COLLECTIVE EXPERT APPRAISAL: SUMMARY AND CONCLUSIONS

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

concerning the assessment of measurement methods for the substances listed in the appendix of the European Directive (EU) 2017/2398

This document summarises the work of the Expert Committee on Health Reference Values (HRV Committee) and of the Working Group on Metrology.

Presentation of the issue

Prior to the transposition of European occupational exposure limits (OEL) into French law, ANSES is mandated by the Ministry of Labour to conduct an assessment of the measurement methods available for the substances listed in the European Directives.

Scientific and legal background

European objectives, intended to protect workers from risks associated with exposure to chemical agents, are set via European directives, in particular in the form of occupational exposure limits (OELs).

Since the European Commission relies on recommendations issued by European scientific expert committees (SCOEL[1] or RAC[2]) for the establishment of European OELs, ANSES does not reassess the health effects of the substances in question when European directives establishing OELs are published.

However, given that neither SCOEL nor RAC undertakes in-depth assessments of the available measurement methods with regard to the European OELs, ANSES is asked to undertake these assessments so that the French Ministry of Labour can have all of the information necessary to establish the binding or indicative nature of the limit values in national law.

Directive (EU) 2017/2398 of the European Parliament and of the Council of 12 December 2017, amending Directive 2004/37/EC, establishes a list of binding occupational exposure limit values for 11 new carcinogens and mutagens[3].
Four of these 11 substances were covered by previous expert appraisals undertaken by ANSES to establish OELs and recommend measurement methods associated with these OEL

[1] SCOEL: Scientific Committee on Occupational Exposure Limits
[2] RAC: Committee for Risk Assessment
[3] Earlier, Directive 2004/37/EC established binding OELs for hardwood dusts, benzene and vinyl chloride monomer. The 11 new carcinogens and mutagens for which binding European OELs have been introduced are as follows: respirable crystalline silica dust, ethylene oxide, 1,2-epoxypropane, acrylamide, 2-nitropropane, o-toluidine, hydrazine, bromoethylene, 1,3-butadiene, chromium (VI) compounds, and refractory ceramic fibres.

proposals. These were hexavalent chromium and its compounds (ANSES, 2010), refractory ceramic fibres (AFSSET, 2009), 1,3-butadiene (ANSES, 2011) and acrylamide (ANSES, 2011). Thus, the measurement methods for these compounds were not reassessed as part of this expert appraisal, since they are already available.

As part of the memorandum of understanding on occupational exposure limits and biological limit values (OELs and BLVs) established between the Ministry of Labour and ANSES, the Directorate General for Labour (DGT) mandated ANSES to undertake the metrological expert appraisal for the following substances only:

- 1,2-epoxyethane (or ethylene oxide) (8h-OEL of 1 ppm, i.e. 1.8 $mg.m^{-3}$),
- 1,2-epoxypropane (8h-OEL of 1 ppm, i.e. 2.4 $mg.m^{-3}$),
- 2-nitropropane (8h-OEL of 5 ppm, i.e. 18 $mg.m^{-3}$),
- o-toluidine (8h-OEL of 0.1 ppm, i.e. 0.5 $mg.m^{-3}$),
- hydrazine (8h-OEL of 0.01 ppm, i.e. 0.013 $mg.m^{-3}$),
- bromoethylene (8h-OEL of 1 ppm, i.e. 4.4 $mg.m^{-3}$).

Organisation of the expert appraisal

ANSES entrusted examination of this request to the Expert Committee on Health Reference Values (HRV Committee). The Agency also mandated the Working Group on Metrology.
The methodological and scientific aspects of the work of this group were regularly submitted to the Expert Committee.
This report has been prepared from metrology reports developed individually for each substance by the Working Group on Metrology. The Working Group reports take into account the additional observations and informations provided by the members of the HRV Committee.
In light of the question asked, the HRV Committee did not examine the relevance of the values laid down by the Directive.
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”.

Description of the method

An assessment report of the measurement methods was prepared by the Working Group on Metrology for each substance and submitted to the HRV Committee, for comments and validation.

Each assessment report presents the various protocols for measuring the respective substance in workplace atmospheres grouped together based on the methods they use. These methods were then assessed and classified based on the performance requirements set out particularly in the French Standard NF EN 482: "Workplace atmospheres - General requirements for the performance of procedures for the measurement of chemical agents" and the decision-making criteria listed in the methodology report (ANSES, 2017).
A list of the main sources consulted is detailed in the methodology report (ANSES, 2017).

These methods were classified as follows:

- Category 1A: the method has been recognized and validated (all of the performance criteria in the NF-EN 482 Standard are met);
- Category 1B: the method has been partially validated (the essential performance criteria in the NF-EN 482 Standard are met);
- Category 2: the method is indicative (essential criteria for validation are not clear enough);
- Category 3: the method is not recommended (essential criteria for validation are lacking or inappropriate).

A detailed comparative study of the methods in Categories 1A, 1B and 2 was conducted with respect to their various validation data and technical feasibility, in order to recommend the most suitable method(s) for measuring concentrations for comparison with OELs.

This overall report was prepared from metrology reports developed individually for each substance. The details concerning the adoption of each measurement method assessment report are given in the following table.

Table 1: Adoption dates of the individual reports by the Working Group on Metrology and by the HRV Committee

Substance		Adoption date	
Name	**CAS number**	**By the WG**	**By the HRV Committee**
bromoethylene	593-60-2	17/05/2018	03/05/2018
2-nitropropane	79-46-9	26/03/2018	03/05/2018
hydrazine	302-01-2	16/10/2018	29/11/2018
1,2-epoxypropane	75-56-9	03/12/2018	25/01/2019
o-toluidine	95-53-4	03/12/2018	25/01/2019
1,2-epoxyethane	75-21-8	16/05/2019	13/06/2019

The overall report, as well as the summary and conclusions of the collective expert appraisal, were adopted by the HRV Committee on 13/06/2019.
This collective expert appraisal work and the summary report were submitted to public consultation from 05/09/2019 to 30/09/2019. The people or organizations that contributed to the public consultation are listed in appendix 7 of the report (only available in French). The comments received were reviewed by the Committee on Health Reference Values who finally adopted this version on the 28/11/2019.

Results of the collective expert appraisal

The Expert Committee on “Health reference values” (HRV Committee) adopted the collective expert appraisal work and its conclusions and recommendations, which are covered in the accompanying report, at its meeting of 28 November 2019 and informed ANSES’s General Directorate.

Conclusions and recommendations of the collective expert appraisal

The assessment of the applicable reference methods for the measurement of occupational exposure levels for the six substances, listed in Directive (EU) 2017/2398 and to be assessed in light of the values established therein, found that each of the six substances has at least one measurement method classified in Category 1B.
1,2-epoxyethane also has a measurement method classified in Category 1A.
The table below summarises the measurement methods recommended by the HRV Committee for each of the six substances.

Table 2: Measurement methods recommended by the HRV Committee

Identification of the substance		Principle of the recommended method		Implementation protocols (References)	Classification for 8h- OEL regulatory technical control	Additional information
Substance	**CAS number**					
bromoethylene	**593-60-2**	Active sampling on an active charcoal tube – Solvent desorption – GC/FID analysis	Active charcoal (400/200) Ethanol desorption	NIOSH 1009 (1994)	1B	The HRV committee recommends measuring bromoethylene by sampling on a tube containing active charcoal at a flow rate of 50 $ml.min^{-1}$. It should be noted that sampling effectiveness can be affected by the presence of other substances in air and that coelution is possible with bromine (Br_2). Given the toxicity of CS_2, the implementation of the method with ethanol desorption should be preferred (NIOSH 1009 protocol). Moreover, given the quantities to be trapped, the capacity of a 100/50 mg tube of active charcoal may be sufficient and would enable the volume of ethanol used for desorption to be reduced.
			Active charcoal (100/50) CS_2 + n-heptane desorption	OSHA ORG-08 (1979)		
2-nitropropane	**79-46-9**	Active sampling on an adsorbent tube Solvent desorption – GC/FID analysis	Chromosorb 106 Ethyl acetate desorption	OSHA 15 (1980) NIOSH 2528 (1994)	1B	To cover the range of 0.1 to 2*8h-OEL, with an 8h sample on Chromosorb 106, a flow rate of 0.0125 $L.min^{-1}$ is necessary. Regarding XAD 4 resin, to cover the range of 0.1 to 2*8h-OEL, two 4h samplings are necessary with a flow rate of 0.1 $L.min^{-1}$. Given the toxicity of CS_2, the implementation of the method with Chromosorb 106 and ethyl acetate desorption should be preferred.
			XAD 4 CS_2 desorption	OSHA 46 (1984)		
hydrazine	**302-01-2**	Active sampling on an impregnated filter Solvent desorption + derivatisation LC-UV analysis	Two glass fibre filters impregnated with sulphuric acid (Gelman 37 mm) Extraction: EDTA disodium Derivatisation: Benzaldehyde	OSHA ORG-108 (1997)	1B	Performing an 8-hour sampling at a flow rate of 1 $L.min^{-1}$

Table 2 : Measurement methods recommended by the HRV Committee (continued)

Identification of the substance		Principle of the recommended method		Implementation protocols (References)	Classification for 8h- OEL regulatory technical control	Additional information
Substance	**CAS number**					
1,2-epoxypropane	**75-56-9**	Active sampling on an adsorbent tube Solvent desorption GC/FID analysis	Anasorb 747 CS_2 desorption	OSHA 88 (1991)	1B	An 8h sample at a flow rate of 10 ml.min^{-1} is necessary to comply with the recommended maximum volume of five litres. Users' attention is drawn to the fact that the desorption solvent (CS_2) is classified as category 2 reprotoxic.
		Active sampling on an adsorbent tube Solvent desorption HBr derivatisation GC/ECD analysis	Active charcoal (400/200) Toluene/CS_2 (99/1) desorption	ZH 1-120-28E/2 (1994) BGI 505-28-02GC (1994)	1B	Given the constraints in terms of flow rate and sampling volume not to be exceeded, two successive 4h samples at a maximum flow rate of 2.4 L.h^{-1} are necessary. These conditions enable the range of 0.1 to 2*8h-OEL to be covered. Users' attention is drawn to the fact that the desorption solvents (toluene and CS_2) are classified as category 2 reprotoxic.
o-toluidine	**95-53-4**	Active sampling on a filter impregnated with sulphuric acid Solvent desorption + derivatisation GC/ECD analysis	Two glass fibre filters impregnated with sulphuric acid Toluene desorption Derivatisation: HFAA (heptafluorobutyric acid anhydride)	OSHA 73 (1988)	1B	Enables o-toluidine to be sampled in a mixed phase. Users' attention is drawn to the fact that the desorption solvent (toluene) is classified as category 2 reprotoxic
1,2-epoxyethane	**75-21-8**	Active sampling on an HBr-impregnated adsorbent tube Solvent desorption – GC/ECD analysis	HBr-impregnated Anasorb 747 (100/50 mg, SKC 226-178) Desorption: Acetonitrile/toluene	OSHA 1010 (2007)	1A	In light of the available data, sampling for eight hours at a flow rate of 25 mL.min^{-1} is recommended. Users' attention is drawn to the fact that the desorption solvent (toluene) is classified as category 2 reprotoxic
		Passive sampling on an HBr-impregnated absorbent material Solvent desorption – GC/ECD analysis	SKC 575-005 badge Desorption: methanol	SKC (2000)	1B	Regarding the other badges (3M 3551 and Assay Technology Chemdisk 555) that can be used when implementing this method, since most of the validation data are not available, it was not possible to assess their applicability in relation to the 8h-OEL.

Validation date of the summary by the Expert Committee: 28 November 2019.

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