

EXHIBIT 20

SUPPLEMENTAL INFORMATION OR PEER REVIEW WORKSHEET

I. STUDY IDENTIFICATION

Active Ingredient Glyphosate
 SB 950 #: 241 Document #: 364-163 (Rebuttal) and 364-142 through 364-148 (individual data to original mouse oncogenicity study report)
 Record #: 48775 (Rebuttal) and 45712-45718 (individual data)
 Addenda to Record #: 937660 (Vol. 1 of original report), 36060 (additional data on male kidneys)
 Addenda to Document #: 364-076 and 364-128, respectively.
 Study Type: Mouse oncogenicity (832)
 Full Study Title: Chronic Feeding/Oncogenicity Study in Mice, BD-77-420.
 (Wording of this glyphosate study title varies between submissions)
 Company Sponsor: Monsanto
 Testing Laboratory: Bio/dynamics
 Final Report Date: 7/21/83 (date of final report, Vol. 76). Vols. 142-148 dated 6/6/86, and Vol. 163 dated 8/26/86.

II. STUDY STATUS

A. Does this supplemental information or "second opinion" review lead to new conclusions regarding the study's acceptability or changes in the status of possible significant adverse health effects, compared to the most recent review?

Yes. Study is now complete and acceptable as an oncogenicity study. There is a possible adverse (oncogenic) effect.

B. Is the Report Complete? yes	Is the Study Acceptable yes
-Meets EPA guidelines?	-Has useful data yes
yes -Minor variances from guidelines?	-Has no useful data
-Major variances from guidelines?	-Insufficient data
-Could be upgraded with additional information (see discussion)	-Other

C. Conclusions: Does the study as reported demonstrate a possible significant adverse health effect?
 yes.

If so, in what area? Oncogenicity (renal tubular adenomas)

D. New "one liner": One or two sentence summary of the study, its status, and the conclusions, taking into account any supplemental information or peer review changes:

Document #s: 364-163 (Rebuttal) and 364-142 through 364-148 (individual data to original mouse oncogenicity study report) Record #s: 48775 (Rebuttal) and 45712-45718 (individual data). Addenda to Record #s: 937660 (Vol. 1 of original report), 36060 (additional data on male kidneys), and Document #s: 364-076 and 364-128, respectively. Oncogenicity, mouse, Bio/dynamics, dated 7/21/83 (final report, Vol. 76). Vols. 142-148 dated 6/6/86, and Vol. 163 dated 8/26/86. Rebuttal review by C. Aldous (11/17/86). Previous reviews by J. Christopher (Vol 1 of report = CDFA Doc. #364-076, reviewed 7/19/85) and J. Remsen Gee (additional data in Doc. #364-128, reviewed 5/1/86). Glyphosate, technical (99.7%). Dosages of 0, 1000, 5000, and 30000 ppm in diets of CD-1 mice. Possible oncogenic effect (renal tubular epithelial adenoma incidence of 0, 0, 1, and 3 in 0, 1000, 5000, and 30000 ppm groups.

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respectively). General systemic toxicity NOEL = 5000 ppm (Effects at 30000 ppm included central lobular hepatocyte hypertrophy in males, central lobular hepatocyte necrosis in males, chronic interstitial nephritis in males, and proximal tubule epithelial basophilia and hypertrophy in females). Report acceptable and complete. Filename = GLYPMO01.241.

NOTE: EPA is requiring a repeat mouse oncogenicity study (EPA publication, "Guidance for the reregistration of pesticide products containing glyphosate as the active ingredient" (June, 1986).

III. NATURE OF SUPPLEMENTAL INFORMATION

The additional data (CDFA Vols. 142-148) are volumes 2-8 of the original report. These volumes include largely individual data of body weight, food consumption, clinical observations, water consumption, hematology, organ weights, histology (including cross-referencing with gross findings), neoplastic lesion summaries identifying individual animal ID numbers, and individual animal fate data.

The rebuttal comments (Vol. 163) include the following responses to J. P. Christopher's review of 7/19/85:

a. (ref JPC concern about an excessively wide weight range among male mice initiated on test):

Only 1 male mouse was outside the $\pm 20\%$ range called for in 1982 guidelines.

b. (ref need for historical tumor data):

Attachment 1 of Vol. 163 provides historical tumor incidence data for male kidneys, non-neoplastic incidence data for male and female kidneys, and lymphoreticular/hematopoietic system tumor data for both sexes.

c. (ref JPC concern about dosage level justification):

A 90-day mouse subchronic study (Bio/dynamics Project No. 77-2111) was cited, in which dosages of 50,000 ppm glyphosate resulted in decreased body weight gains of 24 and 18% in males and females, respectively. The high dosage of 30,000 ppm in the present study was selected to achieve body weight decrements of about 10%.

d. (ref JPC indication that histopathology was performed on three levels of brain and on thoracic and spinal cord sections only on 10 animals per sex per group):

Registrant responds that all brains were examined in three sections, and all spinal cords were examined in the cervical region. Additional sections of spinal cord (thoracic and lumbar regions) were examined in 10 animals/sex/group, as recommended in 1978 guidelines, which were current at the time of this study.

e. (ref indication by JPC and/or Environmental Health Specialist that there was excessive mortality in the study):

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Registrant notes that mortality was well within limitations of 1982 guidelines.

f. (JPC stated that "Pathologist combines M & F for lymphoreticular tumors - not justified): also

(JPC requested historical incidence data for lymphoreticular tumors, renal tubular neoplasms, and chronic interstitial nephritis):

Registrant responds that lymphoreticular tumor incidence data was presented both by sex and combined [see Vol. 076, Tab "Pathology Report, p. 400].

The requested historical data are presented in Attachment 1 of Vol. 163.

IV. DISCUSSION

The responses of the registrant encompassed in items a-f above, combined with the additional data in Vols. 142-148, suffice to make this report complete and acceptable as an oncogenicity study.

The additional data in Attachment 1 of Vol. 163 reported frequencies of most neoplastic and non-neoplastic findings which varied substantially due to inter-study differences in lesion designation. Some commonly-occurring geriatric findings were counted in some studies but not in others (normal evidences of the aging process apparently not being counted by some pathologists as "findings": (chronic) interstitial nephritis being a typical case in point). There was no historical data designation for "proximal tubule epithelial basophilia and hypertrophy", as this effect was designated in Table 1 (located immediately before Table of Contents of final report, Vol. 76). Historical data for liver lesions as described in the above table were not requested by J. Christopher, and were not presented in Attachment 1. The new information does not change the conclusions acknowledged by Monsanto in Table 1, Vol. 76, which will be considered by CDFA as indications of high dose (30000 ppm group) toxicity. These findings are:

1. Central lobular hepatocyte hypertrophy in males.
2. Central lobular hepatocyte necrosis in males.
3. Chronic interstitial nephritis in males.
4. Proximal tubule epithelial basophilia and hypertrophy in females.

None of these findings are considered "significant adverse effects", due to their being restricted to the high dosage groups only.

The incidence of lymphoreticular neoplasms appeared to be somewhat elevated in high dose females compared to controls and other groups (see Vol. 76, Tab "Pathology Report" for a tumor type synopsis, or Vol. 148, Appendices 17A-18B for a more detailed breakdown). When lymphocytic and reticulum cell neoplasms are combined as recommended for analysis of incidence in some representative rodent species (Jan. 23, 1984 draft of EPA Hazard Evaluation Division Standard Evaluation Procedure entitled "Oncogenic

Potential: Guidance for Analysis and Evaluation of Long Term Rodent Studies"), the incidence of lymphoreticular neoplasms in the present study is not out of the historical control data range given in Attachment 1 of Vol. 163. Incidence of controls vs high dose females is not significant by Fisher's exact test. There is thus not a sufficient increase in lymphoreticular neoplasms in high dose females to judge these findings to be a treatment-related effect.

Renal tubular adenomas were noted in Vol. 76, Tab "Pathology Report" as having occurred in one 5000 ppm male and in three 30000 ppm males, but not in any other groups. Vol. 128 reports results of re-examination of previously cut sections and examinations of three additional sections/kidney of all mice on study. It was determined on this re-examination that control male mouse #1028 had a small renal tubular epithelial tumor not previously discovered, which would appear to reduce the likelihood that the findings in the higher two dosage groups was real. The EPA publication, "Guidance for the reregistration of pesticide products containing glyphosate as the active ingredient" (June, 1986, p. 6), states that the control male finding was not considered by EPA HED Toxicology Branch to represent a validated neoplasm: the final EPA determination was that "After examination of the slides, the Agency concluded that this lesion did not represent a pathophysiologically significant change". Historical incidence from Attachment 1 of Vol. 163 indicate only 3 tubular adenomas out of 1159 kidneys examined, two instances being in one study group of 120 kidneys (presumed by this reviewer to represent 60 mice). Although the incidence in the glyphosate study is obviously non-significant by Fisher's exact test whether there be 0 or 1 such neoplasms in controls, the relative rarity of this lesion and the findings of 3 such tumors in 30000 ppm males is sufficient reason to conclude that there is very possibly a treatment effect at the 30000 ppm level.

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Toxicologist

Nov. 17, 1986

Date