



E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED

WILMINGTON, DELAWARE 19898

ENGINEERING DEPARTMENT
LOUVIERS BUILDING

April 11, 1986

Dr. Lester D. Grant
Director, Environmental Criteria
and Assessment Office (MD-52)
U.S. EPA
Alexander Drive and Route 54
Research Triangle Park, NC 27711

Dear Dr. Grant:

This letter is in reply to your letter to me of April 4, 1986 expressing concern about the differences in the blood pressure-log blood lead ($BP-\ln(BPb)$) regression coefficients estimated in analyses of NHANES II data by Du Pont and Dr. Schwartz. I appreciate the opportunity to address some of the statistical issues Dr. Schwartz raised in his memo to you (stamped March 3, 1986) regarding differences between our analysis approaches.

While I fully recognize your needs and associated time constraints for closing on the Addendum to Air Quality Criteria for Lead, it is important to recognize that there are two distinct and important, but perhaps conflicting analysis objectives, that are being confused in Dr. Schwartz' analyses and your intended use of his results:

- (1) Assessment of the validity of the results on the blood pressure-blood lead relationship when not adjusting for sites as reported by Harlan et al (1985) and Pirkle et al (1985).
- (2) Determination of the best estimate of a blood pressure-blood lead relationship in selected age-race-sex groups based on sound statistical procedures that effectively account for important covariates affecting blood pressure and blood lead.

Du Pont's analysis performed prior to the May 1985 CASAC meeting was intended to address only the first objective. That analysis has demonstrated conclusively that the results reported in Harlan et al and Pirkle et al are invalid since adjusting for sites critically affects the magnitude and significance of the

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BP-ln(BPb) coefficient. Reviews of our analysis by CASAC consultants Drs. Ware and Royall as well as by Dr. R. Little (contained in LIA's comments to EPA of March 1986) and Dr. R. A. Bradley (contained in Ethyl's comments to EPA of March 1986) have all confirmed the need to adjust for sites. As such reporting or use of results from any NHANES II analysis not so adjusted is unfounded and a misjustice to the scientific evidence at hand.

The second objective appears to be the one about which you are most concerned now, especially for the white male age group 40-59 years. Although Dr. Schwartz' analyses have incorporated additional covariates significantly related to blood pressure but not considered in Harlan et al and Pirkle et al (and consequently not by Du Pont), I cannot agree that his results satisfy Objective (2). Reliable determination of Objective (2) requires very careful statistical scrutiny well beyond that performed to date. For example, analysis of alternative models such as those suggested by Dr. Royall (see memo to Dr. Weil of August 21, 1985), careful diagnostic evaluation of deviations from model assumptions that could affect estimated coefficients, assessments of the robustness of the relationship across age-race-sex subgroups, evaluation of impact of interactions of other covariates with BPb, etc, are all extremely important to explore. Basing judgements of cardiovascular risk on coefficients not so scrutinized would be scientifically indefensible. Consequently, merely attempting to replicate Dr. Schwartz' analysis would be of no use in accomplishing the second objective. A more complete, comprehensive analysis is in order. A task group guided by either or both of Drs. Ware and Royall and involving Dr. Schwartz, Dr. Bradley and myself appears to be the best way to answer Objective (2) in a reliable and defensible manner and resolve technical differences.

Per your request, on the attached pages I have provided explanations on each of the questions you raised as a result of items of difference identified by Dr. Schwartz in his March 3, 1986 memo to you. Several of these explanations depend on whether the analysis objective is (1) or (2). Differences in the BP-ln(BPb) coefficient between analyses are not due to data centering, age coding errors, suppression of the intercept, weighting, or nonuse of SURREGR. I must say I continue to be troubled by both the character and quality of many of the comments Dr. Schwartz has made orally and in writing on statistical issues during my involvement in environmental proceedings on lead exposure. His March 3, 1986 memo to you is another example. Either he does not comprehend many of the statistical issues or he is deliberately trying to cloud the real issues with rhetoric that sounds convincing to the statistical layman.

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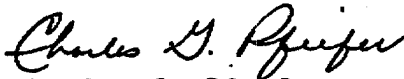
In reference to the summaries in your Table 1, I have noted two typos (other than my name being misspelled). The adjusted Du Pont results for males aged 12-74 are reversed for systolic and diastolic blood pressures and a single asterisk should be appended to the 1.95 coefficient. While you state such a table is for comparative results only, I strongly caution you against presenting any unadjusted results from NHANES II in the Addendum; such results have been acknowledged as wrong and give a biased impression.

I hope the above and attached comments are of value to your office. As I am sure you will agree, this dialogue has helped to prevent continuation of any misconceptions seeded in Dr. Schwartz' memo to you. I look forward to receiving an advance copy of the revised Addendum that you agreed to send at the March 11-12, 1986 CASAC meeting, which is being prepared for anticipated CASAC closure on the Air Quality Criteria Document for Lead later this month. I trust the Addendum will offer a balanced scientific evaluation of all the epidemiological evidence on the blood pressure-blood lead relationship and not selectively emphasize results for any particular age-race-sex groups.

If you require any clarification on points made in this letter or have any additional questions I can help answer, please do not hesitate to ask.

Sincerely yours,

ENGINEERING SERVICE DIVISION
Applied Statistics Group



Charles G. Pfeifer
Consultant Supervisor

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CC: J. M. Pierrard - Du Pont

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