certain forms of chromium VI are irritating to the skin and can lead to skin sensitisation.

The recommended methods for exposure measurement are those that recommend a sampling of the inhalable fraction, and sequential extraction, first of the soluble hexavalent chromium compounds in a pH 8 buffer solution, then the insoluble compounds undergo heated ultrasonic extraction using a strong basic solution, and finally an analysis by ion chromatography with colourimetric detection of the derivative with diphenylcarbazide.

The NIOSH 7605 and OSHA ID 215 (V2) methods can be adapted to include the above recommendations.

ISO 16740 (although its presentation is relatively confused) contains sufficient details of the different stages of extraction and analysis recommended above, to provide a satisfactory experimental protocol by selecting the options.

The MétroPol 84 protocol (new version - September 2008) meets the requirements for sample preparation and its sensitivity is satisfactory for an OELV lowered to $1 \mu\text{g/m}^3$ with the ion chromatography analysis method.

If the recommended OELV is set below a chromium IV concentration of $1 \mu\text{g/m}^3$, the quantification limits of the methods mentioned make their application inadequate.

Finally, the Committee reiterates that:

- the ALARA¹ principle must be applied in the presence of a non-threshold carcinogenic substance:
- as the available data do not allow determination of a STEL, it is recommended not to exceed concentrations corresponding to five times the 8h OELV over 15-minute periods² in order to limit the magnitude of exposure levels for short exposure times.

¹ As Low As Reasonably Achievable

Maisons-Alfort, 17 September 2009

On behalf of the experts of the Committee
François Paquet,
Chairman of the Committee

² For more information, please consult the collective expert appraisal for setting occupational exposure limit values for chemical agents of December 2008, regarding recommendations on occupational exposure limit values intended to limit the size and number of exposure peaks over the working day (Part 1).