COLLECTIVE EXPERT APPRAISAL: SUMMARY AND CONCLUSIONS

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

On the assessment of health effects and methods for the measurement of exposure levels in workplace atmospheres for lead and its inorganic compounds

This document summarises the work of the Expert Committees on "expert appraisal for recommending occupational exposure limits for chemical agents", on "health reference values" and the Working Group on "metrology"

This summary is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text of July 2017 shall prevail.

Presentation of the issue

On 11 March 2013, ANSES was requested by the Director General for Labour to conduct the expert appraisal work required for setting occupational exposure limit (OELs) for lead and its compounds. France currently has 8h-OEL[1] for lead and its compounds of 0.10 $mg.m^{-3}$. The Directorate General for Labour requested ANSES to re-assess this 8h-OEL and the biological limit values (BLV) for lead and its compounds (that is to say 400 $\mu g.L^{-1}$ for men and 300 $\mu g.L^{-1}$ for women) for lead in blood, and, if necessary, propose new occupational exposure limits based on health considerations.

Scientific background

The French system for establishing OELs has three clearly distinct phases:

- Independent scientific expertise (the only phase entrusted to ANSES);
- Proposal by the Ministry of Labour of a draft regulation for the establishment of limit values, which may be binding or indicative;
- Stakeholder consultation during the presentation of the draft regulation to the French Steering Committee on Working Conditions (COCT). The aim of this phase is to discuss the effectiveness of the limit values and if necessary to determine a possible implementation timetable, depending on any technical and economic feasibility problems.

[1] Art. R4412-149 of labour code

The organisation of the scientific expertise phase required for the establishment of OELs was entrusted to AFSSET in the framework of the 2005-2009 Occupational Health Plan (PST) and then to ANSES after AFSSET and AFSSA merged in 2010.

The OELs, as proposed by the Committee are concentration levels of pollutants in workplace atmospheres that should not be exceeded over a determined reference period and below which the risk of impaired health is negligible. Although reversible physiological changes are sometimes tolerated, no organic or functional damage of an irreversible or prolonged nature is accepted at this level of exposure for the large majority of workers. These concentration levels are determined by considering that the exposed population (the workers) is one that excludes both children and the elderly.

These concentration levels are determined by the experts of the Committee based on information available from epidemiological, clinical, animal toxicology studies, etc. Identifying concentrations that are safe for human health generally requires adjustment factors to be applied to the values identified directly by the studies. These factors take into account a number of uncertainties inherent to the extrapolation process conducted as part of an assessment of the health effects of chemicals on humans.

The Committee recommends three types of values:

- 8-hour occupational exposure limit (8h-OEL): this corresponds to the limit of the time-weighted average (TWA) of the concentration of a chemical in the worker's breathing zone over the course of an 8-hour work shift. In the current state of scientific knowledge (toxicology, medicine, epidemiology, etc.), the 8h-OEL is designed to protect workers exposed regularly and for the duration of their working life from the medium- and long-term health effects of the chemical in question;
- Short-term exposure limit (STEL): this corresponds to the limit of the time-weighted average (TWA) of the concentration of a chemical in the worker's breathing zone over a 15-minute reference period during the peak of exposure, irrespective of its duration. It aims to protect workers from adverse health effects (immediate or short-term toxic effects such as irritation phenomena) due to peaks of exposure;
- Ceiling value: this is the limit of the concentration of a chemical in the worker's breathing zone that should not be exceeded at any time during the working period. This value is recommended for substances known to be highly irritating or corrosive or likely to cause serious potentially irreversible effects after a very short period of exposure.

These three types of values are expressed:

- either in $mg.m^{-3}$, i.e. in milligrams of chemical per cubic metre of air and in ppm (parts per million), i.e. in cubic centimetres of chemical per cubic metre of air, for gases and vapours;
- or in $mg.m^{-3}$, only for liquid and solid aerosols;
- or in $f.cm^{-3}$, i.e. in fibres per cubic centimetre for fibrous materials.

The 8h-OELV may be exceeded for short periods during the working day provided that:

- the weighted average of values over the entire working day is not exceeded;
- the value of the short term limit value (STEL), when it exists, is not exceeded.

In addition to the OELs, the Committee assesses the need to assign a "skin" notation, when significant penetration through the skin is possible (ANSES, 2014). This notation indicates the need to consider the dermal route of exposure in the exposure assessment and, where necessary, to implement appropriate preventive measures (such as wearing protective gloves). Skin penetration of substances is not taken into account when determining the atmospheric limit levels, yet can potentially cause health effects even when the atmospheric levels are respected.

The Committee assesses the need to assign an "ototoxic"[2] notation indicating a risk of hearing impairment in the event of co-exposure to noise and the substance below the recommended OELs, to enable preventionists to implement appropriate measures (collective, individual and/or medical) (ANSES, 2014).

The Committee also assesses the applicable reference methods for the measurement of exposure levels in the workplace. The quality of these methods and their applicability to the measurement of exposure levels for comparison with an OEL are assessed, particularly with regards to their compliance with the performance requirements in the NF-EN 482 Standard and their level of validation.

Organisation of the expert appraisal

ANSES entrusted examination of this request to the Expert Committee on expert appraisal for recommending occupational exposure limits for chemical agents (OEL Committee) and to the Expert Committee on "health reference values". The Agency also mandated the Working Group on metrology to assess measurement methods in workplace atmospheres.

The methodological and scientific aspects of the work of this Group were regularly submitted to the Expert Committees. The report produced by the Working Group takes account of observations and additional information provided by the Committee 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".

Preventing risks of conflicts of interest

ANSES analyses interests declared by the experts before they are appointed and throughout their work in order to prevent potential conflicts of interest in relation to the points addressed in expert appraisals.

The experts' declarations of interests are made public on ANSES's website (www.anses.fr).

Description of the method

For the assessment of the health effects:

A summary report was prepared by ANSES's officers and submitted to the OEL Committee, which commented on it and added to it. The summary report was mainly based on the expert appraisal report on "the evaluation of biomarkers of exposure and recommendation for biological limit values and biological reference values for lead and its inorganic compounds" and the reports of US EPA (2006) and ATSDR (2007), supplemented by a bibliographic search carried out until 2016 on the following databases : Medline, Scopus.

The source articles cited as references were reassessed when requested by the Committee.

For the assessment of methods for measuring exposure levels in workplace atmospheres:

A summary report was prepared by the Working Group on metrology and submitted to the OEL Committee, which added its own comments.

[2] Since the publication of the ANSES report of 2014, the "ototoxic" notation has been replaced by the "noise" notation as the "noise" notation has been adopted by the European Scientific Committee and has been adopted in the French regulation for styrene.

The summary report presents the various protocols for measuring lead 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, 2016[3]).

A list of the main sources consulted is detailed in the methodology report (ANSES, 2016).

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.

The collective expert appraisal work and its conclusions and recommendations were adopted on 04 July 2017 by the OEL Committee.

The collective expert appraisal work and the summary report were submitted to public consultation from 05/07/2019 to 05/09/2019. The people or organizations who contributed to the public consultation are listed in appendix of the report (only available in French). The comments received were reviewed by the Committee on “Health Reference Values” (term of office 2017-2020) who finally adopted this version on the 23 January 2020. Two experts abstained. Their position is set out in the Annex 6 of the French report.

Results of the collective expert appraisal on the health effects

Toxicokinetic data

Absorption

Particle deposition in the respiratory tract is influenced by the size of the inhaled particles, age, other physiological factors and airflow in the respiratory tract. Approximately 95% of deposited inorganic lead that is inhaled as submicron particles is absorbed (ATSDR, 2007).

The amount of lead absorbed by the oral route is influenced by the physico-chemical characteristics of the substance (particle size, solubility, nature of the lead derivative, etc.), as well as by the physiological characteristics of the person (age, nutritional status in iron, calcium, etc.). Approximately 40 to 50% of lead contained in food is absorbed in infants and children and 3 to 10% in adults (ATSDR, 2007).

Distribution

Lead absorbed by the digestive tract passes into the bloodstream (ATSDR, 2007). In the blood, 99% of the lead is found in the intra-erythrocyte compartment. Most of the lead found in red blood cells is bound to proteins. Approximately 40–75% of lead in the plasma is bound to albumin (Al-Modhefer *et al*. 1991 et Ong

[3] Note that the methodology for assessing measurement methods was updated in 2020 after the adoption of this report by the Committee on “ Health Reference Values” : https://www.anses.fr/fr/system/files/AIR2020SA0050Ra.pdf

et Lee, 1980 quoted by ATSDR, 2007). Blood lead is then distributed in bone tissue and soft tissues such as the brain, kidneys and liver. It is also found in the male reproductive system (epididymis, seminal vesicles, testes and prostate) as well as in seminal fluid. Lead also passes into breast milk. The concentrations found in breast milk are proportional to the blood concentrations in the mother (the ratio between breast milk and blood is between 0.01 and 0.48). Lead also crosses the placental barrier (INSERM, 1999).

In adults, the half-life of lead in blood and soft tissue is about 30 days (ATSDR, 2007) whereas in bone tissue, the half-life is between 10 and 30 years. Approximately 94% of the body burden of lead in an adult is found in the bones. Bone tissue is an endogenous reservoir of exposure to lead, even when exposure has ceased. Some of the bone lead can therefore be mobilised into plasma under certain pathophysiological conditions. During physiological stresses such as pregnancy, when suffering from a disease or with the age-related reduction in bone mass, and in cases of osteoporosis, the lead stored in the bones is released into the blood again. Accumulated lead can therefore be released into the blood over a person's entire lifetime (INSERM, 1999).

The relative amounts of lead in other tissues, as reported by Schroeder and Tipton (1968 cited by ATSDR, 2007), were distributed in the following manner: liver (33%), skeletal muscle (18%), skin (16%), connective tissue (11%), fat tissue (6.4%), kidneys (4%), lungs (4%) and brain (2%).

Excretion

Lead is excreted in the faeces (25%) and in urine (75%). Urinary excretion occurs by glomerular filtration with low tubular reabsorption. There is also low excretion via tissues rich in sulphur-containing proteins, nails and hair which, like urine and bones, can be used as matrices for screening for biomarkers.

Toxicity

Several effects have been observed as a result of exposure to lead in the workplace. The following critical effects were analysed and discussed:

Acute and subacute toxicity

Acute inorganic lead poisoning can only result from massive ingestion or parenteral administration (Garnier, 2005). There are few data in the literature on acute respiratory toxicity.

Irritation and sensitisation

There are no data in the literature on irritation and sensitisation (dermal and inhalation).

Chronic toxicity

Neurological effects

The neurological effects of lead have been widely documented for exposure above 400 $\mu g \cdot L^{-1}$. However, at lower blood lead levels, subtle effects that are difficult to interpret have been the subject of several studies, some of which are described in this section. The reported neurological effects mainly consist of a decrease in the conduction speed of peripheral sensory and motor nerves. An analysis of the neurological effects of lead was carried out from the various tables in Annex VI of the report by the US EPA (2006), classifying these effects into four categories: posture and stability, cognitive functions, nerve conduction and evoked potentials.

While the studies analysed in the collective expert appraisal report described heterogeneous results, some of them stand out and provide a body of evidence for determining a biological limit value (BLV), in particular the studies by Schwartz *et al*. (2001, 2005) exploring different neurobehavioural functions. The study by Schwartz *et al*. (2005) showed statistically significant effects (decline in performance) with eight positive

tests out of the 11 conducted, corresponding to the transition from the 25th to the 75th percentile. The value of 210 µg·L^{-1} corresponds to the 25th percentile. Accordingly, the absence of effect is not demonstrated for a blood lead level of 210 µg·L^{-1} (25th percentile), resulting in this value being considered as a LOAEL. In their previous article (Schwartz *et al*. 2001), the authors indicated the possibility of a threshold of the order of 180 µg·L^{-1} for blood lead levels (determined graphically by the authors), value below which the effects of lead on certain tests do not seem to be observed and corresponding to a NOAEL.

Kidney effects

In the general population, chronic renal failure was the critical effect selected in ANSES's opinion (ANSES, 2013) (blood lead levels below 15 µg·L^{-1}). In occupational populations, many studies have examined the potential kidney effects of lead. For the purposes of this report, the studied parameters were divided into three categories: indicators of clinical diagnosis, early indicators of glomerular impairment, and early indicators of tubular impairment (proximal and distal). Although their use for diagnostic purposes is tending to grow, especially when screening for nephrotoxicity potentially induced by new drugs, the clinical significance of the early indicators has still not been clearly established (Xie *et al.*, 2013).

In conclusion, it would seem from the identified studies that lead exposure in workers has no measurable effect on renal function or on the early indicators of glomerular effects. The effects on the renal proximal tubules are not consistent as a whole. Although a NOAEL of 150 µg·L^{-1} has been determined for these effects from data on urinary α_1-microglobulin, this effect cannot be regarded as adverse. In accordance with the methodology of the Committee, all the studies included in this section were carried out in the workplace. As they are spread out over time, the "non-exposed" groups in these studies have blood lead levels above the threshold of 15 µg·L^{-1} mentioned at the beginning of this section, which aims to protect the general population from chronic kidney disease. It is therefore impossible to verify the impact of occupational exposure possibly occurring around this low value from the data in this literature. Nevertheless, if there is a causal relationship between occupational exposure to lead measured by the blood lead levels and chronic kidney disease, one would expect to find a dose-effect and dose-response relationship between blood lead levels and the various indicators of kidney damage described here. However, neither the indicators of clinical diagnosis nor the early indicators of glomerular effects clearly show such an effect, even at blood lead levels several tens of times higher than the threshold of 15 µg·L^{-1}. Only one early indicator of tubular effects, urinary α_1-microglobulin, suggests a slight effect on the renal tubule at 10 times the threshold of 15 µg·L^{-1}, whereas the other recognised early indicators of tubular effects show no clear signs of tubular impairment.

Cardiovascular effects

The report by the US EPA (2006) identified a number of studies conducted on occupational populations, including Glenn *et al*. (2003), Schwartz *et al*. (2000), Sokas *et al*. (1997) Tepper *et al*. (2001), Maheswaran *et al*. (1993), Telišman *et al*. (2004), Lee *et al*. (2001), Lustberg *et al*. (2004), Nomiyama *et al*. (2002), Wu *et al*. (1996), and a meta-analysis by Nawrot *et al*. (2002).

According to the report by the US EPA (2006), in the workplace, there is an effect on the variation of blood pressure in workers exposed to lead, for blood lead levels below 400 µg.L^{-1}. However, no increase in the risk of high blood pressure has been observed at blood lead levels below the current BLV of 400 µg·L^{-1} and 300 µg·L^{-1} in women.

The associations between lead in blood and blood pressure during pregnancy require particular focus. These studies are detained in the section on reprotoxicity.

Effects on the immune system

The epidemiological studies suggest an association between exposure to lead and an effect on the immune system in workers, which appeared for blood lead levels higher than the current BLV of 400 µg·L^{-1} (for men).

Effects on the haematopoietic system

The epidemiological studies examined in the biomarkers expert appraisal report (ANSES, 2019) on possible associations between exposure to lead and an effect on the haematopoietic system do not report significant effects in workers for blood lead levels below the current BLV of 400 µg·L^{-1} (for men). There are effects on delta-aminolevulinic acid dehydratase (ALAD) and zinc protoporphyrin (ZPP), which are not significant in health terms.

Genotoxicity and carcinogenicity

The genotoxicity studies show that lead can be responsible for DNA damage and an increase in micronuclei levels. However, there does not appear to be any increase in levels of chromosomal aberrations during exposure to lead. Epidemiological studies carried out in the workplace suggest a relationship between lead and lung or stomach cancer, but the evidence is limited by the presence of various potential confounding factors (co-exposure to arsenic or cadmium, smoking and dietary habits). The National Toxicology Program (NTP 2003 and 2004) and the International Agency for Research on Cancer (IARC, 2006) have concluded that lead compounds are probably carcinogenic (Group 2A, limited evidence in humans and sufficient evidence in animals).

Toxicity on reproduction

Effects on male fertility

Over the last 20 years, many cross-sectional studies have shown associations between occupational exposure to lead and sperm abnormalities (decline in sperm count in particular). These observations are in agreement with the animal data. However, the results are sometimes contradictory and these studies may have methodological limitations (in particular selection bias, variability of the semen analysis and the multitude of factors to be taken into account). The European study by Bonde *et al*. (2002) helped identify a limit to the blood lead level below which the decline in sperm count is unlikely. The NTP reports sufficient evidence of an effect on male fertility above 150 µg·L^{-1} of blood lead, based on the graphic interpretation of the study of Naha (2005), the other studies conducted on workers and analysed by the NTP report effects on fertility on men from 200 µg·L$^{-1.}$ (NTP, 2012).

Effects on female fertility

As the studies were conducted in primarily male work environments, there are insufficient data for assessing the associations between exposure to lead and female fertility. The most recent studies (for lower exposures) do not show significant results.

Snijder *et al*. (2012), in a review of the literature on the impact of occupational exposure on the time needed to conceive, in which two of the studies were conducted in women, did not show any statistically significant effects below the current BLV of 300 µg·L^{-1}.

Developmental effect

Some studies analysed in this collective expert appraisal report quantified the relationship between the level of lead (in maternal or cord blood) and parameters of foetal growth in populations of mothers subjected to low levels of lead exposure. Significant relationships were observed with birth weight in particular.

In conclusion, the analysis of these studies seems to suggest that lead induces reprotoxic effects (intra-uterine growth retardation, low birth weight, risk of spontaneous abortion and delayed postnatal development) at blood lead levels below 100 µg·L^{-1}.

The NTP concludes that there is sufficient evidence of effects, at concentrations below 50 µg·L^{-1} of blood lead, on intrauterine growth and limited evidence for blood lead levels below 100 µg·L^{-1} associated with spontaneous abortions and premature births.

Cardiovascular effects and effects on blood pressure in pregnant women

Concerning pregnant women, eight studies (four cross-sectional, three prospective and one case-control) focused on mean maternal blood lead levels (or cord blood levels for two studies) that were significantly lower than 100 µg·L^{-1}. All showed a relationship between higher blood lead levels and increased blood pressure during pregnancy, or even a risk of hypertension, with the exception of one showing a positive association with bone lead (and not blood lead). In conclusion, these studies show that there is an effect on the variation of blood pressure in pregnant women for blood lead levels below 100 µg.L^{-1}. However, a no-effect threshold can not be identified.

Establishment of OELs

8h-OEL

Choice of the critical effects and point of departure (POD)

IARC has classified lead and its inorganic compounds in Group 2A, "limited evidence of carcinogenicity in humans and sufficient evidence in animals" (IARC, 2006). Based on the results of genotoxicity studies, lead is considered to be an indirect genotoxic agent (INERIS, 2016). Its indirect genotoxicity seems to be linked, on the one hand, to an increase in and modulation of reactive oxygen species and, on the other hand, to its interaction with cellular proteins, including those involved in DNA repair mechanisms (INERIS, 2016). It therefore appears that there is a threshold for lead carcinogenicity. Health Canada (2011, 2017) considers that, based on human carcinogenicity studies, lead is probably carcinogenic but at high concentrations or blood lead levels. The Committee therefore considers that the genotoxic action of lead and its inorganic compounds could be indirect and concludes that there is a concentration threshold for carcinogenicity.

The Committee believes that the human carcinogenicity studies of lead do not enable a proper assessment of the dose-response relationship, since co-exposure to other carcinogens cannot be ruled out.

It should be noted that most studies do not present results on atmospheric lead exposure levels, but describe blood lead concentrations associated with health effects.

As part of its expert appraisal work for the biological monitoring of occupational exposure, the Committee recommended a BLV of 180 µg·L^{-1} for blood lead levels based on two studies (Schwartz *et al*., 2001 and 2005) conducted in a South Korean population monitored over about two years. These studies showed a significant decrease in neurobehavioural performance measured through a battery of standard tests adapted from the WHO Neurobehavioural Core Test Battery and exploring various major neurobehavioural registers such as motor skills, executive functions, cognition and emotions (ANSES, 2019). In addition, for women of childbearing age, the Committee recommended not exceeding the biological reference value (BRV) of 45 µg·L^{-1}, based on the 95th percentile of the ENNS survey values (March 2011) observed in the general population of women aged 20 to 45 years, as it is not possible to identify a specific threshold with no reproductive effect (ANSES, 2019).

Based on the identified health effects and available data, the Committee decided to establish a pragmatic 8-hour OEL for lead and its inorganic compounds on the basis of the neurological effects, using the blood lead level of 180 µg.L^{-1} as the POD (Point Of Departure).

It should be noted that the primary objective of this pragmatic 8h-OEL is to limit atmospheric lead concentrations in working atmospheres and not to protect against possible reprotoxic effects (as no threshold value can be determined at this time).

Calculation of the 8h-OEL

Approach based on PBPK modelling

For the derivation of the 8h-OEL, the expert committee favoured the field studies (that is to stay studies that examined the relationship between blood lead levels and atmospheric lead concentrations in the workplace) over PBPK modelling.

Indeed, the predictive capacity of the Legget model (used by OEHHA) was assessed using data from studies by Griffin *et al.* (1975) and William et al. (1969) where the blood lead levels measured were greater than 250 $\mu g.L^{-1}$. The lead BLV recommended by the expert committee is 180 $\mu g.L^{-1}$ and is outside the predictive capacity domain of the model. At lower concentrations than, for example, the Legget model has been developed, it should have a greater tendency to overestimate exposure and therefore overprotect against low exposures. Indeed, at lower concentrations, there is a zone of linearity in which the transporters (the red blood cells) are not saturated. In the end, while Legget's PBPK model is unlikely to be adequate for blood lead measurements below 250 $\mu g.L^{-1}$, the committee prefers to use the approach based on field studies.

Approach based on field studies

Several organisations (US EPA in 2013, ACGIH in 2001, Safe Work Australia in 2014) have examined the relationship between blood lead concentrations (PbB) and atmospheric lead concentrations (PbAir), by calculating an "air slope factor" or ASF. The ASF reflects the increase in blood lead levels for each increase in lead concentration in the air. According to the US EPA (2013), this relationship is non-linear partly because of saturation at the transport level (in the erythrocytes). In 2001, the ACGIH pointed out that the use of an ASF of 19 $(\mu g \cdot dL^{-1})/(\mu g \cdot m^{-3})$ would correspond to exposure of 0.05 $mg \cdot m^{-3}$ (value recommended by the ACGIH in 2001). However, for the ACGIH, inhalation exposure does not appear to be the main contributor to blood lead levels.

In its report in 2014, Safe Work Australia used this approach to establish an occupational exposure limit value (8 hours). Safe Work Australia identified six epidemiological studies conducted in the workplace and identified the air slope factors (i.e. the relationship between atmospheric concentrations of inhalable lead and blood lead levels (Table 1)). Other studies (other than the six selected) were not included in these calculations, considering that non-airborne exposure (ingestion by hand-to-mouth contact) had been the main contributor to blood lead levels.

Among these six studies selected to determine an ASF, many were conducted while leaded petrol was still in use, which makes a major contribution to blood lead levels (outside the workplace). Safe Work Australia therefore corrected its ASF for background levels when determining the ASF.

In these six studies, for calculating the mean ASF, blood lead levels (not related to occupational exposure) were taken into account in the equation:

$$ASF = (Pb_{BOCC} - Pb_{BBkgd}) \div Pb_{Air}$$

ASF = Average Air Slope Factor between Pb_{BBkgd} and Pb_{BOCC} $(\mu g.L^{-1}).(\mu g.m^{-3})^{-1}$ $Pb_{BOCC} = Pb_B$ $(\mu g.L^{-1})$ in the occupational exposure study associated with the nominated Pb_{Air}
Pb_{BBkgd} = Background Pb_B (µg/L) from the study
Pb_{Air} = Lead concentration in air $(\mu g.m^{-3})$
Pb_B = Lead concentration in blood $(\mu g.L^{-1})$.

The result of the calculation from the six studies is presented in Table 1.

Table 1: Calculation of ASFs from the six epidemiological studies

Reference	Bkgd [a] ($\mu g.L^{-1}$)	Pb_B [b] ($\mu g.L^{-1}$)			ASF [c] $(\mu g.L^{-1}).(\mu g.m^{-3})^{-1}$		
		50 $\mu g.m^{-3}$	**100 $\mu g.m^{-3}$ $\mu g.m^{-3}$**	**150 $\mu g.m^{-3}$**	**50 $\mu g.m^{-3}$**	**100 $\mu g.m^{-3}$**	**150 $\mu g.m^{-3}$**
Pierre *et al*. (2002)	9.9	250	270	310	3	1.7	1.4
Gartside *et al*. (1982)	12	420	440	470	6	3.2	2.3
King *et al*. (1979)	23	480	490	510	5	2.6	1.9
		340	370	410	2.2	1.4	1.2
		480	520	550	5	2.9	2.1
Bishop et Hill (1983)	14	320	360	370	3.6	2.2	1.5
Chavalitnikul *et al*. (1984)	12	320	390	440	4	2.7	2.1
Williams *et al*. (1969)	18	400	500	600	4.4	3.2	2.8
				Average	**4.2**	**2.5**	**1.9**

[a] Bkgd =Background blood lead not associated with workplace lead exposure; [b] Pb_B = Blood lead concentration at the nominated Pb_{Air} concentrations. These are determined from the reported graphical data or the studies regression equation when available.
[c] ASF = Average Air Slope Factor for the contribution of lead in air to Pb_B level. Units $(\mu g.L^{-1}).(\mu g.m^{-3})^{-1}$.

The Committee considers that of the six studies used in the Australian approach, two can be selected on the basis of metrological quality to calculate an ASF (see description in appendix 2 in the French version):

- that of Pierre *et al*. (2002), in which crystal workers were exposed to lead in combination with silicates;
- that of Chavalitnitikul *et al*. (1984), in which workers in a battery manufacturing plant (assembly and bonding stations) were exposed mainly to lead oxides.

These two studies cover only two industry sectors among more than a dozen. They are not representative of all the industry sectors where lead can be used.

The 8h-OEL can be calculated from the following equation:

$$ASF = (PbB_{OCC} - PbB_{Bkgd}) \div PbAir$$

Assuming:

- an ASF of 3 $(\mu g.L^{-1}).(\mu g/m^3)^{-1}$, based on the study by Pierre *et al*. (2002);
- a blood concentration level (Pb_{BBkgd}) for the general French population based on the data from the ENNS survey of 73 $\mu g.L^{-1}$ (95^{th} percentile of the population of the ENNS survey, men and women combined, from 18 to 74 years of age);
- a target blood lead level (BLV) of 180 $\mu g.L^{-1}$ (Pb_{BOCC}),

the atmospheric lead concentration (Pb_{Air}) would be 35.7 $\mu g \cdot m^{-3}$, rounded up to 40 $\mu g \cdot m^{-3}$. This value corresponds to the atmospheric exposure concentration of lead over 8 hours, ensuring that the BLV of 180 $\mu g.L^{-1}$ is not exceeded.

Assuming:

- an ASF of 4 $((\mu g.L^{-1}).(\mu g/m^3)^{-1}$, based on the study by Chavalitnitikul *et al.* (1984),

- a blood concentration level (Pb_{BBkgd}) for the general French population based on the data from the ENNS survey of 73 $\mu g.L^{-1}$ (95^{th} percentile of the population of the ENNS survey, men and women combined, from 18 to 74 years of age),
- a target blood lead level (BLV) of 180 $\mu g.L^{-1}$ (Pb_{BOCC}),

the atmospheric lead concentration (Pb_{Air}) would be 26.8 $\mu g \cdot m^{-3}$, rounded up to 30 $\mu g \cdot m^{-3}$. This value corresponds to the atmospheric exposure concentration of lead over 8 hours, ensuring that the BLV of 180 $\mu g.L^{-1}$ is not exceeded.

The Committee chose the study by Chavalitnitikul *et al.* (1984) and its more protective air slope factor (ASF) of 4 $(\mu g.L^{-1}).(\mu g/m^3)^{-1}$ to calculate the OEL, i.e. an atmospheric lead concentration (Pb_{Air}) of 30 $\mu g.m^{-3}$. This air slope factor was based on a study in a specific sector of activity, battery manufacturing (assembly and bonding stations), in which workers were exposed mainly to lead oxides.

Since the POD was determined from a study conducted with a large number of workers and over a long period of time, no adjustment factor for inter-individual variability was deemed necessary.

The Committee therefore recommends a pragmatic 8h-OEL of 30 $\mu g \cdot m^{-3}$.

The Committee would like to point out that although lead in the air contributes at least partially to the rise in blood lead levels and therefore to the health effects, the best approach to protect workers' health is biological monitoring of occupational exposure to lead.

15min-STEL

The data currently available (acute respiratory toxicity and irritation) do not enable a 15min-STEL to be recommended for lead and its inorganic compounds. Therefore, in accordance with its methodology (ANSES, 2014), the Committee recommends that any occupational exposure to lead and its inorganic compounds over a 15-minute period should not exceed five times the value of the 8h-OEL, i.e. **150 $\mu g \cdot m^{-3}$.**

"***Skin***" ***notation***

Lead is responsible for systemic effects, but in the absence of sufficient data, it was not possible to calculate a skin permeation flux and perform the calculation according to the method of the ECETOC[4].

In the absence of data, **the "skin" notation is not recommended for lead and its inorganic compounds.**

"***Noise***" ***notation***

In 2009, OSHA considered lead as an ototoxic substance. Indeed, several chronic toxicity studies in animals exposed to lead and epidemiological studies in lead-exposed workers suggest that lead has an ototoxic effect caused by a neurotoxic mechanism (OSHA, 2009).

Taking into account the evidence provided by the results of human studies, Vyskocil *et al*. (2011) considered lead as an ototoxic agent. There is no evidence of interaction after combined exposure of workers to lead and noise. Further studies are needed to reach a definitive conclusion on the interaction with noise.

Although lead and its compounds are ototoxic agents, the **"noise" notation is not recommended for lead and its inorganic compounds** due to the lack of available data on possible interaction during co-exposure to lead and noise.

[4] European Centre for Ecotoxicology and Toxicology for Chemicals

Results of the collective expert appraisal on measurement methods in workplace atmospheres

Assessment of the measurement methods for lead in workplace atmospheres

The following table presents the 8 measurement methods that were identified and evaluated and their classification.

Table 2: Classification of methods for measuring lead and its inorganic compounds in workplace atmospheres

N°	Method	Protocol	Category		
			Regulatory control of the 8h-OEL	Monitoring of short-term exposure	Regulatory control of the 15min-STEL
Active sampling of the inhalable fraction – acid mineralisation or direct analysis					
1	Flame atomic absorption spectrometry (F-AAS)	NIOSH 7082 (1994) OSHA id121 (2002) HSE MDHS 6/3 (1998) INHST MTA/MA-025/A16 (2016) DFG Lead (1985)	1B	1B	3
2	Electrothermal/graphite furnace atomic absorption spectrometry (ET-AAS)	NIOSH 7105 (1994) MDHS 6/3 (1998) DFG lead (1985) BGI -505-73-1 (2009)	1B	1B	1B
3	Inductively coupled plasma atomic emission spectrometry (ICP-AES)	NF ISO 15202-2 (2012) NF ISO 15202-3 (2005) INRS MétroPol M122 (2016) NIOSH 7300 (2003); NIOSH 7301 (2003); NIOSH 7303 (2003) NIOSH 7302 (2014) NIOSH 7304 (2014) NIOSH 7306 (2015) OSHA id125g (2002) OSHA id206 (1991)	1B	1B	1B
4	Inductively coupled plasma mass spectrometry (ICP-MS)	NF ISO 30011 (2010) IRSST MA 362 (2010°) OSHA 1006 (2005)	1A	1A	1A
5	X-ray fluorescence spectrometry (direct analysis)	HSE MDHS 91/2 NIOSH – 7702 (1998)	3		
6	Anodic stripping voltammetry	NIOSH 7701 (2016)	2	2	2
7	Rhodizonate-based detection (spot test kit)	NIOSH 7700 (1996)	3		
8	UV/visible photometry	BGIA 6015 (2005)	3(*)		
(*) *method classified in Category 3 due to the absence of validation data*					

The two figures below show the range of validation of the different methods classified in Categories 1B and 2, as well as their limits of quantification with regard to the pragmatic 8h-OEL and the pragmatic 15min-STEL recommended by the Committee.

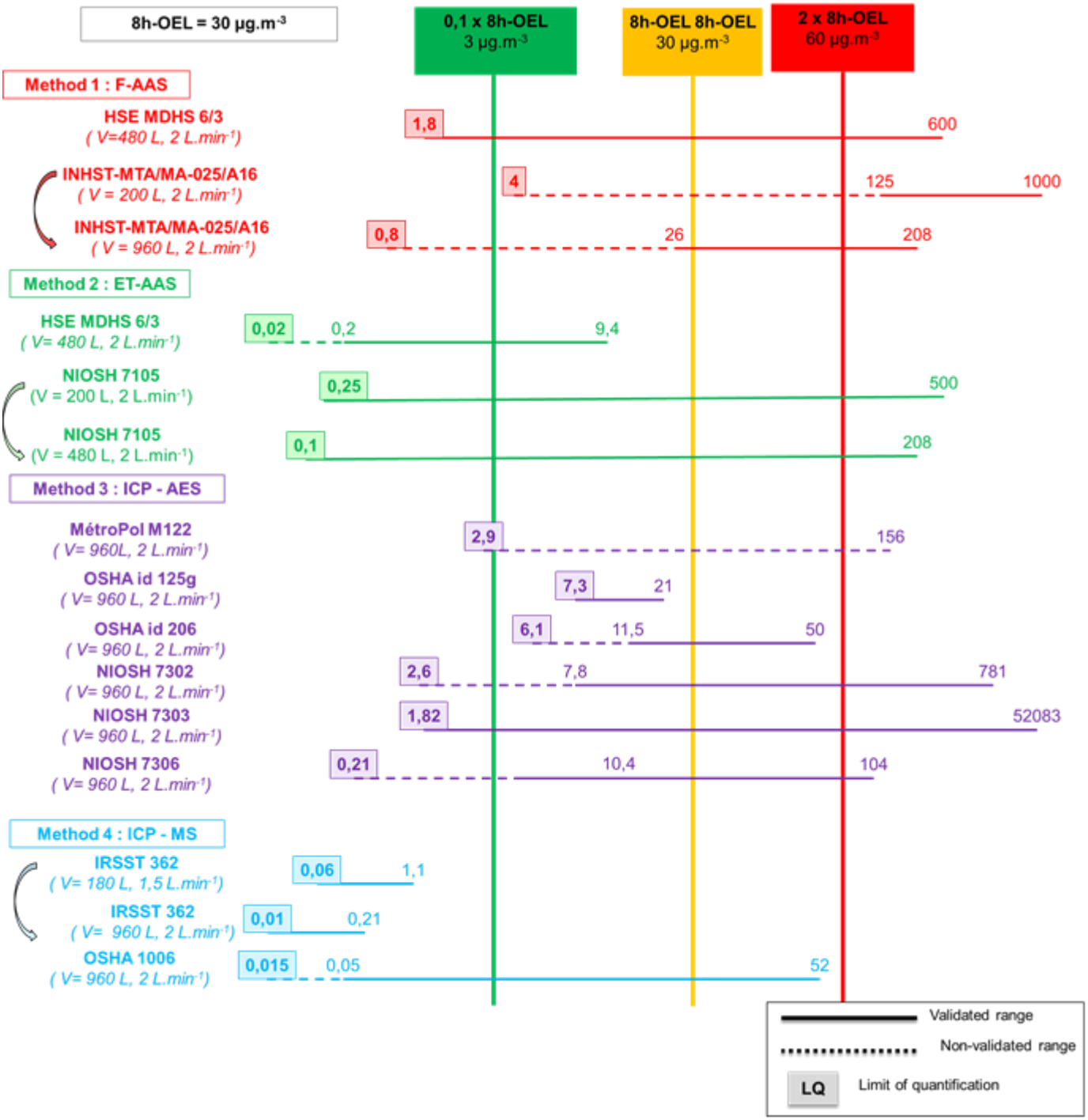
8h-OEL = 30 µg.m-3
0,1 x 8h-OEL
3 µg.m-3
8h-OEL 8h-OEL
30 µg.m-3
2 x 8h-OEL
60 µg.m-3
Method 1 : F-AAS
HSE MDHS 6/3
(V=480 L, 2 L.min-1)
1,8
600
INHST-MTA/MA-025/A16
(V = 200 L, 2 L.min-1)
4
125
1000
INHST-MTA/MA-025/A16
(V = 960 L, 2 L.min-1)
0,8
26
208
Method 2 : ET-AAS
HSE MDHS 6/3
(V= 480 L, 2 L.min-1)
0,02
0,2
9,4
NIOSH 7105
(V = 200 L, 2 L.min-1)
0,25
500
NIOSH 7105
(V = 480 L, 2 L.min-1)
0,1
208
Method 3 : ICP - AES
MétroPol M122
(V= 960L, 2 L.min-1)
2,9
156
OSHA id 125g
(V= 960 L, 2 L.min-1)
7,3
21
OSHA id 206
(V= 960 L, 2 L.min-1)
6,1
11,5
50
NIOSH 7302
(V= 960 L, 2 L.min-1)
2,6
7,8
781
NIOSH 7303
(V= 960 L, 2 L.min-1)
1,82
52083
NIOSH 7306
(V= 960 L, 2 L.min-1)
0,21
10,4
104
Method 4 : ICP - MS
IRSST 362
(V= 180 L, 1,5 L.min-1)
0,06
1,1
IRSST 362
(V= 960 L, 2 L.min-1)
0,01
0,21
OSHA 1006
(V= 960 L, 2 L.min-1)
0,015
0,05
52
Validated range
Non-validated range
LQ
Limit of quantification

Figure 1 : Ranges of validity and limits of quantification for the methods compared to the range from 0.1 to 2 times the pragmatic 8h-OEL recommended by the Committee

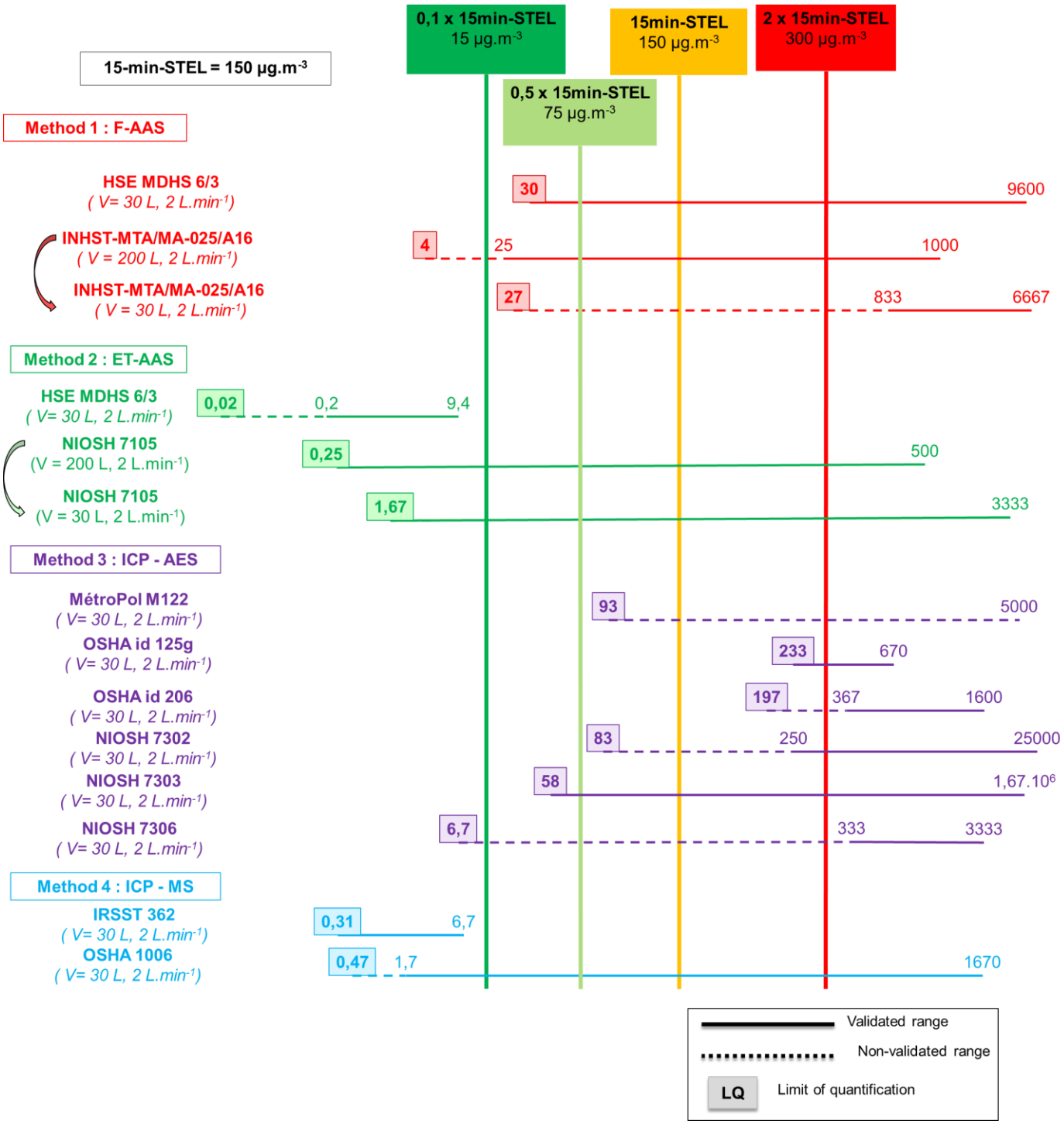
0,1 x 15min-STEL
15 µg.m-3
15min-STEL
150 µg.m-3
2 x 15min-STEL
300 µg.m-3
15-min-STEL = 150 µg.m-3
0,5 x 15min-STEL
75 µg.m-3
Method 1 : F-AAS
HSE MDHS 6/3
(V= 30 L, 2 L.min-1)
30
9600
INHST-MTA/MA-025/A16
(V = 200 L, 2 L.min-1)
4
25
1000
INHST-MTA/MA-025/A16
(V = 30 L, 2 L.min-1)
27
833
6667
Method 2 : ET-AAS
HSE MDHS 6/3
(V= 30 L, 2 L.min-1)
0,02
0,2
9,4
NIOSH 7105
(V = 200 L, 2 L.min-1)
0,25
500
NIOSH 7105
(V = 30 L, 2 L.min-1)
1,67
3333
Method 3 : ICP - AES
MétroPol M122
(V= 30 L, 2 L.min-1)
93
5000
OSHA id 125g
(V= 30 L, 2 L.min-1)
233
670
OSHA id 206
(V= 30 L, 2 L.min-1)
197
367
1600
NIOSH 7302
(V= 30 L, 2 L.min-1)
83
250
25000
NIOSH 7303
(V= 30 L, 2 L.min-1)
58
1,67.10⁶
NIOSH 7306
(V= 30 L, 2 L.min-1)
6,7
333
3333
Method 4 : ICP - MS
IRSST 362
(V= 30 L, 2 L.min-1)
0,31
6,7
OSHA 1006
(V= 30 L, 2 L.min-1)
0,47
1,7
1670
Validated range
Non-validated range
LQ
Limit of quantification

Figure 2 : Ranges of validity and limits of quantification for the methods compared to the range from 0.1 to 2 times the pragmatic 15min-STEL recommended by the Committee

Preliminary remarks

- Sampled fraction

Most of the protocols identified use an aerosol sampling device generally consisting of a 37 mm cassette in a closed (sampling of the inhalable fraction) or open (total dust sampling) configuration.

As all protocols were assessed by spiking with lead solutions, the collection efficiency was not taken into account. The methods were therefore assessed by considering a single sampling device for the inhalable fraction and the associated flow rate for each method, namely the closed 37 mm cassette at a flow rate of 2 $L \cdot min^{-1}$. The only exception was the BGI-505-73-1 protocol using a GSP sampler with a flow rate of 10 $L \cdot min^{-1}$, which was retained for the assessment.

- Mineralisation modes and rate

Different mineralisation modes are proposed in the identified protocols/methods. These digestion modes mainly depend on the material used and the supposed refractory aspect of the collected particles. Within the limits of these two points, they can nevertheless be transposed from one analytical method to another. The performance of the different protocols was established with regard to these digestion modes, which can in most cases influence the associated performance. The assessment of the different methods was therefore implicitly linked to the digestion modes proposed in the associated protocols.

- Environmental conditions and interference with sampler capacity

The influence of these parameters (temperature, humidity, orientation of the sampling device, etc.) must be specified, and if there is no particular indication the method should be classified in Category 2 (ANSES, 2016). The environmental conditions are rarely described in the identified methods. However, the NF EN 13890 standard does not consider these variations as uncertainty components, unlike the NF EN 1076 standard for gaseous compounds. These criteria were not therefore regarded as exclusion criteria in this assessment.

- Storage data

The data on storage of the sample must also be mentioned, otherwise it will be classified in Category 3. This information was not always specified in the protocols studied. However, the NF EN 13890 standard states that with regard to procedures for measuring metals and metalloids in airborne particles, "metals and metalloids and their inorganic compounds are generally stable". This criterion was not therefore regarded as an exclusion criterion.

Method 1

The method involves sampling the inhalable fraction on a cellulose ester or cellulose nitrate membrane and then mineralisation in an acid medium, in order to perform determination by atomic absorption spectrometry with flame atomisation (F-AAS).

It covers the concentration range from 0.1 to 2* pragmatic 8h-OEL and from 0.5 to 2*pragmatic 15min-STEL. The overall expanded uncertainty also complies with the requirements of the EN 482 standard.

The recovery rate was determined by trapping lead on a filter by aerosol generation (NIOSH 7082 protocol), which made it possible to take into account the capture efficiency and mineralisation rate, for load levels within the range of 0.1 to 2* pragmatic 8h-OEL.

It should be noted, however, that interferences were identified without being studied. For this reason, the method has been classified in Category 1B for regulatory control of the pragmatic 8h-OEL and monitoring of short-term exposure. However, since the limit of quantification is greater than 0.1*pragmatic 15min-STEL, the method cannot be used for regulatory control of the pragmatic 15min-STEL and has therefore been classified in Category 3 for this purpose.

Method 2

The method involves sampling the inhalable fraction on a cellulose ester or cellulose nitrate membrane and then mineralisation in an acid medium, in order to perform determination by atomic absorption spectrometry with electrothermal atomisation (ET-AAS).

The method covers the concentration ranges from 0.1 to 2* pragmatic 8h-OEL and from 0.1 to 2* pragmatic 15min-STEL. The overall expanded uncertainty also complies with the recommendations of the EN 482 standard.

Although the mean recovery rate was determined exclusively by spiking materials with lead solutions or solid compounds and without taking into account the capture efficiency, it was determined at load levels included in the validation range.

However, interferences were mentioned without being studied. This is why the method has been classified in Category 1B for regulatory control of the pragmatic 8h-OEL and the pragmatic 15min-STEL, as well as for monitoring short-term exposure.

Method 3

The method involves sampling the inhalable fraction on a filter and then mineralisation in an acid medium, in order to perform determination by inductively coupled plasma atomic emission spectrometry (ICP-AES).

The validation data from the different protocols studied are highly disparate due to the different mineralisation conditions and the different types of filters recommended.

The method covers the concentration ranges from 0.1 to 2* pragmatic 8h-OEL and from 0.1 to 2* pragmatic 15min-STEL, depending on the protocols. The mineralisation rates vary according to the conditions applied, and although they are generally higher than 90%, they may not meet this criterion set by the EN 13890 standard, as for example at the low level tested with the mineralisation recommended by the NIOSH 7301 protocol. Only the OSHA id125g protocol mentions, for determining the recovery rate, tests carried out on wipes spiked on the one hand with solutions and on the other hand with certified reference materials (metal dust). These tests show that the 90% recovery criterion is not met in all cases, particularly for paint dust and dust from indoor environments. These low recovery rates may be related to the very low lead concentration in these reference materials.

The overall expanded uncertainty complies with the recommendations of the EN 482 standard.

The method has therefore been classified in Category 1B for regulatory technical control of the pragmatic 8h-OEL and the pragmatic 15min-STEL, as well as for monitoring short-term exposure.

Method 4

The method involves sampling the inhalable fraction on a cellulose ester membrane. After sampling, the material is mineralised in an acid medium, in order to perform determination by inductively coupled plasma mass spectrometry (ICP-MS).

The method covers the concentration ranges from 0.1 to 2* pragmatic 8h-OEL and from 0.1 to 2*pragmatic 15min-STEL.

Data on the uncertainty of the method are provided. The NF ISO 30011 standard also mentions compliance with the requirements of the EN 482 standard without specifying the details of the calculations. The other validation data (OSHA 1006 protocol) are complete, including tests for validating the influence of the mineralisation method (using a certified reference material), the sampler capacity of the filter membrane and the storage conditions of the collected samples.

The method is therefore classified in Category 1A for regulatory technical control of the pragmatic 8h-OEL and the pragmatic 15min-STEL, as well as for monitoring short-term exposure.

Method 5

This method involves sampling by pumping onto a membrane filter, preferably 37 or 25 mm in diameter depending on the expected dust weight, which will then be analysed directly by X-ray fluorescence spectrometry. A calibration curve with the spiked materials (aerosol generation) is required to perform these quantitative analyses.

To achieve performance that matches the stated performance, this method requires the loading rate and the particle size of the collected sample to be verified. The size of the sampled particles should ideally be less than 2.5 µm. However, this diameter does not correspond to the median aerodynamic diameter of the conventional inhalable fraction. It is also likely that performance will be affected in the case of a sample that is disparate in nature, or of heterogeneous deposition due to the nature of the sampling device. This method also requires specific calibration on the material in question, which can be cumbersome.

The method is therefore classified in Category 3 for regulatory control of the pragmatic 8h-OEL, the pragmatic 15min-STEL and short-term exposure.

Method 6

The method covers the range from 0.1 to 2* pragmatic 8h-OEL by increasing the sampling time and the volume to be sampled. The method also covers the range from 0.1 to 2*pragmatic 15min-STEL. Information is given on the recovery rate assessed under different conditions (lead aerosols generated in the laboratory, samples collected in the workplace and certified reference materials), showing an equivalence of results between this method and alternative methods (ICP-AES and F-AAS) based on previously studied protocol variants (including the mixture of acids used for mineralisation). However, the published mineralisation performance indicates wide variability with a mean close to or less than 90%. It should also be noted that interferences were identified without being studied and that the uncertainty data are very partial and poorly documented.

This is why the method has been classified in Category 2 for regulatory technical control of the pragmatic 8h-OEL and the pragmatic 15min-STEL, as well as for monitoring short-term exposure.

Method 7

This method uses a sampling pump to sample the inhalable fraction on a cellulose ester membrane. The material is then treated with a rhodizonate colorimetric detection kit, marketed by Merck. A yellow/orange colour complex indicates the presence of lead.

This qualitative method is not suitable for comparing OELs. No validation data are available. It is therefore classified in Category 3 for regulatory technical control of the pragmatic 8h-OEL and the pragmatic 15min-STEL, as well as for monitoring short-term exposure.

Method 8

In the BGIA 6015 protocol, which lists the different analytical methods that can be used for the determination of lead, a method corresponding to photometry by UV/visible absorption is mentioned in a summary table.

No data on this method have been published, which leads to this method being classified in Category 3 for the pragmatic 8h-OEL, the pragmatic 15min-STEL and the monitoring of short-term exposure, because it cannot be assessed in the absence of validation data for lead measurement.

Conclusions and recommendations

Among the eight methods identified,

- Four are not recommended for lead measurement, three of which have been classified in Category 3:
    - Method 5 (X-ray fluorescence analysis) which is based on a sampling device for which care must be taken to ensure that the particle size is less than 2.5 µm in order to limit analytical bias (this diameter does not correspond to the particle size range of the inhalable fraction: median aerodynamic diameter > 20 µm). Moreover, it is quite cumbersome to implement (preparation of a calibration curve with dust-spiked filters). The validation data were also studied over a range greater than 0.1 to 2* pragmatic 8h-OEL.
    - Method 7 (colorimetric detection kit), which is an indicative qualitative technique not suited to OEL monitoring.
    - Method 8 (UV/visible absorption photometry), for which there are no validation data specific to lead.

  and one of which has been classified in Category 2: method 6 (anodic stripping voltammetry), mainly because of the lack of an interference study and very partial uncertainty data.
- Method 4 (ICP-MS) has complete validation data. It has therefore been classified in Category 1A for regulatory technical control of the pragmatic 8h-OEL and the pragmatic 15min-STEL for lead, as well as for monitoring short-term exposure.
- Methods 2 (ET-AAS) and 3 (ICP-AES) are partially validated and have been classified in Category 1B for regulatory technical control of the pragmatic 8h-OEL and the pragmatic 15min-STEL for lead, as well as for monitoring short-term exposure.
- Method 1 (F-AAS) is partially validated and has been classified in Category 1B for regulatory technical control of the pragmatic 8h-OEL and the monitoring of short-term exposure. However, this method's limit of quantification is greater than one tenth of the pragmatic 15min-STEL. It has therefore been classified in Category 3 for regulatory technical control of the pragmatic 15min-STEL.

In view of its performance, the Committee recommends in particular Method 4, which uses ICP-MS.

Table 3 shows the methods recommended for measuring lead and its inorganic compounds in workplace atmospheres for the purposes of comparison with the OELs.

Table 43: Recommended methods for measuring lead and its inorganic compounds in workplace atmospheres for comparison with OELs

N°	Method	Protocol	Category		
			Regulatory control of the pragmatic 8h-OEL	Monitoring of short-term exposure	Regulatory control of the pragmatic 15min-STEL
Active sampling of the inhalable fraction - acid mineralisation					
lis	Flame atomic absorption spectrometry (F-AAS)	NIOSH 7082 (1994) OSHA Id121 (2002) HSE MDHS 6/3 (1998) INHST MTA/MA-025/A16 (2016) DFG Lead (1985)	1B	1B	3 (not recommended)
2	Flame atomic absorption spectrometry (ET-AAS)	NIOSH 7105 (1994) MDHS 6/3 (1998) DFG lead (1985) BGI -505-73-1 (2009)	1B	1B	1B
3	Inductively coupled plasma atomic emission spectrometry (ICP-AES)	NF ISO 15202-2 (2012) NF ISO 15202-3 (2005) NIOSH 7300 (2003) NIOSH 7301 (2003) NIOSH 7303 (2003) NIOSH 7302 (2014) NIOSH 7304 (2014) NIOSH 7306 (2015) INRS Métropol M-122 (2016) OSHA id125g (2002) OSHA id206 (1991)	1B	1B	1B
4	**Inductively coupled plasma mass spectrometry (ICP-MS)**	**NF ISO 30011 (2010) IRSST MA 362 (2010) OSHA -1006 (2005)**	**1A**	**1A**	**1A**

Conclusions of the collective expert appraisal

Based on the data currently available, the Committee recommends a pragmatic 8h-OEL of 30 µg·m^{-3} for lead and its inorganic compounds and a pragmatic 15min-STEL of 150 µg·m^{-3}.

It does not recommend either a "skin" or "noise" notation.

It should be noted that the primary objective of this pragmatic 8h-OEL is to limit atmospheric lead concentrations in working atmospheres and not to protect against possible reprotoxic effects (as no threshold value can be determined at this time).

The Committee would also like to point out that although lead in the air contributes at least partially to the rise in blood lead levels and therefore to the health effects, the best approach to protect workers' health is biological monitoring of occupational exposure to lead.

Concerning the methods for measuring lead and its inorganic compounds in the workplace, the Committee recommends one method validated and classified in Category 1A, as well as two methods partially validated and classified in Category 1B for monitoring the pragmatic 8h-OEL, for regulatory technical control of the pragmatic 15min-STEL or for monitoring short-term exposure:

- Method classified in Category 1A:
    - Method 4, involving active sampling of the inhalable fraction on a membrane, acid mineralisation and then determination by inductively coupled plasma atomic emission spectrometry
- Methods classified in Category 1B:
    - Method 2, involving active sampling of the inhalable fraction on a membrane, acid mineralisation and then determination by atomic absorption spectrometry with electrothermal atomisation;
    - Method 3, involving active sampling of the inhalable fraction on a membrane, acid mineralisation and then determination by inductively coupled plasma atomic emission spectrometry.

Method 1 is also partially validated and has been classified in Category 1B for monitoring of the pragmatic 8h-OEL and for monitoring short-term exposure, but is not recommended for regulatory technical control of the pragmatic 15min-STEL due to an insufficient limit of quantification.

In view of its performance, the Committee recommends in particular Method 4, which uses ICP-MS.

The Committee would like to stress that determining the effectiveness of mineralisation is a necessary prerequisite for the implementation of these methods. If there is any doubt about the effectiveness of the chosen mode of mineralisation, depending on the nature of the materials that may be present in the test atmosphere, this effectiveness should be determined for this particular application.

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