Monsanto

JUN 12 1978

FROM (NAME—LOCATION—PHONE): A. W. Dickinson, MISD, General Offices, G3EB

DATE: June 2, 1978

SUBJECT: Review of Aroclor Report

REFERENCE:

TO: P. E. Berteau - A2SC

R. I. Groff G5NC
R. C. Isham B1ND
J. R. G. Ortiz E2NE

The following are my comments on "Bioassay of Aroclor® 1254 for possible carcinogenicity".

1) The statistical procedures employed in the analysis of the data appear to be both proper and thorough. They are, in fact, the conventional tests which are generally applied to data resulting from chronic animal experiments.

2) As noted by one of the subgroup members (page 62), the use of only 24 animals per dose/sex combination is somewhat deficient. It is a more common practice to employ 50 animals per group. In a presentation at the 1977 Gordon Conference on Statistics, David Gaylor expressed the opinion that even 50 animals was not enough and suggested 200 as a more reasonable group size. I feel that the small group size may be at least partly responsible for some of the ambiguity in the findings of this study.

3) It is definitely not legitimate to state that "NCI has determined that Monsanto's PCB is not carcinogenic". All they have done is fail to demonstrate conclusively that it is carcinogenic. If we must make some statement, I would prefer your "there is no conclusive evidence that PCB's cause cancer". I would have some qualms about releasing even this statement without the qualifying (page 62) "It is suggested that Aroclor® 1254 may be a tumor promoter". Perhaps the best position is to make no public statement.

4) In paragraph four of the summary, it is stated that "the combined incidences of lymphomas and leukemias showed a significant dose-related trend in males". The corresponding analysis is described in more detail on page 21 of the report. The significant P value (.009) was obtained as a result of a test for positive dose-related trend. This test utilized data from all 96 male animals and also considered the ordering of the dose levels.

In the latter half of paragraph four, it is stated that "the direct comparisons of each dosed group with those of the matched controls were not statistically significant".

Each of these test is based on a comparison of the 24 animals in a dose group with the 24 animals in the control group. Since these tests employed fewer animals than in the test for trend, it is not surprising that the results are less significant. The final statement that "tumors cannot clearly be related to administration of Aroclor® 1254" is apparently based on a requirement that both the trend and the individual comparisons must be significant in order for a substance to be classified as a carcinogen. In view of the fact that the power of the individual comparisons is limited by the small group sizes, I would view the presence of the positive dose-related trend as a strong warning that the substance may be carcinogenic.

5) Additional results are quoted in the following paragraphs of the summary. The occurrence of hyperplastic nodules is statistically significant as evidenced by the very strong dose-related trend present for both male and female groups. The remaining events cited are small in number and not statistically significant, but may be suggestive because all occurred in the dosed animals and none in the controls.

I am returning your copy of the report but would like to have one for my files. Please let me know if you have any questions.

Best Regards,

A. W. Dickinson

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