

DATE: August 21, 1978

SUBJECT: Roundup-glyphosate Evaluation of Validation of I.B.T. B-1020; 90 day subacute oral toxicity study with CP67573 in albino rats. EPA Reg. No. 524-308 Caswell No. 661A

FROM: William Dykstra, Ph.D.
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WHD 8/22/78

TO: Robert Taylor (25)

Registrant: Monsanto Agricultural Products
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Product Manager: Robert Taylor (25)

Recommendations:

1. The validated report does not impact adversely on the original TB review. The NOEL for glyphosate in diet of rats for 3 months is still considered to be greater than 2000 ppm.

Review

1. Roundup, BTL 71-57; I.B.T. B-1020

a. Original Toxicology Branch Review PP 4G1444, Raymond E. Landolt.

Fifteen rats of each sex were fed the technical material at 0, 200, 600 and 2000 ppm in their daily diet for 90 days. The animals were observed daily for signs of toxicity and weighed weekly. The following hematologic and blood chemistry determinations were made on the control and high level at 45 and 84 days on the study: RBC, WBC, differential hematocrit, hemoglobin, BUN, SAP, SgPT and fasting blood glucose concentration. Uring analysis consisted of determinations for glucose, albumin, and microscopic elements examination; pH and specific gravity at the 45 and 84 day interval. The following organs were weighed: liver, kidney, spleen, gonads, heart and brain. The following tissues were examined microscopically from the control and high dose group: esophagus, stomach, small intestine, cecum, colon, liver, kidneys, spleen, pancreas, urinary bladder, pituitary gland, adrenal gland, testes, seminal vesicle, ovary, bone marrow, thyroid gland, parathyroid gland, salivary gland, prostate gland, heart, aorta, lung, lymph node, skeletal muscle, peripheral nerve, bone, spinal cord, uterus, trachea, eye, optic nerve, and brain. Organ to body weight ratios were determined in all three dosage levels.

Results: No significant abnormalities were reported for any of the parameters investigated for animals fed 200, 600 and 2000 ppm of Roundup for 90 days.

Conclusion: The no-effect level for rats fed glyphosate for 3 months was 2000 ppm.

- b. Package of Materials relating to validation.
1. Certification of Statement signed Monte C. Throdchl, Monsanto Company
 2. Exhibit A.- Curriculum Vitae of G.L. Wesp, Ph.D.
 3. Exhibit B.- Curriculum Vitae of D.W. Fassett, M.D.
 4. Exhibit C - Curriculum Vitae of G.J. Levinskas, Ph.D.
 5. Exhibit D - Audit Statement of G.L. Wesp
There are only the following discrepancies in the raw data and the final report.
 - I. Body Weight: raw data shows 8 discrepancies which do not adversely impact on original review.
 - II. Food Consumption: Means - No raw data to support mean values shown for 13th week. However, this discrepancy does not adversely impact on original review...
 - III. Hematologic data: Discrepancies do not impact on original review.
 - IV. Blood Chemistry: No impact on original review..
 - V. Urine Analysis-No adverse impact on original review.

Histology:

Six discrepancies were noted in individual animal data.

<u>Sex</u>	<u>Animal No.</u>	<u>of group T-III</u>
F	94	Kidney-chronic nephritis, gr. 1
F	106	Liver-Focal hepatitis, gr. 1
F	112	Trachea-chronic tracheitis, gr. 3
F	112	Lung-chronic mur. pneu., gr. 1
F	113	Lung-chronic mur. pneu., gr.1
F	113	Liver-focal hepatitis, gr. 1

Two discrepancies were noted in mean data.

Group

C-M chronic tracheitis- Incidence 9 T-III-M Add kidney-chronic nephritis, incidence 1, grade 1. Histopathological Effects in Livers of T-II animals and control.

3 (3F)

0

20 (10m + 10 F)

20 (10m + 10 F)

New validated data does not adversely impact on original review.

6. Exhibit E - Validation Statement of D.W. Fassett
7. Exhibit F - Response to E.P.A. questions
8. Exhibit G - Stability reports. Do not adversely impact on original review.
9. Marked Copy of I.B.T. Report No. B 1020 showing discrepancies.

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