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OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: April 19, 2006

SUBJECT: Metconazole Human Health Risk Assessments for the Section 18 Request for Control of Soybean Rust on Soybeans

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INTRODUCTION

The Departments of Agriculture of the states of Minnesota (05MN15) and South Dakota (05SD05) have petitioned the Agency requesting a quarantine exemption for metconazole to control soybean rust on soybeans, under Section 18 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). In conjunction with the petition, the petitioners have requested the establishment of temporary tolerances for residues of metconazole on soybeans. The Asian soybean rust pathogen (caused by *Phakopsora pachyrhizi*) has been identified in the continental United States. As a designated biosecurity threat, it is important that control measures be available. Under the proposed use, soybeans could be treated upon the official confirmed identification of soybean rust in the United States. The exemption request is for use of

metconazole alone (Caramba™ fungicide), or in a premix co-pack package with the systemic strobilurin fungicide pyraclostrobin (i.e., as a Headline® Caramba™ Copack fungicide). Acute and chronic dietary risk assessments were conducted, incorporating food and water exposures. In addition, risks to occupational handlers and re-entry workers using metconazole were evaluated.

EXECUTIVE SUMMARY

General Information

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl) cyclopentanol] is an unregistered systemic triazole fungicide. The proposed Section 18 use is to control Asian soybean rust (caused by *Phakopsora pachyrhizi*) on soybeans as a systemic eradicant and a protectant. The petitioner states that metconazole has post-infection activity that can stop pathogen establishment in the early phases of disease development. This is the first Section 18 request for this use. The proposed program will entail application of 420,000 gallons (maximum) of Caramba™ 90 SL [315,000 lb metconazole ai] on 5.6 million acres in South Dakota (primarily in eastern SD) and Minnesota (primarily in southern MN) during 2006. The proposal is for one or two applications of metconazole per season at a maximum application rate of 0.056 lb ai/acre/application. The exemption request is for use of metconazole alone (Caramba™ 90 SL fungicide) or in a premix co-pack package with the systemic strobilurin fungicide pyraclostrobin (i.e., as a Headline® Caramba™ Copack fungicide). Tolerances for pyraclostrobin are established under 40 CFR 180.582 on soybean commodities. The proposed spray intervals between applications are 10 to 21 days on Caramba™ and Headline® Caramba™ Copack fungicide labels; although both labels allow for earlier second applications if monitoring shows disease development or if conditions are conducive for disease infection. The Caramba™ fungicide label and the Headline® Caramba™ Copack fungicide label each propose a pre-harvest interval (PHI) of 21 days, restricted entry interval (REI) of 12 hours, and a livestock feeding restriction for soybean forage and hay.

Toxicology/Hazard Assessment

The toxicology database for metconazole is essentially complete. Extensive details of the toxicology of metconazole are available in the HED memo, "Metconazole: Human Health Risk Assessment for Proposed tolerance on Imported Bananas, D308794, concurrent, B. O'Keefe. The data are sufficient for endpoint selection for exposure risk assessment scenarios and for FQPA evaluation.

Metconazole is a member of the triazole class of systemic fungicides and acts primarily as an inhibitor of ergosterol biosynthesis. Like other conazoles, the primary target organ in mammalian toxicity studies is the liver. Other toxicological effects are seen on the blood, ovaries, and body weight. Developmental studies in rats and rabbits show some evidence of developmental effects (skeletal variations, post-implantation loss, reduction in fetal body weight), but only at dose levels that are maternally toxic.

The Cancer Assessment Review Committee (CARC) for metconazole met on November 2, 2005 (memo, J. Kidwell, TXR# 0054211, 4/14/06). Metconazole is "Not Likely to be

Carcinogenic to Humans" based on convincing evidence that carcinogenic effects are not likely below a defined dose range. A non-genotoxic mode of action for mouse liver tumors was established. No quantification is required.

There are adequate data in the metconazole database to characterize the potential for pre-natal or post-natal risks to infants and children. These data do not suggest that pups are more susceptible, and thus there are no residual uncertainties. The Toxicology Branch and RAB3 toxicity team recommended that the special FQPA factor be reduced to 1X. The metconazole risk assessment team evaluated the quality of the exposure data, and based on these data, also recommended that the special FQPA SF be reduced to 1X.

Appropriate endpoints protective for the most sensitive effects were identified for the acute and chronic dietary exposure scenarios, and for occupational and residential scenarios following dermal and inhalation exposures.

The acute population-adjusted dose (aPAD) for females age 13-49 years is 0.12 mg/kg/day, based on increases in skeletal variations in a developmental toxicity study in rats (NOAEL of 12 mg/kg/day; LOAEL of 30 mg/kg/day). An aPAD was not determined for the general population, including all infants, because an appropriate dose/endpoint attributable to a single dose was not observed in the available oral toxicity studies reviewed.

The chronic population-adjusted dose (cPAD) for all populations is 0.04 mg/kg/day, based on increased liver weights and associated hepatocellular lipid vacuolation and centrilobular hypertrophy in males and females, plus increased spleen weights in females, in a chronic oral toxicity study in rats (NOAEL of 4.3 mg/kg/day; LOAEL of 13.1 mg/kg/day).

Short-term dermal and inhalation exposures were assessed based on effects seen in a 28-day oral toxicity study in rats; i.e., decreased body weight, increased liver and kidney weights, hepatocellular vacuolation and hypertrophy (NOAEL of 9.1 mg/kg/day; LOAEL of 90.5 mg/kg/day). For dermal exposures a 5% dermal absorption factor is applied.

Intermediate-term dermal and inhalation exposures were assessed based on effects seen in a 90-day oral toxicity study in rats; i.e., increased hepatocellular fatty vacuolation and increased spleen weight in females (NOAEL of 6.4 mg/kg/day; LOAEL of 19.2 mg/kg/day). For dermal exposures a 5% dermal absorption factor is applied.

Dietary Exposure & Risk

No tolerances have been established for metconazole. The first food use for metconazole, which proposes a tolerance of 0.10 ppm on imported bananas, is under concurrent review in a separate document (HED memo, "Metconazole: Human Health Risk Assessment for Proposed tolerance on Imported Bananas, D308794, concurrent, B. O'Keefe).

Acute and chronic dietary (food + drinking water) exposure analyses were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, version 2.03), which uses food consumption data from the United States Department of Agriculture's (USDA's) Continuing

Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analyses were performed to support this Section 18 request for metconazole on soybeans and for the use on bananas imported into the U.S.

Acute Dietary Exposure Results and Characterization

An acute dietary exposure assessment was conducted for all proposed food uses (soybeans and imported bananas) and drinking water. Except for water, a conservative (Tier 1) assessment was conducted. The residue levels used in the assessment were the proposed/recommended tolerance levels. The assessment used 100% crop treated.

Estimated concentrations of metconazole in drinking water from use on soybeans were provided by EFED and incorporated directly into the acute assessment. A Tier II drinking water assessment for the proposed use on soybeans was performed using PRZM/EXAMS modeling with index reservoir (IR) scenarios and percent cropped area (PCA) adjustment factors.

The acute (food + drinking water) exposure to metconazole is below HED's level of concern for females 13-49 years old (exposure estimate at the 95th percentile was 0.0013 mg/kg/day and utilizes 1% of the aPAD).

Chronic Dietary Exposure & Risk

A chronic dietary exposure assessment was conducted for all proposed food uses (soybeans and imported bananas) and drinking water. Except for water, a conservative (Tier 1) assessment was conducted. The residue levels used in the assessment were the proposed/recommended tolerance levels. The assessment used 100% crop treated.

Estimated concentrations of metconazole in drinking water from use on soybeans were provided by EFED and incorporated directly into the chronic dietary assessment. A Tier II drinking water assessment for the proposed use on soybeans was performed using PRZM/EXAMS modeling with index reservoir (IR) scenarios and percent cropped area (PCA) adjustment factors.

The chronic (food + drinking water) exposure to metconazole is below HED's level of concern for the general U.S. population and all population subgroups. The chronic dietary exposure estimates utilize 2% of the cPAD for the U.S. population and 5% of the cPAD for children 1-2 years old, the most highly exposed population subgroup.

Risk from Residues in Water

The Agency used the Screening Concentration in Ground Water (SCI-GROW) model to calculate metconazole estimated drinking water concentrations (EDWCs) in ground water and the Pesticide Root Zone Model/Exposure Analysis Model System (PRZM/EXAMS) to calculate EDWCs in surface water. The assessment was based on the proposed use pattern of metconazole on soybeans under this Section 18. Since the use on bananas is on imported bananas, the use on bananas will not contribute to residues in water in the U.S.

The values used in the dietary risk assessment were provided by the Environmental Fate and Effects Division (EFED) in the following memo: *Tier II Drinking Water Assessment for the Use of Metconazole on Soybean* (DP Barcode 319662, Amer Al-Mudallal, 7/28/05). A Tier II drinking water assessment for the proposed use on soybeans was performed using PRZM/EXAMS modeling. Estimated concentrations of metconazole in drinking water from use on soybeans were provided by EFED and incorporated directly into the acute and chronic assessments. Water residues were incorporated in the DEEM-FCID™ in the food categories "water, direct, all sources" and "water, indirect, all sources."

Based on PRZM/EXAMS, the EDWCs of metconazole in surface water are 1.57 µg/L and 0.48 µg/L for acute and chronic (non-cancer) exposures, respectively. For chronic/cancer assessments, the 30-year average from PRZM/EXAMS is 0.34 µg/L. The EDWC for both acute and chronic exposures is estimated as 0.04 µg/L for ground water using the SCI-GROW model.

Non-Dietary Non-Occupational (Residential) Exposure & Risk

There are no non-dietary, non-occupational (residential) uses registered or proposed for metconazole, and therefore, no such exposures are expected from the proposed use of this Section 18 request on soybeans.

Aggregate Risk

Aggregate exposure assessments were perfomed in the dietary section of this document, i.e., for acute and chronic aggregate dietary exposure (food + drinking water). All potential exposure pathways were assessed in the aggregate risk assessment. Dietary (food and drinking water) exposures were considered, as necessary, because there is a potential for individuals to be exposed concurrently through these routes. Because there are no existing or proposed residential uses of metconazole, short- and intermediate-term aggregate risk assessments are not needed.

Occupational Exposure and Risk

Handler Risk: Short- and intermediate-term dermal and inhalation exposures are anticipated for occupational handlers mixing, loading, and applying metconazole to soybean fields. For all mixers, loaders, and applicators, the combined MOEs for short- and intermediate-term exposures range from 2,800 to 53,000, and therefore, do not exceed HED's level of concern, i.e. all MOEs ≥ 100.

Postapplication Risk: This proposed Section 18 use on soybeans involves foliar applications; therefore, there is a potential for short- and intermediate-term dermal exposure to workers entering metconazole-treated areas to perform a variety of agricultural/occupational tasks, and a risk assessment is required. The risk estimates from these exposures do not exceed HED's level of concern (i.e. MOEs ≥ 100) on the day on application. The restricted entry interval (REI) on the proposed label is 12 hours, which is compliance with the worker protection standard (WPS) based on acute toxicity category findings.

Conclusions

For the proposed Section 18 use of metconazole on soybeans to control soybean rust, the exposure and risk estimates for occupational handlers that mix, load, or apply metconazole do not exceed HED's level of concern. Additionally, postapplication exposures do not exceed HED's level of concern. As per WPS rules, workers who re-enter treated fields during the restricted entry interval should wear the same PPE that occupational handlers are required to wear.

Provided the label is revised as indicated below, HED has no objection to the issuance of a Section 18 exemption for the use of metconazole on soybeans in the States of South Dakota and Minnesota. Time-limited tolerances for residues of metconazole should be established to support this Section 18 exemption as follows:

Commodity	ppm
soybean, seed	0.10
aspirated grain fractions	1.0
soybean, meal	0.25
soybean, hulls	1.2
soybean, refined oil	1.2
meat, fat, and meat byproducts of cattle, goat, hog, horse, poultry and sheep	0.02
milk	0.02
egg	0.02

Since feeding of soybean forage and hay to livestock is restricted by the proposed labels, livestock feed items associated with the proposed use on soybeans are seed, aspirated grain fractions, meal, and hulls.

The rotational crop restriction regarding crops not specified on the labels should be revised to read as follows: "Any crop not specified on the labels may be planted into treated areas as follows: 120 days after the last application for root crops and leafy vegetables and 12 months after the last application for all other crops."

DETAILED DISCUSSION

Toxicology Considerations

Hazard Assessment

The toxicology database for metconazole is essentially complete. Extensive details of the toxicology of metconazole are available in the HED memo, "Metconazole: Human Health Risk Assessment for Proposed Tolerance on Imported Bananas", D308794, concurrent, B. O'Keefe. The only data gap is for a two-generation reproduction study with the metconazole 85:15 (cis:trans) isomer mixture. A two-generation reproduction study using cis (>95% cis) metconazole was submitted and is being used in this assessment. The toxicological database for

the cis and cis/trans technicals show similar toxicological profiles and so the two-generation reproduction study with the cis-only isomer should be reasonably sufficient to bridge the data gap until the new study is submitted. The data are sufficient for endpoint selection for exposure risk assessment scenarios and for FQPA evaluation.

Metconazole is a member of the triazole class of systemic fungicides and acts primarily as an inhibitor of ergosterol biosynthesis. Like other conazoles, the primary target organ in mammalian toxicity studies is the liver. Other toxicological effects seen are effects on the blood, ovaries, and body weight. Developmental studies in rats and rabbits show some evidence of developmental effects (skeletal variations, post-implantation loss, reduction in fetal body weight), but only at dose levels that are maternally toxic.

Metabolism studies in rats indicated that metconazole is excreted primarily in the feces with greater than 90% of the administered dose excreted by three days postdosing. Biliary excretion is the major route of elimination. In an experiment in which the triazole ring was labeled, a single high (200 mg/kg) dose of metconazole showed approximately 5% was excreted as free triazole.

The liver is the primary target organ in the mouse, rat and dog following oral exposure to metconazole via subchronic or chronic exposure durations. Other major critical effects observed in oral studies were decreased body weight, decreased body weight gains, and blood (reductions in erythrocyte and/or platelet parameters) effects in the mouse, rat, dog and/or rabbit. Splenic effects including increased spleen weight and hyperplasia were observed in the mouse, rat and dog at dose levels where liver effects were also observed. In dogs, lenticular degeneration (cataracts) was observed at the highest dose tested. At high dietary levels, there is evidence that metconazole is a gastrointestinal irritant in the dog.

The proposed mode of action for metconazole is via inhibition of sterol (ergosterol) biosynthesis in fungi which is consistent with altered cholesterol levels observed in mice and rats. The critical effects are considered relevant to humans because they were observed in at least three species. There was no enhanced susceptibility to the fetuses of rats or rabbits following *in utero* exposure to cis/trans metconazole. In the developmental toxicity study in rats, skeletal variations (predominantly lumbar ribs) occurred in the presence of maternal toxicity (decreased body weight gains). In the prenatal developmental toxicity study in rabbits, developmental effects (increased post-implantation loss and reduced fetal body weights) were observed at the same dose that caused maternal toxicity (decreased body weight gains, reduced food consumption and alterations in hematology parameters). In the two-generation reproduction study in rats with cis metconazole, offspring toxicity (reduced fetal body weights in F1 and F2 offspring) were observed only at the highest tested dose which also resulted in evidence of parental toxicity (reduced parental body weight gains and increased ovarian weight). The chemical is non-genotoxic and not likely to be carcinogenic below a defined dose range based on bioassays in the rat and the mouse combined with a lack of *in vitro* or *in vivo* mutagenicity. The CARC for metconazole met on November 2, 2005 (TXR# 0054211, 4/14/06, J.Kidwell). Metconazole did not demonstrate the potential for neurotoxicity in the four species (mouse, rat, dog and rabbit) tested. NOAELs/LOAELs are well characterized and are used as endpoints for appropriate risk assessments.

Dose-Response

Appropriate endpoints protective for the most sensitive effects were identified for the acute and chronic dietary exposure scenarios, and for occupational and residential exposure scenarios following dermal and inhalation exposures. The following key studies were chosen from the hazard assessment, and used to select endpoints: developmental study in rats (acute dietary exposure scenario for females 13-49 years old); chronic rat study (chronic dietary exposure scenario for the general population and long-term dermal and inhalation occupational and residential postapplication scenarios); 28-day study in rats (incidental oral [short-term] and dermal and inhalation short-term occupational and residential postapplication scenarios); and 90-day study in rats (incidental oral [intermediate-term] and dermal and inhalation intermediate-term occupational and residential post-application scenarios).

The only study in which an effect of concern could be observed following a single dose was the developmental study in rats. This study showed an increase in skeletal variations beginning at a dose of 30 mg/kg/day (LOAEL) which increased in incidence and severity at the highest dose tested (75 mg/kg/day). The NOAEL of 12 mg/kg/day was used as the hazard endpoint of concern following a single, oral dose. Available subchronic and chronic data (all oral studies – 28-day [rat]; 90-day [rat, mouse, dog]; two-generation study [rat]; chronic [rat, dog]; and carcinogenicity studies [rat, mouse]) all show the liver, spleen, kidney, and blood as target organs. These effects were observed in all species and at approximately the same dose in all species. The 28-day LOAEL of 90.5 mg/kg/day shows that liver and kidney damage occurs within a short time frame. Although the liver weight increase and associated histopathology (hypertrophy and vacuolation) and changes in serum enzymes associated with liver changes may be indicative of an adaptive response, the sustained exposures in the 90-day, chronic, and cancer studies show that these effects persist with increasing exposure: LOAELs of 19.2 mg/kg/day [rat] and 50.5 mg/kg/day [mouse] in the 90-day studies; 13.1 mg/kg/day [rat] and 37 mg/kg/day [dog] in the chronic studies; and 13.8 mg/kg/day [rat] and 58.1 mg/kg/day [mouse] in the cancer studies. Importantly, other effects are also seen at these LOAELs: effects on the spleen (rats and mice) and the kidney (rats).

Table 1 Acute Toxicity Profile - Metconazole Test Substance (cis:trans/cis only)

Guideline No.	Study Type	MRID(s)	Results	Toxicity Category
870.1100	Acute oral mouse (cis:trans)	44721512	LD_{50} = 566 mg/kg M/F	III
870.1100	Acute oral rat (cis:trans)	44721512	LD_{50} = 660 mg/kg M/F	III
870.1100	Acute oral rat (cis only)	44721513	LD_{50} = 1459 mg/kg M/F	III
870.1200	Acute dermal rat (cis only)	44721513	LD_{50} > 2000 mg/kg M/F	III
870.1200	Acute dermal rat (cis:trans)	44721512	LD_{50} > 2000 mg/kg M/F	III
870.1200	Acute dermal rabbit (cis:trans)	44721512	LD_{50} > 2000 mg/kg M/F	III
870.2400	Acute eye irritation rat (cis only)	44721513	moderate irritant	III
870.2500	Acute dermal irritation rabbit (cis only)	44721513	non irritant	IV

Table 1 Acute Toxicity Profile - Metconazole Test Substance (cis:trans/cis only)				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.2600	Skin sensitization guinea pig (cis only)	44721513	non sensitizer	-

Table 2 Summary of Toxicological Doses and Endpoints for Metconazole for Use in Human Risk Assessments			
Exposure/ Scenario	**Dose Used in Risk Assessment, Interspecies, Intraspecies and any Traditional UF**	**Special FQPA SF and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (females 13-49 years of age)	NOAEL= 12 mg/kg/day UF = 100 Acute RfD = 0.12 mg/kg/day	Special FQPA SF = 1X aPAD = 0.12 mg/kg/day	**Developmental toxicity study in rats**: LOAEL= 30 mg/kg/day based on increases in skeletal variations.
Acute Dietary (General population including infants and children)	An appropriate dose/endpoint attributable to a single dose was not observed in the available oral toxicity studies reviewed.		
Chronic Dietary (All populations)	NOAEL= 4.3 mg/kg/day UF = 100 Chronic RfD = 0.04 mg/kg/day	Special FQPA SF = 1X cPAD = 0.04 mg/kg/day	**Chronic oral toxicity study in rats**: LOAEL = 13.1 mg/kg/day based on increased liver (M) weights and associated hepatocellular lipid vacuolation (M) and centrilobular hypertrophy(M). Same effects seen in F at 54 mg/kg/day, plus increased spleen wt.
Incidental Oral Short-Term (1 - 30 days)	NOAEL= 9.1 mg/kg/day UF= 100	LOC for MOE = 100	**28-Day oral toxicity study in rats:** LOAEL = 90.5 mg/kg/day based on decreased body weight (M), increased liver and kidney weight and hepatocellular hypertrophy and vacuolation (M/F).
Incidental Oral Intermediate-Term (1 - 6 months)	NOAEL= 6.4 mg/kg/day UF= 100	LOC for MOE = 100	**90-Day oral toxicity study in rats:** LOAEL = 19.2 based on increased spleen wt (F) and hepatic vacuolation (M).
Dermal Short-Term (1 - 30 days)	NOAEL= 9.1 mg/kg/day UF= 100 Dermal absorption rate= 5%	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	**28-Day oral toxicity study in rats:** LOAEL = 90.5 mg/kg/day based on decreased body weight (M), increased liver and kidney weight and hepatocellular hypertrophy and vacuolation (M/F).

Table 2 Summary of Toxicological Doses and Endpoints for Metconazole for Use in Human Risk Assessments

Exposure/ Scenario	Dose Used in Risk Assessment, Interspecies, Intraspecies and any Traditional UF	Special FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal Intermediate-Term (1 - 6 months)	NOAEL= 6.4 mg/kg/day UF= 100 Dermal absorption rate= 5%	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	**90-Day oral toxicity study in rats:** LOAEL = 19.2 mg/kg/day based on increased spleen wt (F) and hepatic vacuolation (M).
Dermal Long-Term (> 6 months)	NOAEL= 4.3 mg/kg/day UF= 100 Dermal absorption rate= 5%	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	**Chronic oral toxicity study in rats:** LOAEL = 13.1 mg/kg/day based on increased liver (M) weights and associated hepatocellular lipid vacuolation (M) and centrilobular hypertrophy(M). Same effects seen in F at 54 mg/kg/day, plus increased spleen wt.
Inhalation Short-Term (1 - 30 days)	NOAEL= 9.1 mg/kg/day UF= 100 Inhalation absorption rate =100%	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	**28-Day oral toxicity study in rats:** LOAEL = 90.5 mg/kg/day based on decreased body weight (M), increased liver and kidney weight and hepatocellular hypertrophy and vacuolation (M/F).
Inhalation Intermediate-Term (1 - 6 months)	NOAEL= 6.4 mg/kg/day UF= 100 Inhalation absorption rate =100%	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	**90-Day oral toxicity study in rats:** LOAEL = 19.2 mg/kg/day based on increased spleen wt (F) and hepatic vacuolation (M).
Inhalation Long-Term (> 6 months)	NOAEL= 4.3 mg/kg/day UF= 100 Inhalation absorption rate =100%	LOC for MOE = 100 Residential LOC for MOE = 100 Occupational	**Chronic oral toxicity study in rats:** LOAEL = 13.1 mg/kg/day based on increased liver (M) weights and associated hepatocellular lipid vacuolation (M) and centrilobular hypertrophy(M). Same effects seen in F at 54 mg/kg/day, plus increased spleen wt.
Cancer (oral, dermal, inhalation)	**Classification: "Not Likely to be Carcinogenic to Humans"**		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

Recommendation for the FQPA Safety Factor

There are adequate data in the metconazole toxicology database to characterize the potential for pre-natal or post-natal risks to infants and children: a two-generation reproduction study in rats (cis-only isomer; one with the cis/trans mixture has been completed and will be submitted in the near future); a developmental study in rats; and several developmental studies with rabbits. The effects seen in these studies do not suggest that pups are more susceptible: pup effects were only seen in the presence of maternal toxicity and, in general, were of comparable or less severity to the effects observed in adults. Thus, there are no residual uncertainties and the Toxicology Branch and RAB3 toxicity team recommended that the special FQPA factor be reduced to 1X.

The metconazole risk assessment team evaluated the quality of the exposure data, and based on these data, also recommended that the special FQPA SF be reduced to 1X. These recommendations are based on the following:

> The acute and chronic dietary assessment consisted of a Tier I food exposure analysis and Tier 2 drinking water exposure analysis. For the food portion of the dietary assessment, the residue levels used in the assessment for bananas and soybeans were the proposed/recommended tolerance levels. For bananas, the recommended tolerance is the method LOQ; however, residues were all less than the LOQ of the method. Tolerances in soybean commodities were based on the maximum reported residues and theoretical processing factors. For the Section 18 on soybeans, theoretical processing factors were used since no soybean processing study was available. The assessments used 100% crop treated. Although not needed at this time, HED could refine the exposure and risk estimates with the following information: 1) a soybean processing study; 2) projected market share/percent crop treated data; 3) anticipated residue data.
>
> The dietary assessment utilizes Tier II drinking water exposure estimates generated by the PRZM/EXAMS model and its associated modeling parameters (i.e., modeling with index reservoir (IR) scenarios and percent cropped area (PCA) adjustment factors). PRZM/EXAMS is designed to provide health protective, high-end estimates of water concentrations which will not likely be exceeded. These estimated concentrations of metconazole in drinking water from use on soybeans were provided by EFED and incorporated directly into the acute and chronic dietary assessments.

Residue Profile

Metabolism in Plants and Livestock

The nature of the residue in plants and livestock is adequately understood for this Section 18. The residue of concern in soybeans and livestock commodities is metconazole (parent). Although no soybean metabolism data are available, metconazole (parent) was the principle

^{14}C-residue identified in all banana matrices in a banana petition (PP#9E05052) currently under review. In the *Metconazole EU Monograph* (Draft Assessment Report - DAR, April 2004; Belgium, January 2004), parent, triazolylalanine, and triazole acetic acid were found in wheat grain and straw; parent and triazolylalanine were found in canola. Parent is adequate as the residue of concern in livestock commodities because of the low residues expected in livestock commodities as a result of the proposed use.

Analytical Enforcement Methodology

Adequate enforcement methods are available to enforce the tolerance expression. The methods determine metconazole as the *cis*- and *trans*- isomers (CL 354801 and CL 354802, respectively).

For soybean commodities, the data collection method was BASF Analytical Method Number 550/0, an LC/MS/MS method. The method determines metconazole as the *cis*- and *trans*- isomers (CL 354801 and CL 354802, respectively). Adequate recoveries were reported for soybean seed, forage, and hay. The limit of quantitation (LOQ) was 0.005 ppm for the *cis*-isomer + 0.005 ppm for the *trans*-isomer (i.e., 0.01 ppm for combined residues).

For soybean raw agricultural commodities, the enforcement method for the Section 18 is DFG Method S19 (MRID 46665405), a gas chromatography method using nitrogen/phosphorus detection (GC/NPD) and confirmation using mass selective detection (MSD). The LOQ for all matrices is 0.01 ppm for each isomer (0.02 ppm for combined residues).

For livestock commodities, the enforcement method is DFG Method S19, a gas chromatography method using nitrogen/phosphorus detection (GC/NPD) and confirmation using mass selective detection (GC/MSD). Adequate recoveries were reported for meat, fat, milk, and eggs. The limit of quantitation (LOQ) for all matrices was 0.01 ppm for each isomer (0.02 ppm for combined residues).

Magnitude of the Residues

Residues of metconazole are not expected to exceed 0.10 ppm in/on soybean seed, 1.0 ppm in aspirated grain fractions, 0.25 ppm in soybean meal, 1.2 ppm in soybean hulls, and 1.2 ppm in soybean refined oil as a result of this Section 18 use. Time-limited tolerances should be established at these levels.

Secondary residues in livestock commodities are not expected to exceed 0.02 ppm as a result of this Section 18 use. Time-limited tolerances should be established at 0.02 ppm for meat, fat, and meat byproducts of cattle, goat, hog, horse, poultry, and sheep; milk, and egg.

Rotational Crop Restrictions

In the *Metconazole EU Monograph* (Draft Assessment Report - DAR, April 2004; Belgium, January 2004), total radioactive residues (TRR) were determined after two applications of metconazole at the rate of 90 g as/ha/application (0.16 lb ai/A/season) with plantback intervals (PBI's) of 30-31 days and 88 days for both carrots and lettuce and 98-99 days for wheat. Total radioactive residues were <0.01 ppm in carrots and lettuce harvested 90-97 days after the last treatment, in wheat forage harvested 310-336 days after the last treatment, and in wheat grain and straw harvested 415-416 days after the last treatment. These data indicate that the proposed 120-day PBI is adequate for root crops and leafy vegetables but may not be adequate for wheat and other crops.

The rotational crop restriction regarding crops not specified on the labels should be revised to read as follows: "Any crop not specified on the labels may be planted into treated areas as follows: 120 days after the last application for root crops and leafy vegetables and 12 months after the last application for all other crops."

International Residue Limits

No CODEX, Canadian, or Mexican MRLs or tolerances have been established for metconazole on soybeans. Therefore, international harmonization is not an issue at this time.

Dietary Exposure Analysis & Risk Estimates

No metconazole tolerances have been established for any food or feed uses, since metconazole is currently an unregistered active ingredient in the U.S. The first proposed Section 3 food use for metconazole, which proposes a tolerance of 0.10 ppm for metconazole on imported bananas, is under concurrent review. Time-limited tolerances of 0.10 ppm on soybean, seed; and 1.0 ppm on aspirated grain fractions will be established in connection with the proposed Section18 for soybeans. Time-limited tolerances on processed commodities will also be established as follows: 0.25 ppm on soybean, meal; 1.2 ppm on soybean, hulls; 1.2 ppm on soybean, refined oil; and 0.02 ppm on livestock commodities. For purposes of this Section 18 on soybeans, the residue of concern is metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] in crop and livestock commodities.

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the Reference Dose (RfD) divided by the special FQPA Safety Factor. For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD.

Acute and chronic dietary (food + water) assessments were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 2.03), which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The assessments used the proposed/recommended tolerance levels for soybean and banana commodities, based on the maximum residue levels from the field trials. The proposed/recommended tolerances for soybean raw agricultural commodities are 0.10 ppm on soybean seed, 1.0 ppm on aspirated grain fractions, and 0.10 ppm on banana. Residues in/on soybean processed commodities, in the absence of processing studies, were calculated using the maximum theoretical concentration factors (from OPPTS 860.1520, Table 3) of 2.2x for soybean meal, 11.3x for soybean hulls, and 12.0x for refined oil. Based on these theoretical processing factors and a tolerance of 0.10 ppm for soybean seed, residues would not be expected to exceed 0.25 ppm in/on soybean meal, 1.2 ppm in/on hulls, and 1.2 ppm in refined oil. Livestock feed items were used in these assessments to estimate the livestock dietary burdens in order to calculate the residue levels in meat, milk, eggs and poultry. Residues in livestock commodities were thus calculated to be $\leq$0.02 ppm, using the livestock metabolism data described above. The limit of quantitation of the method for livestock commodities was 0.01 ppm for each isomer (0.02 ppm for combined *cis*- and *trans*- isomers). The level of 0.02 ppm was used in the assessment for all livestock commodities.

The acute and chronic (food + water) dietary exposure assessments were conducted for all proposed food uses (soybeans and imported bananas) and drinking water. Except for water, a conservative (Tier 1) assessment was conducted. The residue levels used in the assessment were the proposed/recommended tolerance levels. The assessment used 100% crop treated.

Estimated concentrations of metconazole in drinking water from use on soybeans were provided by EFED and incorporated directly into the acute assessment. A Tier II drinking water assessment for the proposed use on soybeans was performed using PRZM/EXAMS modeling with index reservoir (IR) scenarios and percent cropped area (PCA) adjustment factors.

Acute Dietary Exposure Results and Characterization:

The acute dietary assessment was a conservative assessment as described above. The acute (food + drinking water) exposure to metconazole is below HED's level of concern for females 13-49 years old (exposure estimate at the 95th percentile was 0.0013 mg/kg/day and utilizes 1% of the aPAD). EPA generally has no concern for acute exposures below 100% of the acute PAD. Based on all these considerations, EPA concludes that there is a reasonable certainty that no harm will result to the U.S. adult population from acute aggregate dietary exposure to metconazole residues.

Chronic Dietary Exposure Results and Characterization:

The chronic dietary exposure assessment was a conservative assessment as described above. The chronic dietary (food + drinking water) exposure to metconazole is below HED's level of concern for the general U.S. population and all population subgroups. The chronic

dietary exposure estimates utilize 2% of the cPAD for the general U.S. population and 5% of the cPAD for children 1-2 years old, the most highly exposed population subgroup. EPA generally has no concern for chronic exposures below 100% of the chronic PAD because the chronic PAD represents the level at or below which daily aggregate dietary exposure over a lifetime will not pose appreciable risks to human health. Under current EPA guidelines, non-dietary uses of metconazole do not constitute a chronic exposure scenario, and thus are not a factor in chronic aggregate risk. Based on all these considerations, EPA concludes that there is a reasonable certainty that no harm will result to the U.S. population from chronic aggregate dietary exposure to metconazole residues.

Table 3. Summary of Dietary (Food + Water) Exposure and Risk for Metconazole[a,b]

Population Subgroup	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	not applicable*		0.00076	2	not applicable	not applicable
All Infants (< 1 year old)			0.0018	4		
Children 1-2 years old			**0.0021**	**5**		
Children 3-5 years old			0.0018	4		
Children 6-12 years old			0.0012	3		
Youth 13-19 years old			0.00073	2		
Adults 20-49 years old			0.00057	1		
Adults 50+ years old			0.00048	1		
Females 13-49 years old	**0.0013**	**1**	0.00054	1		

[a] The values for the population with the highest risk for each type of risk assessment are bolded.

[b] Reported to 2 significant figures.

* For the U.S. general population and all other populations other than females 13 -49 years old, an appropriate dose/endpoint attributable to a single dose was not observed in the available oral toxicity studies reviewed.

Cancer Dietary Risk

Metconazole is "Not Likely to be Carcinogenic to Humans" based on convincing evidence that carcinogenic effects are not likely below a defined dose range. A non-genotoxic mode of action for mouse liver tumors was established. No quantification is required.

Non-Dietary Non-Occupational (Residential) Exposure Analysis & Risk Estimates

There are no non-dietary, non-occupational (residential) uses registered or proposed for metconazole, and therefore, no such exposures are expected from the proposed use of this

Section 18 request on soybeans.

Drinking Water Exposure

The Agency used the Screening Concentration in Ground Water (SCI-GROW) model, version 2.2, to calculate metconazole EDWCs in ground water and the Pesticide Root Zone Model/Exposure Analysis Model System (PRZM/EXAMS) to calculate EECs in surface water. The assessment was based on the maximum proposed application rate of 0.056 lbs ai/acre with two applications. The modeling was conducted using three different application intervals (7, 14, and 21 days) to represent the range of intervals stated on the labels. Using the 21 day interval between the two applications produced the highest estimated concentration. This could be attributed to a rain event in the meteorology file occurring immediately after the application date. These results may vary with scenarios using different meteorology files. Although the use of the 21 day interval produced the highest estimated concentration, the difference in concentration was very small (insignificant) versus the use of the 7 day interval.

Based on PRZM/EXAMS, the EDWCs of metconazole in surface water are 1.57 µg/L and 0.48 µg/L for acute and chronic (non-cancer) exposures, respectively. For chronic/cancer assessments, the 30-year average from PRZM/EXAMS is 0.34 µg/L. The EEC for both acute and chronic exposures is estimated as 0.04 µg/L for ground water using the SCI-GROW model.

Aggregate Risk

Aggregate exposure assessments were perfomed in the dietary section of this document, i.e., for acute and chronic aggregate dietary exposure (food + drinking water). All potential exposure pathways were assessed in the aggregate risk assessment. Dietary (food and drinking water) exposures were considered, as necessary, because there is a potential for individuals to be exposed concurrently through these routes. Because there are no existing or proposed residential uses of metconazole, short- and intermediate-term aggregate risk assessments are not needed.

Cumulative Risk

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to metconazole and any other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that metconazole has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

Occupational Exposure & Risk

The potential exposures and associated risks for handlers mixing, loading and applying metconazole to soybeans and postapplication workers re-entering fields were based on the proposed labels. The proposed labels are both liquid formulations, i.e., with metconazole alone (Caramba™ 90 SL fungicide) or in a premix co-pack package with the systemic strobilurin fungicide pyraclostrobin (i.e., as a Headline® Caramba™ Copack fungicide). The proposed labels allow two applications of metconazole at up to 0.056 lb ai per acre per application, with a spray interval of 10 to 21 days, a pre-harvest interval (PHI) of 21 days, and a restricted entry interval (REI) of 12 hours. Applications can be made using ground or aerial application equipment. The total approximate acreage to be treated 2.0 million acres in South Dakota, 3.6 million acres in Minnesota, and potentially 36.9 million acres in the United States.

Handler Exposure & Risk

Short- and intermediate-term dermal and inhalation exposures are anticipated for occupational handlers mixing, loading, and applying metconazole to soybean fields. Lacking specific exposure data for these scenarios, they were assessed using surrogate PHED unit exposure data (version 1.1, 1998). Dermal and inhalation exposures are combined in this assessment, since the toxicological endpoints are the same for short- and intermediate-term dermal and inhalation exposures. Table 4 below presents the risks to occupational handlers using metconazole for use on soybeans. For all mixers, loaders, and applicators, the combined MOEs for short- and intermediate-term exposures range from 2,800 to 53,000, and therefore, do not exceed HED's level of concern, i.e. all MOEs $\geq$ 100.

Table 4. Occupational Handler Exposure & Risk Estimates to Metconazole Used on Soybeans to Control Soybean Rust

Route of Exposure	Unit Exposure[1] (mg/lb ai handled)	Application Rate[2] (lb ai/acre)	Units Treated[3] (acres/day)	Average Daily Dose[4] (mg ai/kg bw/day)	Short-Term MOE[5]	Intermediate-Term MOE[5]	Combined Short-Term MOE[6]	Combined Intermediate-Term MOE[6]
Mixer/Loader - Liquid - Open Loading (for Groundboom)								
Dermal w/ gloves	0.023	0.056	200	1.84E-4	49,000	35,000	24,000	17,000
Inhalation	0.0012	0.056	200	1.92E-4	47,000	33,000		
Mixer/Loader - Liquid - Open Loading (for Aerial)								
Dermal w/ gloves	0.023	0.056	1200	1.10E-3	8,200	5,800	4,000	2,800
Inhalation	0.0012	0.056	1200	1.15E-3	7,900	5,600		
Applicator - Groundboom - Open Cab								
Dermal w/ gloves	0.014	0.056	200	1.12E-4	81,000	57,000	39,000	28,000
Inhalation	0.00074	0.056	200	1.18E-4	77,000	54,000		
Applicator - Aerial								
Dermal w/ gloves	0.0022	0.056	1200	1.06E-4	86,000	61,000	53,000	37,000
Inhalation	0.000068	0.056	1200	6.53E-5	140,000	98,000		
Flagger								
Dermal w/ gloves	0.012	0.056	350	1.68E-4	54,000	38,000	34,000	24,000
Inhalation	0.00035	0.056	350	9.80E-5	93,000	65,000		

[1] Unit Exposure = mg a.i./lb a.i. handled from the Pesticide Handler Exposure Database (PHED), Version 1.1, August 1998. Dermal = a single layer of work clothing (i.e., long pants, long-sleeved shirt, shoes plus socks).

[2] Application Rate taken from Section 18 Request, Correspondence with J. Sierk, Minnesota Dept. Agriculture to D. Rosenblatt, 21 March 2005.

[3] Units Treated taken from Science Advisory Council for Exposure, Standard Operating Procedure 9.1, Standard Values for Daily Acres Treated in Agriculture, Rev. 25 SEP 2001.

[4] Average Daily Dose (ADD) = Unit Exposure * Application Rate * Units Treated * Absorption Factor (dermal 5%; inhalation 100%) ÷ Body Weight (60 kg).

[5] Margin Of Exposure (MOE) = LOAEL (mg/kg/day) ÷ ADD (mg/kg/day); where the NOAEL = 9.1 mg/kg/day for dermal and inhalation short-term exposures and 6.4 mg/kg/day for dermal and inhalation intermediate-term exposures.

[6] Combined MOE = $1/[(1/MOE_{Dermal}) + (1/MOE_{Inhalation})]$.

Postapplication Exposure & Risk

This proposed Section 18 use on soybeans involves foliar applications; therefore, there is a potential for short- and intermediate-term dermal exposure to workers entering metconazole-treated areas to perform a variety of agricultural/occupational tasks, and a risk assessment is required. Inhalation exposure is expected to be negligible for postapplication scenarios.

The petitioner did not submit any study data depicting the amount of dislodgeable foliar residue (DFR) to expect on soybeans following application of metconazole end use product. Therefore, HED default assumptions and SOPs were used to determine the DFR values used in this assessment. The transfer coefficients used in this assessment are from an interim transfer coefficient guidance document developed by HED's Science Advisory Council for Exposure using proprietary data from the Agricultural Re-entry Task Force (ARTF) database (SOP#3.1). HED has also identified Transfer Coefficients (TC) (expressed as cm^2/hr) relative to the various activities.

For the proposed use on soybeans, the activities with the highest TC are scouting or irrigating the crop in full foliage stages of crop development with a TC of 1,500 cm^2/hr. Lacking compound specific data, the Agency assumes 20% of the application rate is available as foliar dislodgeable residue on day zero after application. This is adapted from the Science Advisory Council For Exposure SOP No. 003 (7 May 1998 - Revised 7 August 2000).

For short- and intermediate-term postapplication dermal exposures, all activities result in MOEs greater than 100, and therefore, do not exceed HED's level of concern. The short- and intermediate-term MOEs were estimated for "Day 0" exposure (i.e. the day of application), and are presented in Table 5. The restricted entry interval (REI) on the proposed label is 12 hours, which is compliance with the worker protection standard (WPS) based on acute toxicity category findings.

Table 5. Non-Cancer Exposure and Risk Assessment for Occupational Postapplication Activities

Crop Group	Application Rate (lb ai/A)	Dermal Transfer Coefficient (cm^2/hr)	Postapplication Day (t)	Dislodgeable Foliar Residue (DFR)[1] ($\mu g/cm^2$)	Daily Dose[2] (mg/kg/day)	Short- & Intermediate-Term Dermal MOE[3]
Soybean	0.056	100 (hand weeding)	0	0.1256	7.18E-5	130,000/89,000
		1500 (scouting or irrigation)			1.08E-3	8,500/5,900

[1] DFR = Application Rate (lb ai/A) x 4.54E+8 µg/lb x 24.7E-9 A/cm^2 x Percent Residue Available Day 0 (20%)

[2] Daily Dose = [DFR x (0.001 mg/µg) x Dermal Transfer Coefficient x Dermal Absorption Factor (5%) x Exposure Time (8 hr)] / [Body weight (70 kg)]

[3] MOE = NOAEL/Daily Dose; where short-term dermal NOAEL = 9.1 mg/kg/day, and intermediate-term dermal NOAEL = 6.4 mg/kg/day.

References

1. Metconazole EU Monograph (Draft Assessment Report - DAR, April 2004; Belgium, January 2004).

2. Tier II Drinking Water Assessment for The Use of Metconazole on Soybean, D319662, A. Al-Mudallal, 7/28/05.

3. Metconazole: Human Health Risk Assessment for Proposed tolerance on Imported Bananas, D308794, concurrent, B. O'Keefe.

4. Metconazole: Report of the Cancer Assessment Review Committee, TXR# 0054211, 4/14/06, J. Kidwell.

cc: Barry O'Keefe, Registration Action Branch 3, Health Effects Division (7509C)
Michael Doherty, Registration Action Branch 2, Health Effects Division (7509C)

Appendix 1.

DIETARY EXPOSURE

Table 6. Residue Consideration Summary Table

PARAMETER	PROPOSED USE	RESIDUE DATA
CHEMICAL	metconazole	metconazole
FORMULATIONS	Caramba™ 90 SL Headline® Caramba™CoPack (contains Caramba™ 90 SL and Headline (pyraclostrobin)	BAS 555 01F (an SL formulation)
CROP	soybeans	soybeans
TYPE APPLICATION	broadcast foliar; ground or air	broadcast foliar; ground equipment
# APPLICATIONS	two	two
TIMING	postemergence; Caramba ™: Apply at or prior to disease development or early flowering (R1-R3 growth stage), whichever is earlier. Make a second application 10 to 21 days later or earlier if monitoring shows disease development or if conditions are conducive for disease infection. Headline® Caramba™CoPack Apply at early flowering (R1 growth stage) or prior to disease development. Make a second application 10 to 21 days later or earlier if monitoring shows disease development or if conditions are conducive for disease infection.	postemergence; 10 day retreatment interval
RATE/APPLICATION	0.056 lbs ai/A	0.07 lb ai/A
RATE/YEAR or SEASON	0.11 lb ai/A/season	0.14 lb ai/A/season
MAXIMUM RESIDUE	N/A	0.05 ppm in soybean seed (30-day PHI); 0.71 ppm in aspirated grain fractions (31-day PHI); 2.43 ppm in forage (7-day PHI) (label restriction); 3.36 in hay (7-day PHI) (label restriction)

Table 6. Residue Consideration Summary Table

PARAMETER	PROPOSED USE	RESIDUE DATA
RESTRICTIONS	Both Caramba™90 SL label and Headline® Caramba™CoPack label: Do not apply within 21 days of harvest.* Do not make more than 2 applications of metconazole-containing products per season. Do not feed soybean forage or hay to livestock. Do not apply this product through any type of irrigation system. Restricted entry interval (REI) is 12 hours. Apply in no less than 5 gallons per acre (gpa) spray volume by air. Caramba™ 90 SL label only: Do not use less than 15 gpa spray volume by ground. Crops listed on the Caramba™ labels may be planted as soon as practical after last application. Any crop not specified on the labels may be planted into treated areas 120 days after last application. Headline® Caramba™CoPack label only: Do not make more than 2 applications of pyraclostrobin-containing products per season. Crops listed on the labels (Headline®, Cabrio®, Pristine®, and Caramba™) may be planted as soon as practical after last application. Any crop not listed on these labels may be planted into treated areas 120 days after last application.	Preharvest intervals (PHI's) were 7 days for forage and hay and 30-31 days for seed. An adjuvant was added to the spray mixture for all applications.
RESIDUE DATA SOURCE	N/A	BASF Registration Document Number 2004/5000755
PERFORMING LAB	N/A	BASF

* The Caramba ™ label states the preharvest interval is 21 days under "Restrictions and Limitations but 30 days remains under Table 1. This should be revised to 21 days.

Animal Feedstuffs Considerations.

Since feeding of soybean forage and hay to livestock is restricted by the labels, livestock feed items associated with the proposed use on soybeans are seed, aspirated grain fractions, meal, and hulls. No tolerances have been established or proposed for livestock commodities.

Goats: Metabolism data on goats are available (*Metconazole EU Monograph*, Draft Assessment Report - DAR, April 2004; Belgium, January 2004). Goats were fed 14 and 25 ppm in the diet for 3 or 4 days. At 14 ppm, TRR were 0.004 ppm in milk, 0.456 ppm in liver, 0.145 ppm in kidney, 0.004 ppm in muscle, and 0.015 ppm in fat. At 25 ppm, TRR were 0.004 ppm in milk, 0.559 ppm in liver, 0.276 ppm in kidney, 0.005 ppm in muscle, and 0.003 ppm in fat. At 11 ppm in the diet, TRR were <0.002 ppm in milk, 0.317 ppm in liver, 0.148 ppm in kidney, 0.007 ppm in muscle, and 0.006 ppm in fat.

Poultry: Metabolism data on hens are available as part of the *Metconazole EU Monograph* (Belgium, January 2004). Hens were fed 10 ppm in the diet for 28 days. TRR were 0.096 ppm in eggs, 0.6 ppm in liver, 0.327 ppm in kidney, 0.027 in meat, and 0.145 ppm in fat.

Maximum theoretical dietary burdens (MTDBs) for cattle, poultry, and swine are calculated below. HED notes that there is a label restriction: "Do not feed soybean forage or hay to livestock." Also, HED does not expect both soybean hulls and aspirated grain fractions to be fed to livestock (discussion with R. Loranger, July 2005).

Table 7. Maximum Theoretical Residues in the Diet of Beef and Dairy Cattle

Feedstuff	% of Diet	% Dry Matter	Tolerance (ppm)	Dietary Burden (ppm)
soybean meal	15	92	0.25	0.04
soybean hulls	20	90	1.2	0.27
Total	35			0.31

Table 8. Maximum Theoretical Residues in the Diet of Poultry

Feedstuff	% of Diet	Tolerance (ppm)	Dietary Burden (ppm)
soybean meal	40	0.25	0.10
soybean hulls	20	1.2	0.24
Total	60		0.34

Table 9. Maximum Theoretical Residues in the Diet of Swine			
Feedstuff	% of Diet	Tolerance (ppm)	Dietary Burden (ppm)
soybean meal	25	0.25	0.06
aspirated grain fractions	20	1.0	0.20
Total	45		0.26

Based on the goat and hen metabolism studies and the maximum theoretical dietary burdens (MTDBs) calculated above, residues in all livestock commodities are not expected to exceed 0.01 ppm except for 0.02 ppm in poultry liver. For the Section 18, time-limited tolerances should be established for all livestock commodities at 0.02 ppm (the LOQ of the method). Time-limited tolerances should be established at 0.02 ppm for meat, fat, and meat byproducts of cattle, goat, hog, horse, poultry, and sheep; milk, and egg.

Processed By-Products: Soybean processed commodities are meal, hulls, and refined oil. No processing studies have been submitted. Theoretical processing factors (from OPPTS 860.1520, Table 3) are 2.2x for soybean meal, 11.3x for hulls, and 12.0x for refined oil. Based on the theoretical processing factors and a tolerance of 0.10 ppm for soybean seed, residues would not be expected to exceed 0.25 ppm in/on soybean meal, 1.2 ppm in/on hulls, and 1.2 ppm in refined oil. For the Section 18, time-limited tolerances should be established on the processed commodities at these levels.