DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control

March 18, 1983

David Weil Ph.D.
EPA Annex Building
Alexander Drive
Research Triangle, North Caroline 27711

Dear Dr. Weil,

Enclosed are three documents for the NHANES II Time Trend Review Panel:

1) Duplicate measurements differing by more than 7 ug/dl (in response to questions from Dr. Smith)
2) Appendix M: Tabulations by Demographic Variables (at the request of Dr. Smith)
3) Appendix N: Regression Analysis of Urban and Rural Population Subgroups

I hope this information will be of assistance to you and the panel.

Sincerely,

James L. Pirkle

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Duplicate measurements differing by more than 7 ug/dl

When duplicate lead measurements of a whole blood sample differed by more than 7 ug/dl, the analysis of the sample was repeated (again in duplicate) and the results of the repeat analysis were used. Experience with the modified Delves cup technique for measuring lead in whole blood indicated that if duplicate measurements differed by more than 7 ug/dl, it was likely that an unusual, non-random analytical error had occurred. Examples of such errors are: microclots in the whole blood sample, slight misalignment of the Delves cup, uneven distribution of the blood inside the cup and physical deterioration (pitting, hairline cracking) of the cup. These errors can cause a large variation between duplicate measurements. For example, if a microclot (a small aggregate of red blood cells) was dispersed in the duplicate analysis of a whole blood sample, it would contain so many more red blood cells than a typical sample that the duplicate measurement could artifactually be as much as 2 to 3 times higher (e.g. 15 ug/dl to 45 ug/dl). The other sources of error listed could produce changes as large as 50-100%.

The cutoff of 7 ug/dl was selected to detect any lead measurements which might potentially be affected by such errors. Duplicate measurements not meeting the 7 ug/dl cutoff were not included in the final lead concentration calculation in order to insure that the reported lead measurement was not influenced by any of these atypical analytical errors.

For the sake of detail, an analysis was performed to determine what would have happened had these values not been excluded from the final lead concentration calculation. The analysis is meant only to be illustrative since measurements are included which would have been rejected on analytical grounds as described above. Out of the approximately 10,000 whole blood lead samples, 458 were repeated because duplicate measurements differed by more than 7 ug/dl. Thirty-six of these 458 had duplicate measurements which differed by more than 25 ug/dl and clearly were cases of a microclot, pitted cup, alignment problem etc. The remaining 422 samples had a difference

between duplicate determinations greater than 7 ug/dl either from one of the previously mentioned sources (i.e. microclot, cup alignment, etc.) or from random sources of error typically associated with analytical procedures (e.g. pipetting, instrument noise, etc.).

A new lead value was calculated by averaging the duplicates which differed by more than 7 ug/dl with the duplicates of the repeat analysis. Thus four values were averaged together to determine this new lead value. The difference between this new lead value and the reported value is plotted versus time in Figure 1 with a linear regression fit and a 95% confidence interval about the mean. Table 1 gives the linear regression results.

The plot and the regression analysis indicates that in samples that had duplicates greater than 7 ug/dl (about 4.5% of the 9937 NHANES II lead measurements), reporting the repeat measurement (again done in duplicate) did not contribute to a downward trend in the NHANES II blood lead data over time.

Table 1
Regression of difference in calculated new lead value and reported lead value over time (see text for details)

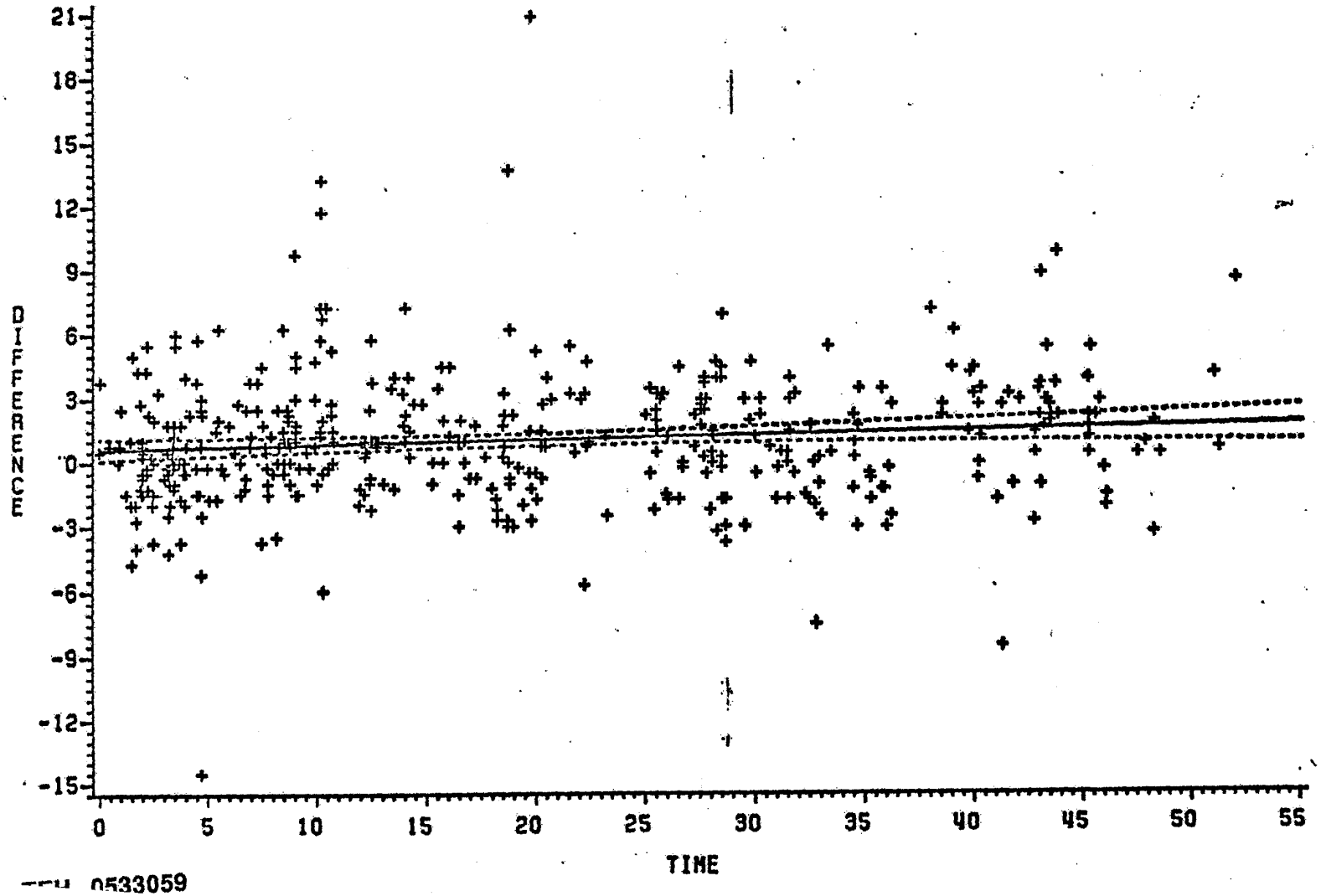
DEP VARIABLE: DIFF

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB>F
MODEL	1	50.480216	50.480216	5.406	0.0205
ERROR	420	3921.905	9.337870		
C TOTAL	421	3972.386			
ROOT MSE		3.055793	R-SQUARE	0.0127	
DEP MEAN		1.080569	ADJ R-SQ	0.0104	
C.V.		282.7949			

VARIABLE	DF	PARAMETER ESTIMATE	STANDARD ERROR	T FOR HO: PARAMETER=0	PROB > |T|
INTERCEP	1	0.605344	0.252791	2.395	0.0171
TIME	1	0.025015	0.010759	2.325	0.0205

DIFFERENCE IN LEAD VALUES CALCULATED USING ONLY REPEAT

MEASUREMENTS VERSUS BOTH INITIAL AND REPEAT
MEASUREMENTS OVER THE NHANES II SURVEY PERIOD
LINEAR REGRESSION FIT WITH 95% CONF. INTERVAL
(SEE DISCUSSION IN TEXT)



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