Glyphosate / TOX UNDATED (10)

To: L. Dale, Ph. D.

RELEASABLE

Thru: Chief, Toxicology Branch

Thru: [redacted] Pesticide Science Officer

From: K.L. Bailey, Toxicology Branch

Subject: Glyphosate (Roundup) #661A

I Points of Note

A. There are accepted tolerances ~~as for~~ for glyphosate in or on ~~goods~~ grain crops, grasses and soybeans as per 40 CFR 180.364.

B. The nitroso derivative of the active ingredient, N-nitrosoglyphosate, has been identified as being present at levels of .2 - .4 ppm in the formulated product, Roundup.

(See M. L. Quaife, Ph. D. 6-29-77 memo, PP6F1861)

C. The Chemistry Branch has concluded, ~~in the 6-9-77 D. Duffy review concerning PP6F1861~~, for certain crops, that the maximum hypothetical residues of nitrosamine would be less than .007 ppm. ~~in the 6-9-77~~ (See D. Duffy 6-9-77 review concerning PP6F1861)

II Metabolism

A. Plant

The Chemistry Branch has in the June 3, 1974 D. Duffy memo concerning PP 461444 concluded that the major metabolic pathway involves the formation of the amino-methylphosphonic acid and glyoxalate via C-N enzymatic bond cleavage. ~~(See attachment for details)~~

(Note: For details consult attached review.)

B. Mammalian Toxicology

The ~~Toxicology~~ Branch has in the May 9, 1974 R. Landolt Memo concerning ~~PP 4G1444~~ PP 4G1444 ~~the~~ concluded the following in relatin to the rat:

1. ~~N-phosphonomethyl glycine rather than animal metabolites.~~ " N-phosphonomethyl-^{14}C-glycine remains unchanged in the rat through three different types of treatment and is excreted in urine and feces as the parent compound. "

2. ~~Conclusion:~~ "The ingested test material was excreted from the body by apparent first order processes so that the amount excreted was directly proportional to the intake. Upon withdrawal, excretion dropped sharply but plateaued temporarily after four days. This excretory plateau during the withdrawal period was due to the excretion of the mobilized tissue residues which were cleared by the kidney or secreted into the intestine with the bile. The cumulative effect was not localized in a single tissue or organ system and was clearly reversibly bound. "

(Note: Fr ~~details~~ details consult attached review)

II Inhalation Toxicity

A. Pyrolysis Products.

No information is at hand concerning the ~~pyrolysis~~ inhalation toxicity of the ~~fogrol~~ pyrolysis products of this compound.

B. Formulated ~~Test~~ Product

The acute rat inhalation LD_{50}, using a 41% formulation, is identified >12 mg/L in the attached R. Landolt review.

IV Pharmacodynamics

A. Toxicity

While there are ample toxicity studies at hand concerning this material, there is no information available concerning the mechanism whereby the ~~sp~~ compound affects mammalian systems.

B. Metabolism

See II ~~Metab~~ Metabolism above.

C. Pharmacokinetics

~~While there is no pharmacokinetic~~

While there is no concrete numerical pharmacokinetic data ~~[illegible]~~ at hand, the attached R. Landolt ~~[illegible]~~ review suggests that mammalian bioretention is not a problem with this compound.

4. other associated reviews

D. Many of the pertinent toxicity studies at hand were performed by IBT and have not, as yet, been validated.

E. For recent Toxicology Branch Reviews consult the following:

1. 10-4-77 M. Quaife re all petitions
2. 1-25-77 M. Quaife re PP 6F1758 and 6H5126
3. 9-12-77 M. Quaife re PP 6G1757 ~~and 6H5152~~ and 6H5125