Monsanto

FROM (NAME & LOCATION) Dept. of Medicine & Environmental Health - P.E. Berteau, A2SC

BO-77-2

DATE: May 26, 1978

cc: R.A. Stohr, B2SC

SUBJECT: Non-human primate study with a PCB conducted at Litton Bionetics

REFERENCE:

TO J.C. Weber, B2SK

For your information, prior to a meeting later today, the following summary provides the most current information regarding the above mentioned study. The most recent data were obtained today in a telephone conversation with Dr. David Martin of Litton Bionetics.

The study was originally designed to investigate the effect of PCB's on the reproductive function of the rhesus monkey in the light of data reported by Allen /e.g. Allen et al. Tox. Appl. Pharm., 30, 440-451 (1974) and Barsotti et al. Food Cosmet. Toxicol. 14, 99-103 (1976)/. The justification for recommending this study is presented in the memorandum of April 9, 1976 from P.L. Wright to G. Roush, Jr., M.D.

Groups of 4 male and 8 female rhesus monkeys have received 0, 5, 25, or 100 µg/kg of a PCB (Aroclor 1254) daily since April 1, 1977. These levels have been recalculated to be approximately equivalent to 0.34, 1.7, and 6.7 ppm in the feed, based upon Allen's information and food consumption of the monkeys. Breeding was started on October 1 and has continued since that time.

RESULTS

1. Fertility

Based upon the most recent information, 7 out of 8 control animals became pregnant, 5 have already delivered; 7 out of 8 low dose animals have become pregnant (1 aborted, 2 have delivered); 6 out of 8 medium dose animals have become pregnant, 5 have delivered; and 3 out of 8 high dose animals become pregnant (2 aborted, 1 delivered a normal infant). Four (4) animals are nursing except 1 premature infant in the medium dose group. No evidence of abnormalities in infants is evident upon gross observations. Thus, female fertility is significantly affected at the 100 µg/kg level. Male fertility, as determined by semen evaluation, has been unaffected.

MONS 002959

IN 10M 12/75

2. Mortality

Two (2) control animals have died due apparently to gastric dilation, one 12 days after the commencement of the study and was replaced and one on March 31, 1978. No deaths have occurred in the low or medium dose groups. Three (3) deaths have occurred in the high dose group. Markedly diminished granulopoiesis was evident upon histological examination of the bone marrow of each of these animals.

3. Hematology

Significantly reduced values of several hematological parameters became evident in the high dose group beginning at month 10 (January 1, 1978) and also at month 12 (March 1, 1978). Significantly reduced hemoglobin was evident in the females, only in the medium dose group at month 12 only. Very recent information has indicated an improvement however. At month 13 (April 1, 1978) depression of hematological parameters was less marked than at month 12, and at month 14 (May 1, 1978) only the hemoglobin in the females on the high dose was depressed, other blood parameters being normal. A few non-dose related abnormalities in these parameters have been noted; these appear to be unrelated to PCB administration.

4. Biochemistry

Possible effects on certain liver function enzymes may be evident in the high dose group, although it is difficult to draw any conclusions. However, there was significantly increased serum iron in the high dose group at months 10 and 12. This finding may be related to the hematological observations and this possibility is being explored further.

5. Clinical Signs

Two (2) of 4 males and 3 of 8 females in the high dose group showed classical signs of PCB toxicity (e.g. edema and wrinkling of eyelids) beginning to be evident during the fourth quarter of feeding. Chloracne has not been noted however.

6. Analysis of Tissues

Problems have been encountered, possibly due to contamination and results are unreliable. This situation is being looked in to.

CONCLUSIONS

The findings so far roughly parallel those of Allen, except for the absence of chloracne. Reduced fertility is clearly evident in females on 100 µg/kg. No signs of a teratogenic effect are evident however. Possible blood dyscrasias are evident at 100 µg/kg, although this situation may be reversing itself even though administration of the PCB is continuing. Clinical signs of PCB intoxication are evident only at 100 µg/kg. Thus, a tentative no-effect level of 25 µg/kg/day with respect to all these parameters can be established (this level is 25 times higher than that established by FDA for human intake of PCB's).

RECOMMENDATIONS

The following suggestions are open for discussion:

1. Continue feeding the PCB for a further 2-3 months with monthly hematological and biochemical evaluation, to determine if there is an adaption to the apparent effect of the PCB on blood parameters.

2. Discontinue feeding the PCB after June 1 and determine if the effect on blood parameters is reversible.

3. Allow infants to nurse for given periods and sacrifice at equal times after birth (say 2 months).

4. Continue the study as before through another breeding season.

5. Discontinue the study on June 1 and sacrifice and necropsy all animals as soon as possible after that time.

Peter E. Berteau

alw