UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

OK

DATE: December 11, 1978

SUBJECT: Roundup; PP#9G2150; Request for establishment of temporary tolerances of 0.2 ppm for combined residues of the herbicide glyphosate and its metabolites aminomethylphosphonic acid in or on the raw agricultural commodities stone fruit (apricot, cherry, nectarine, peach, plum and prune). EPA Registration Number#524-EUP-UT, Caswell#661A (glyphosate)

FROM: William Dykstra, Ph.D
Toxicology Branch/HED

2/11/78 WHO

TO: Dan Dickson & RCB, TS-769
Product Manager#25

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

Chemistry Branch Considerations:

Recommendations:

1. In a memo of 8/22/78 from R. Engler to R. Taylor, the summary of toxicological data base for validated studies is discussed together with a list of additional studies required.

2. Memo of 9/26/78 from M. Quaife to R. Taylor regarding glyphosate data submitted by Monsanto.

3. The proposed temporary tolerances of 0.2 ppm of glyphosate in stone fruit are toxicologically supported. The proposed tolerances will use up only 0.12% of the ADI. Other published and approved tolerances use up 14.07% of the ADI. All tolerances on glyphosate will use up 14.19% of the ADI.

Name of Product: Roundup

(EPA Reg.#524-308)

Total quantity proposed for use: 595 gallons containing 1785 pounds active ingredient.

Time period: Two years

Acerage: 2080 acres

1. Data Considered:

Oral LD_{50} rabbit	3.8 gm/kg (valid)
90-day rat feeding	NOEL 2000 ppm (valid)
90-day dog feeding	NOEL 2000 ppm (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 (valid)
3-generation rat reproduction	NOEL 100 ppm (valid)
18-month mouse oncogenicity	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 gm/kg (cumulative for 3 days)

Mutagenicity Tests

(i) dominant lethal (mice) - negative 10 mg/kg (highest dose); supplemental study, no records of positive controls.

(ii) host mediated assay - negative (valid)

(iii) Ames test - negative (supplemental study, no raw data available)

(iv) Rec-Assay - negative (supplemental study, no raw data available)

2. Studies Desirable

(1) Repeat all supplemental studies and studies so indicated above.

(2) Assessment of oncogenic potential in two species.

3. Evaluation of the ADI

The ADI is based on the NOEL of 100 ppm in a 2 year rat feeding study (most sensitive species). This NOEL equals 5.0 mg/kg/day. A safty factor of 100 is used to calculate the human ADI.

$$\text{ADI} = 5.0 \text{ mg/kg/day} \times \frac{1}{100} = .05 \text{ mg/kg/day}$$

The MPI for a 60 kg person is 3.0 mg/day

$$\text{MPI} = \text{ADI} \times 60 \text{ kg} = .05 \text{ mg/kg/day} \times 60 \text{ kg} = 3.0 \text{ mg/day}$$

4. Tolerances for glyphosate have been established under 40 CFR 180.364.

5. The current action will use up 0.12% of the ADI. Other published, approved and pending tolerances use up 14.07% of the ADI. All glyphosate tolerances will use up 14.19% of the ADI (see computer printout).

6. Conclusions and Recommendations

It is concluded that the reqested temporary tolerances can be toxicologically supported. Only 0.12% of the ADI will be used up by the current action. All tolerances published and approved, will use up 14.19% of the ADI. The recommendations in memo of 8/22/78 from R. Engler to R. Taylor provide sufficient toxicological data to support the present action.

TOX?HED:th:R.Gessert:12-8-78

[illegible] updated 12/6/78

ACCEPTABLE DAILY INTAKE DATA

Rat, NOEL [illegible]		S.F.	ADI	MPI
mg/kg	ppm		mg/kg/day	mg/day/60kg
5.000	100 ppm	100	0.0500	3.0000

Published Tolerances

CROP	Tolerance	Food Factor	mg/day/1.5kg
Grain Crops(68)	0.100	13.79	0.02069
Soybeans(143)	0.200	0.92	0.00275

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

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Unpublished, FR approved F1560,1714,1738,1796,1892,1904,1971,2016,202[illegible]
H5144, H5126

CROP	Tolerance	Food Factor	mg/day/1.5kg
Grapes, inc raisins(66)	0.100	0.49	0.00074
Citrus Fruits(33)	0.200	3.81	0.01144
Sugar,canebeet(154)	0.100	3.64	0.00546
Cottonseed(41)	6.000	0.15	0.01350
Pome Fruits(120)	0.200	2.79	0.00837
Nuts(101)	0.200	0.10	0.00031
Pistachio nuts(210)	0.200	0.03	0.00009
Leafy Vegetables(80)	0.[illegible]00	2.76	0.00828
Root Crop Veg(136)	0.200	11.00	0.03299
Seasoned Veg(143)	0.200	3.66	0.01098
Soybeans(143)	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(35)	1.000	0.75	0.01119
Avocados(6)	0.200	0.03	0.00009
Molasses(98)	2.000	0.03	0.00092

MPI	TMRC	% ADI
3.0000 mg/day/60kg	0.2105 mg/day/1.5kg	7.02

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Current Action 3G2150

CROP	Tolerance	Food Factor	mg/day/1.5kg
Stone Fruits(151)	0.200	1.25	0.00374

MPI	TMRC	% ADI
3.0000 mg/day/60kg	0.2143 mg/day/1.5kg	7.14

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Other Pending Tolerances 8F2070/3G2051,6G1679/6H5105,8G2060,8G2032

CROP	Tolerance	Food Factor	mg/day/1.5kg
Asparagus(5)	0.200	0.14	0.00043
Fish,Shellfish(59)	0.150	1.08	0.00244
Cucurbits(43)	0.050	2.84	0.00213
Fruiting Vegetables(64)	0.050	2.99	0.00225
Small Fruit,berries(149)	0.050	0.83	0.00052
Potable Water(150)	0.050	133.33	0.10000
Sugar,canebeet(154)	4.000	3.64	0.10369
Potatoes(127)	[illegible]	5.43	[illegible]

MPI	TMRC	% ADI
3.0000 mg/day/60kg	0.4258 mg/day/1.5kg	14.19

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