Health Canada Santé Canada

# Evaluation Report for Category A.1.3 Application

**Application Number:** 2011-2152
**Application:** New Active Ingredient - Maximum Residue Limits (MRLs) only
**Product:** Etoxazole Technical
**Registration Number:**
**Active ingredients (a.i.):** Etoxazole [ETX]
**PMRA Document Number : 2297935**

## Background

This active ingredient was previously reviewed under submission 2008-0581 to establish Maximum Residue Limits (MRLs) for grapes, pome fruits, strawberries, and tree nuts under Use Site Category 14 (terrestrial food crops).

## Purpose of Application

The purpose of the application was to establish import MRLs for the active ingredient etoxazole on tea; caneberries (crop subgroup 13-07A); cucurbit vegetables (crop group 9); hops; low growing berries (crop subgroup 13-07G); mint; tomatoes; peppers and eggplants (crop subgroup 8-09B); small fruit vine climbing except fuzzy kiwifruit (crop subgroup 13-07F); tropical fruit (avocado, papaya, star apple, black sapote, mango, sapodilla, canistel, mamey sapote); and stone fruit (crop group 12-09).

## Chemistry Assessment

| | |
|---|---|
| **Active substance** | Etoxazole |
| **Function** | Insecticide |
| **Chemical name** | |
| 1. **International Union of Pure and Applied Chemistry (IUPAC)** | (*RS*)-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl]phenetole |
| 2. **Chemical Abstracts Service (CAS)** | 2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole |
| **CAS number** | 153233-91-1 |
| **Molecular formula** | $C_{21}H_{23}F_2NO_2$ |
| **Molecular weight** | 359.4 |



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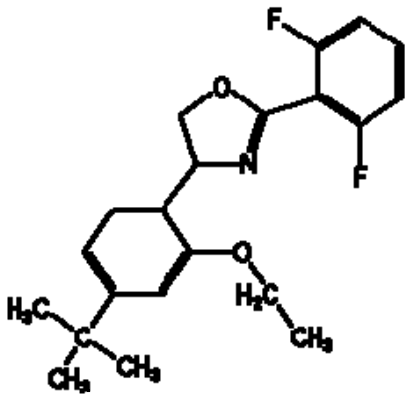
**Structural formula**



**Purity of the active ingredient** 97.2%

**Technical Product—Etoxazole Technical**

| Property | Result |
|---|---|
| Colour and physical state | White crystalline powder |
| Odour | No obvious odour |
| Melting range | 101.5 to 102.5 °C |
| Boiling point or range | The product is a solid |
| Specific gravity at 20°C | 1.2389 |
| Vapour pressure at 25°C | $7.0 \times 10^{-6}$ Pa |
| Ultraviolet (UV)-visible spectrum | pH — $\lambda_{max}$ (nm)<br>Neutral — 220<br>272<br>Acidic — 222.5<br>272.5<br>Basic — 272.5 |
| Solubility in water | $3.99 \times 10^{-5}$ g/L in distilled water at 10 °C<br>$7.04 \times 10^{-5}$ g/L in distilled water at 20 °C<br>$6.69 \times 10^{-5}$ g/L in distilled water at 30 °C |
| Solubility in organic solvents at 20°C | Solvent — Solubility (g/L)<br>Acetone — 309<br>1,2-Dichloroethane — 402<br>Ethyl acetate — 249<br>n-Heptane — 18.7<br>Methanol — 104<br>Xylene — 252 |
| *n*-Octanol-water partition coefficient ($K_{ow}$) | Log $K_{ow}$ = 5.52 at 20 °C |
| Dissociation constant ($pK_a$) | Does not dissociate |

| | |
|---|---|
| Stability (temperature, metal) | The product was found to be stable under elevated temperature. The applicant stated that the technical grade active ingredient was not tested for stability to metals since contact with metals in unlikely in normal product storage and use. |

The methods provided for the analysis of the active ingredient and the impurities in Etoxazole Technical have been validated and assessed to be acceptable for the determinations.

**Health Assessments**

Since there is no impact on the toxicological profile, please refer to the previous Evaluation Report for submission 2008-0581 for the complete toxicity assessment of etoxazole.

The nature of etoxazole in livestock and plants is adequately understood based on the previously reviewed animal metabolism studies (goat and hen), and plant metabolism studies (cotton, orange, eggplant, and apple). Based on these studies, the residue definition for etoxazole in/on plant and livestock matrices is outlined in TABLE 1.

**TABLE 1. Summary of Residue Definition for Etoxazole**

| **Matrix** | | **Dietary Exposure Assessment** | **Enforcement** |
|---|---|---|---|
| Plants | Apple, Orange, Eggplant, Cottonseed | Parent Only | Parent Only |
| Livestock - Ruminant | Muscle, Fat, Milk | Parent Only | Parent Only |
| | Liver, Kidney | Parent, Metabolite 1 | Parent Only |
| Livestock - Poultry | Muscle, Fat, Eggs | Parent Only | Parent Only |
| | Liver, Egg Whites | Parent, Metabolite R-16 | Parent Only |

An LC-MS/MS analytical method (liquid chromatography with dual mass selective detector), and analytical methods modified from previously reviewed enforcement/data gathering methods GC-NPD (gas chromatography with nitrogen-phosphorous specific flame-ionization detector) and GC-MSD (gas chromatography with mass selective detector) were used to quantitate residues of etoxazole in/on the currently petitioned imported crops.

Frozen storage stability of etoxazole was demonstrated in several commodities (mint leaves, avocadoes, tea, hops, tomatoes, bell and non-bell peppers, cucumbers and summer squash) ranging from 3-13 months, therefore providing confidence that residues will not decline to less than 70% of their original value under the actual storage intervals of the samples. Residues of etoxazole in cantaloupes, caneberries and stone fruits were corrected for any noted in-storage dissipation.

Crop field trials were conducted in NAFTA representative growing regions on tomatoes, bell and non-bell peppers, cucumbers, summer squash, cantaloupe, cherry, peach, plum, caneberry, mint leaves, avocado and hops. Crop field trials on tea were conducted in Japan. Trials for tea and avocadoes were conducted at the maximum label rates. Trials for all other commodities were conducted at 2-fold maximum label rates since they were completed before the U.S. established

that a single application per season would be sufficient. The established MRL on grapes will be replaced by the MRL for the Small Fruit Vine Climbing (except fuzzy kiwifruit) Subgroup (CG13-07F). The established MRL on strawberries will be replaced by the MRL for the Low Growing Berry Subgroup (CG 13-07G). A summary of the submitted field trial data is provided in TABLE 2.

**TABLE 2. Summary of Field Trial Data Used to Establish Maximum Residue Limit (MRL)**

| Commodity | Application Method/ Total Application Rate (g a.i./ha) | PHI (days) | Residues (ppm) | | Experimental Processing Factor | Currently Established MRL | Recommended MRL |
|---|---|---|---|---|---|---|---|
| | | | Min | Max | | | |
| Tomato | Foliar broadcast/ 301-304 | 1 | <0.010 | 0.053 | N/A | None | 0.20<br>Peppers and eggplants (crop subgroup 8-09B) |
| Bell pepper | Foliar / 300-314 | 6-8 | <0.010 | 0.042 | N/A | None | |
| Non-bell pepper | Foliar / 296-306 | 6-7 | <0.010 | 0.160 | N/A | None | |
| Cantaloupe | Foliar / 296-311 | 5-8 | 0.016 | 0.119 | N/A | None | 0.20<br>Melons (crop subgroup 9A) |
| Summer squash | Foliar / 304-325 | 6-7 | <0.010 | 0.014 | N/A | None | 0.02<br>Squash and cucumbers (crop subgroup 9B) |
| Cucumber | Foliar / 297-316 | 6-8 | <0.010 | 0.014 | N/A | None | |
| Tart cherry | Foliar / 304-312 | 6-8 | 0.031 | 1.190 | N/A | None | 1.0<br>Stone fruits (crop group 12-09); except plums |
| Sweet cherry | Foliar / 304-321 | 6-8 | 0.130 | 0.280 | N/A | None | |
| Peach | Foliar / 299-309 | 6-8 | 0.113 | 0.494 | N/A | None | |
| Plum | Foliar / 302-307 | 6-7 | 0.023 | 0.102 | N/A | None | 0.15 |
| Caneberry | Foliar / 300-324 | 0 | 0.295 | 1.071 | N/A | None | 1.5<br>Caneberries (crop subgroup 13-07A) |

| **TABLE 2. Summary of Field Trial Data Used to Establish Maximum Residue Limit (MRL)** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Commodity** | **Application** | **PHI** | **Residues (ppm)** | | **Experiment** | | **Recommende** |
| Grape | Foliar/ 296-310 | 13-14 | <0.005 | 0.330 | N/A | 0.5 (Grape only) | 0.5 Small fruits vine climbing, except fuzzy kiwifruits (13-07F) |
| Strawberry | Foliar/ 299-305 | 1 | 0.028 | 0.318 | N/A | 0.5 (Strawberry only) | 0.5 Low growing berries (13-07G) |
| Hops (residues of etoxazole only) | Foliar / 410-428 | 6-7 | 1.980 | 4.180 | N/A | None | 7 |
| | Foliar / 449 | 7 | 3.710 | 4.090 | N/A | None | |
| Mint (leaves) | Foliar / 445-463 | 6-7 | 2.400 | 7.600 | 1.6 (for oil) | None | 15 (Peppermint and Spearmint Leaves) 20 (Peppermint and Spearmint Oil) |
| Avocado | Foliar / 151-156 | 1 | <0.01 | 0.089 | N/A | None | 0.20 |
| Tea | Foliar / 400 | 14 | 2.340 | 7.980 | N/A | None | 15 |

Processing studies were conducted on plums and mint. Concentration was only observed in mint oil (1.6-fold), and thus MRLs for peppermint and spearmint oils at 20 ppm will be required.

Dietary Exposure Assessment

The basic chronic dietary exposure assessment, using consumption estimates coupled with proposed MRLs, demonstrates that consumption of the above imported crops treated with

etoxazole as per Good Agricultural Practices (GAP) will not pose a concern to human health for any segment of the population, including infants, children and seniors.

**Environmental Assessment**

An environmental assessment was not required for this application.

**Value Assessment**

A value assessment was not required for this application.

**Conclusion**

The Pest Management Regulatory Agency has completed an assessment of information available in support of Etoxazole Technical and has found the information sufficient to support the import MRLs on for the active ingredient etoxazole on tea; caneberries (crop subgroup 13-07A); cucurbit vegetables (crop group 9); hops; low growing berries (crop subgroup 13-07G); mint; tomatoes; peppers and eggplants (crop subgroup 8-09B); small fruit vine climbing except fuzzy kiwifruit (crop subgroup 13-07F); tropical fruit (avocado, papaya, star apple, black sapote, mango, sapodilla, canistel, mamey sapote); and stone fruit (crop group 12-09).

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