8-28-97

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 08/28/97

SUBJECT: ID#5F4560. PERMANENT TOLERANCE REQUEST FOR THE USE OF THE NEW CHEMICAL: CLORANSULAM-METHYL IN/ON SOYBEAN, SEED AT 0.02 PPM, IN/ON SOYBEAN, FORAGE AT 0.1 PPM, AND IN/ON SOYBEAN, HAY AT 0.2 PPM.

PRAT Case # 286828 Chemical # 129116
Trade Name: FirstRate EPA Reg # 63719-ETU
Class: Herbicide

TO: Philip Errico, PM#25
Registration Division (7505C)

FROM: Brenda Tarplee, William Dykstra, and Martha Lamont
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Health Effects Division (7509C)

THRU: Melba Morrow, Branch Senior Scientist
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INTRODUCTION

DowElanco is proposing that tolerances be established for the herbicide cloransulam-methyl in/on soybeans, soybean forage, and soybean hay for preplant, pre- and postemergent control of broad leaf weeds.

Cloransulam-methyl (XDE-565 or DE-565) is a triazolopyrimidine sulfonamide: N-(2carboxymethyl-6-chlorophenyl)-5-ethoxy-7-fluoro(1,2,4)triazolo(1,5-C)pyrimidine-2-sulfonamide.

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The petition requests the following tolerances for the herbicide cloransulam-methyl plus its acid, cloransulam calculated as parent ester:

Commodity	Tolerance
soybean, seed	0.02 ppm
soybean, forage	0.1 ppm
soybean, hay	0.2 ppm

Cloransulam-methyl for use on soybeans is formulated as an 84% active wettable granular material packaged in water-soluble packets under the trade name FirstRate herbicide. It is recommended for use in the control of broad leaf weeds at the rates of 0.04 lb ai/A (0.64 oz ai/A) for preplant and preemergent use and 0.016 lb ai/A (0.26 oz ai/A) for postemergent use. One application per season is allowed.

SUMMARY

Occupational exposure and aggregate risk estimates do not exceed HED's level of concern. Establishment of necessary tolerances should not pose an unacceptable aggregate risk to infants, children, or adults. Therefore, HED has no objections to the issuance of tolerances for the use of cloransulam-methyl on soybeans. Tolerances for the residues of cloransulam-methyl (plus its acid, cloransulam calculated as parent ester) in/on soybean, seed at 0.02 ppm; in/on soybean, forage at 0.1 ppm; and in/on soybean, hay at 0.2 ppm should be established to support this petition.

TOXICOLOGICAL ENDPOINTS

DIETARY

1) ***Acute Toxicity.*** For acute dietary risk assessment, the Toxicology Endpoint Selection Committee (TESC, 05/22/97) concluded that this risk assessment is not required, since no acute toxicological endpoints were observed in any of the relevant studies. There was no developmental toxicity up to the highest dose tested in either rats (1000 mg/kg/day) or rabbits (300 mg/kg/day). Additionally, no maternal toxicity was seen in rats at 1000 mg/kg/day [the limit dose] and the maternal toxicity in rabbits at 300 mg/kg/day was due to repeated dosing, manifested as reduced body weight gain, food efficiency, and abortion in 2 rabbits.

2) ***Chronic Toxicity.*** RfD = 0.10 mg/kg/day. The RfD Committee [3/27/97] established the RfD at 0.10 mg/kg/day based on a NOEL of 10 mg/kg/day in one-year dog feeding study [MRID# 43668909] due to increased liver serum enzyme levels and hepatocellular hypertrophy in the liver at the LOEL of 50 mg/kg/day. An uncertainty factor of 100 was used to calculate the RfD. This 100-fold uncertainty (safety) factor is designed to account for inter-species extrapolation and intra-species variability.

NON-DIETARY

1) ***Short-Term Toxicity.*** The TESC (05/22/97) concluded that this risk assessment is not required since the 21-day dermal toxicity studies in rabbits, which were available both for the technical (98.2%; [MRID No. 43668908]) and the formulation (83.6%; [MRID No. 43668915]), had systemic toxicity limited to decreases in RBC, hemoglobin and hematocrit counts in females at 1000 mg/kg/day [highest dose tested, limit dose] with the NOEL in both studies set at 500 mg/kg/day. The NOEL of 500 mg/kg/day will generate MOEs which are substantially higher [>100,000] than the required MOE of 100 and are not needed for risk assessment purposes.

2) ***Intermediate-Term Toxicity.*** For intermediate-term MOE calculations, the TESC [5/22/97] recommended use of the parental NOEL of 10 mg/kg/day from the 2-generation reproduction study in rats (MRID# 43668911). At the LEL of 100 mg/kg/day, there were hypertrophy, vacuolation, and fatty deposits in kidney tubular epithelium [collecting ductules] in both sexes. This risk assessment is required for workers (when intermediate-term exposure scenarios are present). Since this endpoint is derived from an oral study, a dermal penetration estimate of 30% is used for calculating occupational MOEs.

3) ***Chronic Toxicity.*** The TESC determined [5/22/97] that a chronic toxicity endpoint should be based on the NOEL of 10 mg/kg/day, based on increased liver serum enzyme levels and hepatocellular hypertrophy in the liver in the chronic dog study at the LOEL of 50

mg/kg/day. This risk assessment is required for workers (when chronic exposure scenarios are present). Since this endpoint is derived from an oral study, a dermal penetration estimate of 30% is used for calculating occupational MOEs.

4) ***Dermal Penetration.*** Dermal penetration of 30% has been estimated by comparing the LOEL of 300 mg/kg/day in the rabbit oral developmental study [LOEL based on decreased body weight] and the LOEL of 1000 mg/kg/day in the 21-day dermal toxicity study in rabbits [LOEL based on slight anemia].

CANCER

Cloransulam-methyl has been classified as a "not likely" (to be carcinogenic to humans) chemical by the RfD Committee [3/27/97] based on two acceptable studies in Fischer 344 rats and B6C3F1 mice at adequate dose levels. The Committee recommended against performing a carcinogenic risk assessment. The compound is negative for mutagenicity in all acceptable studies.

EXPOSURES AND RISKS

In examining aggregate exposure, FQPA directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor and/or outdoor uses). In evaluating food exposures, EPA takes into account varying consumption patterns of major identifiable subgroups of consumers, including infants and children.

1. From Food and Feed Uses:

Cloransulam-methyl is a new chemical and no tolerances have been established for the residues in or on raw agricultural commodities.

Acute Risk. The acute dietary (food only) risk assessment was not required since no acute oral toxicity was identified from the toxicological database (TESC, 05/22/97).

Chronic Risk. In conducting this chronic dietary risk assessment, HED has made very conservative assumptions -- 100% of soybeans will contain cloransulam-methyl residues and those residues would be at the level of the tolerance -- which result in an overestimation of human dietary exposure. Thus, in making a safety determination for this tolerance, HED is taking into account this conservative exposure assessment.

The proposed cloransulam-methyl tolerances result in a Theoretical Maximum Residue Contribution (TMRC) that is equivalent to the following percentages of the RfD:

U.S. Population	<0.01%
Nursing Infants	<0.01%
Non-Nursing Infants (<1 year old)	0.03%
Children (1-6 years old)	0.01%
Children (7-12 years old)	0.01%

The subgroups listed above are: (1) the U.S. population (48 states); (2) those for infants and children; and, (3) the other subgroups for which the percentage of the RfD occupied is greater than that occupied by the subgroup U.S. population (48 states).

2. *From Drinking Water:*

Based on information provided by EFED (memo, Nelson Thurman; date 7/31/97), cloransulam-methyl is highly mobile and expected to reach water. There are no established Maximum Contaminant Levels for residues of cloransulam-methyl in drinking water. However, based on GENEEC modeling data of surface water, the generic peak is 1.83 ppb for cloransulam-methyl.

In conducting this risk assessment, HED has made very conservative assumptions -- GENEEC modeling data of surface water was used for cloransulam-methyl residues and the maximum (acute) value of 1.83 ppm was used from this model -- which result in an overestimation of dietary exposure from drinking water. Thus, in making a safety determination for this tolerance, HED is taking into account this conservative exposure assessment.

Using this peak surface water value and default water consumption figures, the following drinking water exposures are calculated:

Chronic exposure (adult female) = 0.00183 mg/L x 2 L/day ÷ 60 kg = 6.1×10^{-5} mg/kg/day

Chronic exposure (child) = 0.00183 mg/L x 1 L ÷ 10 kg = 1.83×10^{-4} mg/kg/day

Drinking Water Risk (Chronic only)

The calculations presented below are based on a chronic NOEL = 10 mg/kg/day. The Reference Dose has been established as 0.1 mg/kg/day. Since no toxicological endpoint for acute dietary risk assessments has been identified, acute drinking water risk assessment is not required.

Chronic Drinking Water Risk

For a 10 kg child consuming 1 Liter of water a day, the chronic drinking water risk is calculated as a percent of the RfD:

Percent of RfD = (1.83×10^{-4} mg/kg/day ÷ 0.1 mg/kg/day) X 100 = 0.183%

For a 60 kg female consuming 2 Liters of water a day the chronic drinking water risk is calculated as a percent of the RfD:

Percent of RfD = (6.1×10^{-5} mg/kg/day ÷ 0.1 mg/kg/day) X 100 = 0.061%

3. From Non-Dietary Uses:

Cloransulam-methyl is not currently registered for residential uses.

4. From Cumulative Exposure To Substances with a Common Mechanism of Toxicity:

Cloransulam-methyl is a triazolopyrimidine sulfonamide herbicide. Another member of this class is Flumetsulam [Chemical Assignment List, SRRD (The Pesticide Manual, British Crop Protection Council)].

Section 408(b)(2)(D)(v) of the Food Quality Protection Act requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity". The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also scientific policies and methodologies for understanding common mechanisms of toxicity and conducting cumulative risk assessments. For most pesticides, although the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodologies to resolve the complex scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will increase the Agency's scientific understanding of this question such that EPA will be able to develop and apply scientific principles for better determining which chemicals have a common mechanism of toxicity and evaluating the cumulative effects of such chemicals. The Agency anticipates, however, that even as its understanding of the science of common mechanisms increases, decisions on specific classes of chemicals will be heavily dependent on chemical-specific data, much of which may not be presently available.

Although at present the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments, there are pesticides as to which the common

mechanism issues can be resolved. These pesticides include pesticides that are toxicologically dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case common mechanism of activity will be assumed).

HED does not have, at this time, available data to determine whether cloransulam-methyl has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, therefore, HED has not assumed that cloransulam-methyl has a common mechanism of toxicity with other substances.

DETERMINATION OF SAFETY FOR U.S. POPULATION

1. Acute Aggregate Risk. Acute aggregate risk assessment was not required since no acute toxicity was identified from the toxicological database (TESC, 05/22/97).

2. Chronic Aggregate Risk. Chronic aggregate risks have been determined for food and water using the conservative TMRC exposure assumptions previously described and the conservative model for estimating residues potentially present in drinking water. There are no chronic exposure scenarios for non-dietary uses of cloransulam-methyl which would contribute to the aggregate risk.

HED has concluded that the percentage of the RfD that will be utilized by aggregate exposure [food and water] to residues of cloransulam-methyl ranges from a low of approximately 0.068% [0.007% for food and 0.061% for water] for females 20 years (not pregnant, not nursing) and up to 0.216% [0.183% for water and 0.033% for food] for non-nursing infants (<1 year old). The chronic aggregate risk for the sub-population, females 13+ years also approximates 0.068% of the RfD, and for children 1 through 6, 0.216% of the RfD. Taking into account the completeness and reliability of the toxicity data and this very conservative exposure assessment, HED concludes that there is a reasonable certainty that no harm will result to the general population, and infants and children from chronic aggregate exposure to cloransulam-methyl residues.

3. Short- and Intermediate-Term Aggregate Risk. There are no residential uses of cloransulam-methyl at this time. Therefore, no non-dietary, non-occupational exposure is expected and short- and intermediate-term aggregate risk assessment is not required.

DETERMINATION OF CANCER RISK

Since the RfD Committee determined that this pesticide is "not likely" to cause tumors in humans, a quantitative cancer risk assessment is not required.

ENDOCRINE DISRUPTER EFFECTS

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inert ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disruptor effects.

DETERMINATION OF SAFETY FOR INFANTS AND CHILDREN

In assessing the potential for additional sensitivity of infants and children to residues of cloransulam methyl, HED considered data from developmental toxicity studies in the rat and rabbit and a 2-generation reproductive toxicity study in the rat. Developmental toxicity studies are designed to evaluate adverse effects on the developing organism resulting from maternal pesticide exposure during gestation. Reproductive toxicity studies provide information relating to pre- and post-natal effects from exposure to the pesticide, information on the reproductive capability of mating animals, and data on systemic toxicity.

FFDCA section 408 provides that EPA shall apply an additional 10-fold margin of safety for infants and children in the case of threshold effects to account for pre-and post-natal toxicity and the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a margin of exposure analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. In either case, EPA generally defines the level of appreciable risk as exposure that is greater than 1/100 of the no observed effect level in the animal study appropriate to the particular risk assessment. This 100-fold uncertainty (safety) factor/margin of exposure (safety) is designed to account for inter-species extrapolation and intra-species variability. HED believes that reliable data support using the 100-fold margin/factor rather than the 1000-fold margin/factor when EPA has a complete data base under existing guidelines, when the severity of the effect in infants or children, the potency or unusual toxic properties of a compound, or the quality of the exposure data do not raise concerns regarding the adequacy of the standard margin/factor.

1. Developmental Toxicity Studies.

a. Rats. In the developmental study (MRID# 43003426) in rats, the maternal (systemic) NOEL was 1000 mg/kg/day [Limit Dose; highest dose tested]. The developmental (fetal) NOEL was 1000 mg/kg/day (Limit Dose; highest dose tested).

b. Rabbits. In the developmental toxicity study (MRID# 43718904) in rabbits, the maternal (systemic) NOEL was 100 mg/kg/day, based on reduced weight gain, food efficiency, increased abortions, and cesarean section observations at the LOEL of 300 mg/kg/day (highest dose tested). The developmental (fetal) NOEL was 300 mg/kg/day (highest dose tested).

2. Reproductive Toxicity Studies.

Rats. In the 2-generation reproductive toxicity study (MRID# 43668911) in rats, the maternal (systemic) NOEL was 10 mg/kg/day, based on histopathological alterations of the kidney in both sexes at the LOEL of 100 mg/kg/day. The reproductive/developmental (pup) NOEL was 100 mg/kg/day, based on decreased live pups and increased pup deaths at the LOEL of 500 mg/kg/day.

3. Pre- and Post-Natal Sensitivity

The toxicological data base for evaluating pre- and post-natal toxicity is complete with respect to current data requirements. There are no pre- or post-natal toxicity concerns for infants and children, based on the results of the rat and rabbit developmental toxicity studies and the 2-generation rat reproductive toxicity study.

HED concludes that reliable data support use of the 100-fold margin of exposure/uncertainty factor and that an additional margin/factor is not needed to protect infants and children.

4. Acute Aggregate Risk. An acute aggregate risk assessment is not required, since there is no acute dietary toxicological endpoint for cloransulam-methyl.

5. Chronic Aggregate Risk. HED has concluded that the percentage of the RfD that will be utilized by aggregate exposure (dietary food and drinking water) to residues of cloransulam-methyl ranges from 0.191 percent for nursing infants, up to 0.216 percent for non-nursing infants less than one year old. There are no chronic residential exposure scenarios. Taking into account the completeness and reliability of the toxicity data and this conservative exposure assessment, EPA concludes that there is a reasonable certainty that no harm will result to infants and children from chronic aggregate exposure to cloransulam-methyl residues.

DETERMINATION OF SAFETY TO OCCUPATIONALLY EXPOSED WORKERS

1. Acute data for this formulation were provided to RAB1. The proposed work clothing and personal protective equipment (PPE) which appear on the label are in compliance with the Worker Protection Standard (WPS).

2. Acute data for the technical are available. The proposed restricted entry interval (REI) of 12 hours appearing on the label is in compliance with the WPS requirements.

3. Occupational exposure assumptions and estimates are summarized in Tables 1 and 2, respectively. Worker exposure estimates are based on surrogate data from the Pesticide Handlers Exposure Database (PHED), [memo, C. Lewis, 10/25/95] and/or the PHED Surrogate Exposure Guide (May 1997) with the worker wearing a single layer of clothing plus gloves.

   The resulting exposure assessment is a conservative estimate since the water dispersible granule formulation packaged in water soluble pouches were treated as an open pour, dry flowable (memo, C. Lewis, 10/25/95).

4. Using these exposure assumptions, HED has concluded that the MOEs that will result from the handling and application of Cloransulam-methyl by workers are 2500 for ground mixers/loaders and 14,000 for ground applicators. These MOEs do not exceed HED's level of concern for occupationally exposed workers.

OTHER CONSIDERATIONS

Metabolism in Plants and Animals

1. The nature of the residue in plants and animals is adequately understood. The residue of concern is cloransulam-methyl, parent, plus its acid, cloransulam calculated as parent ester. (HED Metabolism Assessment Review Committee meeting, 08/14/97).

   Cloransulam-methyl was applied as a spray to soybeans at the V5 growth stage at a rate of about 5X the proposed rate. Samples of forage and beans were obtained at intervals during the growth of the test crop and analyzed. XDE-565 after application was found to rapidly degrade into numerous metabolites with an overall half life of the parent of less than a day. Residues of parent in all fractions at all sample times were very low. Residues in forage at 27 days after application (DAA) were less than 0.015 ppm, less than 0.01 ppm in 61 DAA forage, and less than 0.01 ppm in mature beans. Fractions containing the highest levels of radioactivity were cleaned up and subjected to TLC and HPLC. Neither parent nor postulated metabolites were found in any fraction other than 0.006 ppm of parent in 27 DAA forage (memo, J. Garbus, 08/29/96).

Analytical Enforcement Methodology

2. Analytical enforcement methodology (GC/MS) was submitted to EPA, BEAD, Analytical Chemistry Lab (Beltsville) for validation. RAB1 received verbal notification from the laboratory director that the analytical method for cloransulam-methyl in/on soybean seed,

forage, and hay has successfully passed validation requirements. The final report will be delivered by September 5, 1997 (F. Griffith, 08/28/97).

Because of its chemical structure, cloransulam-methyl is a candidate for FDA's Multiresidue Protocols C, D, E, and F. Cloransulam-methyl responded adequately to Protocol C under Level II conditions (GC at 230 degrees C) with an RT 4.5 X that of phosalone. The material failed to respond adequately to Protocols D, E, and F.

The validation data provided by the petitioner on soybean rac's and processed commodities fortified at levels of 0.005 to 0.5 ppm and carried through the analytical method are summarized below:

Matrix	Number	Recovery Range (%)	Recovery Mean and S.D.(%)
Grain	19	71-99	85 ± 6
Forage	18	74-92	87 ± 7
Hay	18	74-104	89 ± 9
Meal	17	70-106	90 ± 11
Hulls	18	92-102	97 ± 3
Crude Oil	18	84-110	97 ± 6
Refined Oil	18	94-105	100 ± 3

The Limit of Quantitation (LOQ) for the method has been set as 0.01 ppm and the Limit of Detection (LOD) of the method has been set as 0.005 ppm

Data from independent laboratory validation of the method on soybean rac's fortified at levels of 0.01 to 0.05 ppm and carried through the analytical method are summarized below:

Matrix	Number	Recovery Range (%)	Recovery Mean plus S.D. (%)
Grain	4	74-86	80 ± 6
Forage	4	92-107	101 ± 7
Hay	4	95-111	104 ± 8

Magnitude of the Residues

3. Based on the field trial data, residues of cloransulam-methyl are not expected to exceed 0.02 ppm in/on soybean, seed; 0.1 ppm in/on soybean, forage; and 0.2 ppm in/on soybean, hay as a result of this use. Tolerances should be established at these levels.

Field trials with soybeans treated with cloransulam-methyl, applied either as a preplant-soil incorporated treatment (PPI - 0.74 oz ai/A) or as a postemergent treatment (PE - 0.16 oz ai/A), were conducted and mature soybeans were obtained 65 - 123 days after the PE treatment or 116-160 days after PPI treatment. Forage and hay were obtained at intervals of 14 to 81 days between application and sampling. No residues of cloransulam-methyl were detected in any of the soybean seed samples from any of the trials (LOD = 0.005ppm). Three forage samples had detectable residues, one was less than the LOQ of 0.01 and the remaining 2 samples containing residues of 0.032 and 0.013 ppm respectively. Seven hay samples contained detectable residue, four of which with residues below the calculated LOQ of 0.016 ppm. The three other soybean hay samples contained residues of 0.052, 0.122, and 0.037 ppm, respectively (memo, J. Garbus, 08/29/96).

4. Based on the results of animal metabolism studies, considering the exaggerated rate of dosing and the low level of residues detected, it is unlikely that significant residues would occur in secondary animal commodities from this use.

Two lactating goats were dosed daily with cloransulam-methyl for 5 days at levels equivalent to about 10 ppm cloransulam-methyl in the diet, 500 times the proposed tolerance proposed for soybeans. Milk, feces, and urine were collected daily and tissue samples taken after five days to be analyzed for total radioactivity. Radioactivity recovered in feces and urine accounted for 99.9% of the administered dose. Liver and kidney tissues were chosen for the identification and characterization of radioactive metabolites. The parent was detected at 0.066 ppm in kidney and at <0.003 ppm in liver. The sum of all postulated metabolites in kidney was less than 10% of TRR or less than 0.05 ppm. Liver tissue did contain a metabolite characterized as XDE-565 acid at 9.5% of TRR or 0.005 ppm. All other metabolites in liver and kidney were present at 0.009 ppm or less. Parent or postulated metabolites were not found at detectable levels in other tissues examined or in blood or milk.

Groups of 10 hens were dosed daily for 5 days at levels equivalent to about 9 ppm cloransulam-methyl in the diet, 450 times the proposed tolerance for soybeans. Eggs were collected throughout the dosing period and after 5 days the eggs and tissues were examined for total radioactivity. Radioactivity recovered in feces and urine accounted for 99.7% of the administered dose. For characterization of the level and distribution of metabolites, liver, muscle tissue, and eggs were extracted and subjected to TLC and HPLC/MS with reference standards of the parent and potential metabolites used as markers in the analyses. XDE-565 was found in eggs at 0.006 ppm, representing 35-40% of the TRR. In liver and muscle the major metabolite was cleavage product 5-ethoxy-7-fluoro-(1,2,4)triazolo[1,5c]pyrimidine-2-sulfonamide (ASTP) representing 49% of the TRR (0.02 ppm) in liver and 57% of the TRR (0.08 ppm) in muscle. The remainder of the radioactivity in all tissues consisted of multiple components that could not be related to the reference standards (memo, J. Garbus, 08/29/96).

Rotational Crop Restrictions

5. No field studies were conducted with rotational crops. The label restrictions on plantback intervals (small grains, 4 months; corn, sorghum, cotton, peanuts, alfalfa, and rice, 9 months; sugar beets, sunflowers, and tobacco, 30 months and a successful field bioassay) are based on confined rotational crop studies due to the potential of phytotoxicity to susceptible plants.

   ^{14}C-labeled cloransulam-methyl was incorporated into confined soil at a rate 1.1-fold that of the maximum proposed preplant use. After 120 days, wheat, lettuce, and potatoes were planted in the treated soil. Samples of wheat forage were taken at the boot stage and samples of lettuce, potato tubers, wheat grain, and wheat straw were obtained at maturity. Samples were examined for total radioactivity. The highest levels were found in wheat straw. After solvent extraction and fractionation, samples were examined for levels of XDE-565 by the proposed analytical method. None of the crop samples contained analytically detectable levels of XDE-565. One identifiable component (triazolopyrimidine sulfonic acid) was found in wheat straw and represented 6.6% of the TRR (0.004 ppm). Another unidentified component accounted for 8.9% (0.006 ppm) of the TRR. No other individual metabolites or resolvable components were detected (LOD = 0.005 ppm). Significant portions of the radioactivity were associated with natural plant components such as starch, lignin, and cellulose (memo, J. Garbus, 08/29/96; and D237713, DowElanco's response dated July 22, 1997).

International Residue Limits

6. Currently there are no international or CODEX MRLs associated with cloransulam-methyl(memo, J. Garbus, 08/29/96).

SUPPLEMENTAL INFORMATION

OCCUPATIONAL EXPOSURE

Table 1. Occupational Exposure Assumptions	
PARAMETER	**ASSUMPTION**
Pesticide Handlers Exposure Database (PHED), Version 1.1[OREB, 10/25/95]	Mixer/Loader (Dry Flowable, Open Mixing and Loading, Single Layer Clothing Plus Gloves): Dermal = 93.2 µg/lb ai handled; Inhalation = 1.03 µg/lb ai handled
	Applicator - Ground (Groundboom, Open Cab, Single Layer Clothing Plus Gloves): Dermal = 14.7 µg/lb ai handled; Inhalation = 0.64 µg/lb ai handled
Work Clothing and PPE	Long-sleeved Shirt and Long Pants, Shoes Plus Socks, Chemical Resistant Gloves
Percent Absorption	Dermal: 30 % [TESC Document, 05/22/97] Inhalation: 100 % [HED Default]
Application Type	Ground
Minimum Finish Spray	Ground: 10 gal/A
Maximum Application Rate	0.048 lb ai/A
Maximum Applications Per Year	One
Acres Treated/Day (Y. NG,BEAD)	200 acres (Based on information provided by DowElanco)
Average Farm Size	400 acres (Based on information provided by DowElanco)
Worker Weight	70 kg (Based on Tox endpoint)
Number of Farms Treated by PCO (Professional Chemical Operator)	Ground: 2

Table 2. Occupational Exposure and Risk Assessment[a]		
Worker	Average Daily Dose[b] (ug/kg/day)	Intermediate-Term MOE[c]
Ground Mixer/Loader	3.25	2500
Ground Applicator	0.57	14000

a MOEs are expressed to two significant figures.
b Average Daily Dose (ADD) = PHED unit exposure (dermal x 30% absorption + inhalation x 100% absorption) x application rate x acres treated/day ÷ kg body weight.
c Intermediate-Term Occupational Exposure MOE = NOEL/ADD (where NOEL = 10 mg/kg/day).

DIETARY EXPOSURE

Deficiencies concerning the product chemistry of cloransulam-methyl (memo, J. Garbus, 08/29/96) were addressed by the registrant (memo, D237713 DowElanco's response dated July 22, 1997).

Table 3. Residue Consideration Summary Table	
PARAMETER	PERTINENT INFORMATION
CHEMICAL	Cloransulam-methyl
FORMULATION	FirstRate herbicide
CROP	Soybeans (grain, forage, hay)
TYPE APPLICATION	Ground
# APPLICATIONS	One
TIMING	Preplant, pre- and postemergent
RATE/APPLICATION	0.04 lbs ai/A for preplantand preemergent 0.016 lbs ai/A for postemergent
RATE/YEAR or SEASON	0.04 lbs ai/A for preplantand preemergent 0.016 lbs ai/A for postemergent
MAXIMUM RESIDUES	Seed: none detected (LOD = 0.005 ppm) Forage: 0.032 ppm Hay: 0.122 ppm
RESTRICTIONS	Aerial application is prohibited; Maximum application rate is 0.048 lb ai/A 14 day interval for forage and cutting of hay; 65 day PHI for beans

Table 3. Residue Consideration Summary Table	
PARAMETER	PERTINENT INFORMATION
PROCESSING DATA	Soybeans from residue trials treated at 5X the proposed label rate were processed into meal, hulls, grain dust fractions, crude oil, and refined oil. The soybeans and fractions were examined for residues of XDE-565. Residues of XDE-565 in the soybeans and all fractions were below the LOD of 0.005 ppm.
ROTATIONAL CROPS	The label restriction on plantback intervals: small grains: 4 months corn, sorghum, cotton, peanuts, alfalfa, and rice: 9 months sugar beets, sunflowers, and tobacco: 30 months and a successful field bioassay (due to potential of phytotoxicity to susceptible plants)
RESIDUE DATA SOURCE	DowElanco (MRID#436689-29 thru 32)
PERFORMING LAB	DowElanco

ADDITIONAL INFORMATION

Attachments: DRES Runs: Chronic: B. Steinwand, 07/18/97
Environmental Fate Assessment: N. Thurman, 08/14/97

cc with Attachments: Brenda Tarplee, William Dykstra, RAB1

cc without Attachments: RAB1, OREB (129116), Caswell File, TOX (T. McMahon)

RDI:RAB1: 08/28/97

CHEMICAL INFORMATION FOR CASWELL NUMBER 129116 DATE: 07/18/97 PAGE: 1

CHEMICAL	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
CLORANSULAM-METHYL Caswell #129116 CAS No. A.I. CODE: 129116 CFR No:	NOEL= 10.0000 mg/kg 0.00 ppm LEL= 50.0000 mg/kg 0.00 ppm ONCO:	HISTOPATHOLOGY OF LIVER INCREASED LIVER ENZYME ACTIVITY	UF -->100 OPP RfD= 0.100000 EPA RfD= 0.000000		

FOOD CODE	FOOD NAME	PETITION NUMBER	TOLERANCE (PPM) NEW	PENDING	PUBLISHED
27010OA	SOYBEANS-OIL	5F4560	0.020000		
28023AA	SOYBEANS-UNSPECIFIED	5F4560	0.020000		
28023AB	SOYBEANS-MATURE,SEEDS DRY	5F4560	0.020000		
28023WA	SOYBEANS-FLOUR, FULL FAT	5F4560	0.020000		
28023WB	SOYBEANS-FLOUR, LOW FAT	5F4560	0.020000		
28023WC	SOYBEANS-FLOUR,DEFATTED	5F4560	0.020000		

TOLERANCE ASSESSMENT SYSTEM ROUTINE CHRONIC ANALYSIS

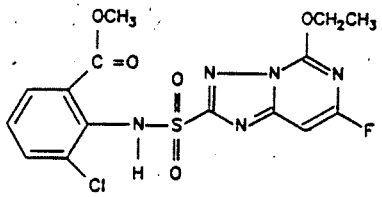
DATE: 07/18/97

CHEMICAL INFORMATION	STUDY TYPE	EFFECTS	REFERENCE DOSES	DATA GAPS/COMMENTS	STATUS
CLORANSULAM-METHYL Caswell #129116 CAS No. A.I. CODE: 129116 CFR No.	NOEL= 10.0000 mg/kg 0.00 ppm LEL= 50.0000 mg/kg 0.00 ppm ONCO:	HISTOPATHOLOGY OF LIVER INCREASED LIVER ENZYME ACTIVITY	UF -->100 OPP RfD= 0.100000 EPA RfD= 0.000000		

POPULATION SUBGROUP	TOTAL TMRC (MG/KG BODY WEIGHT/DAY) CURRENT TMRC*	NEW TMRC**	NEW TMRC AS PERCENT OF RFD	DIFFERENCE AS PERCENT OF RFD	EFFECT OF ANTICIPATED RESIDUES ARC	%RFD
U.S. POPULATION - 48 STATES	0.000000	0.000007	0.006797	0.006797		
U.S. POPULATION - SPRING SEASON	0.000000	0.000007	0.006558	0.006558		
U.S. POPULATION - SUMMER SEASON	0.000000	0.000007	0.006782	0.006782		
U.S. POPULATION - FALL SEASON	0.000000	0.000007	0.007015	0.007015		
U.S. POPULATION - WINTER SEASON	0.000000	0.000007	0.006837	0.006837		
NORTHEAST REGION	0.000000	0.000006	0.006151	0.006151		
NORTH CENTRAL REGION	0.000000	0.000007	0.006838	0.006838		
SOUTHREN REGION	0.000000	0.000007	0.006853	0.006853		
WESTERN REGION	0.000000	0.000008	0.007521	0.007521		
HISPANICS	0.000000	0.000007	0.007105	0.007105		
NON-HISPANIC WHITES	0.000000	0.000007	0.006854	0.006854		
NON-HISPANIC BLACKS	0.000000	0.000006	0.006327	0.006327		
NON-HISPANIC OTHERS	0.000000	0.000007	0.006516	0.006516		
NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.000008	0.007783	0.007783		
NON-NURSING INFANTS (< 1 YEAR OLD)	0.000000	0.000033	0.032617	0.032617		
FEMALES (13+ YEARS, PREGNANT)	0.000000	0.000005	0.004532	0.004532		
FEMALES 13+ YEARS, NURSING	0.000000	0.000006	0.005958	0.005958		
CHILDREN (1-6 YEARS OLD)	0.000000	0.000013	0.012723	0.012723		
CHILDREN (7-12 YEARS OLD)	0.000000	0.000010	0.009784	0.009784		
MALES (13-19 YEARS OLD)	0.000000	0.000007	0.007056	0.007056		
FEMALES (13-19 YEARS OLD, NOT PREG. OR NURSING)	0.000000	0.000006	0.005885	0.005885		
MALES (20 YEARS AND OLDER)	0.000000	0.000005	0.005399	0.005399		
FEMALES (20 YEARS AND OLDER, NOT PREG. OR NURS)	0.000000	0.000005	0.004811	0.004811		

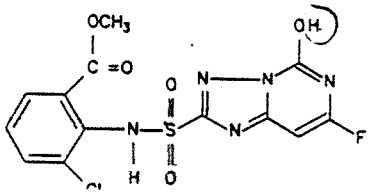
*Current TMRC does not include new or pending tolerances.
**New TMRC includes new, pending, and published tolerances.

Enviro mental Fate Assessment
Cloransulam Methyl and Its Structurally-Similar Transformation Products



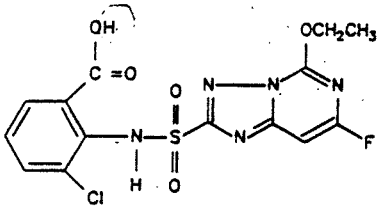
cloransulam methyl

Parent



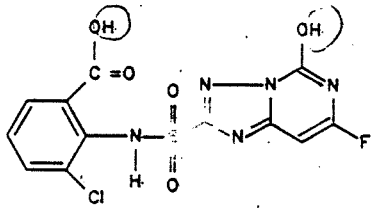
5-hydroxy-cloransulam methyl

Major transformation product in metabolism studies
Peak 17% of applied @ 14 da



cloransulam

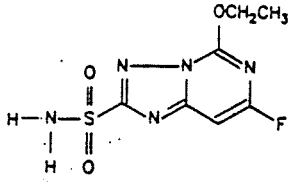
Major transformation product in metabolism studies
Peak 37-38% of applied @ 28 da



5-hydroxy-cloransulam

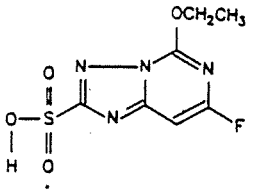
Major transformation product in metabolism studies
Peak 11-21% of applied after 120 days

Additional Transformation Products of Cloransulam Methyl



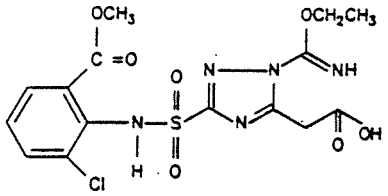
sulfonamide (ASTP)
(aminosulfonyltriazolopyrimidine)

Found in anaerobic metabolism study (27% @ 3[illegible]a)



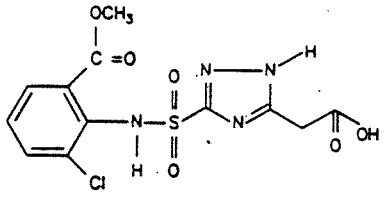
sulfonic acid (TPSA)
(triazolopyrimidine sulfonic acid)

Found in photo[illegible]s studies (22%)



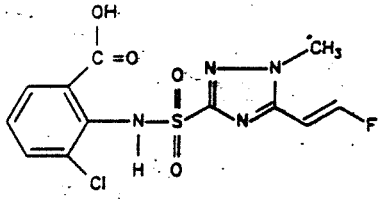
cloransulam methyl imidate

Found in hydrolysis study.
peak 25-29% @ pH 9 (3-5 da)



cloransulam methyl acetic acid

Found in hydrolysis study.
peak 49-54% @ pH 9 (7 da)



cloransulam methyl, fluoroethenyl

Found in anaerobic aquatic metabolism study.
peak 52-66% @ 365 da

Routes of Dissipation

Terrestrial

(1) Aerobic soil metabolism:
Parent only: $t_{1/2}$ ≈ 2-4 weeks
Parent + structurally-similar transformation products:
$t_{1/2}$ ≈ 1-2 months (61 da used for modeling)

(2) Leaching:
Parent: K_d = 0.15-1.49 ml/g; K_{oc} ≈ 43
Transformation products:
apparent K_ds range from 0.2 to 1.8 ml/g

Anticipate that parent, transformation products will be more persistent in subsurface soil horizons, ground water.

Surface Water

(1) Photolysis:
$t_{1/2}$ = 22 min [not expected to persist in clear waters; may persist in surface waters with reduced light penetration, i.e., turbid, high algal growth, etc]
NOTE: The soil photolysis half-life is much longer (30-70 days) and the chemical does not bind. We don't have enough information to know whether the aqueous photolysis rate is typical, an outlier, or the result of other interferences.

Ground Water

Cloransulam-methyl and its structurally-similar transformation products are mobile and persistent enough to reach ground water under certain conditions. These chemicals are likely to persist in ground water.

Estimated Water Concentrations:

Surface Water Concentrations using GENEEC (in ppb)

	PEAK EEC	AVERAGE 4 DAY EEC	AVERAGE 21 DAY EEC	AVERAGE 56 DAY EEC
Cloransulam-methyl	1.83	1.13	0.28	0.10
Cloransulam-methyl & similar products	1.88	1.16	0.28	0.11

No ground water estimates have been made yet.