

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

SUBJECT: Carbaryl, Sevin<sup>(R)</sup>, 1-Naphtyl-N-Methyl Carbamate

DATE: July 17, 1974

FROM:

TO: Mr. Lee TerBush, Acting Chief  
Coordination Branch  
Registration Division (IM-567)

Pesticide Petition No. 2F1220

Union Carbide

Requested tolerance: 0.25 ppm in or on potatoes

The unresolved questions concerning Sevin center around its effects on reproduction (including teratology and mutagenesis).

1. A detailed 3-generation rat reproduction study is contained in the present amendment. This study is also published (Weil et al Tox. and Appl. Pharm. 26: 21-638, 1973). The maximum doses given to rats were 200 mg/kg/day (4000 ppm) in the diet or 100 mg/kg/day by oral intubation (o.i.). The animals receiving Sevin by dietary inclusion showed normal reproduction and signs of slight toxicity on the adults, such as decreased weight increase and increases in number of days after first mating to birth of litter. The animals dosed by o.i. (100 mg/kg/day) showed adequate reproduction as measured by the four reproduction indexes, several toxic effects on the mating animals however were observed, ranging from increased mortality, to decreased weight gain. At a dose of 25 mg/kg/day by o.i. no adverse effects were observed. The no effect level for dietary inclusion was 200 mg/kg/day.

2. The F3b litter was used for a teratology study. The only adverse effects were observed at the o.i. dose of 100 mg/kg/day. The median number of fetuses was reduced from 13 to 11 and the percent of litters with resorption sites was increased from 38.5% to 88.2%. No adverse effect was noted at any other feeding level or o.i. dose. The no effect level for teratogenic effects are thus the same as for the reproduction study.

3. F2b males from the reproduction study were used for a dominant lethal mutagenicity study, by mating them to unexposed virgin females. No effects were noted, except for a not dose related increase in percentage of late fetal death in the 4th week mating cycle.

4. Guinea pig teratology. Pregnant guinea pigs were dosed with 200, 100, 50 and 0 mg/kg/day by o.i. or 300, 200, 100 and 0 mg/kg/day by dietary inclusion. The dosage schedule was for one day, two or three days or up to 14 days. At the higher o.i. doses the continuing dosing had to be

omitted because of toxicity to the mothers. The dietary doses were given at all dose levels at all of the selected time periods. No skeletal or soft tissue anomalies or increased numbers in resorption sites were noted at any level.

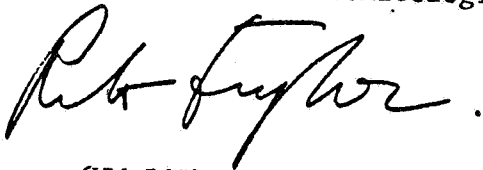
5. A Bionetic study (June 23, 1973) showed no teratogenic effects in 20 rats each fed 375 mg/kg and 200 mg/kg respectively.

6. Teratogenic evaluation in Rhesus Monkeys. Eighty monkeys were used. Their estrus cycle was monitored and pregnancy was initiated. (Only one female did not become pregnant.) The monkeys were then divided into 5 groups @ 16 animals; (i) control group (ii) vehicle control (iii) 0.2 mg/kg, (iv) 2 mg/kg and (v) 20 mg/kg. Carbaryl was administered daily from day 20-38 of gestation, in two equal daily doses. The number of live births, abortions and stillbirths as well as gestation length and birth weights were recorded. No significant differences in these parameters were observed between control and treatment groups. The females underwent clinical observation throughout their pregnancy. No signs of Carbaryl toxicity were detected. Four control and four high dose infants were sacrificed after weaning and they and any other infant dying during the study were autopsied. The cause of infant mortalities (six deaths) was grossly identified as respiratory or G.I. tract infections. Histopathology on the six deaths and 8 sacrificed animals has not been completed.

### Conclusion

The monkey study presented should dissipate any previous concern relating to impairment of primate gestation by Sevin. The rat reproduction study also showed no other than toxic effects on the mothers. The reproduction study showed a NEL of 200 mg/Kg/day or 4000 ppm when Sevin was given with the diet to rats. TB finds that the submitted studies clarify the uncertainties about Sevin's involvement in reproduction anomalies, and the requested tolerance on potatoes can be toxicologically supported.

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Toxicology Branch  
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cc: CB, EEB, Division File, Branch File, PP No. 2F1220

R/D Init: CHWilliams 07-15-74

Init: GEWhitmore S.F.W.

CHWilliams Cms 9/17/74

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MONKEY  
STUDY