

SUBJECT: Roundup - glyphosate Evaluation of Validation of I.B.T. B-566; Three-generation Reproduction Study with CP 67575 in Albino Rats

FROM: William Dykstra, Ph.D
Toxicology Branch

WDD 8/14/78

TO: Robert Taylor (25)

EPA #: 528-308
Caswell #661A

Registrant: Monsanto Agricultural Products
800 N Lindbergh Boulevard
St. Louis, Missouri 63166

Recommendations:

1. The validated I.B.T. B-566 Study does not adversely impact on the original TB review. The study is acceptable as core minimum data and the NOEL for glyphosate in the diet for three generations is ~~greater than 300 ppm.~~ *NOEL = 100 ppm*

Review: Roundup. BTL 71-34, I.B.T. B-566

- a. Original review by Ray Landolt PP4G1444

Eight males and 16 female rats were fed dietary levels of 0, 30, 100 and 300 ppm for the Fo parental generation and each of the following succeeding Flb and F2b generations. The study was terminated following the weaning of the F3b. Animals in all groups were maintained on their respective diets without interruption until their sacrifice, which followed the weaning of the second litters.

Mating trials were initiated when the parental animals were 100 days old. The first litters (Fla, F2a & F3a) obtained were weaned at 21 days post-partum. The parental females were given a 10 day rest period and again mated to obtain the second litter. All females were observed for fertility length of gestation and lactation performance. All pups were examined for physical abnormalities at birth and the number of viable and still born were recorded. The weight of the liver, kidneys, spleen, gonads, heart and brain were recorded, along with the final body weight of each rat.

Statistical analyses were conducted on an absolute organ and upon the organ to body and organ to brain weight ratios. The following tissues were examined microscopically from 5 males and 5 females from each level tested: heart, trachea, lung, liver, pancreas, stomach, small intestines, cecum, colon, spleen, lymph node, kidney, urinary bladder, testes, ovary, prostate, uterus, pituitary gland, adrenal gland, salivary gland, thyroid gland, parathyroid gland, skeletal muscle, bone marrow, peripheral nerve, brain, seminal vesicle, esophagus, spinal cord.

Results

Ingestion of technical material had no adverse effect upon parental body weight or body weight gains. There were no deaths during the investigation which could be attributed to the test material. No untoward behavioral reactions were noted among test or control animals. Organ weight, organ to body weight and organ to brain weight ratios revealed no consistent intergroup differences. All lesions noted during histopathologic evaluation revealed no relationship to the ingestion of the test material. Parameters of reproductive ability were similar for test and control animals during the first (F1a and F1b litters) generation. Animals fed 300 ppm exhibited reduced mating, fertility and pregnancy indices during the first litters of both the second and third generation (F2a and F3a litters). These parameters were comparable to those of the control groups during the second litters (F2b and F3b) breeding periods. The reduced parameters of reproductive ability which were observed during the "a" litters compared favorably with the control group values. There were no intergroup differences with respect to reproductive parameters with either the control or groups fed the 30 or 100 ppm level. No differences between test and control pups which could be attributable to the test material with the number delivered, survival indices, behavioral reactions, external anomalies, growth patterns, or gross and histopathologic exam.

Conclusion

The reproductive no effect level for rats fed glyphosate for three generations is ~~greater than 300 ppm~~. *NCEL = 100 ppm*

b. Package of Materials relating to validation.

1. Certification statement signed by Monte C. Throdahl, Monsanto Company.
2. Exhibit - A Biography of G.L. Wesp, Ph.D.
3. Exhibit - B Biography of G.J. Levinskas, Ph.D

4. Exhibit C - Biography of H.F. Smyth, Jr.

5. Exhibit D - Audit Statement of G.L. Wesp.

I. Body Weight Data, Parental
The discrepancies noted do not adversely impact on original TB review.

II. Individual Reproduction Data

8 errors in number of pups alive on various lactation days.
These errors do not adversely impact on original TB review.

III. Mortality Data

3 discrepancies vs. raw notebook data. These discrepancies do not impact adversely on original TB review.

IV. Organ Weights and Ratios

Discrepancies do not impact adversely on original TB review.

V. Reproductive Performance

3 discrepancies do not impact adversely on original TB review.

VI. Male Fertility
No discrepancies

VII. Population data, Progency

Discrepancies do not impact on original TB review.

VIII. Survival Indices

Discrepancies do not impact adversely on original TB review.

IX. Body Weight Data Weanlings

Discrepancies do not impact on original TB review.

X. Summary of Histopathologic Change

Discrepancies do not impact adversely on original TB review.

6. Exhibit E - Validation statement of H.F. Smyth, Jr.

7. Exhibit F - Responses to EPA Questions.

8. Exhibit G - Stability Reports - Do not impact adversely on original TB review.
9. Marked Copy of IB.T.B.-566 showing discrepancies.

Conclusions

The total of all discrepancies in the validation do not adversely impact on the original TB review

HED/TOX: init: Reto Engler 8/1/78
gjl

£ 8/17/78