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March 21, 1983

Dr. David E. Weil
Project Manager
Environmental Criteria & Assessment Office
MD-52
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

Dear Dr. Weil:

The attached material has been prepared for distribution to the special statistics panel, assembled by EPA to determine to what extent, if any, NHANES II blood lead data can be used reliably to evaluate within study time trends and to correlate these trends with other environmental lead exposure data.

Du Pont has made several submissions to EPA in the matter of the gasoline lead phasedown regulations (Docket No. A-81-36) which contain analyses and viewpoints on many issues bearing on the review of the Air Quality Criteria Document for Lead. As opposed to submitting all these documents, the attached presentation represents a consolidation of only that material relevant to the chartered task of the special panel. Reference is made on several occasions to Du Pont's submission to EPA of October 8, 1982 which the panel already has received.

We would appreciate it if you could distribute this material to the panel in time so they can review it prior to our next session. Seven copies are enclosed for your convenience. We may have additional items for distribution at the next session.

Very truly yours,

J. M. Pierrard
Engineering Fellow

JMP:mep
Attachment

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TEH 0533060

March 18, 1983

DU PONT'S SUBMITTAL TO SPECIAL EPA STATISTICAL PANEL EVALUATING THE NHANES II STUDY FOR THE EPA REVIEW OF THE AIR QUALITY CRITERIA DOCUMENT FOR LEAD

The Second National Health and Nutrition Examination Survey (NHANES II) was conducted by the National Center for Health Statistics to gather health and nutritional data from a representative cross section of the noninstitutionalized U.S. population. The blood lead phase of the program (1) was intended to: (i) provide information for the first time about the distribution of blood lead levels in the general U.S. population, (ii) establish base line estimates for future studies to monitor changes in such exposure over time, (iii) provide normative information for use in health policy and regulatory decisions and (iv) correlate levels of exposure with other health and nutritional parameters.

Chronological analyses of NHANES II blood lead data have revealed a general downward trend during the course of the survey (February 1976 through February 1980). The blood lead trend and a similar trend in national gasoline lead use (see top figure in Attachment 1) have been widely publicized during 1982 in the proceedings of the gasoline lead phasedown regulations. The drop in blood lead levels from beginning of survey to end of approximately 5.8 μg/dl has been largely attributed to gasoline lead as a result of the aforementioned coincidental trends and subsequent analyses by ICF (EPA contractor) and CDC which identified significant associations between blood lead and gasoline lead. Further, ICF (2) has used empirically derived relationships between NHANES II blood lead data and gasoline lead use to (i) forecast the incidence and number of children expected to have elevated blood lead levels under various gasoline lead regulation scenarios for the years 1983 to 1990 and (ii) estimate the proportion of lead in blood that is due to gasoline lead emissions for the period 1976 through 1980.

Du Pont continues to be gravely concerned regarding the quantitative and causal implications of these and related analyses. We do not believe that the NHANES II blood lead data can be used to estimate time trends during the study period, attribute the portion of the decrease due to gasoline lead use or correlate these data with gasoline lead use to answer questions of the type ICF (2) has attempted to do. A key basis for this concern is a gross inconsistency between the observed blood lead level drop from beginning to end of the NHANES II study and that which might have been expected to occur based on reductions in air lead attributable to reductions only in gasoline lead.

One of the best documented and independently assessed relationships used in setting the present air lead standard is the blood lead (μg/dl)-air lead (μg/m^3) slope. Most researchers

have concluded that the slope is in the 1-2 m^3/dl range. (EPA used a value of 2 m^3/dl in setting the current air lead standard.) The composite quarterly average of ambient air lead values at 105 sites across the nation reported by EPA (3) was about 1.25 $\mu g/m^3$ in 1976 and 0.93 $\mu g/m^3$ in 1979, the latest year available. Applying the blood lead/air lead slope of 2 m^3/dl to the estimated national air lead drop of 0.32 $\mu g/m^3$, provides a rough estimate of 0.64 µg/dl for the expected blood lead drop. This estimate differs by nearly one order of magnitude from the decline observed during NHANES II. Because gasoline lead emissions contribute approximately 90% to the lead in air, it is implausible that reductions in gasoline lead have resulted in a substantial portion of the observed decrease in blood lead levels.

The difficulties of avoidance of contamination and of accurate analysis of lead in biological materials recently have been reviewed by the Karolinska Institute (4). As stated in Section 3.3 of the Institute's report (Attachment 2):

> "Studies on commercially available blood collection tubes have shown that diluted nitric acid as well as blood may extract lead and cadmium from certain vials and syringes in quantities which would invalidate any measurement of these metals in blood within the normal range of concentration."

As further stated in Section 2.3 of the Institute's report (Attachment 3):

> "The reviewed studies show that the accuracy and precision of trace metal analysis in biological specimens, especially lead and cadmium in blood and urine, in general appear to be unsatisfactory. This may also hold for laboratories that have gained considerable experience by analyzing a large number of biological samples over many years."

Because of the factors discussed above, it appears plausible that most of the reported decline in blood lead levels may be due to one or more of the following:

1) Biases resulting from sampling itinerary and differential stand-to-stand demographic composition.

2) Bias resulting from inadequate quality control.

3) Contributions from reductions in other sources of lead exposure such as water, food and nonfood (e.g. paint lead) items.

Consequently, Du Pont continues to critically review the NHANES II data and challenge those who use these data to draw unsupportable conclusions.

The following items summarize points that Du Pont has previously raised in submissions to EPA in the matter of the gasoline lead phasedown regulations on the interpretation of the NHANES II blood lead data and its relationship to gasoline lead use.

1. Regional Sampling Variations

Although the NHANES II survey was intended to provide a snapshot of distributional characteristics of all recorded health and nutritional parameters, the study required four years to complete. No controls to insure samples representative of the target population within stands or even within short time periods were imposed. Regarding the scheduled sample itinerary, Annest, et al (1) warned:

> "A possible logistical factor indirectly influencing the blood lead data is the itinerary of the Mobile Examination Centers (MEC's). To minimize the effects of adverse weather conditions on response rates, MEC's were set up in the northern states during the summer and more southern states during the winter. The potential environmental effects on blood lead levels associated with seasonality and geographic location may be confounded, to some undetermined degree, with those associated with degree of urbanization of place of residence."

The breakdown by region of numbers of venous blood leads sampled by six-month periods is shown in the table below. Year-long periods devoid of data occurred in each region at some point during the study. In 1980, samples were taken only in the south.

Sampling Program
Number of Persons Sampled

	Northeast	South	Midwest	West	Total
76-1st half	0	437	41	557	1,035
76-2nd half	0	425	821	226	1,427
77-1st half	470	696	0	0	1,166
77-2nd half	845	267	0	0	1,112
78-1st half	0	0	19	1,193	1,212
78-2nd half	424	0	776	0	1,200
79-1st half	0	240	673	517	1,430
79-2nd half	353	330	208	0	991
80-1st half	0	315	0	0	315
Total	2,092	2,710	2,638	2,493	9,933

2. Differential Urban Representation

The figure shown at the top of Attachment 1 is the plot that Dr. Vernon Houk, CDC, published (5) and presented in public sessions, which shows a correlation between the weighted arithmetic mean NHANES II blood lead levels and gasoline lead use, grouped by six-month (January to June and July to December) intervals. The figure at the bottom of Attachment 1 is an alternative plot showing a similar correlation between the same NHANES II blood lead values and actual percent of urban dwellers (urban categories 1-4 on data tape) represented.

Further simple correlation analyses were performed between weighted geometric mean blood lead levels and weighted sample proportions associated with various demographic categorizations in six-month intervals. These results are presented in Attachment 4 (see (6), Section III, Appendix A). The urban category is defined as in Attachment 1, which the rural area category reflects urban category 8 on the NHANES II data tape. Consistent significant associations occur over many age, race and sex categories for urban and rural dwellers.

3. Impact on Blood Lead Trend After Accounting for Urbanization and SMSA Category

By way of a simple analysis, Du Pont has attempted to underscore the need to take proper and complete account of confounding factors before using NHANES II in a manner for which it was not designed. Preliminary graphical time trends by SMSA category (levels are central city, not central city and not SMSA and are a separate and not dependent classification from urbanization in the NHANES II data base) revealed a decreasing but nonparallel relationship. Regressing $\log_e$ blood lead on terms reflecting urban area (categories 1-4), SMSA category, time, time by SMSA category interactions and age, race and sex main and interaction effect terms confirmed the nonparallelism. (Refer to (6), Section III, Table 1.) Subsequently, another analysis was performed regressing $\log_e$ blood lead on single degree of freedom terms urban area, central city (versus not SMSA) and not central city (versus not SMSA). The residuals of this analysis on 9701 blood lead observations (only white and black races included) reflect adjustments to the dependent variable for urban area and SMSA category. Weighted (by lead weights) geometric mean comparisons between the observed blood lead data and the adjusted blood lead data (exponential of residual plus overall mean) for the first and last six-month periods of NHANES II are given in Attachment 3 (see (6), Section III, Table 2). The results suggest that degree of urbanization and SMSA category may be able to account for a nonincidental portion of the trend.

4. Evaluation of Blind Quality Control Data

Our analysis of the NHANES II blind quality control data is reported in (6), Section III, pages 5-7. This analysis was based on data provided last summer by CDC representing averages of duplicate blind quality control data from low (13.5 µg/dl) and high (25.5 µg/dl) lead bovine pools. In that discussion, it was noted that no blind quality control data were available for the first 334 days or the last 265 days of NHANES II and there were coincidental significant curvilinear effects in both pools.

CDC subsequently pointed out that data were available at the end of the study and the testing time associated with the quality control data must be inaccurate. On January 26, 1983, Dr. Pirkle provided Du Pont another listing of these data with correct time associations. The new listing indicates that quality control testing began 518 days after the start of NHANES II for the low lead pool and 369 days after the start for the high lead pool.

5. Federal Programs to Reduce Lead Exposure

A report of the National Academy of Sciences (7) stated that there are at least eight departments and agencies of the Federal government currently administering programs designed to limit human exposure to lead. Fourteen regulations are identified which are aimed at reducing or eliminating human lead exposure as it occurs through air, water, food and nonfood media (e.g. paint lead). Table C1 of the NAS report (Attachment 6) summarizes these regulations.

Unfortunately, very little data of sufficient quality on the impact of these programs are available to relate to the NHANES II blood lead data. Publications by Jelinek (8) and Schaffner (9) indicate major reductions in food lead levels, particularly those of the processed or canned variety. Table 5 from Jelinek is shown below.

Lead Content, Food for Infants

Product	Mean Level, ppm		
	Early 1970's	1976-1977	1979-1980
Infant Formula, Concentrate a	0.10	0.055	0.02
Infant Juices	0.30 a	0.045 a	0.015 b
Infant Foods, Pureed b	0.15	0.05	0.03
Evaporated Milk a	0.52	0.10	0.08

a Packed in cans b Packed in glass

The paucity of quality data, however, does not allow one to conclude that lead exposure reductions in sources of lead other than via gasoline lead has no, or has an inconsequential, effect on the observed NHANES II blood lead trend; nor does it allow one to conclude that no differential variations in lead exposure from nongasoline sources during NHANES II occurred which is an implicit assumption when trying to forecast blood lead values on the basis of gasoline lead consumption alone.

6. Analyses Relating Blood Lead Levels to Both Gasoline Lead Use and Paint Lead Exposure Variables

These analyses are discussed in detail in Section V of (6). The purpose of these analyses was to demonstrate to the statistical laymen by way of a plausible example the difficulties associated with trying to unambiguously quantify the portion of an observed decline in the incidence of the blood lead levels exceeding thresholds (of 30 μg/dl and 49 μg/dl) with simultaneous reductions occurring in more than one lead exposure source. The data used are from the CDC Lead Poisoning Prevention Program published in the CDC Morbidity and Mortality weekly reports. The results reveal (see (6), Section V, Table 3) that:

- Analyses ignoring gasoline lead use lead to the conclusion that lead paint exposure variables are significantly associated with the incidence of elevated blood lead.
- Analyses ignoring lead paint exposure variables lead to the conclusion that gasoline lead is significantly associated with the incidence of elevated blood lead.
- Analyses accounting for both gasoline lead and lead paint exposure variables lead to the conclusion that lead paint exposure variables are better predictors of incidence of elevated blood lead levels than gasoline lead use. In two of the three incidence responses analyzed, gasoline lead use was not significant at level $p \leq .05$.

Subsequent analyses (see (6), Section V, Table 4) demonstrated that no significant residual time trend remained after accounting for only lead paint exposure variables, while one did after accounting for only gasoline lead use.

These results show that if only data on lead paint exposure were available, one could conceivably arrive at the conclusion that lead paint is the primary, or even only, important exposure factor impacting on the incidence of elevated blood lead. The problem evidenced here and also inherent in all studies relating blood lead to a single lead exposure source such as gasoline lead, is that all lead exposure variables are presumably highly correlated with one another over time (not to men-

tion the inherent problems in the quality of the blood lead data itself). Consequently, the effects and contributions of each can never be unambiguously sorted out. Focusing in on one or a few exposure sources, to the exclusion of others, only exaggerates the confusion. Interpretation of such correlation analyses should always take into account these inherent limitations.

REFERENCES

(1) Annest, J. L., Mahaffey, K. R., Cox, D. H. and Roberts, J., "Blood Lead Levels for Persons 6 Months - 74 Years of Age: United States, 1976-1980," National Center for Health Statistics, Advance Data, Number 79, May 12, 1982.

(2) "The Relationship Between Gasoline Lead Usage and Blood Lead Levels in Americans: A Statistical Analysis of the NHANES II Data" prepared under Contract (68-01-5845) for U.S. Environmental Protection Agency, Office of Policy and Resource Management, Office of Policy Analysis, by ICF Incorporated, December 1982.

(3) "National Trend in the Maximum Quarterly Average Lead Levels, 1970-1979," EPA Office of Air Quality Standards, Data Monitoring Branch.

(4) "Assessment of Human Exposure to Lead and Calcium Through Biological Monitoring," National Swedish Institute of Environmental Medicine and Department of Environmental Hygiene, Karolinska Institute, Stockholm, 1982.

(5) "Blood Lead Levels in U.S. Population," Morbidity and Mortality Weekly Report, Centers for Disease Control, 31, 132-134 (1982).

(6) Supplementary Statement Presented to Environmental Protection Agency in the Matter of Regulation of Fuel and Fuel Additives, Lead Phasedown Regulations Proposal Rulemaking, October 8, 1982, Docket No. A-81-36, Petroleum Chemicals Division, E. I. du Pont de Nemours & Co., Inc.

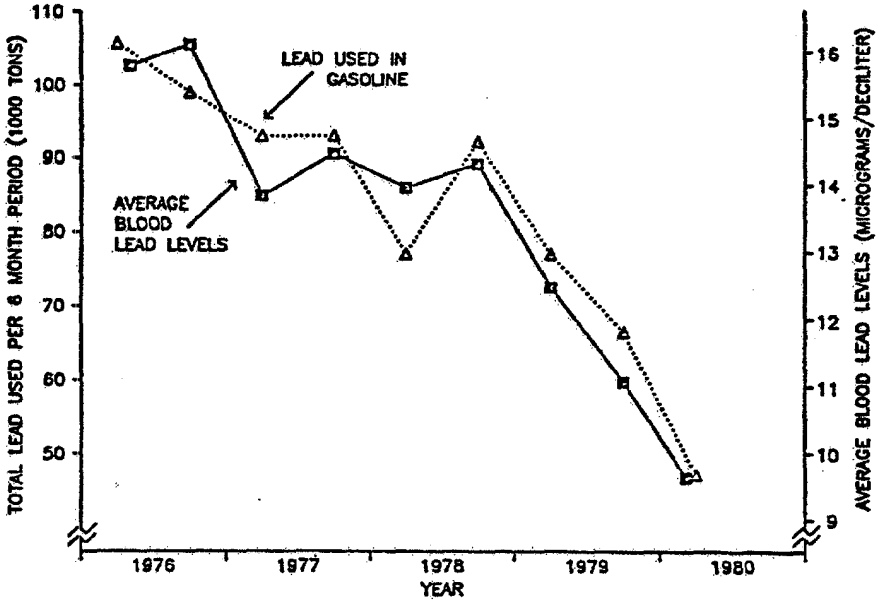
(7) Lead in the Human Environment, National Academy of Sciences, Washington, D.C. (1980).

(8) Jelinek, C. F., "Levels of Lead in the U.S. Food Supply," Food and Drug Administration, Bureau of Foods, Washington, D.C.

(9) Schaffner, A. M., "Lead in Canned Foods," Food Technology, December 1981.

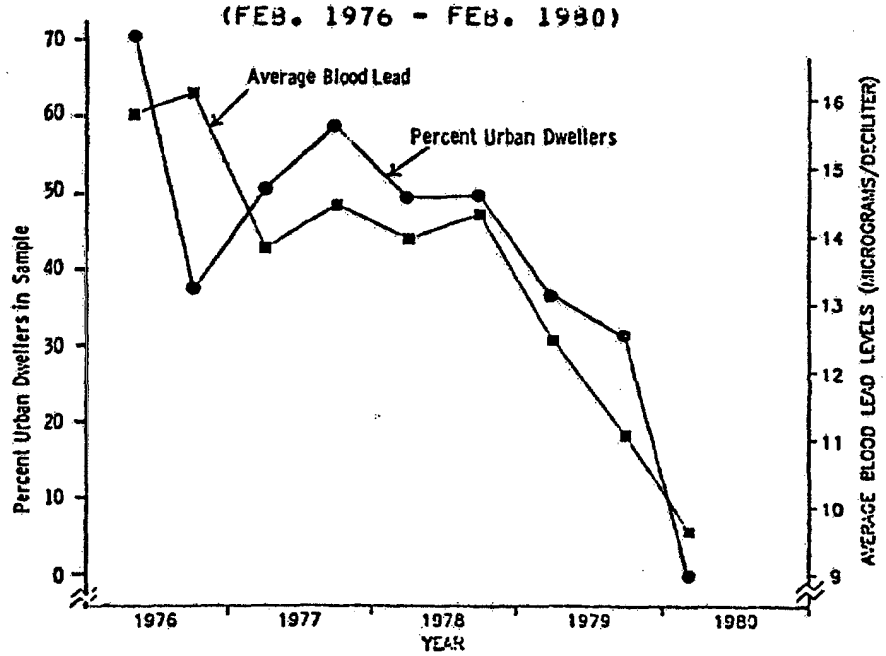
Original Houk Figure

LEAD USED IN GASOLINE PRODUCTION AND
AVERAGE NHANES II BLOOD LEAD LEVELS
(FEB. 1976 - FEB. 1980)



Another Plot of NHANES Data

PERCENT URBAN DWELLERS IN SAMPLE AND
AVERAGE NHANES II BLOOD LEAD LEVELS
(FEB. 1976 - FEB. 1980)



3.3 Preanalytical quality control

There are many possibilities to contaminate biological samples through use of e.g. unsuitable blood collecting vials and contaminated anticoagulants (Zief & Mitchell, 1976; Nackowski et al., 1977; Nise & Vesterberg, 1978). Furthermore, contamination may originate from the skin if not properly cleaned, or from contaminated cleaning solutions (Bratzel & Reed, 1974). Studies on commercially available blood collection tubes have shown that diluted nitric acid as well as blood may extract lead and cadmium from certain vials and syringes in quantities which would invalidate any measurement of these metals in blood within the normal range of concentration (Nise & Vesterberg, 1978).

To avoid contamination as much as possible, evacuated blood collection tubes (Venoject, Terumo Corp., Tokyo, Japan) with heparin from the same batch were provided by the CI after control of the metal content in a suitable number of tubes from the batch. Eight tubes were randomly selected from a box of 100 heparinized blood collection tubes and ten grams of 0.01 M nitric acid added to each tube. After 11 days of storage at room temperature the content of lead and cadmium was analyzed by AAS (ETA). Some tubes were turned over so that the acid came into contact with the rubber caps during storage. The results showed a mean cadmium concentration of 0.06 µg Cd/l in the acid solution, and a lead concentration of less than 0.8 µg Pb/l (both close to the detection limit of the analysis) in all tubes tested. No contamination from the rubber caps was noticed. A similar study on 20 Venoject tubes containing EDTA as anticoagulant showed a mean cadmium content of 0.14 µg Cd/l and a mean lead content of 0.85 µg Pb/l. It was decided to use tubes with heparin since they seemed to contain less metals compared to the tubes with EDTA. If in the future EDTA tubes with low metal content will be available, the use of such tubes may have certain advantages (see Appendix 1).

It was recommended that before collecting blood, the skin should be carefully washed and then cleaned with disposable napkins, saturated with 70% isopropyl alcohol (Medi-Swab, Pharmax Limited, Bexley, U.K.), provided by CI after check for metal content. Written instructions for the sampling of blood were worked out (WHO, 1980a) and a demonstration was made at CI during the meeting in Stockholm in May 1980. The participating institutions were requested to prepare a protocol with information on the personnel collecting the samples, procedures for collection, transport and storage of samples and any additional procedure.

After collection of the blood samples, the blood from each tube was transferred to three 5 ml tubes of polypropylene (washed with diluted nitric acid and deionized water) provided by the CI. They were deep-frozen as soon as possible. One of the three tubes was stored to allow duplicate analysis at the CI or a reference laboratory. Blood not used for the initial analysis was stored to make possible reanalysis at the laboratory if necessary.

The risk of a significant contamination was considered less pronounced for kidney cortex samples owing to the higher concentrations of cadmium in the kidneys than in blood. To avoid contamination to the greatest possible extent and to get comparable samples, the laboratories received a film showing procedures for collection of kidney cortex samples at autopsies. The film was produced by WHO/IAEA in relation to the project "WHO/IAEA Joint Research Programme on Trace Elements in Cardiovascular Diseases (Autopsy Studies)" (Masironi & Parr, 1979). The kidneys were to be opened longitudinally (with e.g. stainless steel knives) and a slice containing the cortex and medulla was to be isolated. From this slice pyelic fat should be eliminated and a portion of the cortex carefully isolated and collected, then put in a suitable container of polypropylene or polyethylene (previously washed with diluted nitric acid and deionized water) and deep-frozen as soon as possible. After collection the samples were kept deep-frozen until analysis. Some of the collected material was kept in storage to enable reanalysis and/or duplicate analysis at a reference laboratory. A description of the procedures used for the kidney cortex collection was prepared by each laboratory and sent to CI.

2.3 Intra- and interlaboratory comparison studies on the analysis of lead and cadmium

To evaluate the accuracy of trace metal analysis in biological materials, a number of intra- and interlaboratory comparison studies have been carried out in the past by different laboratories and organizations. As the results of such studies may be of importance in interpreting the validity of reported data, some of these are summarized below.

The American Industrial Hygiene Association sponsored interlaboratory comparisons to test the accuracy of blood lead analysis (Keppler et al., 1970). In this study samples of spiked blood (200–2910 μg Pb/l) were sent to ten different laboratories to be analyzed by methods routinely used by these laboratories. The overall variation in results was large for both the high and the very low concentrations. Results of up to 4300 μg Pb/l were reported for normal blood and down to 0 μg Pb/l for blood spiked with 1050 μg Pb/l. There was also great variation between results obtained from the same laboratory with time. The problem was not associated with specific analytical techniques.

Donovan et al. (1971) have reported on lead analysis at laboratories in Pennsylvania, USA. In response to an enquiry to 267 different laboratories, 20 laboratories agreed to participate in an intercomparison programme for analysis of lead in urine. Spiked urine (136 μg Pb/l urine) was sent to each laboratory to be analyzed by the method normally used at the laboratory. Reported results ranged from being 10 times lower to 20 times higher than the "true" value. When notified of their inaccuracy, some of the laboratories sought technical assistance. Seven laboratories with relatively good results on lead analysis in urine were later provided with blood samples spiked with 155 μg Pb/l blood. The results reported ranged between 10 and 150 μg Pb/l blood.

In 1972, the reference laboratory of the European Intercomparison Programme (Berlin et al., 1973) sent an aqueous solution of lead nitrate (100 μg Pb/l) and three samples of blood (two from persons occupationally exposed to lead and one from an unexposed person) to 22 different laboratories. Methods used for analyses included atomic absorption spectrophotometry, dithizone extraction and colorimetry, polarography and emission spectrophotometry. For the aqueous solution, results varied from 51 to 180 μg Pb/l, but 70% of the results did not deviate more than 10% from the "true" values. Blood lead levels were reported to range from 140 to 860 μg Pb/l (median: 500 μg Pb/l), 210 to 1170 μg Pb/l (median: 660 μg Pb/l) and 120 to 740 μg Pb/l (median: 410 μg Pb/l) for the three samples, respectively.

Large variations were reported also in "experienced" laboratories by Browne et al. (1974). Samples of heparinized blood (45 in 1973 and 48 in 1974) from lead workers were sent to three different laboratories for analysis by atomic absorption spectrophotometry or anodic stripping voltammetry. Each laboratory had been reported to handle more than 2,000 blood samples per year for lead analysis. The mean difference between results reported by the participating laboratories was as high as 290 μg Pb/l blood in 1973 and 440 μg Pb/l blood in 1974.

In another study (Lerner, 1975) one blood sample obtained from a single person was divided into 35 separate samples and sent to a well recognized laboratory (the Kettering Laboratory) over a period of nine months together with other samples. A considerable variation in lead levels was found with a mean of 191.3 μg Pb/l blood and a standard deviation of 57.2 μg Pb/l. The values ranged from 120 to 420 μg Pb/l blood.

Lauwerys et al. (1975) evaluated the results from 66 European laboratories participating in an interlaboratory comparison programme for the analysis of cadmium, lead and mercury in water, blood and urine. The analytical methods used were atomic absorption spectrophotometry (flame and flameless), anodic stripping voltammetry, colorimetry and neutron activation analysis. There were large variations in results for all the metals and all the media analyzed. As an example three samples of lead in blood showed median values, interlaboratory coefficients of variation (CV) and ranges as follows: median 128 μg Pb/l, CV 52.2%, range 27–490 μg Pb/l; median 227 μg Pb/l, CV 42.9%, range 103–873 μg Pb/l; median 233 μg Pb/l, CV 77.5%, range 10–1150 μg Pb/l. Corresponding results for cadmium in the same blood samples were: median 7 μg Cd/l, CV 168%, range 1–92 μg Cd/l; median 9 μg Cd/l, CV 116%, range 0–73 μg Cd/l; median 10 μg Cd/l, CV 143%, range 0–110 μg Cd/l. The variability of the results, according to the authors, could not be attributed to either the different analytical methods used or to the difference in experience in trace metal analysis at the laboratories.

Paulev et al. (1978) sent blood, urine and aqueous solutions spiked with lead and cadmium to five laboratories, three in Scandinavia and one each in Britain and Canada. Recovery of the added lead in the blood samples (470 μg Pb/l) ranged between 250 and 470 μg Pb/l. The results for two blood samples spiked with cadmium (20 and 67 μg Cd/l) ranged for three laboratories between 10 and 21 μg Cd/l and 40 and 62 μg Cd/l, respectively.

Maher et al. (1979) sent pooled blood from lead workers to 24 laboratories on nine occasions during 1974 and 1977. They tested different methods but found no significant bias that could be attributed to the method of analysis as such. In six different rounds, the coefficient of variation (CV) varied between 1.7% for a sample with a mean value of 575 μg Pb/l and 10.7% for a sample with a mean value of 250 μg Pb/l. The CV did not improve significantly with time. It was concluded that with available methodologies (atomic absorption spectrophotometry, flameless and Delves Cup, dithizone extraction, colorimetry, anodic stripping voltammetry and spectroscopy) the optimum coefficient of variation between laboratories would be about 7%.

Boone et al. (1979) compared the results from 113 laboratories participating in the "Blood Lead Proficiency Testing Program" conducted by the Center for Disease Control, USA, with the results from isotope dilution mass spectroscopy at the U.S. National Bureau of Standards. The blood for the interlaboratory comparison was obtained from cattle orally fed with lead nitrate, and the concentrations ranged from 130 to 1020 μg Pb/l blood. Twelve separate samples were dispatched to each laboratory for analysis. It was concluded that most methods overestimated the lead concentration when the actual concentration was low (less than 400 μg Pb/l blood) and underestimated it when the actual concentration was high (more than 500 μg Pb/l blood). The overall coefficient of variation ranged from 29 to 73% at NBS values of 124 μg Pb/l blood and from 9 to 37% at an NBS value of 1020 μg Pb/l.

The reviewed studies show that the accuracy and precision of trace metal analysis in biological specimens, especially lead and cadmium in blood and urine, in general appear to be unsatisfactory. This may also hold for laboratories that have gained considerable experience by analyzing a large number of biological samples over many years. Of the analytical methods currently available for analyzing trace metals in biological materials, no single method has been found to be distinctly superior to the others.

Correlation Coefficients[1] Between Weighted Geometric Mean Blood Lead and Sample Proportion by Demographic Groups

Demographic Group	Total Sample	Urban Areas 1-4	Rural Area
Race			
White	.084	.896**	-.862**
Black	-.364	-.001	.002
Age			
≤6 Years	.506	.881**	-.587
7-17 Years	.734*	.898**	-.853**
18-74 Years	-.841**	.805**	-.837**
Sex			
Male	.514	.872**	-.879**
Female	-.509	.799**	-.799**
Race x Age			
White, ≤6 Years	.495	.871**	-.741*
Black, ≤6 Years	.505	.715*	.177
White, 7-17 Years	.702	.947**	-.865**
Black, 7-17 Years	.308	.391	.148
White, 8-18 Years	-.344	.866**	-.839**
Black, 8-18 Years	-.650	-.190	-.176
Race x Sex			
White, Male	.203	.915**	-.887**
Black, Male	-.438	-.243	-.177
White, Female	.010	.861**	-.818**
Black, Female	-.349	.064	.232
Age x Sex			
≤6 Years, Male	.194	.892**	-.781*
≤6 Years, Female	.970**	.964**	-.686*
7-17 Years, Male	-.813**	.780*	-.849**
7-17 Years, Female	.636	.811**	-.202
8-74 Years, Male	-.253	.713*	-.804**
8-74 Years, Female	-.621	.785*	-.783*

*Statistically different from zero at .05 test level.
**Statistically different from zero at .01 test level.
(1) Based on nine pairs of data corresponding to 6-month period, starting January 1, 1976 through June 30, 1980.

Blood Lead Levels - Observed and Adjusted for Degree of Urbanization and SMSA Category

		Geometric Mean Blood Lead, µg/dl			
		1st Half 1976	1st Half 1980	△(1)	Effect(2)
Overall					
	Observed	14.8	8.8	6.0	1.8
	Adjusted	13.8	9.6	4.2	
Race					
White	Observed	14.5	8.6	5.9	1.5
	Adjusted	13.7	9.3	4.4	
Black	Observed	16.3	10.8	5.5	2.5
	Adjusted	14.7	11.7	3.0	
Age					
.5-5 Yrs.	Observed	18.5	9.4	9.1	1.8
	Adjusted	17.5	10.2	7.3	
6-17 Yrs.	Observed	13.4	6.9	6.5	1.6
	Adjusted	12.5	7.6	4.9	
18-74 Yrs.	Observed	15.1	9.3	5.8	1.8
	Adjusted	14.1	10.1	4.0	
Race by .5-5 Yrs.					
White	Observed	17.8	8.7	9.1	1.5
	Adjusted	17.1	9.5	7.6	
Black	Observed	21.6	12.7	8.9	3.3
	Adjusted	19.4	13.8	5.6	

(1) Difference between first two columns.
(2) Effect on trend when accounting for degree of urbanization and SMSA category.

448

TABLE C.1 Federal Regulatory Actions Governing Human Exposure to Lead

Medium through Which Exposure Occurs	Federal Agency	Specific Exposure Pathway Being Controlled	Federal Regulations	Citation
Nonfood Substances				
Lead paint in housing	Housing and Urban Development	Exposure of children to lead-based paint on surfaces of residential structures.	Notification to purchasers and tenants of HUD-associated housing constructed prior to 1950 of the hazards of lead-based paint poisoning.	24 CFR 35.5
			Prohibition against the use of lead-based paint in HUD-associated housing.	24 CFR 35.14
			Elimination of lead-based paint hazards in HUD-associated housing.	24 CFR 35.24
			Elimination of lead-based paint hazards in federally owned properties prior to sale for residential habitation.	24 CFR 35.56
			Prohibition against the use of lead-based paint in federal and federally assisted construction or rehabilitation of residential structures.	24 CFR 35.62
Lead paint in housing	Health, Education, and Welfare	Exposure of children to lead-based paint on surfaces of residential structures.	Grants to develop local programs for detection and treatment of lead-based paint poisoning and for the identification and elimination of the hazards of lead paint in residential structures.	42 CFR 91
Lead in paint, and toys and furniture with painted surfaces	Consumer Product Safety Commission	Exposure of children to lead-based paint on surfaces of residential structures, toys and furniture.	The following consumer products have been declared as banned hazardous products: (1) paint and other similar surface coatings containing more than 0.06 percent lead. (2) toys and other articles intended for use by children that bear paint containing more than 0.06 percent lead. (3) furniture that bears paint containing more than 0.06 percent lead.	16 CFR 1303.4
Air				
Ambient air	Environmental Protection Agency	Exposure of the general population and especially young children (1-5 yrs.) to airborne lead from motor vehicles combusting leaded gasoline.	No gasoline refiner shall exceed an average lead content of 0.5 g Pb/gal after October 1, 1979, averaged over a three-month period.	40 CFR 80.20
Ambient air (including dust and dirt)	Environmental Protection Agency	Exposure of the general population and especially young children (1-5 yrs.) to airborne lead from stationary and mobile emissions sources.	The national primary and secondary ambient air quality standards for lead are 1.5 $\mu g/m^3$, maximum arithmetic mean averaged over a calendar quarter.	40 CFR 50.12

449

TABLE C.1 (*continued*)

Medium through Which Exposure Occurs	Federal Agency	Specific Exposure Pathway Being Controlled	Federal Regulations	Citation
Water				
Drinking water	Environmental Protection Agency	Exposure of the general population to lead in drinking water supplied by public water systems.	The interim national primary drinking water maximum contaminant level for lead is 50 μg/l.	40 CFR 141.11
Food and Eating Utensils				
Apples, apricots, celery, peaches, pears, strawberries, tomatoes, and several other specific fresh fruits and vegetables	Environmental Protection Agency	Exposure of the general population to lead arsenate pesticide residues in or on raw agricultural commodities.	The tolerance for lead arsenate pesticide residues in or on ten designated raw fruits or vegetables is limited to 7 ppm of combined lead.	40 CFR 180.194
Citrus fruits			The tolerance for lead arsenate pesticide on citrus fruits is limited to 1 ppm of combined lead.	
Ceramic dinnerware, enamelware and pewter	Food and Drug Administration	Exposure of general population to lead that is leachable from pottery glazes.	The action level for leachable lead from ceramic work is 7.0 μg/ml, 5.0 μg/ml and 2.5 μg/ml for flatware, small hollow ware, and large hollow ware, respectively.	FDA Administrative Guideline 7417.00
Silver-plated hollow ware	Food and Drug Administration	Exposure of the general population to lead that is leachable from silver-plated hollow ware.	The action level for leachable lead from silver-plated hollow ware for use by adults is 7.0 μg/g. The action level for leachable lead from silver-plated cups intended for use by infants is 0.5 g/ml.	FDA Administrative Guideline 7417.01
Occupational Exposures				
Occupational exposures to lead in all industries covered by OSHA except construction and agriculture	Occupational Safety and Health Administration	Exposure to airborne lead in the workplace.	50 μg/m averaged over an 8-hour period.	29 CFR 1910.1025