Monsanto

FROM (NAME—LOCATION—PHONE) Dept. of Medicine & Environmental Health T.L. Leet

DATE : December 19, 1984 cc. W.J. McCarville - G3WD

SUBJECT : Northwestern Medical Study -
Peer Review Committee Meeting

REFERENCE :

TO : W.R. Gaffey - G2WE

The Peer Review Committee met in Chicago on December 12, 1984 to discuss the protocol for the proposed Northwestern medical study. The participants included the following:

Peer Review Committee

Mark R. Cullen, M.D. - Yale School of Medicine
George Lathrop, M.D., Ph.D. - JRB Associates
Richard Monson, M.D. - Harvard School of Public Health
Lynne Moody, M.D., M.P.H. - NIOSH
Robert Waldman, M.D. - University of West Virginia School of Medicine

Northwestern School of Medicine

Daniel O. Hryhorczuk, M.D., M.P.H.
Victoria Persky, M.D.
Warren H. Wallace, M.D.
James R. Webster, M.D.

Monsanto Company

Terry L. Leet, M.P.H.
George Roush, Jr., M.D.
James H. Spraul, M.D.

The items that were discussed at the meeting are summarized below. In general, the committee members appeared to be very interested in the proposed medical study and were very eager to offer suggestions based on prior experience from other related studies, e.g. the Ranch Hand study and the NIOSH dioxin morbidity study.

Overall, the committee members focused on the study design, specifically the definition of the study population and the ascertainment of health status. All of the members were in favor of including terminated employees in the study, and thought that the omission of this group would limit the scope and the credibility of the study. In addition, the members thought that the maintenance workers should be studied as a separate group, since they may have worked in any of the four exposed departments. The committee members debated whether to use all maintenance workers or only those who were employed after 1970. If Monsanto can identify all maintenance workers

who were assigned to zone I (which included the chlorophenol and pentachlorophenol units) after 1970, the committee members favored including this subset over all maintenance workers, since Monsanto can also identify from the chloracne registry those maintenance workers who spent 200 or more hours in the chlorophenol and pentachlorophenol units. (Comment: Since the meeting, I have spoken with Ken Storms and Pat Riley at the Krummrich plant and they informed me that it would be nearly impossible to identify the zone(s) that a maintenance worker was assigned until 1982, and doubted that we could obtain any additional information from the accounting department.) The committee was asked to consider the possibility of excluding workers with less than three or even six months of employment at the Krummrich plant to reduce the number of terminated employees that would have to be traced. By requiring three months employment, approximately 50% of the terminated employees would be eliminated. However, no decision regarding this restriction was made during the meeting.

Another major decision regarding the study population was to exclude the external controls. The committee thought that any exposure from employees in the internal control group would be minimal, even though they may have been assigned to one of the exposed departments for a few weeks while in the utility department. Furthermore, the committee had some reservations about interpreting the data if there was an excess in disease among the exposed group when compared to the internal controls but not the external controls, and vice versa.

Other comments included the large number of job changes (10 to 20 jobs) per employee while working at Krummrich and whether or not to restrict the study population to those who lived within a 100- or 300-mile radius of the plant. The large number of job changes per employee was explained partly by the fact that the Krummrich employees are unionized and the employees often bid for better paying jobs. Because of this program, the Krummrich employees will have many different jobs during their employment. In addition, some of the departments, including the pentachlorophenol unit, may not have been the most desirable place to work, and some of the employees may have left the departments soon as they possibly could. Regarding the idea of imposing a maximum distance before including an employee in the study, no decision was made. However, the committee would like Monsanto to determine where the active and retired employees are presently residing.

With respect to ascertainment of health status, the committee concentrated on the inclusion of additional tests. The items that were mentioned are as follows:

- use the National Opinion Research Center (NORC) at the University of Chicago to administer the questionnaires, or to at least train the Northwestern interviewers. This was recommended since NORC designed the questionnaires that were used in the Ranch Hand study and Northwestern plans to use the same or some of the questions from the Ranch Hand questionnaire.

- administer the reproductive questionnaire over the telephone and send a computer printout of the individual's responses to the participant a week later for verification.

- collect quantititave data for smoking histories (pack-years), alcohol consumption (type of beverage and amount consumed), and constipation (amount of stress, number of bowel movements per day).

- add questions about amount of exercise to use for the HDL analysis. Possibly consider using the HAINES scale.

- add "de-drumming" questions to the military history questions.

- substitute a registered record administrator for an internist for retrieving and coding data from participant's earlier medical records.

- eliminate the tests concerning anxiety and sleep, since it requires too much participation and provides very little data.

- measure blood pressure in the sitting position only (not sitting and supine) and measure peripheral pulse.

- screen for basal cell carcinoma and call those that may have cancer back for a biopsy, if it appears that there is an excess of basal cell carcinoma in the study population. Provide additional training for the dermatologist by asking him/her to review known chloracne cases with Dr. Suskind or Dr. Taylor.

- Check with Drs. Felman and/or Baker concerning reliability of neurobehavorial testing for participants over 55 years of age, since there is some concern that the

validity of the test decreases with age. May want to consider testing a smaller sample using the Halsted Ray 10 battery, although it takes three to five hours to complete.

- Use a laboratory that uses the DuPont ACA500 for analyzing SMAC's, since this machine provides more accurate estimates and has less variability.

- Use Scripps Laboratory in California to conduct immune tests, since they are considered the best immunological lab in the country. Actually, Bioscience sends their samples to Scripts.

- Use Mayo Clinic to conduct porphyrin profiles. If Northwestern requests a complete profile from Mayo, then Northwestern can eliminate the test for delta-aminolevulonic acid. Be sure to ask participant if he/she is diabetic and whether they gave a complete 24-hour urine sample.

- Inform the participant about his/her health by providing an exit interview, a follow-up letter, and an 800 toll free long distance number for any questions that the participant may have later. Offer the participant the choice of having Northwestern send the medical records to his/her personal physician, to Monsanto as part of their annual physical, or to the participant.

Other items discussed during the meeting were about data analysis, implementation and study limitations. With respect to data analysis, the committee members suggested that Northwestern use SAS or FLOW GEMINI as the software package for data management, and recommended using BMDP for log linear analysis. Furthermore, the NIOSH dioxin exposure matrix will not be completed any earlier than March 1985, and Northwestern has retained Paul Levy as their statistician.

Regarding implementation and study limitations, the following comments were made. If Northwestern decides to include terminated employees in the study, they or Monsanto will need to use the services of a research company, e.g. NORC or Equifax, to help determine where the terminated employees are residing. Northwestern should determine why certain employees refuse to participate in the study. JRB Associates has developed a questionnaire to obtain this information. Either the employees should be told to expect a nine-hour "executive" medical examination or Northwestern should consider speading the exams over a two-day period. Along this line, it was suggested that less important exams, e.g. chest X-rays and

EKG, could either be eliminated or considered an option for those employees who would like to return on the weekend. Furthermore, the committee recommended that Northwestern run a pilot on volunteers who will not be in the study to determine how long the examinations will take and if there are any hitches in their organizational plans.

The meeting concluded with Northwestern expressing their appreciation for the time spent by the committee members and the suggestions that were made during the meeting. Northwestern will review the comments and will revise the protocol. They hope to send the revised protocol to Monsanto and the peer review committee by the first part of January 1985.

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