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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

**MEMORANDUM**

Date: 12/19/2007

Subject: Pyroxsulam. Petition for the Establishment of Permanent Tolerances for Use on Wheat. Summary of Analytical Chemistry and Residue Data. Petition Number 6E7101.

| | | | |
|---|---|---|---|
| DP#: | 335462 | Decision Number: | 369826 |
| PC Code: | 108702 | MRID Nos.: | 46908305-46908308, 46908310, 46908311, 46908315, 46908317-46908319, and 46908454 |
| 40 CFR 180. | Not Yet Established | | |
| Chemical Class: | Triazolopyrimidine herbicide | | |

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This document was originally prepared under contract by Dynamac Corporation (2275 Research Blvd, Suite 300; Rockville, MD 20850; submitted 11/05/2007). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

**Executive Summary**

Dow AgroSciences has submitted a petition, PP#6E7101, proposing the establishment of permanent tolerances for residues of pyroxsulam [N-(5,7-dimethoxy[1,2,4]triazolol[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide] in/on wheat. Pyroxsulam is a new systemic post-emergence triazolopyrimidine herbicide intended for control of a wide spectrum of grass and broadleaf weeds in wheat. Pyroxsulam is a Group 2 herbicide (i.e., an acetolactate synthase inhibitor).

Dow AgroSciences is seeking a trilateral review for registration of pyroxsulam in the U.S., Canada, and Australia. The review of the various aspects of the tolerance petition (i.e., the toxicology, residue chemistry, and environmental fate information) was performed as a collaborative effort between the three countries. The Australian Pesticides and Veterinary Medicines Authority (APVMA) reviewed the residue chemistry data for radiolabeled studies and analytical methods, while Canada's Pest Management Regulatory Agency reviewed storage stability data and the crop field trials conducted in Canada.

Dow is proposing tolerances for residues of pyroxsulam *per se* in/on the following raw agricultural commodities:

| | |
|---|---|
| Wheat, forage | 0.04 ppm |
| Wheat, grain | 0.01 ppm |
| Wheat, hay | 0.01 ppm |
| Wheat, straw | 0.01 ppm |

The residue of concern for both tolerance expression and risk assessment is the parent compound, pyroxsulam. The rationale for these decisions is discussed in detail in the associated risk assessment (Memo, D335496, D. Dotson, 12/19/2007).

In conjunction with this petition, Dow has submitted a FIFRA Section 3 request to register a 7.5% water dispersible granule (WDG) formulation of pyroxsulam (GF-1274 Herbicide, EPA File Symbol No. 62719-LAO) and a 0.25 lb/gal oil dispersion (OD) formulation (GF-1674 Herbicide, EPA File Symbol No. 62719-LAI), both containing the safener cloquintocet-mexyl, for use on wheat. The petitioner has indicated that the 7.5%WDG formulation is intended for registration in the U.S. only, while the 0.25 lb/gal OD formulation is intended for registration in the U.S., Canada, and Australia. The products are proposed for use as a single postemergence broadcast application in the fall or spring to wheat at the 3-leaf to jointing stage (Zadoks 31) at 0.016 lb ai/A for the 7.5% WDG formulation and 0.013 lb ai/A for the 0.25 lb/gal OD formulation. A 7-day pregrazing interval for forage is proposed as well as a 7-day precutting interval for hay. A 60-day preharvest interval (PHI) is proposed for both grain and straw.

No U.S. tolerances are established for pyroxsulam, and there are currently no established Codex, Canadian, or Mexican MRLs. Tolerances are established under 40 CFR §180.560 for residues of the safener cloquintocet-mexyl when used as an inert ingredient in pesticide formulations containing either clodinafop-propargyl or pinoxaden at 0.1 ppm for wheat forage, hay, grain, and straw. A petition to amend the tolerance expression to include use as a safener with pyroxsulam is under separate review (PP#7E7194).

The qualitative nature of the residue in wheat is adequately understood for the purposes of this petition based on an acceptable wheat metabolism study. HED has determined that the residue of concern in wheat is pyroxsulam *per se*. In wheat, pyroxsulam is metabolized via demethylation of the 5- or 7- ether group of the pyrimidine ring to form 5-OH-XDE-742 or 7-OH-XDE-742. In the study, the metabolism was relatively rapid. The majority of the residues in forage samples collected 7 days after treatment (DAT) were comprised of either 5-OH-XDE-742 or its conjugate. Only low levels of parent were detected in samples from 7-DAT forage and hay harvested 51 DAT. Minor metabolites including 7-OH-XDE-742 and 5,7-di-OH-XDE-742 were also identified. The presence of low levels of the metabolites ADTP, XDE-742 sulfonic acid, and XDE-742 sulfonamide indicates that cleavage of pyroxsulam occurred across either side of the sulfonamide nitrogen bridge between the pyridine and triazolo-pyrimidinyl heterocyclic rings.

The metabolism of pyroxsulam in rotational crops appears to be similar to that observed in primary crops. Pyroxsulam was not identified at the 30-day plantback interval in any rotational crop commodity. Metabolites 5-OH-XDE-742 and 7-OH-XDE-742 were identified in potato tops (0.007 ppm), and wheat hay and straw (≤0.002 ppm), respectively. Two metabolites, XDE-742-cyanosulfonamide and 6-Cl-7-OH-XDE-742, that had not previously been identified in primary crops were found at low levels (≤0.005 ppm) in rotational crops. These metabolites were previously identified as soil metabolites in an aerobic degradation study. Although tolerances are not needed at this time, for the currently proposed use HED has determined that the residue of concern in rotational crops is pyroxsulam *per se*.

The qualitative nature of the residue in livestock is adequately understood for the purposes of this tolerance petition. The nature of the residue determination is based on an acceptable poultry metabolism study and an unacceptable goat metabolism study. HED has determined that the residue of concern in poultry commodities is pyroxsulam *per se*. HED is unable to determine the nature of the residue in ruminants because of discrepancies in the submitted goat metabolism study. The data in the goat metabolism study are sufficient enough for HED to determine that tolerances are not required for ruminant commodities. The data that pertain to the quantity and distribution of TRR in urine, feces, tissues, and milk are acceptable. However, there are discrepancies in the data that pertain to the separation and identification of the metabolites in the different tissues, milk, urine, and feces.

The results of the poultry metabolism study indicate that there was no significant metabolism or transformation of pyroxsulam in poultry, with the majority of the administered dose being excreted in the urine and feces as unchanged pyroxsulam. Pyroxsulam residues were not readily transferred into eggs or edible tissues of poultry following oral administration. Limited metabolism via demethylation of the 5- or 7- ether group of the pyrimidine ring was observed in poultry excreta, and cleavage across the sulfonamide nitrogen bridge was observed in poultry liver. In the goat metabolism study, the majority of the TRR were in the urine and feces. Most of the pyroxsulam was excreted. TRR in muscle, kidney, liver, and adipose tissue ranged up to 0.013% of the dose (liver, PY-label, 0.022 mg equiv/kg). TRR in milk ranged up to 0.003% of the dose (0.031 mg equiv/kg). Because of discrepancies in the study report, it is not possible to determine which metabolites were found in the tissues and excreta or the quantities of those metabolites that were present.

Based on the results of the livestock metabolism studies and the calculated dietary burdens for livestock, HED has concluded that tolerances for livestock commodities are not required as a result of the proposed use of pyroxsulam on wheat; therefore, no data pertaining to enforcement methods, storage stability data, or feeding studies for livestock are required to support this petition. If additional uses are requested in the future, or if the registrant proposes a higher application rate to wheat, additional studies might be needed, and tolerances might be needed for animal commodities.

The petitioner has proposed an acceptable LC/MS/MS method, Method GRM 04.17 for the enforcement of tolerances in wheat commodities. This method was also used for data collection in the storage stability study and crop field trials submitted with this petition. The method determines residues of pyroxsulam *per se*. The validated limit of quantitation (LOQ) is 0.01 ppm. Method GRM 04.17 has been adequately validated and has undergone a successful independent laboratory validation (ILV) trial and a radiovalidation trial. In addition, the method includes an acceptable confirmatory procedure. The method was submitted to the Analytical Chemistry Branch (ACB) of the Biological and Economic Analysis Division (BEAD). The ACB concluded that the method appeared to meet the 860.1340 Guidelines for an acceptable method. Furthermore, the lab determined that it did not need to perform a method validation because the registrant's method validation data and the ILV data appear satisfactory.

Adequate PAM I multiresidue methods testing data have been submitted. These data indicate that pyroxsulam cannot be quantified by the FDA PAM I multiresidue methods. Although pyroxsulam is not adequately recovered through the multiresidue protocols, which are GC-based, it is successfully recovered through the German DGF S19 multiresidue method which is LC/MS/MS- based.

Adequate storage stability data are available supporting the sample storage conditions and durations from the wheat field trials. The available data indicate that residues of pyroxsulam are stable under frozen storage conditions for up to 6 months in wheat forage, grain, and straw, as well as in potato, soybean, spinach, and tomato. Samples from the wheat field trials were stored frozen for approximately 6 months.

Adequate field trial data for wheat are available. Twenty wheat field trials were conducted in Canada during the 2005 growing season reflecting application of pyroxsulam with cloquintocet-mexyl added as a safener. Following a single application of the 0.25 lb/gal OD formulation at 0.013 lb ai/A (15 g ai/ha), maximum residues of pyroxsulam were 0.036 ppm in/on forage harvested 7-14 days after treatment (DAT), <0.01 ppm in/on hay at 28-43 DAT, and <0.01 ppm in/on grain and straw at 50-110 DAT.

The Agency previously examined Canadian and European field trial data to determine whether residue data from these trials can be used to support U.S. risk assessment and tolerance setting (Memo, D332115, D. McNeilly, 12/19/2007). The Canadian field trial studies were reviewed in detail, but the European field trial studies were not. HED concluded that, for this case only, it was acceptable to make use of the available Canadian and European data to establish tolerances on wheat commodities in the U.S. and to assess risk without requiring additional U.S. trials (Chem SAC meeting minutes, 10/18/2006). The submitted data are adequate for several reasons. (1) Twenty trials were performed in Canada. This number is equal to that recommended in the OPPTS Series 860 Guidelines. (2) Seven of the field trials were performed in NAFTA growing

zones that extend into the U.S. (3) The Canadian field trials were performed using the OD formulation. The European field trials were performed using the WDG formulation at a slightly exaggerated rate. As a result, field trials were performed using both formulations. (4) Data are available for both wheat and winter wheat. (5) The results of the European field trial data are consistent with the results of the Canadian field trial data. Residues in grain, hay, and straw were below the LOQ of 0.01 ppm in all samples. In the Canadian trials, the highest residue value in forage was 0.036 ppm and in the European trials, the highest residue value was 0.059 ppm. In the Canadian trials, the highest residue value in straw was <0.01 ppm and in the European trials, the highest residue value was 0.022 ppm. The submitted field trial data support tolerances of 0.01 ppm for wheat grain and hay, 0.03 ppm for wheat straw, and 0.06 ppm for wheat forage.

A wheat processing study was not submitted in support of the subject petition. The Agency previously concluded that a processing study for wheat was not required based on the results of the wheat metabolism study, in which residues in wheat grain were very low (ND-0.001 ppm) following application of pyroxsulam at approximately 2x the maximum proposed application rate, and the petitioner's claim that exaggerated rate trials are not possible because of phytotoxicity. Residue data for aspirated grain fractions are not required because, under the proposed use pattern, pyroxsulam is to be applied during the vegetative growth stage, prior to the formation of seed heads.

No field rotational crop data were submitted in support of the subject petition. The Agency has concluded that these data are not required. The available confined rotational crop data are adequate to support the proposed plantback intervals.

**Regulatory Recommendations and Residue Chemistry Deficiencies**

HED has examined the residue chemistry database for pyroxsulam and has determined that, pending submission of a revised Section F and Section B (see requirements under Directions for Use), there are no residue chemistry issues that would preclude granting registration for the requested use of pyroxsulam or establishment of tolerances for residues of pyroxsulam *per se* as follows:

| | |
|---|---|
| Wheat, forage | 0.06 ppm |
| Wheat, grain | 0.01 ppm |
| Wheat, hay | 0.01 ppm |
| Wheat, straw | 0.03 ppm |

In the revised Section F, the registrant needs to propose a tolerance of 0.06 ppm for wheat, forage and a tolerance of 0.03 ppm for wheat, straw.

860.1200 Directions for Use

- The 7-day precutting interval for hay is not supported by the available data and should be revised. The available data support a 28-day precutting interval for hay.

In the study report for the goat metabolism study, there were discrepancies between the values given in tables accompanying the chromatograms and the values entered into the tables in which the data were reported. As a result, it is not possible to determine which values were the correct ones. A revised study report is not needed for the current tolerance petition, however. In the future, if the registrant requests tolerances for commodities that have animal feed items associated with them, HED recommends that the registrant submit a revised goat metabolism study report.

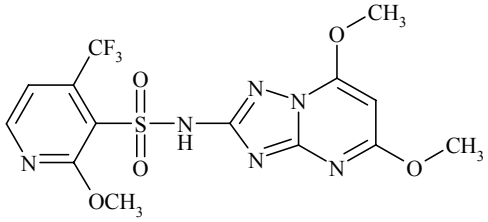
The petitioner should also be advised that, for any future amended uses on wheat or for expansion of pyroxsulam use to other cereal grains or grasses, field trial data should include analysis for residues of parent compound as well as the free and conjugated forms of the 5-OH-XDE-742 metabolite. HED also notes that, for any significant increase in the total seasonal application rate, a new confined rotational crop study would be needed or the registrant should submit limited field rotational crop studies. In these studies the registrant should analyze for residues of metabolites such as the 5- OH-XDE-742 and 7- OH-XDE-742 metabolites and XDE-742 cyanosulfonamide.

## Background

Dow AgroSciences has proposed permanent tolerances and requested registration of two pyroxsulam end-use products for use on wheat, a 7.5% WDG (GF-1274 Herbicide, EPA File Symbol No. 62719-LAO) and a 0.25 lb/gal OD (GF-1674 Herbicide, EPA File Symbol No. 62719-LAI). Both formulations also contain the safener cloquintocet-mexyl. This is the first proposed use of pyroxsulam in the U.S. Under the current action, Dow is seeking a trilateral review for registration of pyroxsulam in the U.S., Canada, and Australia.

The nomenclature and the physicochemical properties of pyroxsulam are summarized in Tables 1 and 2. The chemical names and structures of pyroxsulam and its transformation products are presented in Attachment 1.

**Table 1. Pyroxsulam Nomenclature**.

| | |
|---|---|
| Compound |  |
| Common name | Pyroxsulam |
| Company experimental name | XDE-742 |
| IUPAC name | *N*-(5,7-dimethoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide |
| CAS name | *N*-(5,7-dimethoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide |
| CAS registry number | 422556-08-9 |

| **Table 1. Pyroxsulam Nomenclature**. | |
|---|---|
| End-use product (EP) | GF-1274 Herbicide (7.5% WDG formulation) and<br>GF-1674 Herbicide (0.25 lb/gal OD formulation) |

| **TABLE A.2. Physicochemical Properties of Pyroxsulam.** | | |
|---|---|---|
| Parameter | Value | Reference |
| Melting point | 208.3°C | Product Chemistry Review of XDE-742 Technical |
| pH | 4.06 at 24.4°C (1% wt/wt aqueous solution | |
| Density | Relative: 1.62 g/cc at 20°C<br>Bulk: 0.383 g/cc at 22.6°C | |
| Water solubility ( 20°C) | 0.0164 g/L (pH 4)<br>3.20 g/L (pH 7) | |
| Solvent solubility (mg/L at 20°C) | Xylene: 352, Octanol: 730, Heptane: <10<br>Acetone: 27,900, Methanol: 10,100<br>Ethyl Acetate: 21,700<br>1,2 Dichloromethane: 39,400 | |
| Vapor pressure at 20°C | $<7.5 \times 10^{-10}$ Pa at 20°C | |
| Dissociation constant ($pK_a$) | 4.67 between pH 3.9 and 5.5 | |
| Octanol/water partition coefficient Log($K_{OW}$) | 1.08 (pH 4)<br>-1.01 (pH 7) | |
| UV/visible absorption spectrum | Neutral pH : λmax = 297 nm<br>Molar absorptivity = 8,000 | |

## 860.1200 Directions for Use

Dow provided draft labeling, dated 7/26/06, for a 7.5% WDG (GF-1274 Herbicide; EPA File Symbol No. 62719-LAO) and a 0.25 lb/gal OD (GF-1674 Herbicide; EPA File Symbol No. 62719-LAI), both containing the safener cloquintocet-mexyl. The 7.5% WDG formulation is intended for registration in the U.S. only, while the 0.25 lb/gal OD formulation is intended for registration in the U.S., Canada, and Australia. The use pattern is presented in Table 3.

According to the draft labels, the 7.5% WDG is intended for use on winter wheat and the 0.25 lb/gal OD is intended for use on spring and winter wheat (including durum). The petitioner stated in the administrative materials for the petition that both products will be applied to winter and spring wheat, including durum.

| **Table 3. Summary of Directions for Use of Pyroxsulam** | | | | | | |
|---|---|---|---|---|---|---|
| Applic. Timing, Type, and Equip. | Formulation [EPA Reg. No.] | Applic. Rate (lb ai/A) | Max. No. Applic. per Season | Max. Seasonal Applic. Rate (lb ai/A) | PHI (days) | Use Directions and Limitations |
| Wheat | | | | | | |
| Postemergence, Broadcast, Ground or Aerial | 7.5% WDG (62719-LAO) | 0.016 | 1 | 0.016 | 7 (forage and hay)<br>60 (grain and straw) | Apply fall or spring to wheat at the 3-leaf to jointing stage (Zadoks 31) in ≥10 gal/A using ground equipment and ≥5 gal/A using aerial equipment. |

| Table 3. Summary of Directions for Use of Pyroxsulam | | | | | | |
|---|---|---|---|---|---|---|
| Applic. Timing, Type, and Equip. | Formulation [EPA Reg. No.] | Applic. Rate (lb ai/A) | Max. No. Applic. per Season | Max. Seasonal Applic. Rate (lb ai/A) | PHI (days) | Use Directions and Limitations |
| | 0.25 lb/gal OD (62719-LAI) | 0.013 | | 0.013 | | Use of a nonionic surfactant (0.25-50% v/v), crop oil concentrate (0.8% v/v), or a methylated seed oil (1.0% v/v) is required. |

The following crop rotation intervals are proposed:

- 1 month for wheat
- 9 months for barley, field corn, grasses, millet, oats, popcorn, seed corn, sweet corn, sorghum, alfalfa, canola, chickpea, soybean, dry bean, field pea, flax, lentil, mustard, potato, safflower, sugar beet, and sunflower
- 12 months for other crops not listed.

The label states that, when the product is applied in a tank mix combination, all applicable use directions, precautions, and limitations on each manufacturer's label must be followed. No specific tank mix partners are specified; however, tank mixing with products containing dicamba or amine formulations of 2,4-D or MCPA or with products containing boron is prohibited. Use of an adjuvant is prohibited when the product is applied in combination with other EC formulations. Application through any type of irrigation system is prohibited. A 4-hour reentry interval (REI) is proposed for the 7.5% WDG, and a 24-hour REI is proposed for the 0.25 lb/gal OD.

*Conclusions*. The submitted labels are adequate to allow evaluation of the submitted residue data relative to the proposed use.

The proposed use directions are supported by the available field trial data with the following exception:

- The submitted data do not support a 7-day precutting interval for hay. This restriction should be revised as the data support a 28-day precutting interval for hay.

The use of the safener cloquintocet-mexyl as a spray adjuvant in the submitted crop field trials would normally not be sufficient to support the use of the spray adjuvants listed on the product labels. The adjuvants that are listed include surfactants, crop oil concentrates, and methylated seed oils. These adjuvants are added to the spray mixture to increase exposure to the plant and may result in higher residues. Although the crop field trials do not reflect use of these adjuvants, the requirement for use of these adjuvants in spray mixtures does not need to be removed from the labels in this case based on the nature of the use (early season application at very low rate, most samples <LOQ residues, quantifiable residues maximum about 0.06 ppm and found only in livestock feeds).

**860.1300 Nature of the Residue - Plants**

DER Reference: 46908305.der.doc

Two radio-labeled forms of [$^{14}$C]-XDE-742 were formulated with the blank granulated formulation GF-1274 (i.e., the formulation without active). The $^{14}$C radiolabel was positioned on either the pyridine ring (PY-label) or the triazolo-pyrimidinyl ring (TP-label). A single foliar application of each radio-labeled form was made to spring wheat at an application rate equivalent to 0.034 lb ai/A (37.5 g ai/ha). The application rate used in the study corresponds to 2.1x the maximum proposed application rate to wheat. Plants were harvested from each plot on the day of application (0 days after treatment, DAT) and at stages representing early forage (7 DAT), hay (51 DAT) and maturity (92 DAT). At maturity, plants were separated into straw and grain.

Each sample was homogenized and analyzed by oxidative combustion. Surface radioactivity was removed from the 0 and 7 day forage harvest samples by brief immersion of each sample in acetonitrile. Sub-samples of homogenized early forage, hay, and straw tissues were extracted with aqueous acetonitrile. Further extractions were conducted, as appropriate, with acidified aqueous acetonitrile and 1 N HCl at reflux. Where samples contained sufficient radioactivity, extracts were partitioned against ethyl acetate to determine the amount of organo-soluble residues.

On the day of application, plant tissues contained 1.960 (PY) and 1.266 mg/kg (TP) XDE-742 equivalents. Subsequently the total radioactive residues (TRR) in each commodity showed a decline. The TRR measured in early forage (7 DAT), hay, straw, and grain from the experiment with the PY-label were 0.707, 0.111, 0.034 and 0.001 mg equiv/kg respectively. The corresponding values for the TP-label were 0.203, 0.081, and 0.023 mg equiv/kg for forage, hay, and straw, respectively, and <LOD (<0.002 µg equiv/kg) for grain.

Unchanged XDE-742 accounted for >95% of the TRR (1.217-1.889 mg equiv/kg) in forage samples 0 DAT.

The relatively low levels of XDE-742 in forage samples from day 7, accounting for 5.7-6.5% of the TRR (0.012-0.046 mg equiv/kg) indicate that metabolism of XDE-742 is rapid. Residues of 5-OH-XDE-742 and its conjugate were the predominant residues in day 7 forage samples, accounting for a total of 60-68% of the TRR (0.118-0.485 mg equiv/kg). The remainder of the extractable radioactivity was comprised of minor metabolites including 7-OH-XDE-742 and 5,7-di-OH-XDE-742, each accounting for <2% TRR in respective samples, as well as a number of minor unidentified metabolites. The presence of low levels of XDE-742 sulfonic acid and XDE-742 sulfonamide in PY labeled samples, and ADTP in TP labeled samples is indicative of cleavage of XDE-742 across either side of the sulfonamide nitrogen between the pyridine and triazolo-pyrimidinyl heterocyclic rings. Less than 3% of the TRR could not be extracted from forage samples.

Residues of 5-OH-XDE-742 and its conjugate were the predominant residues in hay samples, accounting for a total of 45-52% of the TRR (0.036-0.058 mg equiv/kg). Minor metabolites, as identified in the day 7 forage samples, comprised the remainder of the radioactivity. Approximately 11% of the TRR from each sample could not be extracted.

Attempts were made to extract radioactivity from straw samples; however, because of the low TRR levels (0.023-0.034 mg equiv/kg) in each sample, extracts contained insufficient residues

for identification. Approximately 40% of the TRR (0.009-0.014 mg equiv/kg) from each sample could not be extracted.

Residues in grain were too low (<LOD-0.001 mg equiv/kg) to attempt characterization or identification of residues.

Results indicate that the metabolism of XDE-742 in wheat is via the demethylation of the 5 or 7 ether group of the pyrimidine ring to form 5-OH-XDE-742 or 7-OH-XDE-742. The metabolism of XDE-742 was relatively rapid, with the majority of the radioactive residue 7 DAT being accounted for as either 5-OH-XDE-742 or its conjugate. Only low levels of parent were detected in samples from 7 and 51 DAT. Minor metabolites including 7-OH-XDE-742 and 5,7-di-OH-XDE-742 were also identified. Very low levels of a metabolite identified as ADTP were identified in TP labeled samples, while XDE-742 sulfonic acid and XDE-742 sulfonamide were detected in PY labeled samples. The presence of these metabolites indicates that cleavage of XDE-742 occurs across either side of the sulfonamide nitrogen between the pyridine and triazolo-pyrimidinyl heterocyclic rings.

*Conclusions*. The submitted wheat metabolism study is adequate to satisfy data requirements. Based on the submitted study, the nature of the residue in wheat is adequately understood. For the purposes of this petition, the residue of concern is the parent compound, pyroxsulam (Memo, D335496, D. Dotson, 12/19/2007).

**860.1300 Nature of the Residue - Livestock**

DER References: 46908307.der.doc (Goat)
46908306.der.doc (Hen)

Ruminants

The purpose of this study was to investigate the nature of radioactive residues present in goat tissues, milk, and excreta collected from goats dosed with [$^{14}$C]-XDE-742 labeled in either the pyridine-ring (PY) or triazolopyrimidine-ring (TP). The test substances were orally administered for 7 consecutive days, corresponding to a dose level of 0.4 mg/kg body weight or the equivalent of 12 ppm in the feed. This feeding level is equivalent to 190-240x the ruminant dietary burden (see dietary burden calculations, Table 6).

Milk, urine, and feces were collected daily. The animals were sacrificed within 24 hours of administration of the final dose. Tissues, including liver, muscle, fat, and kidney were collected and assayed to determine total radioactive residues (TRR).

The TRR and % of administered dose are summarized in Table 4 below. A total of 84.24% and 92.86% of the administered radioactivity was recovered following administration of the TP and PY labeled doses, respectively. The majority of the radioactivity was excreted in the urine and feces: 82.66% for the TP-dosed goat, and 91.35% for the PY-dosed goat. For both labels, the percentages of eliminated radioactivity in urine and feces were similar, i.e., 37% in urine for both labels and approximately 45% or 54% in feces for the TP and PY labels, respectively.

A total of 0.026% and 0.028% of the dose was recovered in milk from the animals dosed with the TP and PY labeled doses, respectively, indicating that very little of the administered dose is transferred to the milk.

At sacrifice, radioactive residues in all tissues, blood, and bile were low. The highest percentage of radioactivity as a function of administered dose was in liver at 0.013% for the PY label and 0.008% for the TP label. TRR in liver were equivalent to 0.013 mg equiv/kg for the TP dose and 0.022 mg equiv/kg for the PY dose. TRR in kidney were equivalent to 0.013 mg equiv/kg for the TP dose and 0.025 mg equiv/kg for the PY dose. Although the percentage of administered dose found in kidney was lower than in liver (0.002% PY and 0.001% TP), the actual concentrations of radioactivity in kidney were comparable to those in liver, for both labels.

**Table 4. Total Radioactive Residues (TRR) in Tissue and Excreta**

| Matrix | TP-label | | PY-label | |
|---|---|---|---|---|
| | % of Dose | mg equiv/kg | % of Dose | mg equiv/kg |
| Urine | | | | |
| Application Day 1 | 4.46 | 4.239 | 0.64 | 0.730 |
| Application Day 2 | 6.91 | 4.047 | 7.34 | 6.639 |
| Application Day 3 | 5.37 | 5.964 | 5.97 | 4.895 |
| Application Day 4 | 4.04 | 4.899 | 3.78 | 7.063 |
| Application Day 5 | 5.57 | 5.594 | 7.19 | 4.875 |
| Application Day 6 | 5.88 | 4.454 | 6.21 | 6.226 |
| Application Day 7 | 5.47 | 4.188 | 6.52 | 4.959 |
| Sub-total urine | 37.70 | | 37.65 | |
| Feces | | | | |
| Application Day 1 | 1.93 | 2.221 | 2.23 | 1.699 |
| Application Day 2 | 6.30 | 5.657 | 6.14 | 3.938 |
| Application Day 3 | 7.82 | 10.535 | 11.25 | 8.814 |
| Application Day 4 | 4.80 | 5.589 | 6.32 | 4.589 |
| Application Day 5 | 6.57 | 8.111 | 12.22 | 9.247 |
| Application Day 6 | 7.56 | 8.942 | 7.35 | 6.525 |
| Application Day 7 | 9.98 | 9.226 | 8.19 | 10.750 |
| Sub-total feces | 44.96 | | 53.70 | |
| Cage Wash | 0.777 | -- | 0.693 | -- |
| Milk | | | | |
| Application Day 1 (am/pm) | 0.001/0.002 | 0.005/0.004 | 0.001/0.001 | 0.003/0.002 |
| Application Day 2 (am/pm) | 0.002/0.003 | 0.012/0.006 | 0.002/0.002 | 0.007/0.003 |
| Application Day 3 (am/pm) | 0.003/0.001 | 0.031/0.003 | 0.003/0.001 | 0.019/0.003 |
| Application Day 4(am/pm) | 0.002/0.001 | 0.009/0.003 | 0.002/0.001 | 0.009/0.003 |
| Application Day 5(am/pm) | 0.002/0.002 | 0.010/0.004 | 0.005/0.001 | 0.025/0.001 |
| Application Day 6(am/pm) | 0.003/0.001 | 0.016/0.004 | 0.003/0.002 | 0.018/0.004 |
| Application Day 7 (am/pm) | 0.003/0.000 | 0.015/0.001 | 0.003/0.001 | 0.018/0.002 |
| Sub-total milk | 0.026 | | 0.028 | |
| Muscle | 0.004 | 0.001 | 0.010 | 0.003 |
| Adipose tissue | 0.001 | 0.003 | 0.001 | 0.007 |
| Kidney | 0.001 | 0.013 | 0.002 | 0.025 |
| Liver | 0.008 | 0.013 | 0.013 | 0.022 |
| Blood | 0.004 | 0.006 | 0.006 | 0.011 |
| Bile | 0.000 | 0.010 | 0.000 | 0.008 |
| Gut | 0.047 | 0.016 | 0.048 | 0.017 |

| Table 4. Total Radioactive Residues (TRR) in Tissue and Excreta | | | | |
|---|---|---|---|---|
| Matrix | TP-label | | PY-label | |
| | % of Dose | mg equiv/kg | % of Dose | mg equiv/kg |
| Gut contents | 0.456 | 0.115 | 0.447 | 0.115 |
| Stomach | 0.022 | 0.007 | 0.031 | 0.009 |
| Stomach contents | 0.235 | 0.023 | 0.235 | 0.025 |
| Urine in bladder | 0.003 | 0.270 | 0.001 | 0.166 |
| | | | | |
| % of Total Administered Dose | 84.24 | -- | 92.86 | -- |

Where samples contained sufficient radioactivity for further characterization and identification, residues were extracted and analyzed by radio-high performance liquid chromatography (HPLC). In the study report that was submitted to the Agency, there were discrepancies between the values given in tables accompanying the chromatograms and the values entered into the tables in which the data were reported. As a result, it is not possible to determine which values were the correct ones. The following discussion is based on the assumption that the values given with the chromatograms are the correct ones.

Aliquots of urine were mixed with scintillation cocktail and analyzed without any additional treatment. Feces were homogenized and suspended in distilled water. Aliquots of these suspensions were freeze dried and solubilized prior to analysis.

Proteins in each milk sample were precipitated twice with acetonitrile. The extracts were combined, concentrated, reconstituted in mobile phase and centrifuged. TRR in the final extract and post extracted solids (PES) were measured. The final extract was analyzed by radio-HPLC.

Liver and kidney were the only edible tissues with TRR levels greater than 0.01 mg/kg. Samples of these tissues were extracted with acetonitrile followed by acetonitrile:water. The combined extracts were partitioned against hexane to reduce the lipid content. The PES were refluxed with 6N HCl overnight and then neutralized with 6N NaOH. The aqueous extracts were reacted with dimethoxypropane to convert the aqueous fraction to acetone and methanol. The acetone/methanol extracts were concentrated and centrifuged to remove precipitated material. The solid material was extracted with acetonitrile and the extracts were combined with the acetone/methanol extracts. The combined extracts were analyzed by radio-HPLC.

The TRR, proportion of radioactivity in various extracts, and the proportion of XDE-742 and its metabolites were similar in samples with both labels.

In urine samples from both labels, unchanged XDE-742 accounted for approximately 95% of the TRR. The remainder of the extracted radioactivity was comprised of 7-OH-XDE-742, 5,7-di-OH-XDE-742 and unidentified metabolites. No single metabolites accounted for more than approximately 5% of the TRR. In the feces, unchanged XDE-742 accounted for 75-80% of the TRR. The remainder of the extracted radioactivity, which accounted for <10% of the TRR, was comprised entirely of 7-OH-XDE-742.

TRR in milk were low and entirely comprised of unchanged XDE-742 (0.007-0.012 mg equiv/kg). The majority of the administered dose was excreted in milk within 12 hours of

dosing. With consecutive doses, a plateau in milk was observed between 3 and 5 days after commencement of dosing.

The only tissues containing sufficient radioactivity for characterization and identification were the liver and kidney. Residues in these tissues were comprised largely of unchanged XDE-742 which comprised 42-63% of the TRR (0.008-0.010 mg equiv/kg) in kidney samples and 41-64% of the TRR (0.008-0.009 mg equiv/kg) in the liver. Small amounts of 5,7-di-OH-XDE-742 (up to 1.2% TRR, ≤0.001 mg equiv/kg) were identified in PY labeled liver and kidney samples. The remainder of extractable residues in samples from both labels was comprised of at least two unidentified metabolites, which accounted for ≤14.2% of the TRR (0.004 mg equiv/kg) in liver and kidney.

The results indicate that there was no significant metabolism or transformation of XDE-742, with the majority of administered dose being excreted rapidly in the urine and feces as unchanged XDE-742. The metabolites 5,7-di-OH-XDE-742 and 7-OH-XDE-742 were identified in the urine, and 7-OH-XDE-742 in the feces as minor components of the residue. The proportion of XDE-742 and its metabolites were similar in samples for both labels, indicating that there was no significant cleavage of the molecule across the sulfonamide nitrogen between the pyridine and triazolo-pyrimidinyl ring.

XDE-742 residues are not readily transferred into milk or edible tissues of ruminants following oral administration. The only radioactive component identified in milk, accounting for ≥95% of the residue was unchanged XDE-742. Of the edible tissues, only liver and kidney contained TRR levels greater than 0.01 mg/kg. Other than parent, the only identifiable component of the residue was 5,7-di-OH-XDE-742, present at 0.001 mg equiv/kg.

Poultry

[$^{14}$C]-XDE-742, labeled in either the pyridine ring (PY) or the triazolo-pyrimidine ring (TP) was orally administered to laying hens for 7 days at the nominal rate of 10 mg ai/kg feed/day in the diet (equivalent to 0.839 mg a.i/kg bw; approximately 1400x the poultry dietary burden (Table 6). Eggs and excreta were collected daily. The animals were sacrificed within 24 hours of the final dose and the following tissues were collected: liver, muscle (breast and thigh), fat (abdominal), and skin with subcutaneous fat.

Each sample was homogenized and analyzed by oxidative combustion to determine TRR. Only liver and excreta contained sufficient radioactivity to allow further characterization and identification of residues. Liver and excreta were extracted in acetonitrile:water. Liver extracts were subjected to more extensive extraction using hexane with partitioning against ethyl acetate. The post extracted solids were further refluxed with 1.0 N HCl, and the extracts partitioned against ethyl acetate. Where extractable radioactivity was greater than 0.01 mg eguiv/kg, the samples were analyzed by HPLC along with reference standards of possible metabolites. Where confirmation of the residues was required, samples were re-analyzed in a second HPLC system and by thin layer chromatography (TLC).

A total of 99% and 104% of the administered dose was recovered from the hens administered $^{14}$C-TP-XDE-742 and $^{14}$C-PY-XDE-742, respectively. The dose was almost entirely excreted, with 99% of the $^{14}$C-TP-XDE-742 and 104% of the $^{14}$C-PY-XDE-742 dose present in the

excreta. Eggs from hens treated with either label each contained less than 0.01% of the dose. During the dosing period the residue levels in eggs tended to increase slightly, with a plateau being reached on about day 3. The maximum radioactive residues in eggs were 0.0047 mg/kg on day 5 in $^{14}$C-TP-XDE-742 labeled samples, and 0.0044 mg/kg on day 7 in $^{14}$C-PY-XDE-742 labeled samples. Residues in all edible tissues collected at sacrifice were also less than 0.01% of the administered dose for both labels. Tissue residues were relatively consistent between radiolabels. Residues of $^{14}$C-TP-XDE-742 in the various tissues were as follows: muscle (<0.010 mg/kg), liver (0.010 mg/kg), fat (<0.010 mg/kg), and skin with fat (0.0043 mg/kg), while residues in $^{14}$C-PY-XDE-742 were: muscle (0.010 mg/kg), liver (0.019 mg/kg), fat (<0.010 mg/kg), and skin with fat (<0.010 mg/kg).

The liver contained a low concentration of radioactivity that consisted of parent, polar compounds, and non-extractable residue. In the $^{14}$C-TP-labeled liver, 27.4% TRR (0.003 mg equiv/kg) was comprised of parent, while 13.4% TRR (0.001 mg equiv/kg) was due to polar compounds. The metabolite ADTP comprised 4.5% TRR (<0.001 mg equiv/kg) and unidentified metabolites comprised 25% TRR (0.002 mg equiv/kg). The remaining 29.4% TRR (0.003 mg equiv/kg) was not extractable from the $^{14}$C-TP-labeled liver.

The $^{14}$C-PY-labeled liver contained 14.9% TRR as XDE-742 (0.003 mg equiv/kg), and 29.1% TRR (0.006 mg equiv/kg) as polar components. Another 15.0% TRR (0.003 mg equiv/kg) was extractable from the $^{14}$C-PY-labeled liver using acid hydrolysis, and was shown to contain multiple components that were of intermediate polarity. The remaining 33.2% TRR (0.006 mg equiv/kg) was not extracted from the $^{14}$C-PY-labeled liver.

In summary, the XDE-742 administered to laying hens was almost entirely excreted in the urine and feces as unmetabolized parent (≥90% TRR in the day 7 excreta). Individually, less than 4% TRR in day 7 excreta was observed to be either the 5-OH or 7-OH metabolites, thus indicating metabolism of XDE-742 by de-methylation of the 5 or 7 ether groups of the pyrimidine ring. A very small amount of radioactivity, (<0.01% of the TRR in each sample, <0.020 mg equiv/kg), was found in the liver. The radioactivity in the liver was characterized as parent (*ca*. 15-30% TRR), ADTP (<5%), and a range of unidentified polar components (*ca*. 15-45% TRR). The 5-OH or 7-OH metabolites were not found in liver samples following administration of either label.

*Conclusions*. The submitted poultry metabolism study is adequate to satisfy data requirements. Based on the submitted study, the nature of the residue in poultry is adequately understood. The residue of concern in poultry commodities is the parent compound, pyroxsulam. The goat metabolism study is not adequate to satisfy data requirements, however. The TRR values in tissues and excreta are acceptable. However, because of the internal discrepancies in the values that relate to the characterization, identification, and distribution of residues in various tissues, the goat metabolism study as a whole is unacceptable. These latter discrepancies do not affect HED's determination that tolerances are not needed for animal commodities because that decision was based on the TRR values in tissues and milk (see Section 860.1480 Meat, Milk, Poultry, and Eggs, below).

## 860.1340 Residue Analytical Methods

DER References: 46908311.der.doc (includes review of MRID 46908454)
46908308.der.doc (includes review of MRID 46908310)

Plant commodities

*Enforcement methods:* Dow AgroSciences LLC Analytical Method GRM 04.17 was developed for the quantitative determination of residues of pyroxsulam in agricultural commodities representative of acidic, dry, and wet crops. The method was validated "in house" and has also undergone an ILV trial.

Residues of pyroxsulam were extracted from the crop samples by homogenizing and shaking with an acetonitrile/water solution. Aliquots of each extract were diluted with 0.1 N hydrochloric acid and purified using solid-phase extraction (SPE). The SPE plate was washed with a methanol/water solution and the pyroxsulam eluted with acetonitrile. The eluate was diluted with stable-isotope labeled internal standard ($^{15}N_3$-XDE-742) in a methanol/water mobile phase containing 2 mM ammonium acetate. The final solution was analyzed by liquid chromatography with positive-ion electrospray ionization (ESI) tandem mass spectrometry (LC/MS/MS).

LC/MS/MS affords a highly specific method for quantitation of pyroxsulam by matching retention times with standards in conjunction with monitoring the MS/MS ion transitions of pyroxsulam at *m/z* 435.1/195.2 and the pyroxsulam stable isotope at *m/z* 438.1/198.2. A second LC/MS/MS method using a different selectivity column provided confirmation of pyroxsulam by matching retention times with standards in conjunction with monitoring the MS/MS ion transitions of XDE-742.

The data gathering/enforcement method was validated over the concentration range 0.01-1.0 mg/kg in plant matrices that included representative acidic, dry, oily, and wet crops as well as processed grain fractions. A summary of results is provided in Table 5. Individual recovery values for each control sample fortified at the proposed LOQ of 0.01 mg/kg and 100x the proposed LOQ were within 70-110% of the fortification concentration, with few exceptions. The average recovery values for each control sample fortified at the proposed LOQ and 100x the proposed LOQ were within 70-120% of the fortification concentration. The relative standard deviation (RSD) of replicate recovery measurements did not exceed 20% at or above the LOQ. Thus Method GRM 04.17 was demonstrated as being suitable for the detection and determination of XDE-742 residues in plant matrices with a validated LOQ of 0.01 mg/kg.

**Table 5. Summary of Recovery Results from Method Validation of Agricultural Commodities using the Data-Gathering Analytical Method GRM 04.17.**

| Matrix | Fortification Level (mg/kg) | % Recoveries Obtained (n= number samples) | Mean Recovery ± SD (RSD) |
|---|---|---|---|
| Acidic Crops | 0.01 - 1.0 | 87 - 99 (20) | 92 ± 3.5 (3.8) |
| Dry Crops | 0.01 - 1.0 | 69 - 108 (36) | 86 ± 7.2 (8.4) |
| Oily Crop | 0.01 - 1.0 | 77 - 101 (20) | 87 ± 6.8 (7.8) |
| Wet Crops | 0.01 - 1.0 | 69 - 90 (16) | 79 ± 6.0 (7.6) |
| Processed Products from Wheat Grain | 0.01 - 1.0 | 83 - 106 (24) | 92 ± 5.9 (6.4) |

An ILV of Method GRM 04.17 was undertaken to confirm the accuracy, reliability and LOQ. The results from the ILV were consistent with those of the data gathering method, and provided confirmation of the LOQ.

To determine the efficiency of the extraction procedures used in Method GRM 04.17, samples of wheat containing aged radio-labeled residues were obtained from the wheat metabolism study discussed above (see Section 860.1300, Nature of the Residue in Plants). Subsamples of 7 DAT wheat treated with $^{14}C_2$-PY-XDE-742 and a control were analyzed to determine the extraction efficiency of GRM 04.17. Liquid scintillation counting (LSC) of several aliquots of the raw extracts demonstrated that 90% of TRR were extracted, indicating that the method is acceptable for the extraction of XDE-742 in wheat samples. LC/MS/MS-based results demonstrated a recovery of 87% for Method GRM 04.17.

Dow AgroSciences Analytical Method GRM 04.17 has been demonstrated as being suitable for the quantitative determination of residues of pyroxsulam in representative acidic, dry (including processed products), oily, and wet crops for the purposes of data gathering and enforcement. The method was validated in house and by ILV over the concentration range of 0.01-1 mg/kg for acidic, oily, wet, and dry (unprocessed) matrices, with a validated LOQ of 0.01 mg/kg.

The method was submitted to the Analytical Chemistry Branch (ACB) of the Biological and Economic Analysis Division (BEAD). The ACB concluded that the method appeared to meet the 860.1340 Guideline for an acceptable method (electronic communication, C. Stafford, 11/15/2007). Furthermore, the lab determined that it did not need to perform a method validation because both the registrant's method validation data and the ILV data appear satisfactory.

*Data collection method:* Method GRM 04.17 was used for data collection for samples from the storage stability study and wheat crop field trials submitted in conjunction with this petition. Adequate concurrent method recovery data were submitted with the studies.

*Conclusions*. The submitted residue analytical method data are adequate to satisfy data requirements for the subject petition. The proposed enforcement method for plant commodities, LC/MS/MS Method GRM 04.17, determines residues of pyroxsulam *per se*, and has been adequately validated and has undergone a successful ILV trial and a radiovalidation trial. In addition, the method includes an acceptable confirmatory procedure. Method GRM 04.17 was forwarded to BEAD/ACB, who concluded the method appeared adequate to meet the 860.1340 Guideline.

Method GRM 04.17 was also used for data collection in the storage stability study and crop field trials submitted with the petition, and was adequately validated concurrently with these studies.

**860.1360 Multiresidue Methods**

FDA PAM I Multiresidue Method

DER Reference: 46908315.der.doc

Pyroxsulam was tested in accordance with OPPTS 860.1360 and selected multiresidue methods (MRMs) described in Protocols A, C and G of the United States Food and Drug Administration (FDA) Pesticide Analytical Manual, Volume I (PAM I). The decision tree provided in Appendix II of the PAM I was referenced to determine the appropriate protocols for the analysis of the test substance.

Pyroxsulam was not evaluated by Protocol A Section 401 DL1, as pyroxsulam is not an N-methylcarbamate. Pyroxsulam was determined to be non-fluorescent according to procedures outlined in Section 401 DL2 of Protocol A. Pyroxsulam was detected and quantitated successfully using non-chemical specific GC modules DG-1 and DG-13, but not DG-18, as outlined in Protocol C. Module DG-15, specific for sulfur compounds, and modules DG-5 and DG-17, specific for nitrogen compounds, were unsuitable for the detection and quantitation of pyroxsulam. Pyroxsulam was determined to be insoluble in solvents necessary for testing with Protocols D, E, and F. When tested according to the parameters detailed in Protocol G, pyroxsulam was chromatographable, but not quantifiable.

*Conclusions*. The submitted multiresidue method testing data for pyroxsulam are acceptable. These data indicate that pyroxsulam cannot be quantified by the FDA PAM I multiresidue methods. The data will be forwarded to FDA for further evaluation.

European Union Multiresidue Method

DER Reference: 46908315.der.doc

In addition, a multi-residue enforcement method for the determination of pyroxsulam in plant materials, animal commodities, soil, and body fluids was developed based on the Modular Multi Residue Enforcement Method L 00.00-34 of the Official Collection of Test Methods (§35 LMBG), which is based on European Multi-Residue Analytical Method DFG S19. Only the components of the method relating to the analysis of plant materials and animal commodities have been included in this summary.

Extraction Module E1 of the multi-residue enforcement method was adapted and used for the preparation of plant (tomato, orange, rape seeds) and animal commodity (whole milk, whole egg, bovine meat and liver) samples. Samples were homogenized and extracted with acetone:water. Sodium chloride was added to the extract which was subsequently partitioned with ethyl acetate/cyclohexane. The phases were allowed to separate and the upper organic phase was filtered and concentrated. Ethyl acetate was added to the residue. Sodium sulfate/sodium

chloride and cyclohexane were added to the extract prior to gel permeation chromatography (GPC) clean-up, where necessary.

Extraction Module E2 was applied to the preparation of wheat grain, and Extraction Module E3 was applied to the preparation of orange samples during method development. Both methods were similar to Extraction Module E1 apart from minor variations to the extraction procedure and solvent volumes. GPC clean-up was not applied to wheat grain samples. Following method development, Extraction Module 1 was applied to orange samples.

Extraction Module E6 was applied to the analysis of bovine fat. Samples of bovine fat were dissolved in ethyl acetate/cyclohexane.

Extraction Module E7 was assessed for preparation of rape seed (canola) samples during method development. Rape seeds were added to a beaker containing calcium silicate, celite and acetonitrile:acetone. The suspension was homogenized, filtered, and calcium silicate was added. The concentrated residue in the organic phase was dissolved in ethyl acetate/cyclohexane for GPC clean-up. Following method development, Extraction Module E1 was applied to rape seed samples.

Gas chromatography with mass spectrometric detection (GC/MS) is the primary detection technique outlined in the European Multi-Residue Analytical Method DFG S19. The GC/MS methodology was tested and found to be inadequate because of partial decomposition of the analyte and insufficient sensitivity.

Alternative analytical methodology using liquid chromatography with tandem mass spectrometric detection (LC/MS/MS) was successfully applied using two different ion transitions (Q1/Q3 *m/z* 435.1/194.7 and Q1/Q3 *m/z* 435.1/81.9.)

Using the LC/MS/MS methodology, individual recovery values for fortified sample matrices were within the EPA acceptance range of 70-120%, with the exception of a single recovery in whole oranges (67% in a sample fortified at 0.1 mg/kg).

Average recoveries were within the EU acceptance range of 70-110%. The relative standard deviation of replicate recovery measurements did not exceed the level of 20% at or above the LOQ, and interferences were negligible (≤20% of the response of the XDE-742 at the LOQ of 0.1 mg/kg for plant materials, animal commodities, and soils). The LOQ validated for plant and animal matrices is 0.01 mg/kg.

An ILV trial on Method DFG S19 was conducted according to the methodology described in Study No 051001. The ILV was also used to support the stated LOQ of 0.01 mg/kg in representative crops (tomatoes and wheat grain) and animal tissues (milk and ground beef). With the exception of a minor modification for the extraction of mammalian tissues, the ILV was undertaken as per Study ID 051001. Both average and individual recoveries were acceptable, and the LOQ of 0.01 mg/kg in plant and animal matrices was confirmed.

Extraction, cleanup, and separation methodology of Method DFG S19 were found to be suitable, with minor modifications, to the standard modules. Detection using the prescribed GC/MS methodology resulted in a very low sensitivity, which was probably due to degradation of the

compound during injection or analysis on the column. It was concluded that the use of GC/MS according to DFG S19 is not suitable for the analysis of pyroxsulam. Using an LC/MS/MS determination technique within the modular European Multi-residue Analytical Method DFG S19, it was demonstrated that this methodology was highly sensitive and is a specific determination method for the detection and determination of residues of pyroxsulam for enforcement purposes.

*Conclusions*. Adequate PAM I multiresidue methods testing data have been submitted. These data indicate that pyroxsulam residues cannot be determined using the FDA multiresidue methods. Although pyroxsulam is not adequately recovered through the PAM I multiresidue protocols, which are GC based, it is successfully recovered through the German DGF S19 multiresidue method which is LC-MS/MS based.

**860.1380 Storage Stability**

DER Reference: 46908317.der.doc

Samples of wheat commodities from the submitted crop field trials were stored frozen (-20ºC) for up to 6.4 months prior to analysis for pyroxsulam.

In support of the sample storage conditions and durations from the crop field trials, Dow AgroSciences submitted a study investigating the storage stability of pyroxsulam in/on various crop commodities.

Samples of spinach, tomato, potato, soybean, wheat grain, wheat straw, and wheat forage (shoot) were homogenized and spiked with pyroxsulam (prepared in methanol at 5.0 µg/mL) at a level of 0.10 mg/kg and were stored at approximately -20$^{o}$C for 6 months. Under these conditions, residues of pyroxsulam were stable in all crops. The study also reported on freezer storage stability of pyroxsulam, 5-OH-XDE-742, 7-OH-XDE-742, and 6-Cl-7-OH-XDE-742 in soil, but these results are not included in this review.

Method GRM 04.17 was used to analyze residues of pyroxsulam in crop samples. The LOQ is 0.01 ppm and the reported LOD is 0.003 ppm.

The data from this interim report indicate that residues of pyroxsulam are stable at -20$^{o}$C for up to 6 months in spinach, tomato, potato, soybean, as well as in wheat grain, straw, and forage (shoot).

*Conclusions*. The submitted storage stability data are adequate, and support the storage durations and conditions for samples of wheat commodities from the submitted crop field trials. No additional data are required to support the subject petition.

**860.1400 Water, Fish, and Irrigated Crops**

There are no proposed uses that are relevant to this guideline topic.

### 860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

### 860.1480 Meat, Milk, Poultry, and Eggs

There are livestock feedstuffs associated with the proposed use of pyroxsulam on wheat. The maximum dietary burdens of pyroxsulam to livestock, based on reasonably balanced diets, are presented in Table 6. The calculated dietary burdens are 0.063 ppm for beef cattle, 0.050 ppm for dairy cattle, 0.007 ppm for poultry, and 0.005 ppm for swine. In the given calculations, wheat forage makes a significant contribution to the diets of both beef and dairy cattle. In practice, however, wheat hay would be used to a much greater extent than wheat forage (ChemSAC minutes, 11/21/2007). As a result, the actual dietary burdens for beef and dairy cattle would be much lower than those given in Table 6. The values given considerably overestimate the actual pyroxsulam dietary burdens of both beef and dairy cattle.

**Table 6. Calculation of Dietary Burdens of Pyroxsulam Residues to Livestock.**

| Feedstuff | Type[1] | % Dry Matter[2] | % Diet[2] | Recommended Tolerance (ppm) | Dietary Contribution (ppm)[3] |
|---|---|---|---|---|---|
| **Beef Cattle** | | | | | |
| Wheat forage | R | 25 | 25 | 0.06 | 0.060 |
| Wheat, milled byproducts | CC | 88 | 20 | 0.01 | 0.003 |
| Untreated CC | CC | 88 | 40 | N/A | -- |
| Untreated PC | PC | 92 | 15 | N/A | -- |
| TOTAL BURDEN | -- | -- | 100 | -- | **0.063** |
| **Dairy Cattle** | | | | | |
| Wheat forage | R | 25 | 20 | 0.06 | 0.048 |
| Untreated R | R | 40 | 25 | N/A | -- |
| Wheat grain | CC | 89 | 20 | 0.01 | 0.002 |
| Untreated CC | CC | 88 | 20 | N/A | -- |
| Untreated CC | PC | 92 | 15 | N/A | -- |
| TOTAL BURDEN | -- | -- | 100 | -- | **0.050** |
| **Poultry** | | | | | |
| Wheat grain | CC | 88 | 70 | 0.01 | 0.007 |
| Untreated CC | CC | 89 | 10 | N/A | -- |
| Untreated PC | PC | 92 | 20 | N/A | -- |
| TOTAL BURDEN | -- | -- | 100 | -- | **0.007** |
| **Swine** | | | | | |
| Wheat, milled byproducts | CC | 88 | 50 | 0.01 | 0.005 |
| Untreated CC | CC | 88 | 30 | N/A | -- |
| Untreated PC | PC | 92 | 20 | N/A | -- |
| TOTAL BURDEN | -- | -- | 100 | -- | **0.005** |

[1] R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.
[2] OPPTS 860.1000 Table 1 Feedstuffs (draft update October 2006).
[3] Contribution = ([tolerance/% DM] x % diet) for beef and dairy cattle; contribution = ([tolerance] x % diet) for poultry and swine.

No feeding studies were submitted with the subject petition. Dow requested a waiver from the requirement based on the following: (1) the ruminant and poultry metabolism studies indicate that pyroxsulam is rapidly absorbed and excreted by livestock; therefore, residues would not be readily transferred into milk, eggs, or edible tissues; and (2) the estimated dietary burdens for ruminants and poultry were very low in comparison to the feeding levels used in the metabolism studies, suggesting that no detectable residues would be detected in livestock commodities.

The ruminant metabolism study was conducted at an exaggerated rate corresponding to approximately 190-240x the dietary burdens calculated above for beef and dairy cattle, and the poultry metabolism study was conducted at a rate corresponding to approximately 1400x the dietary burden for poultry. The beef and dairy cattle diets were very conservative for the reasons stated above. TRR were 0.025 ppm in goat liver and kidney and 0.031 ppm in milk. In poultry, TRR were ≤0.0047 ppm in eggs and tissues except liver. In liver, TRR were ≤0.019 ppm and residues of pyroxsulam itself were 0.003 ppm. Based on these data, HED concurs that the proposed use of pyroxsulam on wheat is not likely to result in finite residues in livestock commodities.

*Conclusions*. Based on the exaggerated rates used in the livestock metabolism studies (190-240x for ruminants and 1400x for poultry) and the resulting low TRR in milk and edible tissues, HED concludes that there is no reasonable expectation of residues of pyroxsulam in livestock commodities (40 CFR §180.6(a)(3)) as a result of the proposed use on wheat. No feeding studies are required to support the subject petition, and no tolerances are required for livestock commodities.

## 860.1500 Crop Field Trials

DER Reference: 46908319.der.doc
Residue Chemistry Memo dated 10/10/06, D. McNeilly
Minutes of 10/18/06 ChemSAC meeting, 11/9/06

Dow submitted field trial data supporting the use of pyroxsulam on wheat. The results of the wheat field trials are discussed below and are summarized in Table 7. Samples from the submitted wheat crop field trials were analyzed for residues of pyroxsulam, the safener cloquintocet-mexyl, and its metabolite cloquintocet acid. The data for the safener and its metabolite will be addressed under separate review (PP#7E7194).

**Table 7. Summary of Canadian Residue Data from Crop Field Trials with Pyroxsulam.**

| Crop matrix | Total Applic. Rate lb ai/A (g ai/ha) | PHI (days) | Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT[1] | Median | Mean | Std. Dev. |
| **WHEAT (proposed use = 0.013-0.016 lb ai/A total application rate, 60-day PHI)** | | | | | | | | | |
| Pyroxsulam | | | | | | | | | |
| Forage | 0.013-0.014 (14.3-15.6) | 7-14 | 40 | <0.010 | 0.036 | 0.035 | <0.013 | <0.010 | <0.007 |
| Hay | | 28-43 | 40 | <0.010 | <0.010 | <0.010 | <0.010 | <0.010 | - |
| Grain | | 50-110 | 40 | <0.010 | <0.010 | <0.010 | <0.010 | <0.010 | - |
| Straw | | 50-110 | 40 | <0.010 | <0.010 | <0.010 | <0.010 | <0.010 | - |

[1] HAFT = Highest average field trial result.

Twenty wheat trials were conducted in Canada in Zones 5 (2 trials in Ontario), 7 (5 trials in Saskatchewan), 7A (3 trials in Alberta), and 14 (2 trials in Alberta, 4 trials in Manitoba, and 4 trials in Saskatchewan) during the 2005 growing season. At each test location, pyroxsulam was applied once at the 31-33 BBCH stage of growth as the 0.25 lb/gal OD formulation (GF-1674) at 0.013 lb ai/A (15 g ai/ha). The application rate used in the trials is 1x the maximum proposed application rate for the 0.25 lb/gal OD formulation and 0.8x the maximum proposed rate for the 7.5% WDG formulation. The safener cloquintocet-mexyl was added to the spray mixture at 0.8% v/v, and it was applied at 0.040 lb ai/A (45 g ai/ha). Wheat commodities were harvested at PHIs of 7-14 days for forage, 28-43 days for hay, and 50-100 days for grain and straw.

Analytical Method GRM 04.17 was used to analyze residues of pyroxsulam. The reported LOD and LOQ are 0.003 and 0.01 ppm, respectively. Method 04.17 was shown to be an acceptable data gathering method, as the concurrent recoveries of pyroxsulam from all wheat matrices ranged from 80-99% for spiking levels of 0.01-1.50 ppm.

Samples were stored for a maximum of 189 days. Pyroxsulam has been demonstrated to be stable under frozen storage conditions for 180 days. Therefore, no additional storage stability data are required to support the results of the field trial data for wheat.

In the field trials that were performed, maximum residues of pyroxsulam were 0.036 ppm in/on forage harvested at 7-14 DAT, <0.01 ppm in/on hay at 28-43 DAT, and <0.01 ppm in/on grain, and straw at 50-110 DAT. Residue decline data show that pyroxsulam residues decreased in both forage and hay after the day of treatment. The results of the wheat field trials are summarized in Table 7.

*Conclusions*. The submitted wheat field trial data are adequate to satisfy data requirements. The studies adequately reflect the proposed use pattern.

The Agency previously examined Canadian and European field trial data to determine whether residue data from these trials can be used to support U.S. risk assessment and tolerance setting (Memo, D332115, D. McNeilly, 12/19/2007). The Canadian field trial studies were reviewed in detail, but the European field trial studies were not. HED concluded that, for this case only, it was acceptable to make use of the available Canadian and European data to establish tolerances on wheat commodities in the U.S. and to assess risk without requiring additional U.S. trials (Chem SAC meeting minutes, 10/18/2006). The submitted data are adequate for several reasons. (1) Twenty trials were performed in Canada. This number is equal to that recommended in the OPPTS Series 860 Guidelines. (2) Seven of the field trials were performed in NAFTA growing zones that extend into the U.S. (3) The Canadian field trials were performed using the OD formulation. The European field trials were performed using the WDG formulation at a slightly exaggerated rate (0.017 lb ai/A). As a result, field trials were performed using both formulations. (4) Data are available for both wheat and winter wheat. (5) The results of the European field trial data are consistent with the results of the Canadian field trial data. Residues in grain, hay, and straw were below the LOQ of 0.01 ppm in all samples. In the Canadian trials, the highest residue value in forage was 0.036 ppm and in the European trials, the highest residue value was 0.059 ppm. In the Canadian trials, the highest residue value in straw was <0.01 ppm and in the European trials, the highest residue value was 0.022 ppm.

The submitted field trial data support tolerances for residues of pyroxsulam *per se* at the LOQ of 0.01 ppm for wheat hay and wheat grain, a tolerance of 0.03 ppm for wheat straw, and a tolerance of 0.06 ppm for wheat forage. Additional field trials conducted in the U.S. are not required.

**860.1520 Processed Food and Feed**

DER Reference: None
Residue Chemistry Memo dated 10/10/06, D. McNeilly

A wheat processing study was not submitted in support of the subject petition. The Agency previously concluded that a processing study for wheat was not required in consideration of the following: (1) in the wheat metabolism study, residues in wheat grain were very low (ND-0.001 ppm) following application of pyroxsulam at approximately 2x the maximum proposed application rate; and (2) the petitioner reported that exaggerated rate trials are not possible because of phytotoxicity. Residue data for aspirated grain fractions are not required because, under the proposed use pattern, pyroxsulam is to be applied during the vegetative growth stage, prior to the formation of seed heads.

*Conclusions*. No processing data are required to support the subject petition.

**860.1650 Submittal of Analytical Reference Standards**

An analytical standard for pyroxsulam, with an expiration date of May 2009, is currently available in the EPA National Pesticide Standards Repository (electronic communication, Dallas Wright, ACB, 11/13/07).

**860.1850 Confined Accumulation in Rotational Crops**

DER Reference: 46908318.der.doc

The purpose of this study was to characterize the radioactive residues in the raw agricultural commodities of rotational crops planted 30 days after the application of $^{14}$C-XDE-742.

Applications of $^{14}$C-XDE-742-TP (triazolo-pyrimidine label; TP label) and $^{14}$C-XDE-742-PY (pyridine label; PY label) were made to confined, outdoor plots of sandy loam soil at rates of 0.0161 lb ai/A (18.11 g ai/ha) and 0.0169 lb ai/A (18.92 g ai/ha), respectively. The target application rate was 0.0167 lb ai/A (18.75 g ai/ha; approximately 1x the maximum proposed seasonal application rate for wheat). Soil samples were taken from all plots at the time of application (0 days after treatment, DAT) and immediately prior to planting crops (30 DAT). After ageing the test plots for 30 days, potatoes, lettuce, and wheat were planted in the plots.

Total radioactivity in the soil samples was determined by oxidative combustion followed by liquid scintillation counting (LSC). Assays of the soil at 0 DAT indicate that an average of 76.6% and 82.4% of the TP and PY labeled test material, respectively, had reached the target. In the soil cores collected at planting (30 DAT), an average of 56.7% and 85.8% of the applied TP and PY labeled test material, respectively, remained in the soil. HPLC analysis of the soil at

both 0 and 30 DAT indicate that the majority of the extracted radioactivity is unchanged parent XDE-742. A small proportion of the radioactivity eluted in the same region as the standards for the 5-OH-XDE-742 and/or 7-OH-XDE-742 metabolites.

Total radioactive residues (TRR) in mature plant samples were determined by oxidative combustion followed by LSC. TRR from plant matrices are summarized below. The TRR in crops from the $^{14}$C-XDE-742-PY treatment ranged from 1 to 12 times as high as TRR in crops from the $^{14}$C-XDE-742-TP treatment. TRR were <0.01 mg/kg in all rotational crop matrices from the 30-day plantback interval except potato tops, wheat hay, and wheat straw from the $^{14}$C-XDE-742-PY treatment.

**Table 8 Total Radioactive Residues (TRR) in Potatoes, Lettuce and Wheat.**

| Matrix | Plant-back interval (days) | $^{14}$C-XDE-742-TP | $^{14}$C-XDE-742-PY |
|---|---|---|---|
| | | ppm | ppm |
| Potato tops-mature | 30 | 0.003 | 0.036 |
| Potato tubers-mature | 30 | <LOQ | 0.001 |
| Lettuce-mature | 30 | 0.001 | 0.006 |
| Wheat forage | 30 | 0.001 | 0.002 |
| Wheat hay | 30 | 0.003 | 0.020 |
| Wheat grain | 30 | 0.001 | 0.001 |
| Wheat straw | 30 | 0.006 | 0.023 |

Only potato tops, wheat hay, and wheat straw from the $^{14}$C-XDE-742-PY treatment contained sufficient radioactivity to allow further characterization. Samples were extracted using acetonitrile:water followed by sequential partitioning with a range of organic solvents. Selected organic and aqueous phases were analyzed by HPLC. No parent compound was found in any of the plant extracts analyzed. Based on co-chromatography with reference standards, the following metabolites were tentatively identified at ≤0.007 mg/kg in potato tops, wheat hay, and wheat straw: 5-OH-XDE-742 in potato tops (at 0.007 mg/kg); 7-OH-XDE-742 in wheat hay and straw (at ≤0.002 mg/kg); XDE-742 cyanosulfonamide in potato tops and wheat hay (at ≤0.005 mg/kg), and 6-Cl-7-OH-XDE-742 in wheat hay (at 0.002 mg/kg). The majority of the TRR (32.1-49.5% TRR, 0.008-0.012 ppm) was accounted for as unidentified metabolites.

The presence of radioactivity in rotational crop samples is evidence that XDE-742 and/or its metabolites will be taken up from the soil and translocated within the plant. Where uptake of XDE-742 occurs, initial metabolism is likely to result in the formation of 5-OH-XDE-742 and 7-OH-XDE-742 metabolites. Also, it is possible that the 5-OH-XDE-742 and 7-OH-XDE-742 metabolites, present in the soil at the time of planting, could be taken up from soil into plant tissue. Conversion of the 7-OH-XDE-742 to the 6-Cl-7-OH-XDE-742 metabolite is proposed as an additional transformation. The presence of the XDE-742 cyanosulfonamide metabolite in some samples indicates that cleavage of the parent and/or its hydroxylated metabolites occurred across the triazolo ring. It is likely that the XDE-742 cyanosulfonamide metabolite is further degraded to aqueous soluble or non-extractable residues. The petitioner also noted that metabolites 6-Cl-7-OH-XDE-742 and XDE-742 cyanosulfonamide were identified in a detailed study of aerobic degradation.

It is concluded that the metabolites of XDE-742 may be present at low levels in raw agricultural commodities from rotational crops planted 30 days after direct application of XDE-742 to soil at a rate of 0.0167 lb ai/A (18.75 g ai/ha). Residues of unchanged XDE-742 are not anticipated in

harvested commodities. No individual metabolites are expected to be present at a level greater than 0.01 ppm.

*Conclusions*. The submitted confined rotational crop study is adequate to satisfy data requirements for the present use on wheat. Based on the submitted study, the nature of the residue in rotational crops is adequately understood. For the purposes of this petition, the residue of concern is the parent compound, pyroxsulam. Two metabolites, XDE-742-cyanosulfonamide and 6-Cl-7-OH-XDE-742, that had not previously been identified in primary crops were found at low levels (≤0.005 ppm) in rotational crops; these metabolites were previously identified as soil metabolites in an aerobic degradation study.

The Agency concludes that field rotational crop studies are not needed at this time. For purposes of the proposed use on wheat, the available data support the proposed crop rotation intervals:

- 1 month for wheat;
- 9 months for barley, field corn, grasses, millet, oats, popcorn, seed corn, sweet corn, sorghum, alfalfa, canola, chickpea, soybean, dry bean, field pea, flax, lentil, mustard, potato, safflower, sugar beet, sunflower
- 12 months for other crops not listed.

**860.1900 Field Accumulation in Rotational Crops**

DER Reference: None

No field rotational crop data have been submitted. Based on the submitted confined rotational crop study, HED has concluded that no rotational crop tolerances are needed, and no field rotational crop studies are required to support the proposed plantback intervals.

*Conclusions*. No field rotational crop data are required to support the proposed use on wheat.

**860.1550 Proposed Tolerances**

HED has determined that the terminal residue of concern in wheat is pyroxsulam *per se* (Memo, D335496, D. Dotson, 12/19/2007). The tolerance expression proposed in the tolerance petition is appropriate.

Adequate field trial data for wheat are available reflecting the proposed use pattern. The available field trial data support a tolerance for residues of pyroxsulam in/on wheat forage at 0.06 ppm, wheat straw at 0.03 ppm, and both wheat grain and wheat hay at 0.01 ppm. HED's tolerance generator for NAFTA-harmonized tolerances was not used to determine tolerance levels for wheat commodities because >60% of the residue values for each commodity were below the LOQ. The recommended tolerances for wheat commodities are presented in Table 9.

Based on the results of the wheat metabolism study and crop field trials, tolerances for wheat processed commodities and aspirated grain fractions are not required.

No Codex, Canadian, or Mexican MRLs have been established for pyroxsulam.

| **Table 9. Tolerance Summary for Pyroxsulam.** | | | |
|---|---|---|---|
| Commodity | Proposed Tolerance (ppm) | Recommended Tolerance (ppm) | Comments; *Correct Commodity Definition* |
| Wheat, forage | 0.04 | 0.06 | |
| Wheat, grain | 0.01 | 0.01 | |
| Wheat, hay | 0.01 | 0.01 | |
| Wheat, straw | 0.01 | 0.03 | |

## References

Pyroxsulam: Use of Residue Data from Canadian and E.U. Residue Field Trials for Risk Assessment and Tolerance Setting for a Low Use Rate Herbicide, Pyroxsulam, D332115, D. McNeilly, 12/19/07.

Minutes of 10/18/06 ChemSAC Meeting, HED's Chemistry Science Advisory Council, 11/9/06.

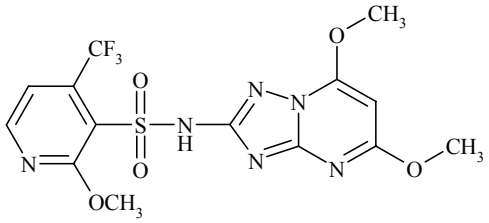
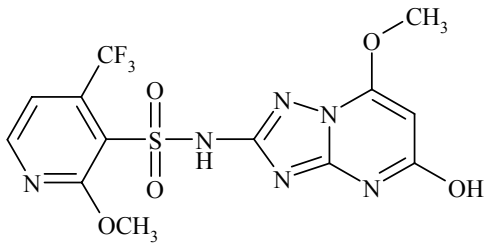
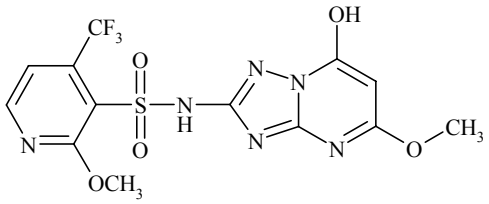
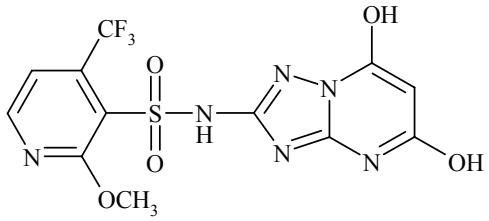
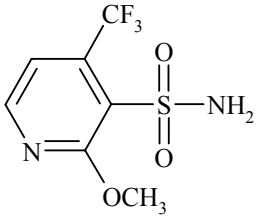
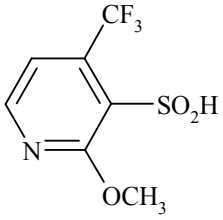
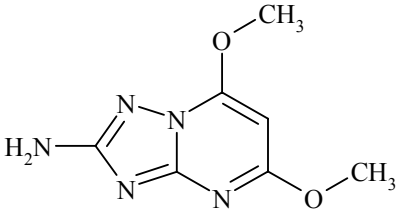
Attachments:
1. International Residue Limit Status Sheet
2. Chemical Names and Structures of Pyroxsulam and Metabolites

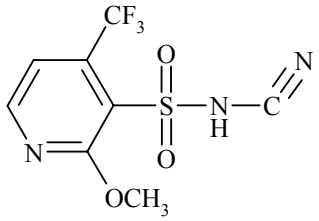
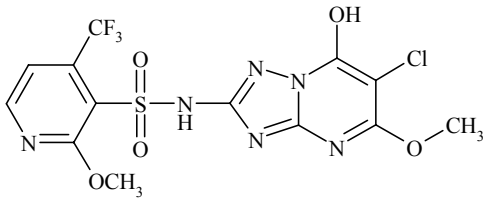
Attachment 1

# INTERNATIONAL RESIDUE LIMIT STATUS

| | | | |
|---|---|---|---|
| Chemical Name: N-(5,7-dimethoxy[1,2,4]triazolol[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide | Common Name: Pyroxsulam | X Proposed tolerance<br>9 Reevaluated tolerance<br>9 Other | Date: 10/17/07 |

| | | | |
|---|---|---|---|
| Codex Status (Maximum Residue Limits) | | U. S. Tolerances | |
| X No Codex proposal step 6 or above<br>□No Codex proposal step 6 or above for the crops requested | | Petition Number: PP#6E7101<br>DP#: D344313<br>Other Identifier: | |
| Residue definition (step 8/CXL): N/A | | Reviewer/Branch: Christina Swartz/Doug Dotson/RAB2 | |
| | | Residue definition: Pyroxsulam *per se* | |
| Crop (s) | MRL (mg/kg) | Crop(s) | Tolerance (ppm) |
| | | Wheat, forage | 0.04 |
| | | Wheat, grain | 0.01 |
| | | Wheat, hay | 0.01 |
| | | Wheat, straw | 0.01 |
| Limits for Canada | | Limits for Mexico | |
| X No Limits<br>□ No Limits for the crops requested | | X No Limits<br>□No Limits for the crops requested | |
| Residue definition: N/A | | Residue definition: N/A | |
| Crop(s) | MRL (mg/kg) | Crop(s) | MRL (mg/kg) |
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |
| Notes/Special Instructions: S. Funk, 10/17/2007. | | | |

| **ATTACHMENT 2. Chemical Names and Structures of Pyroxsulam and Metabolites.** | | |
|---|---|---|
| Common name; Company code | Chemical name | Chemical structure |
| Pyroxsulam; XDE-742 | *N*-(5,7-dimethoxy[1,2,4]triazolol-[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridine-sulfonamide |  |
| 5-OH-XDE-742 | *N*-(5-hydroxy-7-methoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide |  |
| 7-OH-XDE-742 | *N*-(7-hydroxy-5-methoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide |  |
| 5,7-di-OH-XDE-742 | *N*-(5,7-dihydroxy[1,2,4]triazolo[1,5-*a*]pyridimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide |  |
| XDE-742 sulfonamide | 2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide |  |
| XDE-742 sulfonic acid | 2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonic acid |  |
| ADTP | 5,7-dimethoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-amine |  |

| **ATTACHMENT 2. Chemical Names and Structures of Pyroxsulam and Metabolites.** | | |
|---|---|---|
| Common name; Company code | Chemical name | Chemical structure |
| XDE-742 cyanosulfonamide | *N*-cyano-2-methoxy-4-(trifluoromethyl)-pyridine-3-sulfonamide |  |
| 6-Cl-7-OH-XDE-742 | *N*-(6-chloro-7-hydroxy-5-methoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-pyridine-3-sulfonamide |  |