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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: Tebuconazole (ELITE 45 DF). Registration for use on cherry, peach and nectarine and Tolerance Petition for residues in or on cherry and peach.
DP Barcode No. D210245.
Submission No. S478587.
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ACTION:

Review of Miles, Inc. registration amendment petition for use on cherry, peach and nectarine and of a petition to establish permanent tolerances for Tebuconazole in/on peaches and nectarines.

Tolerances are proposed for Tebuconazole in or on the following agricultural food or feed commodities:

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Food or Feed Commodity	Proposed tolerance:
Cherry	4.0 ppm
Peach	1.0 ppm

CONCLUSIONS

1. Toxicology Branch II has no objections to the approval of these requests if the residue chemistry data are acceptable to Chemistry Branch (I/II) and if granting of these petitions will not result in dietary risk (% RfD occupied) exceeding 100% of the RfD.

2. It is recommended that the Acute Toxicity Category for Eye Irritation of the formulation ELITE 45 DF (tebuconazole) be changed from II to III.

DETAILED CONSIDERATIONS

I. Toxicology Profile

The toxicology profile of Tebuconazole is summarized in Table 1. There are no data gaps in the toxicology database for tebuconazole.

II. Issues

A. Carcinogenicity:

Tebuconazole has been evaluated for carcinogenicity by the HED Carcinogenicity Peer Review Committee (CPRC). The CPRC concluded that tebuconazole should be classified as group C - possible human carcinogen and recommended that for the purpose of risk characterization the Reference Dose (RfD) approach should be used for quantification of human risk.

B. Teratogenicity:

Tebuconazole was evaluated for carcinogenicity by the HED Developmental Toxicity Peer Review Committee (DTPRC). The DTPRC concluded that developmental toxicity was induced in mice, rats, and rabbits via the oral route of administration. The lowest NOEL (10 mg/kg/day) is observed in mice. Equivocal maternal toxicity was observed at an oral dose level of 100 mg/kg/day in the mouse and at 30 mg/kg/day in the rat. Developmental toxicity was not induced in the rat or mouse at the highest dose tested via the dermal route (1000 mg/kg/day). The DTPRC recommended that the mouse dermal NOEL of 1000 mg/kg/day be used in assessing developmental toxicity risk associated with occupational exposure to tebuconazole.

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Table 1. Toxicology profile for Tebuconazole. Guideline Numbers are as listed in CFR 158.340.

	REQUIRED	SATISFIED
§81-1 ACUTE ORAL TOXICITY - RAT	Y[1]	Y
§81-2 ACUTE DERMAL TOXICITY - RABBIT	Y	Y
§81-3 ACUTE INHALATION TOXICITY - RAT	Y	Y
§81-4 PRIMARY EYE IRRITATION - RABBIT	Y	Y
§81-5 PRIMARY DERMAL IRRITATION - RABBIT	Y	Y
§81-6 DERMAL SENSITIZATION - GUINEA PIG	Y	Y
§82-1 90-DAY FEEDING - RAT	Y	Y
§82-1 90-DAY FEEDING - DOG	Y	Y
§82-2 21-DAY DERMAL - RABBIT	Y	Y
§82-4 SUBCHRONIC INHALATION	N	N/A
§82-5 21-DAY DELAYED NEUROTOXICITY	N	N/A
§83-1 CHRONIC FEEDING - RAT (COMBINED §83-2)	Y	Y[2]
§83-1 CHRONIC FEEDING - DOG	Y	Y
§83-2 ONCOGENICITY STUDY - RAT	Y	Y
§83-2 ONCOGENICITY STUDY - MOUSE	Y	Y
§83-3 TERATOGENICITY - RABBIT	Y	Y
§83-3 TERATOGENICITY - RAT	Y	Y
§83-4 TWO-GENERATION REPRODUCTION --RAT	Y	Y
§84-2(a) GENE MUTATION	Y	Y
§84-2(b) STRUCTURAL CHROMOSOME ABERRATION	Y	Y
§84-4 OTHER GENOTOXIC EFFECTS	Y	Y
§85-1 GENERAL METABOLISM	Y	Y
§85-2 DERMAL PENETRATION	Y	Y
END-USE FORMULATION (ELITE 45 DF):		
§81-1 ACUTE ORAL TOXICITY - RAT	Y	Y
§81-2 ACUTE DERMAL TOXICITY - RABBIT	Y	Y
§81-3 ACUTE INHALATION TOXICITY - RAT	Y	Y
§81-4 PRIMARY EYE IRRITATION - RABBIT	Y	Y[3]
§81-5 PRIMARY DERMAL IRRITATION - RABBIT	Y	Y
§81-6 DERMAL SENSITIZATION - GUINEA PIG	Y	Y

[1] Y = YES; N = NO; YES: indicates that the DER is Minimum, Guideline or Acceptable.
[2] Submitted as a combined chronic/carcinogenicity study.
[3] Toxicity Category for eye irritation changed from II to III.

C. Reference Dose (RfD):

The Reference Dose (RfD) of tebuconazole is 0.01 mg/kg b.wt./day based on a no-observed-effect-level (NOEL) of 1 mg/kg b.wt./day in dogs and an

uncertainty factor of 100 . A more recent 1-year dog study [MRID 420306-01 and 425372-01] defined a NOEL of 100 ppm (approx. 2.96 and 2.94 mg/kg b.wt./day in males and females, respectively). The review of this study has been transmitted to the RfD Committee for evaluation of its impact on the RfD of tebuconazole.

D. Pending Regulatory Actions: There are no pending regulatory actions with respect to the registration of this chemical.

E. Change in Eye Irritation Category for ELITE 45 DF .

In a review of a primary eye irritation study of Folicur 45% DF [Primary Eye Irritation of FOLICUR (HWG 1608) 45% Dry Flowable in Albino Rabbits, Study No. 87-333-07, MRID No. 40995918], the test material was assigned Toxicity Category II, based on the presence of scores of 1 for redness and swelling on day 8 of observation. The Registrant has presented the point of view that a Draize score of 1 is not a positive effect for the redness and chemosis endpoints according to the FIFRA Guideline for Eye Irritation Studies, thus, eye irritation produced by ELITE 45 DF can be considered to have cleared within 7 days or less (Category III).

The Agency agrees with this point of view and it is recommended that the Acute Toxicity Category for Eye Irritation of the formulation ELITE 45 DF (tebuconazole) be changed from II to III.

Table 2. Acute Toxicity Summary of Tebuconazole (Technical and 45% DF).

Guideline	Study Type	Species	Dose (Purity	Results	MRID No.	Tox Cat	CORE Grade
Technical							
81-1	Acute Oral	Rat (Wistar)	500-5000 mg/kg; (Tech. 97.1% purity)	LD_{50} (fasted): ♂: >5000 mg/kg; ♀: 3933 mg/kg LD_{50} (unfasted): ♂: 4264 mg/kg; ♀: 3352 mg/kg	407009-17	3	Minimum
81-2	Acute Dermal	Rat (Wistar)	1000-5000 mg/kg; (Tech. 97.1% purity)	LD_{50} : ♂ & ♀: > 5000 mg/kg;	407009-17 412908-01	3	Guideln.
81-3	Acute Inhalation	Rat (Wistar)	371 mg/m³ (aerosol) 5093 mg/m³ (dust); (Tech. 96.2% purity)	LC_{50} (4-hours, aerosol): > 371 mg/m³; LC_{50} (4-hours, dust); > 5093 mg/m³; (No deaths)	407009-22	2	Guideln.
81-4	Pri. Eye Irr.	Rabbit (HC:NZW)	(Tech. 96.3% purity)	Mildly irritating	407009-25	3	Guideln.
"	"	"	(Tech 97.1% purity)	Non irritant	407009-17	3	Minimum
81-5	Pri. Derm. Irr.	Rabbit (HC:NZW)	(Tech. 97.1% purity)	Non irritant	407009-17	4	Minimum
"	"	Rabbit	(Tech. 96.6% purity)	Non irritant	409959-10	4	Minimum
81-6	Derm. Sensitiz.	Guinea pig (DHPW)	25% in aqueous Cremophor; (Tech. 97.4% purity)	No evidence of skin sensitization using the Buehler test.	407009-28 412908-02	-	Minimum
Formulation: ELITE 45 DF							
81-1	Acute Oral	Rat	(46.2% a.i)	LD_{50} (fasted): ♂: 4865 mg/kg; ♀: 2593 mg/kg	409959-15	3	Minimum
81-2	Acute Dermal	Rat	(46.2% a.i)	LD_{50}: > 2000 mg/kg (♂ & ♀)	409959-16	3	Minimum
81-3	Acute Inhalation	Rat	(45.3% a.i.)	LC_{50} (4 hours): > 0.97 mg/l	409959-17 420759-01	3	Minimum
81-4	Pri. Eye Irrit.	Rabbit	(46.2% a.i.)	Irritation cleared within 7 days or less	409959-18	3[1]	Minimum
81-5	Pri. Derm. Irrit.	Rabbit	(46.2% a.i.)	Not a primary dermal irritant	409959-19	4	Minimum
81-6	Dermal Sensitiz.	Guinea pig	(45% a.i.)	Positive when tested by the Buehler topical closed patch test method	411539-01	-	Guideline

[1] Category changed from 2 to 3 based on consideration that a Draize score of 1 is not a positive effect for the redness and chemosis endpoints.

Table 2. Non-Acute Toxicity Summary of Tebuconazole Technical.

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
-	Feed. 3 week	Rat (Wistar)	Oral gavage	0, 30, 100 or 300 mg/kg/day for 28 days plus 28 days recovery. (Tech., 97.0% purity)	NOEL = 30 mg/kg/day. LEL = 100 mg/kg/day (based on hematology changes and clinical chemistry parameters).	407009-32	Supplem.
-	Inhl. 3 week	Rat (Wistar)	Inhalation	0, 1.2, 10.6, or 155.8 mg/m^3; 6 hour/day for over 3 weeks. (Tech., 96.2% purity)	NOEL = 10.6 mg/m^3/day. LEL = 155.8 mg/m^3/day (based on piloerection and induction of liver N-demethylase).	407009-35	Supplem.
-	Feed. 30 day	Dog (Beagle)	In diet	0, 500 or 5000 ppm in the diet, for 30 days. (Tech., 93.4% purity)	NOEL = 500 ppm. LEL = 5000 ppm (based on elevated alkaline phosphatase). Range-finding study.	407009-35	Supplem.
-	Feed. 8 week	Mice (SPF)	In diet	0, 500 or 2000 ppm for 8 weeks or 0, 125, 500, or 2000 ppm for 5 days. (Tech., 96.9% purity) Range finding study for carcinogenicity.	Systemic toxicity (8 week study) consisted of increased absolute and relative liver weight associated with increased liver necrosis, vacuolization, and lipidosis at both dose levels. Microsomal enzymes (5 day study) were induced at both dose levels. Range selected for carcinogenicity study was 0, 20, 60 & 180 ppm.	407009-33	Supplem.
82-1 (a)	Feed. 3 month	Rat (Wistar)	In diet	0, 100, 400, or 1600 ppm for 13 weeks. (Tech., 93.4% purity)	♂: NOEL = 400 ppm. LEL = 1600 ppm (based on decreased b.wt. and b.wt. gain, adrenal vacuolation and spleen hemosiderosis). ♀: NOEL = 100 ppm. LEL: 400 ppm (based adrenal vacuolation).	407009-30	Minimum
82-1 (b)	Feed. 3 month	Dog (Beagle)	In diet	0, 200, 1000 or 5000 ppm for 13 weeks. (Tech. 93.4% purity)	NOEL = 200 ppm. LOEL = 1000 ppm (based on decreased b.wt. and b.wt gain, food consumption and increased liver N-demethylase activity). Lens opacity in all HDT ♂ and 1 ♀; cataracts in 3/4 ♀.	407009-34	Minimum

Table 2. Non-Acute Toxicity Summary of Tebuconazole (Continued).

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
82-2	Dermal 3 week	Rabbit (NZW)	Dermal	0, 50, 250, or 1000 mg/kg/day, 5 days/week for 3 weeks (Tech. 97.1% purity)	No significant systemic effects were seen. NOEL = > 1000 mg/kg (limit test).	407009-17	Guideln.
83-1 (a) & 83-2(a)	Feed. Combined Chronic/Carcino-genicity Study	Rat [Bor:WISW (SPF Cpb)]	In diet	0, 100, 300, or 1000 ppm (♂: 5.3, 15.9, or 55 mg/kg bw; ♀: 7.4, 22.8, & 86.3 mg/kg) for 2 years. (Tech. approx. 95% purity)	Not oncogenic at the levels tested. NOEL = 100 ppm. LEL = 300 ppm (based on b.wt. depression; decreased Hb, hematocrit, MCV and MCHC; increased liver enzymes.	407009-39; 408164-01	Minimum
83-1 (b)	Feed. chronic	Dog (beagle)	In diet	0, 40, 200, or 1000 (1-39 wk) & 2000 ppm (40-52 wk) for 1 year. (Tech. 96.9% purity)	NOEL = 40 ppm. LEL = 200 ppm (based on ocular lesions: lenticular and corneal opacity; and hepatic toxicity: changes in the appearance of the liver and increased siderosis). This study was used to define the oral RfD for tebuconazole. With an uncertainty factor of 100, and a NOEL of 1 mg/kg/day, the RfD of tebuconazole was set at 0.01 mg/kg/day. A more recent dog study (see below) will be evaluated for its impact on the RfD.	407009-39 408164-01	Minimum

Table 2. Toxicity Summary of Tebuconazole (Continued).

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
83-1 (b)	Feed. chronic	Dog (beagle)	In diet	0, 100, or 150 ppm for 1 year; (♂: 0, 3.0, 4.4 mg/kg/day; ♀: 0, 2.9, 4.5 mg/kg/day). (Tech. 96.0% purity)	NOEL: 100 ppm. LEL = 150 ppm (based on adrenal effects in both sexes). In males there was hypertrophy of adrenal zona fasciculata cells amounting to 4/4 at 150 ppm and to 0/4 at 100 ppm and in controls. Other adrenal findings in males included fatty changes in the zona glomerulosa (3/4) and lipid hyperplasia in the cortex (2/4) at 150 ppm vs. 1/4 for both effects at 100 ppm and control dogs. In females there was hypertrophy of zona fasciculata cells of the adrenal amounting to 4/4 at 150 ppm and to 0/4 at 100 ppm and 1/4 in controls. Fatty changes in the zona glomerulosa of the female adrenal amounted to 2/4 at 150 ppm and to 1/4 at 100 ppm and in controls. **This study will be evaluated for its impact on the RfD of the compound.**	420306-01 425372-01	Minimum
83-2(b)	Carcinogenicity	Mice (NMRI)	In diet	0, 20, 60, or 180 ppm for 21 months; (♂: 5.9, 18.2, & 53.1 mg/kg/day & ♀: 9.0, 26.1, 80.5 mg/kg/day (Tech. 95.1% purity)	The compound was not carcinogenic at the levels tested. Adequate levels for carcinogenicity testing were not achieved. The HDT resulted in slight liver toxicity (increased bilirubin and weight, associated with centrilobular and periportal vacuolation and lipid deposition); increased adrenal cortical size and hyperplasia and increased pancreatic interstitial edema.	407009-41	Supplem.

Table 2. Toxicity Summary of Tebuconazole (Continued).

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
83-2	Carcinogenicity	Mice (NMRI)	In diet	0, 500, or 1500 ppm for 91 weeks; (♂: 84.9, & 279 mg/kg/day & ♀: 0, 103.1, & 365.5 mg/kg/day) (Tech. 96.2% purity)	Statistically significantly decreased body weights and increased food consumption were reported that were consistent with decreased food efficiency at 500 and 1500 ppm in males and at 1500 ppm in females. Clinical chemistry values dose-dependent increases in plasma GOT, GPT and AP) for both sexes were consistent with hepatotoxic effects at both 500 ppm and 1500 ppm. Relative liver weight increases reached statistical significance at both 500 and 1500 ppm in males and at 1500 ppm only in females. Histopathology included dose-dependant increases in hepatic panacinar fine fatty vacuolation, statistically significant at 500 and 1500 ppm in males and at 1500 ppm in females. Other histopathology included significant oval cell proliferation in both sexes at 1500 ppm and dose-dependent ovarian atrophy that was stat. significant at 500 and 1500 ppm. MTD was achieved at or around 500 ppm. Neoplastic histopathology consisted of statistically significant incidences of hepatocellular neoplasms: adenomas (35.4%) and carcinomas (20.8%) at 1500 ppm in males and carcinomas only (26.1%) at 1500 ppm in females. In addition, there was a dose-related, but not statistically significant, increase in histiocytic sarcomas in both sexes. Examination of historical control data indicated that the histiocytic sarcoma incidences are not biologically significant.	421750-01 424693-00 424693-01	Minimum
83-3	Developmental Toxicity	Rat (Wistar)	Oral (gavage)	0, 10, 30, or 90 mg/kg/day, 6-15 d of gestation. Range finder. Tech. 98.2% ai.	Minimally toxic at the HDT: slight depression of maternal body weight. Doses selected for main study: 0, 30, 60, and 120 mg/kg/day.	407009-42	Supplem.

Table 2. Toxicity Summary of Tebuconazole (Continued).

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
83-3	Developmental Toxicity	Rat (Wistar)	Oral (gavage)	0, 30, 60, or 120 mg/kg/day, 6-15 d of gestation. (Tech. 98.3% purity)	Maternal NOEL: 30 mg/kg/day. Maternal LEL: 60 mg/kg/day (based on elevation of absolute and relative liver weights). Developmental NOEL: 30 mg/kg/day. Developmental LEL: 60 mg/kg/day (based on delayed ossification of thoracic, cervical and sacral vertebrae, sternum, limbs and an increase in supernumerary ribs).	407009-43	Minimum
"	"	"	Dermal	0, 100, 300, or 1000 mg/kg/day, on a 25 cm^2 area, 6 hour/day, 6-15 d of gestation. (Tech. 97.4% purity)	No maternal or developmental toxicity noticed at any dose level: (maternal or develop.) NOEL : 1000 mg/kg/day, (maternal or delop.) LEL > 1000 mg/kg/day.	414508-01	Supplem.
"	"	Rabbit (Chinchilla)	Oral (gavage)	0, 30, 100 or 300 mg/kg/day, 6-18 d of gestation. (Tech. 98.2% purity).	Range Finder. Maternal NOEL: 100 mg/kg/day. Maternal LEL: 300 mg/kg/day (based on reduced body weight gain and 100% preimplantation losses). The doses selected were: 0, 10, 30, & 100 mg/kg/day by gavage.	407009-44	Supplem.
"	"	"	"	0, 10, 30, or 100 mg/kg/day, 6-18 of gestation. (Tech. 98.2% purity).	Maternal NOEL: 30 mg/kg/day. Maternal LEL: 100 mg/kg/day (based on a minimal depression of body weight gains and food consumption). Developmental NOEL: 30 mg/kg/day. Developmental LEL: 100 mg/kg/day [based on increased postimplantation losses and frank malformations in 8 fetuses of 5 litters (e.g. peromelia in 5 fetuses/4 litters; palatoschisis 1 fetus/1 litter)].	407009-45	Minimum
"	"	Mice (NMRI/ORIG)	"	0, 10, 20, 30, 100 mg/kg/day, 6-15 d of gestation. (Tech. 97.4% purity).	Range finder. Maternal toxicity/physiological effects (Vacuolation, & elevations in AST, ALP and AP) occurred at all dose levels. Reduction in MCV in parallel with reduced hematocrit occurred at doses $\geq$ 20 mg/kg/day. The liver was the target organ Maternal NOEL: 10 mg/kg/day. Maternal LOEL: 20 mg/kg/day	408215-01	Supplem.

Table 2. Toxicity Summary of Tebuconazole (Continued).

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
83-3	Developmental Toxicity	Mice (NMRI/ORIG)	Oral (gavage)	0, 10, 30, 100 mg/kg/day, 6-15 d of gestation. (Tech. 93.6% purity).	Maternal NOEL: 10 mg/kg/day. Maternal LEL: 20 mg/kg/day [based on a companion maternal toxicity study (also MRID 48215-01), otherwise no maternal toxic effects in the subject study]. Developmental NOEL: 10 mg/kg/day. Developmental LEL: 30 mg/kg/day [based on the increase in the number of runts (weight < 1.3 g)].	408215-01	Minimum
"	"	"	Dermal	0, 100, 300, or 1000 mg/kg/day, 6 hour/day, 10% of body surface, 6-15 d of gestation. (Tech. 98.1% purity)	No evidence of maternal toxicity was seen in this study. However a companion study (same strain and dosing protocol, MRID 420103-01) showed apparent maternal NOEL of 100 mg/kg and maternal LOEL of 300 mg/kg (based on histopathology and ALT/GPT increase). Based on statistically significant increases in fetal incidences of skeletal variations coupled to marked increases in their litter incidences (e.g. bipartite sternebrae 20% in controls increased to 40% at the HDT) a tentative developmental NOEL and LEL were defined at 300 and 1000 mg/kg/day. The HED Peer Review Committee (PRC) for developmental and reproductive toxicity recommended (5/7/92) that the tentative dermal NOEL of 300 mg/kg/day in mice be changed to 1000 mg/kg/day. The PRC recommended that the mouse dermal NOEL of 1000 mg/kg/day be used in assessing developmental toxicity risk associated with occupational exposure to tebuconazole.	420103-01	Minimum

Table 2. Toxicity Summary of Tebuconazole (Continued).

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
83-3	Developmental Toxicity	Mice (NMRI/ORIG)	Dermal	0, 100, 300, or 1000 mg/kg/day, 6 hour/day, 10% of body surface, 6-15 d of gestation. (Tech. 96.0% purity)	Companion study for dermal teratogenicity in mice. Liver microsomal enzymes were significantly ($p < 0.01$) elevated at the MDT and HDT. Periportal fatty deposition in the liver at the MDT and HDT. ALT (GPT) increased in dose-related fashion and statistically significantly elevated at the HDT. NOEL = 100 mg/kg/day, and LEL 300 mg/kg/day (based on histopathology and increased liver enzyme levels).	420103-01	Minimum
83-4	2 Generation Reproductive Toxicity	Rat (Wistar)	In diet	0, 100, 300, or 1000 ppm for 2 generations. (Tech. 95.2% purity).	Maternal NOEL: 300 ppm. Maternal LEL: 1000 ppm (based on depressed body weights, increased spleen hemosiderosis, and decreased liver and kidney weights). Reproductive NOEL: 300 ppm. Reproductive LEL: 1000 ppm (based on neonatal birth weight depression).	407009-46	Minimum
84-2	Mutagenicity Ames test	Salmonella sp.	-	37.5-2400 µg/plate. (Tech. 96.6% purity)	Non mutagenic with or without metabolic activation.	407009-47 407009-48	Acceptable
"	Mutagenicity HGPRT	CHO cells	-	12.5-2000 µg/plate (No cytotoxicity). (Tech. 96.6% purity).	Non mutagenic with or without metabolic activation.	407009-49	Unacceptable
"	Mutagenicity Dominant lethal	Mice	-	2000 mg/kg, only one dose. No positive controls. (Tech. 93.5% purity).	Negative	407009-50	"
"	Mutagenicity Micronucleus Assay	Mice	-	200, 500, or 2000 mg/kg. (Tech. 95.3% purity).	Negative	407009-51	Acceptable
"	Mutagenicity S. Chr. Exch.	CHO cells	-	Tech. 96.5% purity.	Negative with metabolic activation (15-120 µg/ml) or without metabolic activation (4-30 µg/ml).	407009-52	Acceptable
"	Mutagenicity In vitro cytogenetics.	Human lymphocytes	-	30-300 µg/ml (no cytotox. without activation. (Tech. 96.5% purity).	Negative with or without metabolic activation.	407009-53	Unacceptable

Table 2. Toxicity Summary of Tebuconazole (Continued).

Guideline	Study Type	Species	Route	Dose	Results	MRID No.	CORE Grade
84-4	Mutagenicity DNA damage/repair	E.Coli	-	625-1000 µg/plate (no growth with inhibition demonstrated). (Tech. 97.1% purity).	Negative with or without metabolic activation.	407009-55	Unacceptable
-	Mutagenicity Unscheduled DNA synthesis	Rat primary hepatocytes	-	0.504-25.2 µg/ml. Tech. 96.5% purity).	Negative	408164-02	Acceptable
85-1	Metabolism	Rat	I.V. & oral (Gavage)	1 or 20 mg/kg [phenyl-^{14}C] > 99% purity or [triazole 3,5-^{14}C] > 98.4% purity Tech. non-labeled 99.5% purity.	98.1% of the oral dose is absorbed. Over 87% of the dose excreted in urine and feces within 72 h of dosing. At sacrifice (72 hours post-dosing) total residue (- GI tract) amounted to 0.63% of the dose. A total of 10 compounds identified in excreta. A large fraction of the identified metabolites corresponded to successive oxidation steps of a methyl group of the test material. At the higher dose (20 mg/kg) changes in detoxication patterns may be occurring.	40959-11 40959-12 421762-02 425083-01	Minimum
85-2	Dermal penetration	Rat	Dermal	Triazole 3,5-^{14}C] > 99.66% purity Tech. non-labeled 94.7% purity. Solvent used: ethanol	In rats dosed dermally at actual doses of 0.604, 5.85, 52.4 and 0.547 µg/cm^2 the percent of dose absorbed by 24 hours amounted to 27.77, 27.06, 23.01, and 6.38% of the applied dose, respectively. The amount which remained on the application site after soap and water wash increased with dose, and amounted at 24 hours to 24.7, 24.40, 32.02, and 53.11% of the above applied doses, respectively.	409959-13	Acceptable