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PP# 9G2152: Larvin in Cottonseed and Soybeans. Evaluation of analytical method and residue data.

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The Union Carbide Corporation proposes tolerances for combined residues of the insecticide Larvin (UC 51762), dimethyl N,N'-[thiobis[(methylimino)carbamoyloxy]]bis[ethanimidothioate], and its metabolite methomyl, S-methyl N-[(methylcarbamoyl)oxy]thioacetamide in or on the following commodities.

Cottonseed	0.4 ppm
Soybeans	0.1 ppm
Soybean straw	0.02 ppm

There are no tolerances established for Larvin. However, the metabolite, methomyl, is an insecticide with established tolerances on a variety of commodities at levels of 0.1-40 ppm (§180.253). These tolerances include levels of 0.1 ppm for cottonseed, 0.2 ppm for soybeans, and 10 ppm for soybean forage.

The proposed tolerances are to cover residues resulting from an experimental program which entails the use of 2,200 pounds of active ingredient on 1,000 acres of cotton and soybeans. The experimental program is to take place in 20 states in the major cotton and soybean growing areas of the United States.

Conclusions

1. [redacted] is not sufficiently identified to determine if it is cleared for use under §180.1001.

2. The nature of the residue in plants and animals is adequately understood. The parent compound UC51762 and its metabolite methomyl are the significant components of the residues.

3. An adequate analytical method is available for the determination of residues of UC51762 and methomyl.

4. Residues in cottonseed, soybeans, and their byproducts (oil, meal, soapstock), or soybean straw are not likely to exceed the proposed tolerances.

5. Residues are not likely to occur in eggs, milk, and meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep as a result of the proposed uses [180.6(a)(3)].

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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Recommendation

Toxicological considerations permitting, we recommend for the proposed tolerances.

For permanent tolerances, the following data should be submitted:

[redacted] This identification is necessary in order to determine if the inert ingredient is cleared for use under §180.1001.

2. A step should be included in the residue method which frees conjugated metabolites.

3. Additional residue data for cottonseed and soybeans which reflect maximum proposed conditions of use (i.e., maximum application rate and number of applications with samples collected at proposed treatment-to-harvest intervals).

4. Residue data which show if residues occur in the byproducts of cottonseed and soybeans (hulls, oil, meal, soapstock). If residues appear in these items and at levels greater than in the seeds, then food additive tolerances to cover such residues will be necessary.

5. Livestock (cattle, poultry) feeding studies which show if ingested residues are stored in eggs, milk, and tissues.

Detailed Considerations

Proposed Uses

LARVIN 500 Insecticide, an aqueous flowable formulation containing 44% active ingredient (a.i., or 4.18 lb. a.i./gal), is proposed for use on cotton and soybeans when insects first appear. Repeat applications are to occur as necessary, by ground or air, usually at 5-7 day intervals for most pests.

Cotton: apply at rates of 0.33-0.9 lb act/A depending upon level of infestation. Livestock are not to graze fields, and no application is to occur less than 7 days before harvest (PHI).

The metabolite methomyl is an insecticide which is registered for use on cotton. Ground or aerial, foliar applications are permitted at rates of 0.45-0.67 lb act/A at 3-5 day intervals. A maximum of 3 applications is permitted with a 15-day PHI.

Soybeans: apply at rates of 0.23-0.45 lb act/A depending on level of infestation. Treated forage is not to be fed to livestock, and no application is to occur less than 28 days before harvest (PHI).

Methomyl is registered for use on soybeans with ground or aerial foliar applications of 0.22-0.45 lb act/A. A PHI of 14 days is imposed.

The registered uses for the metabolite methomyl are not likely to adversely affect the total level of residues of Larvin on cottonseed and soybeans. The use of Larvin entails an experimental program of limited scope, and the crops are not likely to be exposed to methomyl during the experimental program. Therefore, the registered methomyl uses are not likely to present a residue problem.

Manufacturing Process

[redacted]

MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED [redacted] The petitioner should be asked to more fully identify this component. If the component is not cleared under §180.1001, then clearance should be obtained.

Nature of the Residue
Metabolism in Plants

The pesticide chemical UC51762, dimethyl N,N'-[thiobis[(methylimino) carbonyloxy]]bis[ethanimidothioate], is absorbed, metabolized, and translocated by plants (cotton, soybeans, corn, wheat, cabbage, carrots). The chemical is extensively degraded and/or metabolized and eliminated from the plant as the volatile compounds carbon dioxide and acetonitrile. The chemical is, to some extent, completely degraded and its elements reincorporated into naturally - occurring plant constituents. A minor pathway for detoxification is conjugation, and/or binding with plant constituents.

The major components of plant residues are the parent compound UC51762 and its metabolite methomyl, S-methyl N-[(methylcarbamoyl)oxy] thioacetamide. The metabolites methomyl oxime, methomyl sulfoxide, and the methylol of methomyl (hydroxymethyl methomyl) appear as minor components of plant residues (usually less than 10% of the residue). The metabolites appear in the free and conjugated and/or bound forms. The conjugated and/or bound forms usually represent less than 10% of the plant residues. (See Figure 1 of accompanying chart for metabolic pathways).

Cotton

Greenhouse studies were performed in which 5-6 week old cotton plants were treated by stem injection with radiolabelled UC51762 (acetyl-C^{14}-label). The plants were sampled at 7, 14, 21, and 28 days and examined for C^{14}-radioactivity.

The cotton plants contained six free or non-conjugated components at seven days. These components represented 53% of the radioactivity present. Three of the components were identified: the parent compound UC51762 (48%); methomyl (4%); and, methomyl oxime (trace, <0.1%). The parent compound generally decreased with time so that at 28 days, it represented only about 0.1% of the free residue. Methomyl remained relatively steady over the 7-28 day period and was 5.4% of the free components at 28 days. The methomyl oxime represented only trace residues over the 28-day period. The unidentified components showed a greater level of residues at 28 days than at 7 days.

The cotton plants also contained 7 components conjugated with sugars. These components were a maximum of 3% of the applied radioactivity at 14 days and had declined to 1.2% at 28 days. Three of these components were identified (all metabolites): methomyl (maximum of 0.24% of applied); hydroxymethyl methomyl (maximum of 0.58% of applied);

and, methomyl oxime (maximum of 0.21% of applied). The conjugated residues generally increased from 7-14 days and decreased with time thereafter.

The unextracted cotton plant residues increased from 0.7-2.6% (7-14 days) and decreased thereafter to 1.5% of the recovered radioactivity at 28 days. Radioactivity lost thru volatilization ranged from 35% of recovered activity at 7 days, increased to 65% at 14 days, and reached a maximum of 70% at 28 days. The volatilized components consisted primarily of acetonitrile and carbon dioxide.

Studies on the volatilization of radioactive C^{14}-UC51762 were carried out in 4-week old cotton plants. C^{14}-UC51762 was applied to the top surfaces of leaves for one treatment and stem injection for another treatment. The plants were collected at intervals of 1, 4, and 7 days and examined for radioactivity.

Volatilization was greater from the leaf surface than from stem injection of UC51762.

A second greenhouse study was performed in which radiolabelled C^{14} UC51762 (acetaldehyde-1-C^{14}) was spread with a brush on the upper leaf surfaces of cotton plants when the flower buds were started. (The treatment is reported to be equivalent to 1.0 lb UC51762/A). The plants were maintained in the greenhouse until the bolls were mature. The senescent leaves were collected for examination. A small branch was removed after 14 days treatment to examine for evidence of absorption and translocation of residues of UC51762.

The mature bolls were collected for examination. The seed were delinted, and both the lint and the delinted seed were examined for radioactivity. The senescent leaves were also collected and examined for radioactivity. The unextracted plant residue was also examined. Analyses and characterization of residues were performed with the procedures noted in the first cotton plant study.

The leaves contained the major portion of the applied radioactivity. The lint had 0.05% of the applied dose and the seed had 0.09% of the applied dose. The petitioner maintains that these data indicate poor absorption and translocation of UC51762 or its metabolites from leaves to other parts of the plant. We concur with this conclusion. The low level of radioactivity in the seed precluded identification of components of the residue.

Fractionation and isolation of the leaf residue showed organo-soluble and water-soluble components. There were 11 organo-soluble components (approximately 37% of the leaf activity). The organo-soluble phase represents free or unbound components. Four components were identified and the remaining 7 were not identified. Those identified were the parent compound, UC51762 (about 60% of the organo-soluble activity); methomyl (about 34%); methylol of methomyl (hydroxymethyl methomyl, 1.4%); and, methomyl oxime (0.4%). The unidentified components were less than 5% of the organo-soluble residue.

The water-soluble residue represents conjugated components which were freed thru enzymatic hydrolysis. The components were about 9.7% of the leaf activity. There were nine conjugated compounds. Three components were identified and 6 were not. The identified compounds were glycosyl conjugates of the metabolites methomyl, hydroxymethyl methomyl, and methomyl oxime. The identified components were about 58% of the conjugated residue. However, the conjugated residue was less than 10% of the leaf activity. Approximately 34% of the bound residue was not affected by the enzymatic hydrolysis. The unextracted leaf residue made about 20% of the leaf residues. These data suggest that some of the bound radioactivity represents reincorporated C^{14}-radioactivity. The presence of radioabelled components which did not correspond to authentic standards further suggests that some of the unidentified components are naturally-occurring, radiolabelled plant constituents.

Two volatile components, carbon dioxide and acetonitrile, accounted for the major portion of the radioactivity lost from the leaf surface of treated plants by volatilization. Less than 3% of the applied radioactivity remained in the plant tissues. About 70% is lost as carbon dioxide and acetonitrile during the first 28 days. Thus, UC51762 appears to be rapidly metabolized to methomyl and methomyl oxime which are subsequently converted to sugar conjugates and/or degraded to carbon dioxide and acetonitrile. These components are then lost thru volatilization.

The major components of cotton plants are the parent compound UC51762 and its metabolite methomyl. The metabolites methomyl and methomyl oxime appear as sugar conjugates. The data indicate that unidentified components (free and bound) are naturally-occurring C^{14}-labelled components (e.g., the absence of N-S and N-C bonds and the absence of the behavior characteristics of authentic standards).

The major metabolic pathway for UC51762 in cotton involves hydrolysis of UC51762 to methomyl which is subsequently degraded thru methomyl oxime to carbon dioxide and acetonitrile. Methomyl and methomyl oxime are also conjugated with sugars to form glycoside esters.

Analysis of Samples

The samples are extracted by blending with an acetonitrile:acetone: water mixture which is centrifuged and filtered. The plant residue is dried and examined for radioactivity by combustion to carbon dioxide followed by liquid scintillation counting.

The filtrate is partitioned into organo-soluble and water-soluble fractions. The organo-soluble fraction is concentrated, purified, and analyzed using one- and two-dimensional thin layer chromatography (TLC). The purified components are further characterized using mass spectrometric techniques.

A portion of the water-soluble fraction is concentrated and incubated with the enzymes beta-glucosidase or gluculase. The incubated mixture is extracted with an acetonitrile:chloroform mixture and partitioned into an aglycone fraction and an aqueous fraction. The aglycone fraction is concentrated and purified by TLC. The purified aglycones are further characterized by mass spectrometry and nuclear magnetic resonance (NMR) techniques.

The unhydrolyzed aqueous fraction is digested with dilute hydrochloric acid, extracted with an acetonitrile:chloroform mixture, and partitioned into an organo-soluble fraction and an aqueous fraction. The organo-soluble fraction is concentrated, and any volatile components are collected as condensate or in a cold trap. The radiolabelled components are characterized by TLC and gas chromatography using a gas proportional counter.

Volatilization Studies

Four week old cotton plants were placed in a metabolism bell jar, and any evolved volatile components were collected at various intervals of 1, 4, and 7 days. The evolved components were characterized by gas chromatography using a gas proportional counter.

Soybeans

Soybean plants were treated with radiolabelled C^{14}-UC51762 by stem injection. Plant samples were collected 7 days later and examined for radioactivity. The methods of analysis and characterization were the same as those used in the preceding cotton plant studies.

The plant residue consisted primarily of free UC51762 and its metabolite methomyl (about 37% of the plant radioactivity). Trace levels of free methomyl sulfoxide (0.3%) and methomyl oxime (0.2%) were also present. Five of 9 components were unidentified. Glucoside conjugates (8 components) were also present and represented less than 2% of the plant radioactivity. The identified conjugated components were methomyl and methomyl oxime.

Approximately 12% of the bound residue was not hydrolyzed by the enzyme system. About 3.6% of the plant radioactivity was not extracted, and some 46% of the applied radioactivity was lost thru volatilization as acetonitrile and carbon dioxide.

As in the cotton plant studies, a portion of the C^{14}-activity appeared to be reincorporated into naturally-occurring plant components.

Corn and Wheat Plants

3 week old corn and wheat plants were separately treated with radiolabelled C^{14}-UC51762 by stem injection. Plant samples were collected at 7 days after treatment and examined for radioactivity. The methods of analysis and characterization of residues were the same as those used in the preceding plant studies.

Plant residues of corn and wheat were similar and consisted of 10 free components (about 60% of activity in plants) of UC51762. The identified components were UC51762 and its metabolites methomyl, methomyl sulfoxide, and methomyl oxime. UC51762 and methomyl accounted for 94-98% of the free components. The remaining 6 free components were unidentified and accounted for less than 1% of the free components.

Nine conjugated components were noted and accounted for about 1.4% of the radioactivity in the plants. The identified conjugated components were methomyl, methomyl sulfoxide, and methomyl oxime. About 7-14% of the plant radioactivity was not hydrolyzed by the enzyme digestion. Some 3-14% of the radioactivity was unextracted plant residues, and 25-53% of the radioactivity was volatile components. The volatile components have been identified as primarily acetonitrile and carbon dioxide.

The unidentified components did not match any of 12 standard components on TLC in any of 10 solvent systems used. These data suggest that such components represent C^{14}-activity which has been reincorporated in naturally-occurring plant constituents.

Cabbage Plants

Greenhouse studies were performed with radiolabelled C^{14}-UC51762 applied by stem injection to six-week old cabbage plants. The plants were sampled at 7, 14, 21, and 28 days and examined for residues of UC51762. The plants were analyzed and residues characterized by the methods used in the preceding studies.

The plants consisted of 13 free components (about 34% of plant radioactivity). Five of these were identified: the parent UC51762 (27%); methomyl (6%); N-hydroxymethyl methomyl (0.08%); methomyl sulfoxide (0.04%); and, methomyl oxime (0.4%). Thirteen conjugated components were noted and represented about 2% of the total plant radioactivity. Four of these were identified: methomyl; N-hydroxymethyl methomyl; methomyl oxime; and, methomyl sulfoxide.

About 11% of the plant radioactivity was not hydrolyzed enzymetically, and up to 18% of the plant radioactivity was not extracted from the plant.

The unidentified components did not correspond to any of the 12 authentic standards on TLC in any of 10 solvent systems. These data suggest that the unidentified components are naturally occurring plant constituents containing reincorporated C^{14}-activity.

The free and conjugated metabolites tended to increase initially with time, then to decrease over the 7-28 day period. The parent compound decreased slowly with time.

The volatile components (acetonitrile and carbon dioxide) showed a different pattern. These components increased with time from 36% at 7 days to 45% of the applied radioactivity at 28 days. This is consistent with behavior observed in other plants.

Carrot Plants

A greenhouse study was performed in which radiolabelled C^{14}-UC51762 was spread over the top surfaces of 6-week old carrot plants. The plants were harvested 28 days after treatment and examined for radioactivity. The samples of tops and roots were examined by the procedures used in the cotton studies.

The tops contained the major portion of the residue with only trace activity in the roots. A large amount of unchanged UC51762 was present in the foliage. The low activity in the roots indicate little translocation of the parent or its metabolites occurred from the leaves to the roots. Additionally, less volatilization of residues appeared to occur from carrot leaves as with the plants in the preceding studies. Due to the low level of radioactivity in the roots, no characterization of residues was attempted.

The carrot tops contained 88% of the applied radioactivity as 10 free components. Four of these components were identified: UC51762 (79%); methomyl (8%); N-hydroxymethyl methomyl (0.15%); and, methomyl oxime (0.09%). There were 9 bound or conjugated components (less than 1% of the plant radioactivity) in the tops. Three of these components were identified: methomyl; N-hydroxymethyl methomyl; and, methomyl oxime. Less than 1% of the radioactivity represented components that were not hydrolyzed by the enzymes. Less than 1% of the radioactivity represented unextracted plant residues, and 9.5% of the applied radioactivity was volatilized primarily as acetonitrile and carbon dioxide. Only about 0.06% of the applied activity was present in the roots.

Metabolism of Methomyl in Plants

Cotton

A greenhouse study was performed in which radiolabelled C^{14}-methomyl was applied by stem injection to 4-week old cotton plants.

The plants were harvested at 7 days after treatment and examined for C^{14}-radioactivity. The methods of analysis used were those employed in the preceding plant studies.

The plants contained 10 radioactive components in the free or unbound form. These represented about 12% of the applied radioactivity. Two components were identified: methomyl (about 10% of the applied radioactivity); and, methomyl oxime (about 0.1% of the applied activity). Thus, methomyl and its oxime metabolite represented about 84% of the free components.

Seven conjugated components were noted in the plants. (These were 5% of the applied radioactivity). One of the components was identified: methomyl oxime - which was about 10% of the components. Approximately 21% of the applied activity was not hydrolyzed by enzyme treatments, and 17% of the applied activity was not extracted from plant material. About 45% of the applied radioactivity was volatilized primarily as acetonitrile and carbon dioxide.

The unidentified components did not match any of the authentic standards when compared using two-dimensional thin layer chromatography and six different solvent systems. These data suggest that the radioactivity represents C^{14}-activity reincorporated into naturally-occurring plant constituents.

Corn

Greenhouse studies were performed in which radiolabelled C^{14}-methomyl was injected into stems of 3-week old corn. The plants were harvested 7 days after treatment and examined for radioactivity. The methods of analyses were those used in the preceding studies.

The plants had 8 free radioactive components which represented 36% of the applied radioactivity. Three of the components were identified: methomyl sulfoxide (1% of applied activity); methomyl (34%); and, methomyl oxime (0.3%).

The plants had 12 conjugated or bound components (about 2% of the applied activity). Three of these components were identified: methomyl sulfoxide, methomyl, and methomyl oxime. About 7% of the bound compounds were not hydrolyzed by enzymes. About 4.4% of the applied radioactivity was not extracted from the plant. Approximately 50% of the applied radioactivity was volatilized and primarily as acetonitrile and carbon dioxide.

The unidentified components failed to match any of the authentic standards when compared using two-dimensional TLC and 6 different solvent systems. These data suggest that the unidentified radioactive components represent C^{14}-activity which has been reincorporated into naturally-occurring plant constituents.

Animal Studies

Rats

UC51762 is rapidly absorbed, metabolized, and excreted by the rat. Some residues are retained in tissues and organs.

A rat was orally administered a single dose of radiolabelled C^{14}-UC51762 (acetaldehyde-1-C^{14}) at a level of 16 mg/kg body weight. The animal was sacrificed 15 minutes later, and tissues and organs were examined for radioactivity. Radioactivity was distributed throughout the organs and tissues.

Approximately 66% of the administered activity was recovered. The remainer is presumed by the petitioner to be volatilized. The volatilized components are believed to consist primarily of acetonitrile and carbon dioxide. Of the recovered radioactivity, 40% was found in the alimentary canal; 6.8% was found in tissues (kidney, 18.5 ppm; lung, 6.8 ppm; liver, 12.4 ppm; spleen, 3.3 ppm; muscle, 3 ppm; heart, 4.3 ppm; fat, 0.7 ppm); 1% in plasma; 2.8% in red blood cells; and 16% in the remaining carcass.

Of the residues in the alimentary canal, the stomach had about 96% organo-soluble residues (free UC51762 and/or its metabolites) and 4% water-soluble residues (possibly bound or conjugated metabolites). Generally, the small intestine had 91-99% water-soluble activity and 3-9% organo-soluble activity. The residues in the stomach consisted primarily of the parent UC51762 (59%), the metabolites methomyl (31%), methomyl oxime (2%), methomyl sulfoxide (0.2%), methomyl sulfoxide oxime (0.3%), 4 unidentified components (2%), and water-soluble activity (4%). Methomyl sulfoxide and methomyl sulfoxide oxime are believed by the petitioner to be artifacts formed by the oxidation of the corresponding components methomyl and methomyl oxime. This conclusion is supported by the fact that when methomyl and methomyl oxime were subjected to the analytical procedure, small amounts of methomyl sulfoxide and methomyl sulfoxide oxime were formed.

Analytical Procedures

Radioactivity in the various extracts of samples was determined using liquid scintillation techniques. Tissues were macerated, and samples were combusted to radiolabelled $C^{14}O_2$. This activity was then determined by liquid scintillation counting.

Samples were extracted by blending with acetonitrile/water, filtered, and aliquots were examined for radioactivity. The extractable radioactivity was divided into organo-soluble and water-soluble phases by partitioning the acetonitrile/water extract with chloroform. Aliquots were taken from the organo-soluble and water-soluble phases and examined separately for radioactivity.

The organo-soluble phase was concentrated and examined by two dimensional TLC. Radioactivity in the TLC spots was determined by scraping the spots from the TLC plate and counting of the radioactivity by liquid scintillation techniques.

Cow

A lactating cow was given a single oral dose of radiolabelled C^{14}-UC51762 (acetaldehyde-1C-label) equivalent to approximately 327 ppm in the feed. Collection of milk samples was begun 6 hours after dosing and continued at 12 hour intervals. Urine samples were collected via catheterization, and feces samples were collected at intervals of 3-72 hours following dosing. Blood samples were collected at intervals also. At 72 hours after dosing, the cow was sacrificed and tissue samples were collected. All samples were examined for C^{14}-radioactivity.

Sixty-six percent of the administered radioactivity was eliminated as carbon dioxide and acetonitrile within the first 72 hours of dosing. The urine had 5% of the administered radioactivity, the feces had 11%, and the milk had about 5%. Residues in the milk reached a maximum of 7.3 ppm UC51762-equivalent residues after 18 hours of dosing. At the end of the treatment period (72 hours), about 10% of the administered radioactivity was noted in the tissues, primarily in the liver (9.1 ppm UC51762-equivalent residues).

UC51762 is metabolised step-wise by thiolysis to methomyl, followed by hydrolysis to the methomyl oxime which is subsequently metabolized to acetonitrile. The acetonitrile is then metabolized to acetamide which is then hydrolyzed to acetic acid which enters the intermediary metabolism cycles of the animal. This results in, ultimately, the production of carbon dioxide which is expired.

The milk contained no residues of the parent UC51762 or its initial metabolite methomyl. These components were found in small amounts and only in the feces. Residues in the milk were acetonitrile, acetamide, and natural components containing reincorporated C^{14}-activity (lactose, lactoalbumin, casein, lipids).

The radioactivity was highest in liver, and this organ was chosen for characterization studies. Most of the extractable material (16%) was acetonitrile and acetamide. The unextractable material (84%) is possibly C^{14} atoms reincorporated into naturally occurring liver tissue components (proteins, glycogen, lipids).

Most of the urinary radioactivity partitioned into the aqueous phase (69-87%). Additionally, the urine contained C^{14}-urea. This further supports the conclusion that UC51762 is degraded with its constituent atoms being reincorporated into naturally-occurring components. Acetonitrile accounted for 11-28% of the urine activity. Free UC51762 and its metabolites were 0.3-6.6% of the urine radioactivity.

Residue Analysis

Radioactivity in samples was determined by liquid scintillation counting techniques. Organic extracts, aqueous samples and extracts, and TLC silica gel scrapings were counted directly. Tissues, feces, blood, and unextractable activity is determined following total combustion to $C^{14}O_2$, absorption in counting solutions, and subsequent counting of activity by liquid scintillation counting techniques.

Characterization and/or identification of radioactive residues were performed with two-dimensional TLC in 5 different solvent systems using authentic standards, gel permeation column chromatography, gas chromatography using a thermal conductivity detector, and a gas proportional radioactivity detector. Aqueous fractions were also subjected to enzymatic hydrolysis with beta-glucuronidase and sulfatase enzymes. However, no aglycones were released thru these treatments. Thus, conjugates of UC51762 metabolites, if present, were at insignificant levels according to the petitioner. Analyses and characterizations were also performed using Nuclear Magnetic Resonance Spectroscopy (NMR), Infra-red Spectrometry (IR), and Mass Spectrometry (MS).

The nature of the residue in animals is similar to that in plants. The significant components of the residue is the parent compound UC51762 and its metabolite methomyl.

Photochemical Transformation
Buffer Solutions:

The photolysis of radiolabelled C^{14}-UC51762 (acetyl-$1C^{14}$-label) in buffer solutions was studied using ultra-violet light under aerobic conditions for 12 days. The buffer solutions were at pH6 and contained 5 ppm UC51762.

Approximately 10% degradation of UC51762 occurred over a 12-day period. The half-life of UC51762 was calculated to be about 81 days. The metabolite methomyl was the major photolysis product (7% of total activity at 12 days). Lesser levels of other metabolites were also noted: UC51762 monosulfoxide (2.5%); methomyl oxime (0.3%); methomyl sulfoxide (0.3%); methomyl sulfoxide oxime (0.4%); unknowns (0.5%); and, water-soluble, unidentified activity (0.4%).

Photolytic degradation of UC51762 involved oxidation to the monosulfoxide, cleavage of the N-S-N skeleton to form methomyl, and hydrolysis of the methyl carbamate ester to form methomyl oxime. Methomyl and its oxime is further oxidized to yield methomyl sulfoxide and its oxime. Methomyl sulfoxide could also have been formed from the monosulfoxide thru cleavage of the N-S-N moiety. Additionally, hydrolysis of methomyl sulfoxide could have yielded methomyl sulfoxide oxime.

Soil surfaces:

The surface photodegradation of UC51762 was studied using radiolabelled C^{14}-UC51762 on 3 different soil types under laboratory conditions. UC51762 degraded more rapidly in a light textured soil (Norfolk Sandy Loam; half-life, 8 hours) than in heavier textured soils (California silt clay loam and Texas sandy loam). Photodegradation is believed to be related to the adsorption of UC51762 to the soil. The stronger UC51762 is adsorbed (California and Texas soils), the more it is protected from the action of light. It is therefore more stable on heavier soils.

The residues on the soil surfaces consist of UC51762 and its metabolites: methomyl; methomyl oxime; and volatile products, probably acetonitrile. After 24 hours of photolysis, about 83% of the radioactivity was volatilized (Norfolk Sandy loam), 13% in California silt clay loam, and 28% in Texas Sandy loam. The parent UC51762 was 12-69% of the activity during the 24-28 hour period, and the metabolites were <6%-37%.

Degradation of UC51762 in Soils

The three soil types in the above study were treated with radiolabelled C^{14}-UC51762 in the greenhouse at two different temperatures (15°C and 25°C) under aerobic and anaerobic conditions for periods up thru 62 days. Samples were taken at periodic intervals and examined for radioactivity.

The metabolite methomyl was the primary degradation product in all soils under all conditions with a half-life of less than 2 days. Methomyl was extensively degraded in non-sterile soils to carbon dioxide or acetonitrile under aerobic and anaerobic conditions, respectively. Both carbon dioxide and acetonitrile generally accounted for greater than 70% of the applied dose after 14 days.

Extractable residue declined to less than 2% in 14-28 days. The extractable residues consisted primarily of UC51762 and its metabolites methomyl and its oxime under aerobic conditions. Under anaerobic conditions the residue consisted primarily of polar materials.

Unextractable C^{14}-residues increased gradually and plateaued at 20-30% of the initial treatment. The unextractable residues were primarily C^{14}-radioactivity which had been reincorporated into soil organic matter (i.e., fulvic and humic acids).

In summary, UC51762 on soil surfaces is degraded to methomyl which is oxidized to the methomyl oxime. The oxime is ultimately converted to acetonitrile which is lost thru volatilization. Some of the soil residues are completely degraded, and the atoms reincorporated into natural occurring organic constituents.

Figure 1

Metabolic pathways of UC 51762 in plants

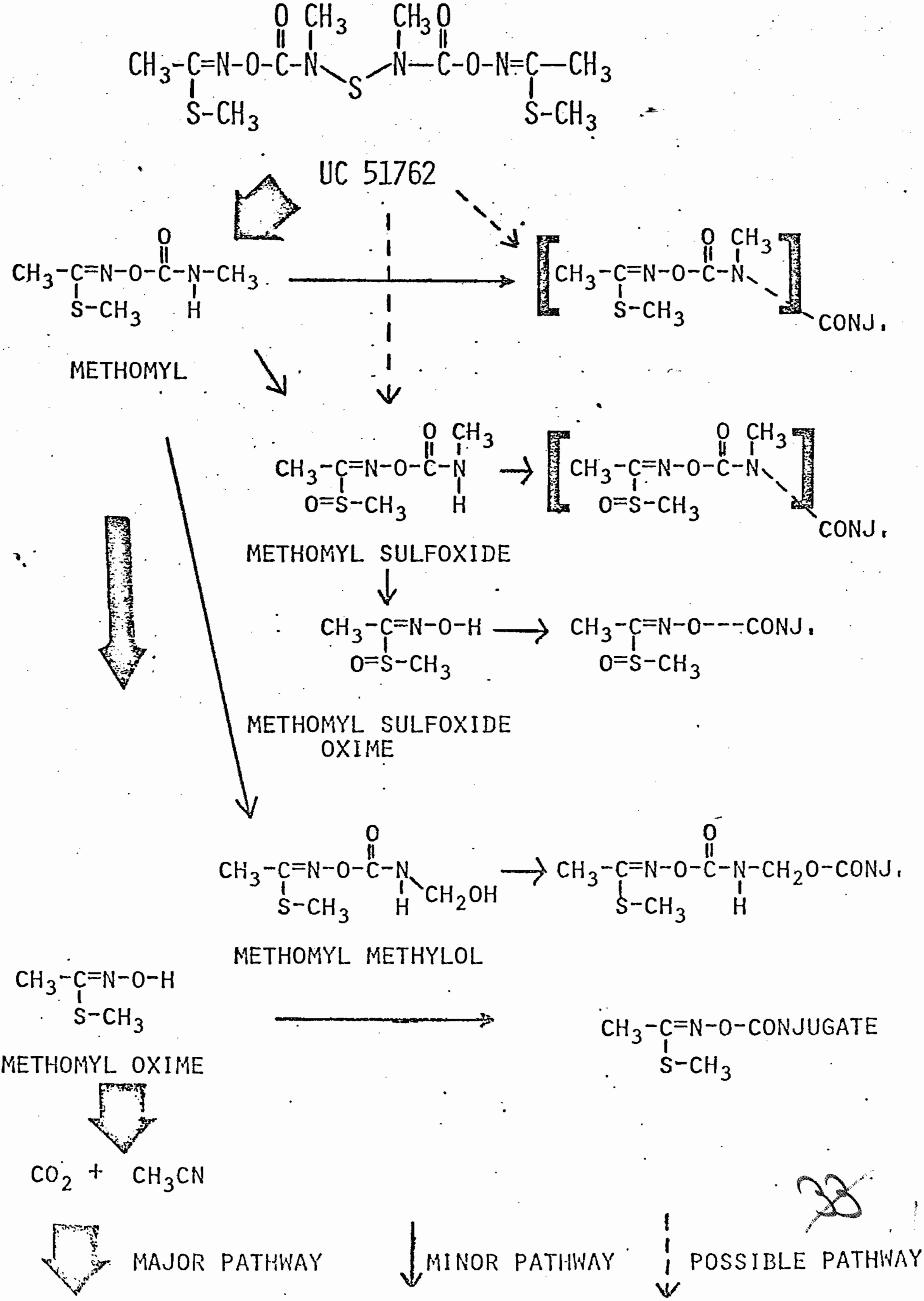


Figure 2

Metabolic pathway of UC 51762 in animals

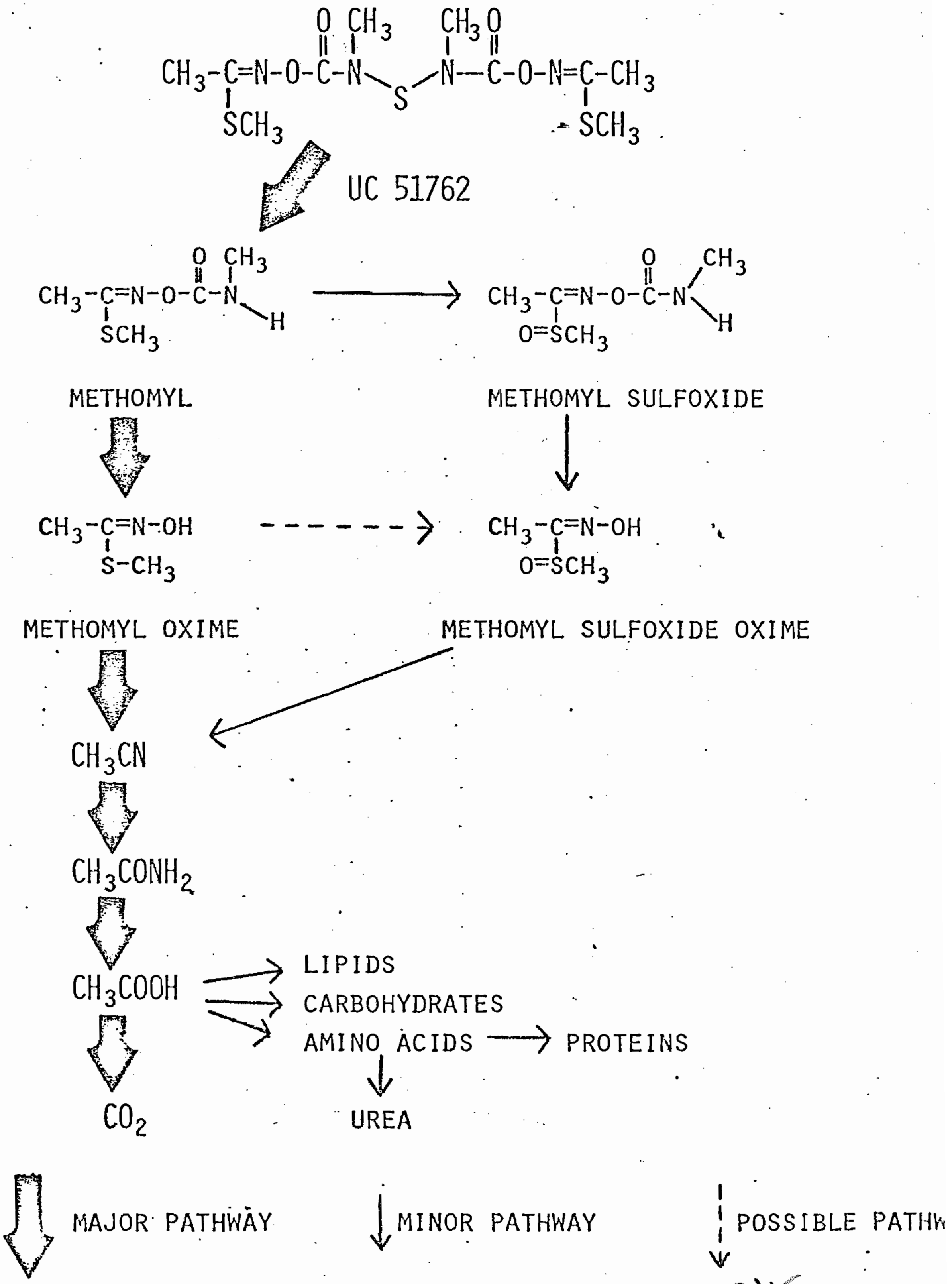


Figure 3

Photolysis of UC 51762 in pH 6 buffer solution

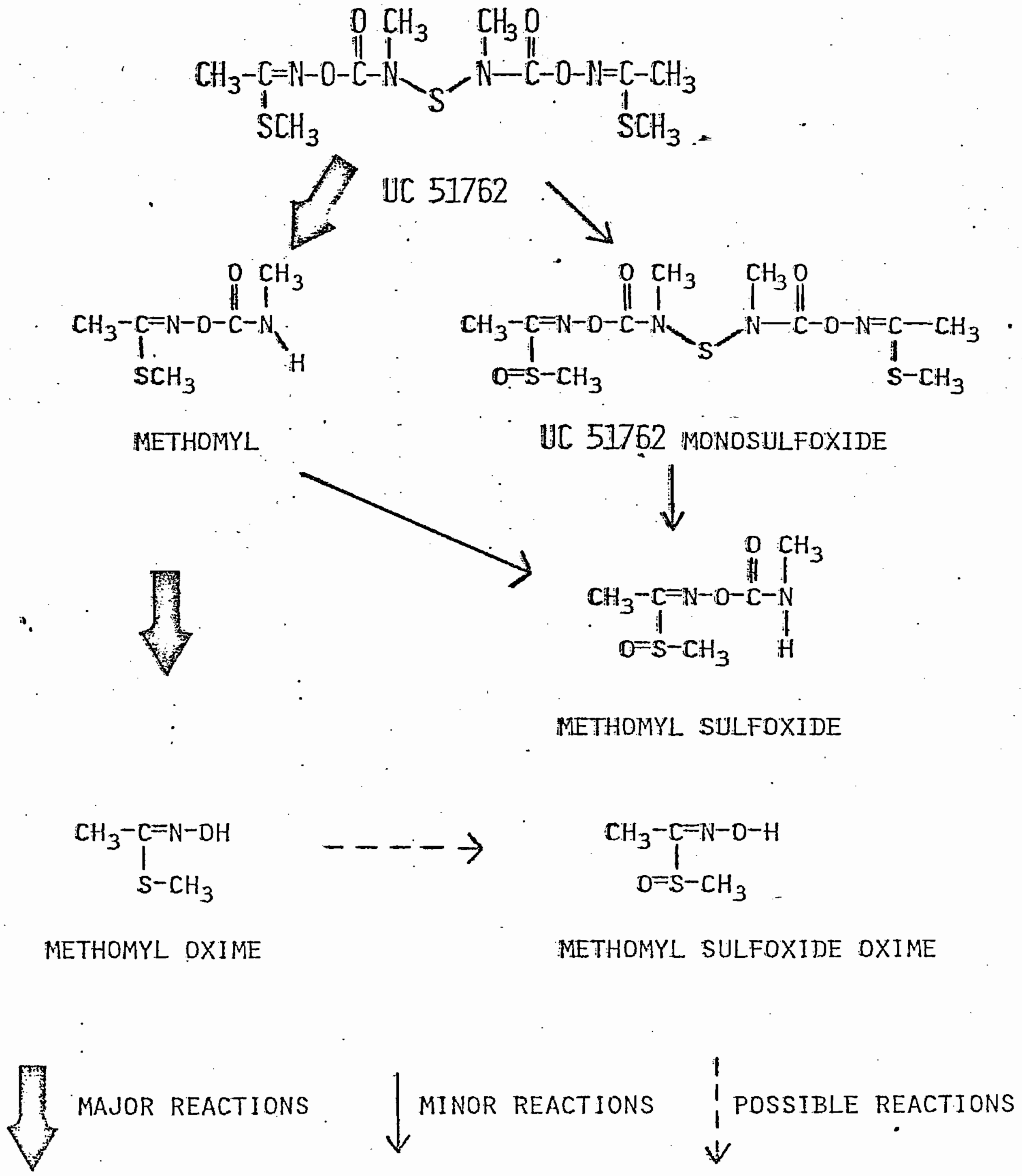
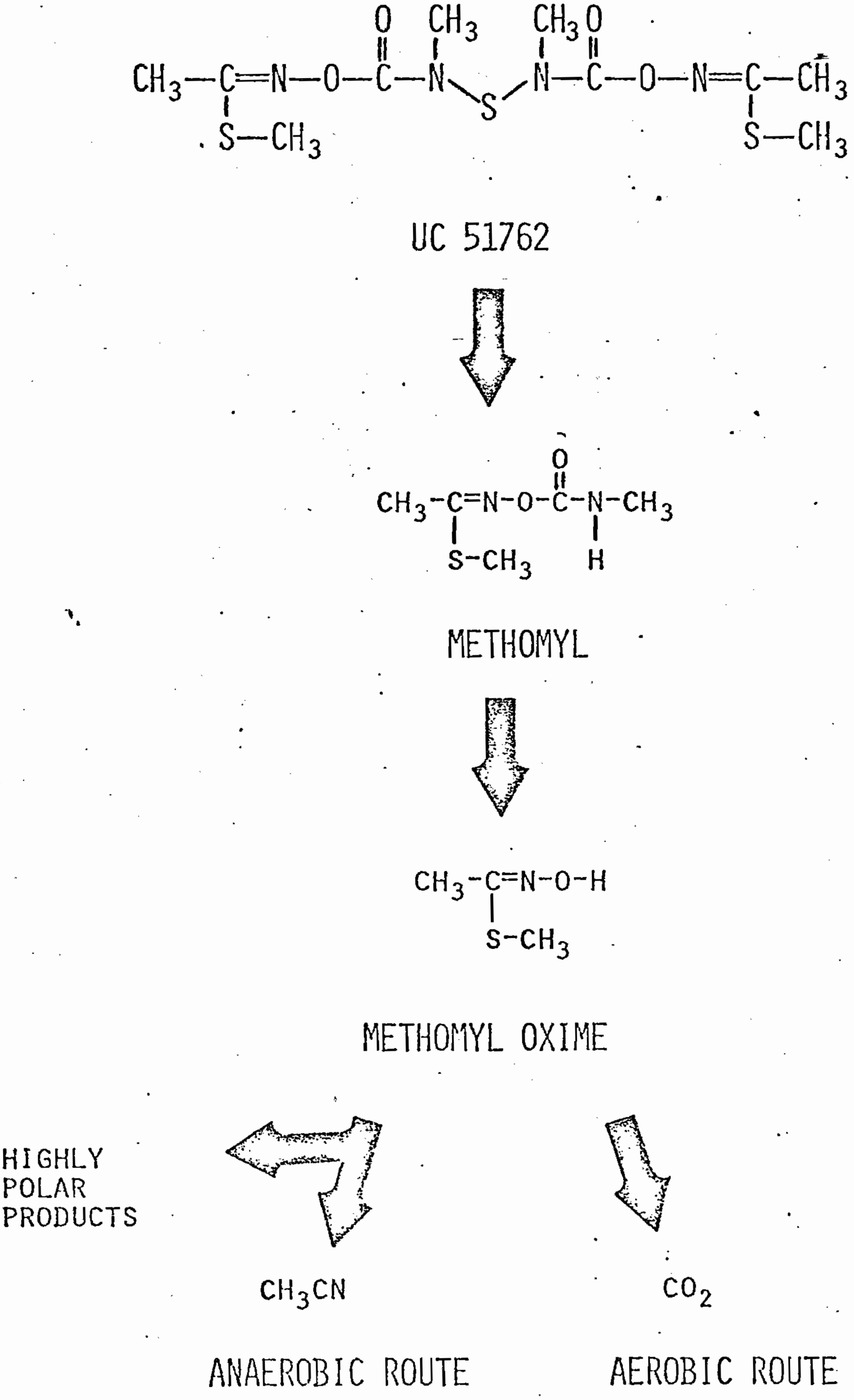


Figure 4

Degradation of UC 51762 in soils



Analytical Method

The method determines residues of UC51762, methomyl, and methomyl oxime in cottonseed, soybeans, and straw. The residues are extracted by blending with acetone followed by a partitioning between acetonitrile and hexane. The residues are further cleaned up using column chromatography. The residues are then hydrolyzed under basic conditions which convert UC51762 and methomyl to the methomyl oxime. The oxime is determined by gas chromatography using a flame photometric detector which is sensitive to sulfur-containing compounds. The results are expressed as total residues of UC51762.

The extraction efficiency of the method was tested by multiple extraction of residues from field-treated samples and samples fortified with UC51762 or methomyl. Samples of cottonseed were extracted 4 times, and the first two extractions were combined. The first two extractions removed 95-99% of UC51762-equivalent residues. Thus, the first two extracts are sufficient to remove the residues of UC51762 from treated samples.

Untreated (control) samples of cottonseed, soybeans, cotton foliage, and soybean foliage had no detectable UC51762-equivalent residues (<0.02 ppm).

Control samples of cottonseed and soybeans were separately fortified with UC51762, methomyl, and methomyl oxime at levels of 0.02-2.0 ppm. Recoveries were 73-95%.

The method is adequate for the determination of residues of UC51762 and its metabolite methomyl in cottonseed and soybeans.

For a permanent tolerance, a step should be included in the residue method which frees conjugated metabolites.

Residue Data

Soybeans

Samples were obtained from crops in Mississippi, Iowa, Oklahoma, North Carolina, Texas, South Carolina, Georgia, Louisiana, and Nebraska. The crops had received 1-4 applications (1-6 for soybean foliage) at rates of 0.23-1.0 lb. act./A. Samples were collected at intervals after the last treatment (PHI) of 26-77 days (soybean seed) and 0-77 days (soybean green foliage and straw).

Soybean seed had residues of ≤0.02-0.03 ppm due to 1-2 applications at 0.23-0.50 lb. act/A and PHIs of 26-39 days. Residues in the soybean seed from 1-4 applications at rates of 0.23-1.0 lb. act/A (up to 2.2X maximum) were ≤0.02-0.05 ppm at PHIs of 48-77 days.

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Two soybean seed samples (21 samples were analyzed) had aberrant residue levels. One sample which had received 1 application at 0.25 lb. act/A had a level of 0.12 ppm at a PHI of 71 days. Another sample which had received 1 application at 0.5 lb. act/A had a residue level of 2.0 ppm. The residue levels are greatly at variance with the levels in other samples and must be considered suspect.

No residue data are submitted which show the level of residues in the soybean byproducts (meal, oil, and soapstock). However, based on the level of residues in the soybeans, it is not likely that residues, if any, in the byproducts would exceed the level in the soybeans.

Residues in soybeans seed or its byproducts are not likely to exceed the proposed tolerance from the proposed uses.

Samples of green forage and straw were obtained from crops which had received 1-6 applications at rates of 0.25-0.90 lb. act/A and harvested at intervals of 0-77 days after the last treatment. Residues in green forage were 34-177 ppm at 0-day; 11-63 ppm at 1-3 days; <0.02-13 ppm at 7-21 days; and, <0.02 (N.D., none detected at the 28-day PHI.

Residues in the straw were <0.02 ppm (N.D.) at 48-77 days after the last treatment.

We conclude that residues in green soybean foliage are not likely to exceed the tolerance proposed for the soybeans (0.1 ppm) under the proposed uses. Additionally, residues in the straw are not likely to exceed the proposed tolerance (0.02 ppm).

For a permanent tolerance, additional residue data for soybeans which reflect maximum proposed conditions of use (i.e., maximum application rate and number of applications with samples collected at the proposed PHI) will be needed. Additionally, residue data will be needed which show if residues occur in the oil and meal. If residues occur in these items and at levels greater than in the seed, then food additive tolerances to cover such residues will be necessary.

Cottonseed

Samples were obtained from crops in Texas, Louisiana, Oklahoma, Georgia, Arkansas, Mississippi, South Carolina, and North Carolina. The crops had received 1-16 applications at rates of 0.2-3.0 lb. act/A. Samples were collected at intervals of 6-62 days after the last application. Overall residues were N.D. (<0.02 ppm)-1.9 ppm. Residues due to approximate proposed conditions of use (multiple applications at rates of 0.33-0.9 lb. act/A with a 7-day PHI) were a maximum of 0.37 ppm (due to a 6-day PHI and 8 applications at 1.0 lb. act/A). Exaggerated dosages (8 applications at 2X and 3X rates) yielded residues of 0.67 ppm and 1.9 ppm, respectively, at the 6-day PHI. Residues at longer PHIs (24-62 days) and 1-16 applications at slightly exaggerated rates (0.2-1.33 lb act/A) were N.D. - 0.15 ppm.

The data representing the proposed PHI are meager, but are sufficient for the purposes of this temporary tolerance. We conclude that residues in cottonseed are not likely to exceed the proposed tolerance of 0.4 ppm from the proposed use.

Cotton Foliage

Samples were obtained from crops in Louisiana, Texas, and North Carolina which had received 1 or 11 applications at rates of 0.75 lb. act/A and 1.0 lb act/A. Residues averaged 111-199 ppm at 0-day; 14-209 ppm at 1-3 days; 0.5-110 ppm at the proposed 7-day PHI; and, <0.02-48.5 ppm at 14-21 days.

The data for cotton foliage show that residues are high and variable. These data support the livestock grazing restriction.

Cotton byproducts

No data are submitted to show the level of residues in cottonseed byproducts (hulls, oil meal and soapstock). However, based on the level of residues in cottonseed, we would not expect residues in the byproducts to exceed the proposed cottonseed tolerance of 0.4 ppm. For a permanent tolerance, data showing the level of residues in cottonseed byproducts will be needed.

Meat and Milk

Cottonseed, cottonseed meal, soapstock, soybeans, soybean hulls, soybean meal, and soybean straw are used as livestock feeds. Livestock are not permitted to graze treated cotton fields, and treated soybean forage is not to be fed to livestock. This removes these items as sources of livestock feed.

The maximum likely ingestion levels for livestock are as follows: cattle (0.1 ppm); poultry (0.05 ppm); swine (0.04 ppm); horses (0.02 ppm); goats and sheep (0.04 ppm). The cow metabolism study show that greater than 80% of the ingested residues is eliminated by the animal, and a significant portion of the retained residue represents reincorporated radioactivity.

In view of the foregoing, we conclude that residues are not likely to occur in eggs, milk, meat, fat, and meat byproducts of livestock due to the proposed use [§180.6(a)(3)].

For permanent tolerances and additional tolerances in which feed items are involved, livestock feeding studies (cattle, poultry) will be needed to show if ingested residues occur in eggs, milk, and tissues.

TS-769:RCB:ASMITH:sdb:X77484:RM810:CM#2:12/17/79
cc: EEB, EFB, TOX, CHM (3)
RDI:RJHUMMEL,11/21/79:JGCUMMINGS,11/21/79