V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

The American Conference of Governmental Industrial Hygienists (ACGIH)\(^61\) has reviewed previous standards for lead in the work environment, and has commented that there are few meaningful data relating to the threshold limit value, probably because most authorities rely primarily on other tests for estimating lead hazards, such as urinary and blood leads, urinary coproporphyrin and ALA, as well as examination of the blood for stippled cells.

Nevertheless, attempts were made to control occupational lead poisoning by establishing acceptable air levels to guide engineering control measures. Although the point is not documented, it seems that at one time an air limit value of 0.5 mg/m\(^3\) was used. In the 30's and 40's, a value of 0.15 mg/m\(^3\) was a common, but often unachieved, goal based on a recommendation of a 1928 PHS survey of storage battery workers published in 1933.\(^62\)

This value continued to be the one most often accepted until 1957, when the ACGIH increased the TLV to 0.20 mg/m\(^3\), based in part on data of Elkins\(^5\) showing that exposure at 0.20 mg/m\(^3\) would result in urinary excretion at 0.20 mg/liter.

In 1971, the Conference recommended lowering of this value back to 0.15 mg/m\(^3\). This appears to have been based in part on the recommendations of the International Subcommittee for Occupational Health, Permanent Commission and International Association of Occupational Health \(^63\) at a 1968 meeting in Amsterdam, and on the results of the study by Williams, King, and Walford. \(^47\)
The International Subcommittee recommended a time-weighted average concentration for a 40-hour week of 0.15 mg/m³, on the basis that it corresponded to an acceptable blood concentration of 0.07 mg/100 ml.

The current workroom air standard established under the Occupational Safety and Health Act of 1970 (published in Part 1910.93 of the Federal Register, Volume 36, Number 157, pages 15101-15107, dated August 13, 1971) is 0.2 mg/m³; this is a time weighted average, and is based on American National Standards Institute Z37.11-1969. This ANSI standard provided no basis for its recommendation.

Basis for Recommended Environmental Standard and Biologic Monitoring

(See Appendix V - NIOSH Testimony Presented at DOL Hearing on a Lead Standard.)

Earlier in this century, efforts to reduce occupational lead poisoning were based on adherence to hygienic workroom air guides. As more knowledge developed, increasing attention was given to blood and urinary lead levels as guides to reduction of occupational poisoning. Concomitantly, there was increasing attention to better lead analyses. There was also an increasing knowledge of the relationship between levels and rates of absorption and excretion, blood lead levels, and health status.

The PHS study by Dreessen et al. was undertaken during the period that the workroom air guide of 0.15 mg/m³ was accepted, but failure to achieve control of airborne lead to this level was common, so findings of slight effects among workers in lead-using industries by Dreessen and co-workers did not invalidate the guide. Though not documented, it appears that many industries have rotated their workers to various jobs to keep blood lead levels below 0.08 mg/100 g; thus, exposure to unsafe workplace air levels did not result in adverse effects on health.
Consequently, there is a little definitive information from experience in the United States and other countries on the suitability of 0.15 or 0.20 mg/m³ as an air-lead level to which workers can be safely exposed over a working lifetime.

However, much experience has accrued to show that absorption of lead in amounts resulting in blood lead concentrations of 0.08 mg/100 g or less will not lead to adverse effects on health, and there is information from studies in other countries relating airborne lead levels to blood lead.

It was previously concluded (III. Biologic Effects of Exposure; Correlation of Exposure and Effect) that a blood lead level of 0.08 mg/100 g is useful for delineating acceptable from nonacceptable lead absorption. While levels below 0.08 mg/100 g are indicative of acceptable occupational lead absorption and, if also representative of past absorption of lead by an individual person, also indicative of insignificant risk of lead poisoning, it should not be concluded that lead poisoning will occur if blood lead levels exceed 0.08 mg/100 g. However, there is an increasing risk of poisoning as levels increase above 0.08 mg/100 g, so absorption of lead should be held to amounts that will result in blood lead levels less than 0.08 mg/100 g. As Kehoe 65 has stated, "...lead poisoning occurs in man only when certain well-defined conditions have been fulfilled" and that this is quantitatively applied by "...the relationship between the current rate and the extent of the absorption of the inorganic compounds of lead, and the concentration of lead in an accessible tissue of the living body, namely, the blood." Thus, a biologic standard of 0.08 mg of lead per 100 g of whole blood is recommended; it provides a margin of safety in adults,
but probably not in children. The extent of this margin of safety is not known, but it seems likely that there will be few, if any, cases of lead poisoning below 0.09 mg/100 g.

Kehoe also pointed out the usefulness of urinary lead as an index of current absorption of lead, but added that it was a quantitatively less certain index than blood lead. It may be consistent with this view that Williams, King, and Walford found that the best correlation between airborne lead and biochemical index of effect was with blood lead (r = 0.90) and less correlation with urinary lead (r = 0.82). The study of Williams and co-workers indicates that blood levels of 0.08 mg/100 ml is associated with a urinary lead level of 0.20 mg/liter. It has been commonly accepted that 0.20 mg/liter is a safe level in urine, based in part on the findings of Elkins. However, it is important to note that Elkins' studies involved calculation of specific gravity of urine to a value of 1.024. The studies of Williams et al. also calculated urinary specific gravity to 1.024. (Urinary lead levels of 0.20 mg/liter, adjusted to a specific gravity of 1.024, would be 0.133 mg/liter if the specific gravity were calculated to 1.016.) Thus, the conclusion of Zielhuis that urinary lead greater than 0.15 mg/liter, uncorrected for specific gravity, represents unacceptable absorption of lead is consistent with the selection of a biologic standard for urinary lead of 0.20 mg/liter, so long as the specific gravity correction is used.

ALA and coproporphyrin assays, and blood examinations for hemoglobin, reticulocytes, and stippled cells are useful in the assessment of worker health, but are less useful than blood lead as a single criterion for
interpreting the acceptability of lead absorption, since no one of these measurements is a specific index of lead absorption, as is urinary or blood lead.

It should be emphasized that blood lead and urinary lead are good indices of current absorption of lead (in the absence of anemia or absorption of chelating agents), but are not necessarily indications of body burden of lead or of the state of health of the individual. Bone lead is probably more indicative of total body burden than is blood lead, but it is not feasible to sample bone for routine lead assay. As to state of health, overabsorption of lead by an individual in the past may have led to a high body burden of lead and may also have contributed to a state of current ill-health in the individual, all without causing currently high blood or urinary levels of lead.

Since the studies of relationship between health and airborne lead levels are inadequate, it is concluded that an air standard should be recommended from data on the relationship between airborne lead and biochemical indices of effect, most importantly, blood lead. There are several studies that point to 0.15 mg/m$^3$ as the level of airborne lead that will result in biochemical indices showing acceptable absorption of lead, in other words, showing that occupational exposure at 0.15* mg/m$^3$ will not result in adverse effects on the health of workers.

Tsuchiya and Harashima$^{46}$ studied storage battery workers in Japan and compared airborne lead with urinary lead, urinary coproporphyrin, basophilic stippling of erythrocytes, and, as an index of anemia, specific gravity of blood. They recommended airborne lead levels on the basis of acceptable

*See appendix V for basis for revised recommendation for an occupational exposure to inorganic lead.
levels of these biochemical indices. On the basis of acceptable urinary lead levels of 0.15 mg/liter, corrected to a specific gravity of 1.024, they recommended a threshold limit value of 0.10 mg/m$^3$. If a higher urinary lead level is accepted, as recommended in the preceding discussion of the relationship between acceptable lead absorption and urinary lead excretion, a higher air standard would result. It should be noted that the workers studied by Tsuchiya and Harashima worked 8 to 10 hours, 6 days a week, and they observed that a higher air level would have been recommended for a 40-hour week.

The study most directly relevant to the development of a recommended workplace air standard is the study of Williams, King, and Walford. Their data (Table X-5), from studies of storage battery workers stable in their employment (40-hour work week, no job change in the past year, no recent absence or sickness, no change in overtime or productivity), showed that exposure at 0.15 mg/m$^3$ resulted in a mean blood lead of 0.060 mg/100 ml. Were mean blood lead the criterion of effect, an air standard much higher than 0.15 mg/m$^3$ could be recommended, but in order to keep most or all workers' blood lead below 0.084 mg/100 ml (0.080 mg/100 g), it is believed that a mean of about 0.060 mg/100 ml should be achieved. The data of Williams and associates does not provide a basis for interpreting the percentage of workers exposed at 0.15 mg/m$^3$ that will have blood levels above 0.084 mg/100 ml. However, it is believed that a small percentage will have blood lead levels at or above 0.084 mg/100 ml or 0.080 mg/100 g, so it is recommended that workers be monitored biologically, by periodic assays of blood lead, or of blood and urinary lead.
Stankovic also compared airborne lead with blood and urinary lead, and in workmen exposed to lead at 0.15 mg/m³ and below, the highest individual blood lead found was 0.06 mg/100 g, and the highest urinary lead 0.12 mg/liter. However, the number of workers exposed at or near 0.15 mg/m³ was not stated, so his finding of 0.06 mg/100 g as the highest individual blood lead is not believed to contradict the previously stated inference that some workers exposed at 0.15 mg/m³ will have blood lead levels at or above 0.08 mg/100 g (especially those workers absorbing abnormal amounts of lead from nonoccupational sources).

It is of interest that conclusions of experts support the recommended standard, but since data and arguments supporting their conclusions were not presented, their recommendations have not been given weight in deriving the recommended occupational air standard.

The rationale for the recommended work practices and sanitation practices was principally derived from Kehoe. They are normal industrial hygiene procedures used to control occupational exposures to various dusts and fumes.

If worker exposures exceed 40 hours a week, the same TWA of 0.15 mg/m³ should be used unless exposures so greatly exceed 40 hours a week that nonworking (excretion) time is significantly reduced; exposures up to 50 hours a week should not significantly affect the time for excretion of absorbed lead. However, maintenance of the same TWA means a proportionate reduction in average concentration as exposures exceed 40 hours a week. To achieve a TWA of 0.15 mg/m³, the average concentration should be 0.15 mg/m³ for a 40-hour week and 0.12 mg/m³ for a 50-hour week.
**Basis for Environmental Sampling and Analytical Method**

Various methods of sampling air and of analysis of these samples have been considered, and recommended methods are presented in Appendixes I and II.

The recommended method of sampling air involves collection of 100 liters of air or more, use of breathing zone samplers with sampling at a rate of 2 liters/min., and collection on 0.45μ cellulose membrane filters. Other sampling rates and other collection media (filter paper, nitric acid impinger, electrostatic precipitation) are capable of giving equivalent results. The recommended procedure is described in Appendix I.

For analysis of lead in blood, atomic absorption spectrophotometry and dithizone colorimetry were considered. Appreciable consonance can be demonstrated between results obtained with atomic absorption and dithizone methods. Both methods have been used for analysis of air samples, and both are concluded to be capable of giving accurate results. After a review of the several procedures involving atomic absorption spectrophotometry, it was concluded that no one of these procedures has been sufficiently standardized. Individual laboratories get excellent results with a specific procedure, but these procedures have not been compared in a number of laboratories. Dithizone colorimetry, on the other hand, has been used for a long time and has been thoroughly studied. The procedures, interferences, sensitivity, and replicability have been studied and are described by Keenan, Byers, Saltzman, and Hyslop. The recommended procedure is described in Appendix II.

Dithizone colorimetry is a wet chemical method requiring equipment found in most chemical laboratories, but requires meticulous attention to detail and to the prevention of loss and the exclusion of contamination.

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Results of lead analysis by this method obtained by well trained technicians are often superior to results obtained by other methods of analysis.

**Basis for Biologic Analytical Method**

Blood lead was selected as the best method, and urinary lead as an acceptable method, for judging lead absorption, for reasons discussed in earlier sections (see "Basis for Recommended Environmental Standard and Biologic Monitoring").

Specific details for collection of biologic specimens for lead analysis have been described in a booklet *Methods for determining lead in air and in biological materials*, published by the American Public Health Association. Keppler et al.\(^7\) described the initiation of interlaboratory evaluations of lead in an attempt to improve accuracy and reproducibility of laboratory analyses through a system of accreditation. Subsequent reports\(^7\) have described some of the results, from which it is apparent that lead analysis is subject to significant error unless a very high degree of care is used.

Methods for the collection of blood and urine are described by Keenan et al.\(^7\) (Appendix II). While lead-free Vacutainers are convenient, any lead-free tube can be used for collection and shipment or storage of blood prior to analysis. No aliquots can be taken unless blood-clotting has been prevented, either by taking aliquots before clotting or by prevention of clotting, e.g., by heparinization. Single use needles ("throw-aways") are acceptable, but must be lead-free, thus must not be lead-soldered.
Methods for the determination of lead in biological materials include dithizone colorimetry,\textsuperscript{72,73,78} spectrography,\textsuperscript{79} polarography,\textsuperscript{80} and atomic absorption spectrophotometry.\textsuperscript{69,71,81} In addition, many biochemical tests, reviewed by Chisolm,\textsuperscript{82} have been developed; these depend on the lead-induced upset in heme synthesis. Among these biochemical tests are determination of coproporphyrin excretion,\textsuperscript{83} urinary ALA\textsuperscript{26,84} and ALA-D in blood.\textsuperscript{85,86} Additional methods, such as cell stippling, porphobilinogen determinations, and examination of intranuclear inclusion bodies have received less acceptance. These biochemical indices are not recommended at this time. They can be sensitive, perhaps too sensitive, but they are not specific for lead, and are judged to be less useful than blood and urinary lead determinations for estimating the absorption of lead. However, future developments may resolve some of the present objections to the routine use of these indices of alterations of heme synthesis in the assessment of lead absorption.

The dithizone procedure is recommended for analysis of lead in blood and urine. As discussed in the previous section (Basis for Environmental Sampling Method), the method is capable of good results if meticulous attention is given to details, including sources of contamination and loss. Cholak\textsuperscript{87} has stated that with careful control the procedure can detect as little as 0.5 µg, with a precision of ± 0.5 µg, and that, with modifications, as little as 0.2 ± 0.1 µg can be determined. The recommended method as described by Keenan et al.\textsuperscript{72} is given in Appendix II. Bismuth is a possible, but uncommon, interfering substance, which can be removed by extraction.
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VII. APPENDIX I

METHOD FOR SAMPLING OF LEAD IN AIR

Lead dust or fume is collected on 0.45 μm cellulose membrane filters mounted in either 2- or 3-piece filter cassettes. Air is drawn through the filter by means of a pump at a rate of 2 liters a minute (not less than 1 nor more than 4 liters per minute). A minimum sample of 100 liters shall be collected. Larger sample volumes are encouraged provided the filters do not become loaded with dust to the point that loose material would fall off or the filter would become clogged.

With each group of samples, one filter, labeled as a blank, shall be submitted; no air shall be drawn through this filter.

The sample cassettes, if shipped, must be packed in a suitable container to prevent damage in transit. Loss of sample shall be prevented; loss of loose deposits on the filter can be prevented by mounting a clean filter in the cassette on top of the sample filter.

Ash the filter and analyze for lead as described in Appendix II.

Other collection methods shown to be equivalent may be used.