Monsanto

ENVIRONMENT, SAFETY & HEALTH

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September 28, 1988

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Dear Dan:

Everybody and his brother (that is to say, Friedlander, Gaffey, Garrett, Haselhorst and Leet) has reviewed the preliminary draft report, each of us taking the sections that he or she was best qualified to review. Our comments are attached.

Some of the comments are editorial, some are matters of fact, and some represent our opinions or questions about the text. I hope they will be helpful to you. Some of them may affect the tables that will go into the final report.

Yours sincerely,

William R. Gaffey, Ph.D.
Epidemiology Director

/jf

cc: B.R. Friedlander w/copy of comments
J.T. Garrett " " "
B.L. Haselhorst " " "
T.L. Leet " " "

DSW 476038.0942

STLCOPCB4043103

Comments on Preliminary Draft Report Titled

"Epidemiologic Investigation of the Health Status of Monsanto Employees with Past Exposure to Chlorophenols, Chlorphenoxy Acid Esters and Their Dioxin Contaminants at the W.G. Krummrich Plant in Sauget, Illinois"

Pages 1-4.

Acronyms are given for a number of substances (e.g. 2,4-D) and tests (e.g. BUN). They should be spelled out the first time they are used, followed by the acronym in parentheses.

Page 3, first paragraph.

Dr. Tillman said that these weight variations did not seem to him to be unusual.

Page 4, Sec. 2.3.3.

The first two sentences are a nonsequitur and should be removed.

Page 5, Sec. 2.4.2.

Second line. "1982" should be "1986".

Third line. Something should be added to the effect that no adjustment was made for smoking because the data were not easily available.

Fourth line. "investigating" should be "investigated".

Sixth line. "selected" should be inserted between "with" and "subcohort".

Page 6.

After first sentence put (MEHI) in parentheses.

Page 7, Sec. 4.2.1.

No rationale for why some hypotheses are "primary" and some are "secondary".

Page 9, Sec. 4.3.

Here and elsewhere, proprietary names like Santobrite should be followed by TM the first time they are used, with a footnote saying that it is a registered trade mark of the Monsanto Company.

DSW 476038.0943

STLCOPCB4043104

Page 15, Table 4.1.

1931. S-036 should be in parenthesis.
1964. S.G. should be spelled out.

Page 17, first line.

The term "snift gas" should be replaced by "revaporized chlorine (known in the plant as "sniff gas")."

Page 22, Table 4.2.

Did the A and B operator also assist the Premium Operator? Replace question marks with an asterisk and explanatory footnote.

Pages 37 and 51.

The word "fines" is a generic term used here in specific senses that are not appropriate. On page 37, next to last line, replace "fines" with "materials" and on page 51, Table 4.10, in 1961, replace "fines" by "particulate products". The usage elsewhere is correct.

Page 83, Sec. 4.4.1.1.

Title and first sentence. Since cohorts are identified independently of outcome, and these people had to be alive to get into the study, the term "group" may be more appropriate.

Definition of exposed cohort. The implication here is that chloracne alone did not qualify a person as being exposed. On page 94, Sec. 4.5.2, the opposite is implied. On page 136, Sec. 5.6, it is apparent that people were called exposed if they worked in the appropriate departments according to their work histories or if they had chloracne and stated that they had worked in the appropriate departments. In other words, the criterion for exposure appears to be different for those with chloracne and those without. Some clarification is needed here and in the other cited sections.

Last paragraph. Salaried controls were not included in the main study. It might be appropriate here to explain why salaried people were included only in the pilot study. In the last sentence MEHI does not have to be spelled out.

Page 85a, Table 4.17.

The age ranges go over 100. ~~In~~ Is some comment needed?

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Page 86, first complete paragraph.

We studied the mortality experience of the whole plant, so this could not explain the difference in the percents whose vital status is unknown in the exposed and controls. The explanation seems to be that one way not to be exposed was to work for a shorter time. Therefore there were more terminations in the control group who had to be followed, therefore more persons with unknown vital status.

Tables 4.17 and 4.18 vs. Tables 8.1, 8.2, 8.3. The labels "Exposed" and "Control" are used in both sets of tables, but it is clear that Tables 4.17 and 4.18 deal with "potential" or "eligible" persons while Tables 8.1 etc. deal with those who were actually examined. The labels should be different in the first set of tables.

Page 91, Sec. 4.5.1, first paragraph.

There were actually four sources. One was hard copies of employment records prior to MEHI.

Page 96, Sec. 4.5.1.1, first sentence.

No need to define the acronym MEHI. "hourly" should precede "worker" and "after 1935" should precede "at".

Page 92, first five lines.

Is the statement about Dr. Davis correct?

Page 93, fifth line.

"assigned" should replace "misclassified"

Page 94, third line from bottom.

Why capitalize "Department"?

Page 95, Sec. 4.5.2.2.

The classification by exposure department needs clarification. First, the implication is that there was no one with a mixed exposure. We know this is not true because in the succeeding tables the numbers of people in each of these categories do not add up to the "Total Exposed" given in the tables.

Second, the category "maintenance workers on the chloracne registry" must include some people (perhaps all of them) with chloracne. Therefore, in the succeeding tables, almost all of which show a fifth category called "chloracne", that category must overlap the other categories. A table showing the numbers in each group, and the numbers with mixed exposures, would be helpful.

DSW 476038.0945

STLCOPCB4043106

Page 96, first complete paragraph.

Reliance in self-reporting was necessary because plant records were not available for those terminated before 1970.

Page 97, Sec. 4.6, last line.

There is no Table 19.

Page 100, Sec. 4.6.2, second line.

Delete "b".

Page 103, Sec. 4.6.9, third line

"Sensortec" should be "Sensortex".

Page 104, third line.

There is no Table 4.19.

Page 107, sec. 4.8.2.1, first paragraph.

In item (3), should it be pointed out that the subjects, when asked, did not recall any such discrepancies?

Page 108, Sec. 4.8.2.3.

Should it be pointed out that the groups were randomized with respect to time of examination in order to eliminate time-of-day bias?

Page 109, Sec. 4.9.

If there are to be power calculations after the fact, they should be done for tests of means as well as for tests of prevalence. However, after a test has been done the power is not relevant. What is relevant are the confidence intervals that were obtained. It can happen that a test which is a priori not powerful can give a confidence interval that rules out the alternative.

Page 117, second full paragraph, second and third lines.

Johns, not John's and Holmes, not Homes.

Page 122, last paragraph, fifth line.

Insert after "to" the phrase "a six digit job class code beginning with"

STLCOPCB4043107

Page 148, Sec. 6.5.8, third line

One "n" in Marilyn.

Page 122, last paragraph, eighth line.

Add to the end of the sentence the parenthetical expression (this accounted for about two percent of the sample).

Page 125, Sec. 5.4.1, fourth line.

(83.2%) should be (83.3%)

Page 136, second line.

"that" should be "than".

Page 142, second paragraph, fifth line.

"of" should be "or".

Page 143, last line.

"coordinator" should be "manager".

Page 145, second line.

Insert the sentence - The van was also inspected by Mr. Paul Kalicki from the Illinois Department of Nuclear Protection.

Page 145, Sec. 6.5.3.

second line - change "coordinator" to "manager"
third line - change "electrocardiogram" to "electrocardiogram/ blood pressure".

Page 146, third line.

After first sentence insert - At that time each one was given an ID bracelet with a 4 digit study number and the first 4 letters of the last name for purposes of quality control, but which included no indication of exposure status.

Page 146, first paragraph, last line.

Change "coordinator" to "manager". Add the sentence - All participants completed a final exit interview prior to leaving the examination site.

Page 146, Sec. 6.5.6, fifth line.

Remove "ed" from "administered".

Page 148, Sec. 6.5.8, second line.

Date is April 7, 1986.

STLCOPCB4043108

Page 149, Sec. 6.5.10, sixth line.

"At" should be "A".

Page 151.

Should be some comment on which records were lost. Were they for people who terminated before some date?

Page 154, Table 7.1.

What do the initials mean?

Page 157, Sec. 7.6, third paragraph.

Fisher's Exact test is usually a one-sided test. Chi-square is a two-sided test. For these associations and the p-values in the regression tables, was a one-sided or a two-sided test used?

Page 158, Sec. 7.6.1, first paragraph.

The exposure classification, except for the chloracne category, is redundant with Sec. 4.5.2.2 and needs clarification.

Page 161, Sec. 7.6.4.

Chloracne as defined here is a mixture of cumulative incidence and prevalence. This implies that the investigators consider chloracne a marker for relatively heavy exposure. This is perfectly proper, but should be mentioned so that readers will not interpret the chloracne figures as being incidence or prevalence.

Page 194, Sec. 8.3.1, second paragraph, third line.

Phrase (2) does not seem to make sense.

Page 197, Table 8.17.

The number in Maintenance cannot be greater than the corresponding number in Table 8.16. One of the two entries must be incorrect.

Tables 8.19, 8.20, 8.21, 8.22.

Apparently Table 8.19 includes people who worked in more than one production department and therefore do not appear in Tables 8.20, 8.21, or 8.22. It would be helpful to restate in the text that Tables 8.20, 8.21 and 8.22 do not add up to Table 8.19. (The pages for these tables are misnumbered.)

DSW 476038.0948

STLCOPCB4043109

Tables 8.30-8.32.

Pages are misnumbered.

Page 232, Table 8.40

The number in "Only 236" is 278. It was never more than 260 in previous tables of the examined group. Is this an error?

Table 8.50 and text.

In several places in this table (Pattern Memory is one example) Department 236 did significantly worse than the controls while the other three exposure groups did very well. Because the people in 236 were a majority of the "All exposed" group the latter group also was significantly worse than the controls. The results for Department 236 and for "All exposed" are presented as if they were two independent conclusions, when in fact the latter is caused by the former. As stated, the findings for "All exposed" falsely imply that the result is pervasive in the exposed group, which it generally is not.

Tables 8.51 to 8.69.

What are the numbers in square brackets in the left column?

STLCOPCB4043110