Brief guide to analytical methods for measuring lead in blood

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Brief guide to analytical methods for measuring lead in blood.

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Contents

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1. Purpose and scope

This document provides a brief overview of analytical methods commonly used for measuring lead in blood. It is primarily aimed at informing public health personnel and policy-makers who are not laboratory specialists but who may need to develop plans for population screening and other public health actions related to human exposure to lead. The document lists well-established analytical methods for measuring lead in blood and briefly describes some of their characteristics, including their advantages and disadvantages. It also highlights, for various types of applications and scenarios, the considerations that need to be taken into account when selecting an analytical method and when deciding about whether to establish a laboratory service for lead measurement or whether to contract it out. This document does not aim to provide an exhaustive description of analytical methods and protocols or to make specific recommendations regarding methodologies or specific instruments. More exhaustive reviews of this subject are available elsewhere (*1*), and links to further information and reading are provided in section 7.

2. Background

Lead is a toxic metal whose widespread use has caused extensive environmental contamination and health problems in many parts of the world. Human exposure to lead is estimated to account for 143 000 deaths every year and 0.6% of the global burden of disease (*2*). Lead is a cumulative toxicant that affects multiple body systems, including the neurological, haematological, gastrointestinal, cardiovascular and renal systems. Chronic exposure commonly causes haematological effects, such as anaemia, or neurological disturbances, including headache, irritability, lethargy, convulsions, muscle weakness, ataxia, tremors and paralysis. Acute exposures may cause gastrointestinal disturbances (anorexia, nausea, vomiting, abdominal pain), hepatic and renal damage, hypertension and neurological effects (malaise, drowsiness, encephalopathy) that may lead to convulsions and death. Children are particularly vulnerable to the neurotoxic effects of lead, and even low levels of exposure can cause serious and, in some cases, irreversible neurological damage. Childhood lead exposure is estimated to contribute to about 600 000 new cases of children with intellectual disabilities every year (*3*).

The clinical diagnosis of lead poisoning can be difficult when there is no clear history of exposure, because poisoned individuals can be asymptomatic, and signs and symptoms, when they are present, are relatively nonspecific. Laboratory investigations are the only reliable way to diagnose lead-exposed individuals and therefore play an essential role in the identification and management of lead poisoning and in the assessment of occupational and environmental lead exposure.

Today, laboratories primarily assess lead exposure with whole blood lead measurements. Although a number of other human tissues and fluids, such as hair, teeth, bone and urine, also reflect lead exposure, the concentration of lead in whole blood has gained wide acceptance as the most useful tool for screening and diagnostic testing (*1*, *4*). In very young children, the lead level in whole blood is an indicator mainly of recent exposure, although there can be variable (but not dominant) input to total blood lead concentration from past

accumulation of lead in the body. In adults, particularly in lead workers, the past accumulation can be a more prominent contributor to total blood lead concentrations.

3. Available analytical methods

A number of laboratory methods are available to determine blood lead concentrations (*1*, *5*–*9*). The most common are atomic absorption spectrometry (AAS), anodic stripping voltammetry (ASV) and inductively coupled plasma mass spectrometry (ICP-MS). In addition, a simple to use, portable device using ASV technology is available for performing blood lead measurements at point of care. These methods differ significantly in their analytical capacities (e.g. limits of detection, accuracy), costs (e.g. purchase and maintenance costs, laboratory infrastructure required, reagents and supplies) and technical requirements (e.g. sample preparation, calibration, skilled personnel). These factors, taken in conjunction with the setting and resources of the laboratory, will influence the decision about the choice of method.

The required limit of detection is an important consideration. In many countries, there has been a successive reduction in the blood lead concentration considered to be of clinical concern. This reflects the growing body of evidence suggesting that there may be no threshold concentration of lead in the body below which there are no adverse health effects (*10*). In addition, public health measures in a number of countries have succeeded in reducing the mean blood concentration in populations. An example is the USA, where the geometric mean blood lead concentration in the population has decreased from 15–17 µg/dl in the mid-1970s (*11*) to the current value of below 2 µg/dl (*12*). These two factors have increased interest in measuring ever-lower blood lead concentrations and created a need for analytical methods that can perform at low levels of detection. In situations where population or subpopulation blood lead concentrations are still elevated, some older technologies with higher levels of detection may still be applicable.

Further discussion about different analytical methods is provided in the sections below and summarized in Table 1.

3.1 Atomic absorption spectrometry (AAS)

AAS is based on the fact that free atoms absorb light at wavelengths characteristic of the element of interest. The amount of light absorbed can be correlated in a linear fashion to the concentration of the analyte in the sample. To conduct an AAS measurement, the lead-containing sample must first be processed by the instrument so as to generate ground-state atoms as a vapour within the light path of the instrument. This process, called atomization, can be done using either a flame (flame atomic absorption spectrometry, or FAAS) or an electrothermal source, most often a graphite furnace (graphite furnace atomic absorption spectrometry, or GFAAS). Although FAAS and GFAAS have similar detection principles, they differ greatly in their applicability to direct measurement of lead in blood (e.g. limits of detection, sample size, sample preparation).

Table 1. Overview of analytical methods for blood lead measurement

Method	Strengths	Limitations
Flame atomic absorption spectrometry (FAAS)	• Requires only basic laboratory expertise • Rapid analysis • Small sample size using Delves cup (50–100 µl) • Low purchase and running costs • Relatively few interferences • Robust interface	• Relatively high detection limit (~10 µg/dl) • Time needed for sample digestion/preconcentration if not using Delves cup • Large sample size needed for nebulization methods • Should not be left to run unattended
Graphite furnace atomic absorption spectrometry (GFAAS)	• Good detection limit (<1–2 µg/dl) • Small sample size • Moderate purchase and running costs • Some multielement capacity • Relatively few interferences (although more than with FAAS) • Widely used, available from multiple vendors	• Longer analysis time • Requires some laboratory expertise (more than FAAS) • Greater potential spectral interference than with FAAS
Laboratory anodic stripping voltammetry (ASV)	• Good detection limit (2-3 µg/dl) • Low purchase and running costs • Rapid • Small sample size (~100 µl) • Relative simplicity of equipment	• Requires some laboratory expertise (similar to GFAAS) • Sample pretreatment needed • Some factors might affect measurement (e.g. presence of copper) • Becoming less available
Portable ASV	• Portable; measurement at point of care possible • Simple to use; does not require skilled laboratory personnel • Very low purchase and running costs • Reasonably good detection limit for a portable device (3.3 µg/dl) • Rapid	• Not as accurate as other methods • Can determine levels only up to 65 µg/dl • Levels above 8 µg/dl should be confirmed by a laboratory method
Inductively coupled plasma mass spectrometry (ICP-MS)	• Excellent method detection limit (~0.1 µg/dl) • Rapid • Small sample size (50–100 µl) • Relatively few, well-understood, spectral interferences • Isotopic measurements possible • Economic if very large number of samples • Multielement capability	• High purchase and running costs • Highly skilled laboratory operator required

3.1.1 Flame atomic absorption spectrometry (FAAS) (5, 13)

FAAS uses an acetylene–air or a nitrous oxide–acetylene–air laminar flame to atomize lead at temperatures in the order of 2000–3000 °C, depending on the gas mix. The limit of detection of FAAS for blood lead depends on sample preparation and the method used. Delves cup methods, for example, enable the use of 50–100 µl sample sizes with a limit of detection in the order of 10–30 µg/dl. By comparison, using nebulization methods, the limit of detection is around 100 µg/dl, and larger samples are needed. Even the lowest achievable limit of detection is too high for FAAS to be useful for screening in populations with low background blood lead concentrations.

FAAS devices can be fitted with an autosampler, which enables large numbers of samples to be processed. Because they use a flammable gas, however, FAAS devices should not be left to run unattended. Owing to its relative simplicity of use, rapidity, relative freedom from interferences and moderate cost, FAAS has been used for decades and is still in routine operation in many parts of the world. In many countries, however, FAAS has largely been superseded by GFAAS, which can determine much lower blood lead concentrations.

3.1.2 Graphite furnace atomic absorption spectrometry (GFAAS)

GFAAS uses an electrically heated graphite tube to vaporize and atomize the analyte at temperatures up to 3000 °C prior to its detection. Sample volumes of 10–50 µl can be analysed. Because the entire sample is atomized within a small volume, a dense atom population is produced. This technique is therefore very sensitive. Methods have been developed that can measure lead concentrations down to below 0.1 µg/dl (*6, 14*); however, in routine use, the limit of detection is in the order of 1–2 µg/dl. GFAAS is currently one of the most commonly used methods for determining lead concentrations in blood. GFAAS is subject to greater potential interference than FAAS. This potential for interference has been reduced by improved instrumentation design and by the application of various matrix modifiers. GFAAS, however, requires trained laboratory personnel to be set up and operated accurately.

Modern GFAAS instrumentation is reliable, accurate and precise. GFAAS devices are usually equipped with an autosampler, which allows for large numbers of samples to be processed and better precision. The fact that GFAAS uses inert gas means that it can safely be operated unattended. Several manufacturers market GFAAS instruments that are readily configured for blood lead testing. GFAAS can be used for limited sequential analysis of multiple elements (e.g. lead and cadmium) in a single sample. It can be set up to measure a wide range of elements as a single element per sample.

3.2 Anodic stripping voltammetry (ASV)

3.2.1 Laboratory ASV devices

To conduct an ASV measurement, a reference electrode and a thin-film mercury graphite electrode are placed in the blood sample. A negative potential is then applied to the mercury electrode for several seconds, which causes lead and other cations present in the sample to concentrate on the surface of the negatively charged mercury electrode. The direction of the potential is then reversed to give an increasingly larger potential over several minutes. As the voltage reaches a specific and characteristic voltage for lead, all such ions are released (stripped) from the electrode, thereby producing a current that can be measured. The current

produced is proportional to the number of lead ions released and can be compared with calibration solutions to determine the lead concentration in the sample. This analytical technique requires that lead be decomplexed and available as the free Pb^{2+} aqueous cation and therefore involves sample preparation.

Although ASV can be used to measure a number of elements, it is mainly used to determine lead in blood, and some ASV instruments specially designed for this application are commercially available. Depending on the sample preparation used, the instrument requires calibration with blood-based materials, which are commercially available.

ASV can be used on microlitre sample volumes. Some commercial laboratory ASV devices can measure lead concentrations in the range of 1–100 µg/dl; however, best reproducibility is obtained at blood lead concentrations above 10 µg/dl (*1*, *15*, *16*). There are a number of factors that can potentially interfere with the measurement of lead using ASV. These include the presence of co-reducible metals that may give false peaks, the use of reagents that complex lead and alter its reduction potential, the presence of chelating agents or elevated copper concentrations (which might be increased during pregnancy or in other physiological states) in the sample. In addition, it is important to ensure quality control of electrodes and purity of the reagents (*1*). For these reasons, ASV requires a skilled operator to obtain optimum method performance.

Because of its good sensitivity to detect relatively high blood lead concentrations in the general population and its relatively low cost, ASV used to be one of the most common approaches to lead analysis, at least until the 1990s. Although ASV is still in use by some laboratories, those needing to measure very low blood lead concentrations (e.g. laboratories serving populations with low mean blood lead concentrations) have changed to more sensitive and precise techniques.

3.2.2 Portable ASV device

An ASV-based handheld instrument for the determination of lead in blood at the point of care has been developed, in collaboration with the United States Centers for Disease Control and Prevention. The initial instrument, named “LeadCare”, was commercialized in 1997 and became known as “LeadCare I” when the “LeadCare II Blood Lead Test System” was commercialized in 2006. LeadCare II is classified by the United States Food and Drug Administration (USFDA) as CLIA-waived* (i.e. it has a lower level of complexity with fewer regulatory requirements). This device does not require skilled laboratory personnel for its operation and has been approved by the USFDA for use at non-traditional laboratory sites, such as clinics, schools and mobile health units. It is also a useful tool for point-of-care blood lead analysis in epidemiological studies at locations where transport of blood samples to an appropriate reference laboratory is difficult.

The device allows the determination of blood lead concentrations within 3 minutes using a 50 µl sample of capillary (finger tip) blood or venous blood. The reportable range of blood

* The USFDA is responsible for the categorization of commercially marketed in vitro diagnostic tests into one of three CLIA (Clinical Laboratory Improvement Amendments of 1988) regulatory categories based on their potential for risk to public health: tests of high complexity; tests of moderate complexity; and waived tests.

lead concentrations is 3.3–65 µg/dl (17). Use at the point of care allows for the immediate collection of venous blood for confirmation of elevated lead levels by a reference laboratory. The single-use sensor, sample container, reagents and calibration equipment are provided as disposable units that are precalibrated by the manufacturer. Comparison of this device with a reference method (GFAAS) showed that it was reasonably accurate, precise and simple to use in the hands of people unaccustomed to performing laboratory tests (17). This device is now routinely used for screening purposes in some countries. However, the manufacturer recommends that a lead concentration at or above 8 µg/dl in any sample be confirmed by another method.

3.3 Inductively coupled plasma mass spectrometry (ICP-MS)

ICP-MS is a multielement technique that uses an inductively coupled plasma (a very high temperature ionized gas composed of electrons and positively charged ions) source to atomize the sample and subsequently ionize the atoms of interest (1, 5, 9). The ions are extracted from the plasma and passed through a mass spectrometer, where they are separated and measured based on their mass-to-charge ratio. The efficiency of the inductively coupled plasma in producing ions from the atoms of interest in the aerosolized sample, coupled with the high selectivity of the quadrupole (which filters the ions), the high amplification of ionic signals striking the detector and the low background noise of the detector, provides very low instrument detection limits (parts per trillion to low parts per billion) for most elements. ICP-MS method detection limits for direct analysis of lead in blood are approximately 0.1 µg/dl. ICP-MS is less tolerant than GFAAS of heavy matrices, so the dilution of blood samples prior to aspiration into the plasma is necessary; therefore, ICP-MS devices usually require skilled laboratory technicians for operation at the highest standards.

Whereas other methods can measure only one or a few elements at a time, ICP-MS can measure multiple elements from a single sample as small as 50–100 µl. This would be an important consideration for laboratories wishing to measure a number of elements in addition to lead. In addition, ICP-MS enables the determination of the isotope ratio of the lead present in a sample, which makes it possible to identify whether the lead came from a particular source.

The purchase cost of an ICP-MS device is high, but it has a high productivity and becomes comparatively economical when many samples and/or elements need to be determined.

4. Important aspects of laboratory practice

In analytical toxicology, even the most sophisticated and accurate equipment will provide incorrect results if the samples have not been appropriately collected and handled, if the equipment has not been used correctly or if analytical protocols have not been followed. The primary concerns associated with current measurements of blood lead concentrations are unrecognized contamination and insufficient quality assurance (QA). These issues are briefly discussed in the following sections.

4.1 Preventing external contamination of samples

Lead is pervasive and can contaminate samples in numerous ways, including during sample collection, sample storage and transport, and sample manipulation. The quality of sample collection and handling is therefore a crucial aspect for the biomonitoring of lead. Specific protocols are available for the different analytical methods, including from manufacturers and standardization agencies, but general precautions apply universally. In all cases, sample collection equipment and containers, including needles and caps, must be certified as lead free, prescreened to measure their lead content or scrupulously acid-washed. Another important aspect for blood collection is the thorough cleansing of the puncture site before blood collection - this is particularly important for finger-tip (capillary) samples, which are highly likely to be contaminated where there is environmental exposure to lead. If blood samples are being collected in the field efforts should be made to set up a clean location for the sample collection. Capillary blood lead measurements can be used for initial screening purposes, and may be used for diagnosis. Since, however, such samples may be more prone to contamination a venous blood sample is preferred, and is recommended when initial measurements are considered elevated.

Sample handling within the laboratory also entails some risk of contamination. These risks can be significantly reduced by implementing adequate QA measures. Laboratories should be as close to lead free as possible, and laboratory staff should be properly trained to prevent sample contamination. Tasks involving high concentrations of lead (e.g. analysis of environmental samples) should not be performed in the same laboratory area as biological sample testing. Sample preparation should be performed in a clean environment, ideally in an International Organization for Standardization class 5 setting (i.e. having no more than 10^5 particles per cubic metre of air) or better. This can be achieved by preparing samples in a laminar flow biological safety cabinet (e.g. a class B2 cabinet). Laboratories should try to minimize the amount of air particulates (i.e. dust and/or outdoor particulates) in the laboratory and in the area where open sample tubes will be located during analysis. Instrument autosamplers should be covered.

4.2 Quality assurance (QA)

QA refers to all the steps that must be taken to assure that the laboratory results are reliable. It covers the utilization of scientifically and technically sound practices for laboratory investigations, including the selection, collection, storage and transport of specimens and the recording, reporting and interpretation of results. It also refers to training and management designed to improve the reliability of investigations. From the point of view of an analysis, QA can be divided into two stages: 1) initial assessment of an analytical method as to its practicability and trueness, which includes linearity, specificity, recovery, calibration standards, blanks and interference; and 2) subsequent quality assessment.

Quality assessment refers to the quality of the analytical results. It has two components:

1) internal quality control, which is a set of procedures used by the staff of a laboratory for continuously assessing results as they are produced in order to determine whether they are reliable enough to be released;

2) external quality assessment (EQA), which is a system for objectively checking laboratory performance using an external agency.

Further information on laboratory QA and quality management and examples of EQA programmes specific for blood lead are available from various sources (*18–23*).

The precision and accuracy of the measurement are particularly important for blood lead analysis, as the blood lead concentrations measured will determine medical treatment and the need for environmental investigations. It is therefore crucial that the laboratory conducting the investigation follow adequate QA measures, including, if possible, EQA. Enrolment in a national and/or international accreditation scheme is advisable.

Longitudinal biomonitoring has additional requirements for long-term QA that will assure that method accuracy and precision are maintained over the length of the investigation (frequently many years), rather than simply assurance of measurements made on a specific day or group of days. In these investigations, sufficient overlap of successive quality control pools, long-term tracking of performance in EQA schemes and method comparison studies as methods are updated over time are all important factors in ensuring the maintenance of QA over time, so that the assessment of drifts in population exposure levels over time can be made with confidence.

5. Considerations for method selection

Several factors need to be taken into account when selecting an analytical method for the determination of blood lead concentrations. Some of these are briefly described below.

5.1 Purpose and circumstances

Method selection will greatly depend on the purpose for the measurement and the circumstances surrounding the analytical investigation. Important parameters that must be clearly defined before a method is selected include:

- the limit of detection required;
- the accuracy and precision needed;
- the turnaround time desired;
- the number of samples to be analysed;
- the need/possibility to perform analysis at the point of care;
- the need to confirm the environmental source of exposure (through isotopic analysis);
- any regulatory or legal issues surrounding the measurement.

Practical examples of scenarios are provided and discussed in section 6.

5.2 Availability of operational equipment

Method selection will also depend on the operational equipment available. Although a specific method or device might, in theory, be the best option for a given task, it might not be

available when needed. Other operational devices should be identified and carefully reviewed with regard to their suitability for the analysis to be conducted. Consideration should be given to the length of time and logistics required for the transportation of supporting supplies and/or biological samples to and from the locations of equipment planned for use in the analytical work. Consideration should also be given to the availability of service support for the equipment (i.e. technical support, repair services and preventive maintenance services).

If no suitable methods or devices are available locally, the analysis might be outsourced to an external laboratory (if necessary at an international level), or suitable equipment might be purchased. In the latter case, the large amount of time required to set up and validate a new instrument (up to several months) must be taken into account.

5.3 Ease of use and availability of skilled personnel

Some methods are very simple to use and do not require trained laboratory personnel, whereas others can be run effectively only by skilled laboratory staff. Factors to consider will include the level of automation available, the condition of the instrumentation and service support available, the degree of accuracy and precision required, and the amount of maintenance that will be needed. If the analytical equipment is old, this increases the need for skilled personnel, particularly if the equipment is no longer supported by a local company. If using the analysers at the point of care, there is a need to plan for environmental conditions that could increase the difficulty of the analytical exercise. These include environmental contamination risks, availability of resources for adequately washing patients' hands, temperature requirements of the analysers, and the availability and quality of the electricity supply.

Some other specific issues include the following:

- Portable ASV devices are very user friendly and do not require trained laboratory technicians.
- FAAS systems are usually relatively easy to set up and run, but do require some laboratory expertise. This is particularly true if there is a need to measure lower blood lead concentrations, as more sophisticated protocols will be needed.
- GFAAS systems are somewhat more difficult to set up and maintain and require laboratory expertise.
- Laboratory ASV devices require some level of expertise to properly address factors that might affect the accuracy of the measurement.
- ICP-MS generally requires highly skilled laboratory personnel to achieve superior results and reliable, high-quality data.

When skilled personnel are needed but unavailable, it might be necessary or more effective (depending on circumstances) to outsource the analysis to an external (if necessary international) laboratory, rather than to train local laboratory staff.

5.4 Analysis costs and availability of financial resources

The analysis costs and financial resources available must be precisely assessed before selecting an analytical method. The true costs are often underestimated.

If the analysis is conducted locally with existing devices, running and maintenance costs must be taken into account. Whereas some devices require only relatively cheap reagents, others have relatively high operating and maintenance costs, including special gases, lamps, tubes, high-purity reagents and standards, a reliable and consistent power supply, and cooling water. Using older equipment, especially if there is no local maintenance support, can increase costs.

If a new device must be acquired, purchase cost but also installation costs to adapt the laboratory to device requirements (e.g. fume extraction, gas installations, electrical and water supply) and running and maintenance costs must be considered. In addition, training and salary costs for laboratory personnel should be taken into account.

If the analysis is conducted by an external laboratory, additional costs, such as sample transport and collection, must be taken into account.

5.5 Quality assurance

Adherence to strict QA measures is crucial to assure the accuracy and validity of the blood lead concentration analysis. If QA cannot be ensured by a laboratory for a specific method, it might be necessary to use a different method or to outsource the analysis to another laboratory, if necessary at the international level.

6. Scenarios

This section presents some typical scenarios in which blood lead measurements are required, with pointers to some of the considerations that will influence the choice of analytical method.

6.1 Suspected intoxication

Determination of the blood lead concentration is crucial for the investigation of suspected cases of lead intoxication. Severe cases of acute and chronic lead intoxication occur and have been reported in virtually all countries. Intoxication can affect a single individual (e.g. a child who has ingested a fishing weight, leaded paint flakes or a lead paint–coated toy; an adult involved in the informal recycling of lead batteries) or a group of people (e.g. lead poisoning outbreaks caused by environmental contamination from processing lead-rich ore; outbreaks arising from use of contaminated ayurvedic medicines or spices).

When investigating a suspected lead intoxication, the rapid availability of results is an important requirement, in particular if exposure levels are acutely life-threatening. A low limit of detection is generally not required. Methods or devices available locally might therefore be preferred to avoid loss of time for sample shipment (in particular if international transport is required). Analysis at the point of care using a portable ASV device might be an advantage,

in particular for rapid patient triage. If a portable device is used, it is recommended that samples with lead concentrations above 10 µg/dl be reanalysed by a diagnostic method (e.g. laboratory ASV, GFAAS or ICP-MS) to confirm the lead concentrations. Analysis of blood lead concentrations for patients undergoing chelation therapy, however, requires a very accurate method and strict QA measures.

6.2 Exposure assessment

Determination of blood lead levels may be required as part of a health risk assessment for a population at risk of being exposed to lead, such as villagers living in the vicinity of a lead-processing factory. Health risk assessments include an exposure assessment step to estimate or measure the magnitude, frequency and duration of exposure to lead, along with the number and characteristics of the population exposed. Although different approaches to evaluate human exposure to lead exist, blood lead concentrations are often used as markers of exposure.

Determination of blood lead concentrations as part of an exposure assessment will require a method with a high level of accuracy (to enable accurate comparison of results with future or past measurements) and a low limit of detection (to determine low levels of exposure). The ability to identify the environmental source of exposure through isotopic analysis might also be useful. If measurements are likely to be used to support legal action, it is crucial that a strict QA process be ensured, ideally including international accreditation and EQA. If a large number of measurements are needed, financial factors may also need to be taken into consideration.

6.3 Screening

Because lead-poisoned individuals are often asymptomatic, the measurement of blood lead concentrations is often used to screen for poisoned individuals in a population at risk or in the general population. Screening programmes usually cover relatively large populations. More affordable analytical methods might, therefore, be preferred in this context. The ability to conduct the analysis at the point of care using a portable ASV device might be an asset. If one is interested in determining the (usually low) exposure level of the general population, a highly accurate method with a low limit of detection might be preferred. Strict QA measures should be ensured.

6.4 Occupational health

The measurement of blood lead concentrations is often part of the routine monitoring of workers active in the lead industry or other work involving lead. In many countries, the regular monitoring of blood lead concentrations of such workers is required by legislation, which also provides for the suspension or removal from further exposure of those with blood lead concentrations above certain values.

In this context, a method with a high level of accuracy is preferred to allow comparison of results with future and past measurements. Strict QA measures should be ensured. If a large

number of measurements are needed, financial aspects might also need to be taken into consideration.

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