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DATE: August 22, 1978

SUBJECT: Glyphosate tolerances
Summary of tox data base. Caswell No. 661A

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We have recently reviewed the validated studies in support of the pesticide Glyphosate. Below follows a 8 point summary. The reviews on the validated studies are separately contained in Glyphosate file.

1. Data Considered :

Oral LD ₅₀ rabbit	3.8 g/kg (valid)
90-day rat feeding	NOEL 2000 ppm, highest dose (valid)
90-day dog feeding	NOEL 2000 ppm, highest dose (valid)
Teratology (2 studies) rabbit	NOEL 30 mg/kg/day (highest dose) (repeat studies with a higher dose)
2-year dog feeding	NOEL 300 ppm (highest dose) (valid)
3-generation reprod. (rat)	NOEL 300 ¹⁵⁰ ppm (highest dose) (valid)
18-month mouse feeding	No carcinogenic potential at 300 ppm (highest dose). Study must be repeated since too many animals are missing.
2-year rat feeding	NOEL 100 ppm, effects at 300 ppm. Study is adequate to determine toxic effects but only marginal with respect to oncogenic evaluation since too few animals examined. As reported study shows no oncogenic potential.
Neurotoxicity (hen)	negative 7.5 g/kg (cumulative for 3 days)

Mutagenicity tests:

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|----------------------------|--|
| (i) dominant lethal (mice) | negative 10 mg/kg (highest dose) supplemental study, no records of positive control. |
| (ii) host mediated assay | negative (acceptable study) |
| (iii) Ames test | negative (supplemental study, no raw data available) |
| (iv) Rec-assay | negative (supplemental study, no raw data available) |

2. Studies desirable

- (i) Repeat all supplemental studies and studies so indicated above,
- (ii) Assessment of oncogenic potential in two species

3. Registrant should be informed about the studies to be repeated.

4-6 See attached computer printout. Since there are a number of tolerances pending they are all grouped under "Current action". Those listed under "Other pending tolerances" are temporary tolerances.

7. There was a pending regulatory action against Glyphosate, based on its contamination with N-Nitrosoamine. It is our understanding that this issue has been resolved.

8. a) The main deficiencies in the data base are:

- (i) lack of adequate Teratology studies, it is however concluded that the studies at hand together with the reproduction study show that Glyphosate has a low potential for showing reproductive effects.
- (ii) the oncogenic potential of Glyphosate is not fully elucidated. The lifetime mouse and rat studies; however, provide adequate assurance that Glyphosate has a relatively low oncogenic potential. This assurance, however, is only valid on an interim basis, adequate oncogenic studies should be initiated as soon as possible.

(iii) several mutagenicity tests could not be validated; they too should be repeated at the earliest possible date.

b) A further assurance of low risk associated with Glyphosate is found in the fact that on a theoretical basis the exposure via the diet would be relatively low at present. It is suggested, however, that the data base for Glyphosate is rechecked in the future should the TMRC reach about 10% of the ADI. An evaluation of the repeat short-term studies (teratology, mutagenicity) and interim reports on the long-term studies will be necessary at that time.

Reto Engler, Ph.D.

Attachment

File last updated 8/18/78

ACCEPTABLE DAILY INTAKE DATA

RAT, Older NOEL	S.F.	ADI	MPI
mg/kg ppm		mg/kg/day	mg/day/60kg
5.000 100.00	100	0.0500	3.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day/1.5kg
Grain Crops (64)	0.100	13.79	0.02069
Soybeans (148)	0.200	0.92	0.00275

MPI	THRC	% ADI
3.0000 mg/day/60kg	0.0234 mg/day/1.5kg	0.78

Current Action F'S-1560,1733,1758,1798,1851,1892,1904,2016,1971

CROP	Tolerance	Food Factor	mg/day/1.5kg
Grapes, inc raisins (60)	0.100	0.49	0.00074
Citrus Fruits (33)	0.200	3.61	0.01144
Sugar, cane & beet (154)	0.100	3.64	0.00546
Cottonseed (41)	6.000	0.15	0.01350
Pome Fruits (126)	0.200	2.79	0.00637
Nuts (101)	0.200	0.10	0.00031
Pistachio nuts (210)	0.200	0.03	0.00009
Leafy Vegetables (80)	0.200	2.76	0.00828
Root Crop Veg (138)	0.200	11.00	0.03299
Seed & Pod Veg (143)	0.200	3.66	0.01096
Soybeans (148)	6.000	0.92	0.08263
Liver (211)	0.100	0.03	0.00005
Kidney (203)	0.100	0.03	0.00005
Palm Oil (202)	0.100	0.03	0.00005
Coffee (36)	1.000	0.75	0.01119

MPI	THRC	% ADI
3.0000 mg/day/60kg	0.2095 mg/day/1.5kg	6.98

Other Pending Tolerances 8F2070/G2051, 8F2021/G2020, 6G1679/H5106,

CROP	Tolerance	Food Factor	mg/day/1.5kg
Asparagus (5)	0.200	0.14	0.00043
Fish, shellfish (59)	0.150	1.06	0.00244
Cucurbits (49)	0.050	2.84	0.00213
Fruiting Vegetables (60)	0.050	2.99	0.00225
Small Fruit, berries (146)	0.050	0.83	0.00062
Stone Fruits (151)	0.050	1.25	0.00094
Potable Water (198)	0.050	133.33	0.10000
Avocados (6)	0.200	0.03	0.00009
Sugar, cane & beet (154)	1.900	3.64	0.10369
Potatoes (127)	0.000	5.43	0.00000

MPI	THRC	% ADI
3.0000 mg/day/60kg	0.4221 mg/day/1.5kg	14.07