

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 **di(2-ethylhexyl)phthalate (DEHP)** **[CAS no.: 117-81-7]**

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 undertaken 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 limit values (OELVs) for some twenty substances including di(2-ethylhexyl) phthalate (DEHP).

1. BACKGROUND AND PURPOSE OF THE REQUEST

Under a Circular¹, France has established an indicative 8h-OELV of 5 mg.m³ for DEHP.

The Directorate General for Labour asked the Agency to reassess this value and, if necessary, to propose new occupational exposure limits based on health considerations.

¹ Circular of 13 May 1987 supplementing the Annex to the Circular of 19 July 1982 on the acceptable values for concentrations of certain hazardous substances in workplace atmospheres

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 final report from this collective expert appraisal 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 DEHP (June 2010). This report was approved by the OEL Committee in its session of 10 June 2010.

3. ANALYSIS AND CONCLUSIONS OF THE EXPERT COMMITTEE

Considerations to be taken into account when setting OELVs

In accordance with the conclusions of the collective expert appraisal report on the "**Assessment of health effects and methods for measuring workplace exposure for di(2-ethylhexyl) phthalate (DEHP)**", the Expert Committee on expert appraisal for recommending occupational exposure limits for chemical agents recommends the following for DEHP:

- setting an **8 hour occupational exposure limit value (8h-OELV) of 0.8 mg/m³**.
The aim of this recommendation is to prevent potential harmful effects on fertility that may occur in the workplace. This value was determined based on a critical dose (NOAEL) identified in the study by David *et al* (2000) on oral exposure in rats. By extrapolation, the critical dose calculated for inhalation in rats was 7.6 mg.m⁻³. An uncertainty factor of 9 was applied to take into account inter-individual variability and route-to-route extrapolation (oral versus inhaled);

Critical effect	Critical dose	UF	8h-OEL by inhalation
Effects on fertility David <i>et al.</i> , 2000 Study on oral exposure in animals	Oral NOAEL for rats = 5.8 mg/kg/day <u>Route-to-route extrapolation</u> Assumptions: 100% absorption by inhalation in rodents and 75% bioavailability by inhalation in humans Inhalation NOAEL in rats = 7.6 mg.m⁻³ <u>Extrapolation to humans</u> Inter-individual variability	9: 3x3 UF _S 3 UF _H 3	 8h-OEL = 0.8 mg.m⁻³

- although the teratogenic and foetotoxic effects of DEHP have been established and justify the proposal of a short term limit value (STEL) to limit acute exposure to this substance, such a value cannot be recommended based on the data that are currently available. Indeed, the studies relating to these effects do not enable to

establish dose-response relationships for acute exposure. Therefore, it is recommended to not exceed 5 times the recommended 8h-OEL over a 15 minute period² (4 mg/m³) to limit exposure levels over short periods;

- not assigning the “**skin**” notation since there are quantitative data that suggest that dermal exposure does not substantially increase the body burden.

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

An analysis of the scientific literature shows that validated measurement methods are available for assessing occupational exposure. These methods, provided that the experimental protocols are adapted, should be capable of measuring the 8h-OEL of 0.8 mg.m⁻³.

Therefore, the Expert Committee recommends **the method of sampling with a sorbent tube and/or filter, solvent desorption, gas chromatography with flame ionisation detection.**

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 the following for DEHP:

- setting an **8-hour occupational exposure limit value of 0.8 mg.m⁻³**; the OEL Committee’s analysis of studies considered robust for establishing an OELV indicates that the recommended 8h-OEL should also prevent developmental effects;
- **not exceeding 5 times the 8h-OEL over a 15 minute period² (4 mg.m⁻³)** to limit exposure levels over short periods;
- not assigning the “**skin**” notation.

In accordance with the assessment of OEL measurement methods undertaken for DEHP, ANSES recommends the **method of sampling with a sorbent tube and/or filter, solvent desorption, gas chromatography with flame ionisation detection.**

Furthermore, the French Agency for Food, Environmental and Occupational Health & Safety would like to underline that:

- replacing DEHP (an agent with known reproductive toxicity) with less harmful substances or processes should be a priority in the prevention of chemical risk in France;
- the ALARA³ principle should be applied in the presence of this substance;

² 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).

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³ As Low As Reasonably Achievable

- pregnant and breastfeeding women should not be assigned to or maintained in workstations that are exposed to DEHP;
- workers should be informed of the recognised reprotoxic effects of DEHP (effects on fertility, teratogenic and foetotoxic effects) and this information should encourage women to declare their pregnancies as early as possible.

In addition, ANSES recommends continuing this expert appraisal work by developing biological reference values that may be used for the biological monitoring of exposure. These values would improve the French regulatory framework for preventing chemical risk in the workplace.

The Director General

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