UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY

AND POLLUTION PREVENTION

MEMORANDUM

DATE: 24-MAY-2017

SUBJECT: **Ametoctradin (BAS 650F). Human Health Risk Assessment** for Amended Use on Imported Hops

PC Code: 119210	DP Barcode: D435382
Decision No.: 520001	Registration No.: NA
Petition No.: 6E8500	Regulatory Action: Tolerance Amendment
Risk Assessment Type: Single Chemical Aggregate	Case No.: NA
TXR No.: NA	CAS No.: 865318-97-4
MRID Nos: 49978301, 50202401 and 50202402	40 CFR: §180.663

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This document provides HED's conclusion of EFSA review of the submitted data in support of amended use on hops as it relates to amended import tolerance and human health risk assessment.

1.0 EXECUTIVE SUMMARY

Ametoctradin, a fungicide, was registered in 2012 for a variety of crops. HED determined that based on toxicity considerations, there are no risk concerns from exposure to the parent or its metabolites and degradates. Therefore, an exemption from the requirement of a tolerance was deemed appropriate for amectoctradin. However, in light of the petitioner's desire for tolerances/maximum residue limits (MRLs) for international trade purposes, HED recommended that the parent compound, in harmonization with other global partners, be used for enforcement and risk assessment purposes; likewise, HED recommended that tolerance levels be harmonized with the global partners.

BASF has submitted a tolerance petition to amend the existing ametoctradin tolerance for residues in hops from the established tolerance of 10 parts per million (ppm) to 100 ppm. The petitioner has made this request to accommodate the importation of hops grown in the European Union into the United States. BASF did not submit residue field trial data on hops as required by the *NAFTA Guidance Document on Data Requirements for Tolerances on Imported Commodities in the United States and Canada (December 2005).* Instead the petitioner submitted this request under OPP's pilot program where they have provided the review by European Food Safety Authority (EFSA) of residue field trial data conducted in Germany to support the increase in the hop tolerance to 100 ppm. BASF is requesting that the United States Environmental Protection Agency (USEPA) rely on the *Reasoned Opinion on the Modification of the Existing MRL for Ametoctradin in Hops - European Food Safety Authority (EFSA), Parma, Italy* dated October 22, 2014 (MRID 49978301) to support the amendment to the tolerance.

EFSA concluded that the field trial data and processing studies are adequate and support an increase of the MRL to 100 ppm. BASF submitted to HED an analytical method validation study as well as an independent method validation (ILV) report in support of the proposed analytical enforcement method. HED reviewed both documents and deemed them satisfactory. HED has not identified any residue chemistry issues that would prevent the Agency from increasing the hops import tolerance from 10 ppm to 100 ppm in order to harmonize with the European Union.

2.0 HED RECOMMENDATIONS

2.1 Data Deficiencies/Conditions of Registration

- None

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

Analytical methods for the determination of ametoctradin residues in plant commodities were assessed during peer review under Directive 91/414/EEC (NL, 2009; EFSA, 2012b). A method based on methanol/water extraction, clean up and final quantification by HPLC-MS/MS was proposed for enforcement purposes. The method was validated for the determination of ametoctradin residues in high water content (tomato, potato), high acid content (orange) and dry commodities (wheat), at the limit of quantification (LOQ) of 0.01 mg/kg (EFSA, 2008). EFSA concluded that the analytical method is not fully validated for dried hops and therefore, additional data had to be provided to confirm that the proposed analytical method is suitable to enforce ametoctradin residues in dried hops. Subsequently, the USEPA contacted BASF and inquired about the need for additional data. BASF submitted a method validation study for dried hops (S. Richter and S. Djedovic, BASF Study ID 772934, 06-OCT-2016) in addition to an independent method validation report (T. Link, BASF Study ID 772935, 22-NOV-2016) which were reviewed by HED and deemed satisfactory. No further data are required.

2.2.2 International Harmonization

HED has examined the residue chemistry database for ametoctradin. There are no residue chemistry issues that would preclude amending the import tolerance without U.S registration for the residues of ametoctradin on hop, dried cones as noted in Table 2.2.2.1 below. The current tolerance expression complies with the 2009 Knizner guidance on tolerance expressions. The amended tolerance should be established under 40 CFR §180.663 (a) for hop, dried cones, as follows:

Table 2.2.2.1 Tolerance Summary for Ametoctradin

Commodity	Established Tolerances (ppm)	Proposed Tolerances (ppm)	HED-Recommended Tolerance (ppm)	Comments
Hop, dried cone	10	100	100	Harmonization with EU

2.2.3 Revisions to Petitioned-For Tolerances

There are no revisions to the petitioned-for tolerances.

2.3 Label Recommendations

As the petitioned uses are for imported crops, the USEPA has no jurisdiction over the contents of the foreign labels. HED notes that the labels were reviewed by EFSA.

3.0 INGREDIENT PROFILE

3.1 Chemical Identity

The structure and nomenclature of ametoctradin are reported in Tables 3.1.1 and 3.1.2.

TABLE 3.1.1 Ametoctradin Nomenclature.

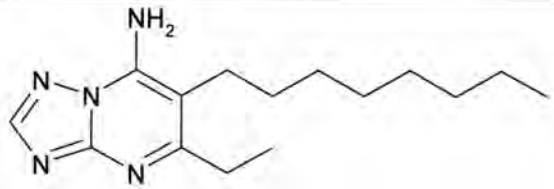
Compound	
Common name	Ametoctradin
Company experimental name	BAS 650 F
IUPAC name	5-ethyl-6-octyl[1,2,4]triazolo[1,5-*a*]pyrimidin-7-amine
CAS name	5-ethyl-6-octyl[1,2,4]triazolo[1,5-*a*]pyrimidin-7-amine
CAS registry number	865318-97-4
End-use product (EP)	BAS 650 00F, Zampro and Orvega

TABLE 3.1.2 Physicochemical Properties of Technical Grade Ametoctradin.

Parameter	Value	Reference
Melting point	197.7°C to 198.7°C	MRIDs: 47700007, 47700008, 47700009, 4700011, 4700012, 47700013, 47700014, 47700017
pH	pH 5.7 at 20°C	
Density	1.12 g/cm^3 at room temperature	
Water solubility	0.14 mg/L at 20°C	
Solvent solubility	Solvent Solubility (g/100mL) Methanol 0.72 Toluene 0.01 n-Heptane <0.001 Ethylacetate 0.08 Dichloromethane 0.30 Acetone 0.19 Acetonitrile 0.05 Dimethylsulfoxide 1.07	
Vapor pressure	2.1 x 10^{-10} Pa at 20°C	
Dissociation constant, pK$_a$	2.78	
Octanol/water partition coefficient, Log(Kow)	4.4 at 20°C (neutral pH)	
UV/visible absorption spectrum	UV molecular extinction ε [l mol^{-1} cm^{-1}]: Methanol pure, pH 7.6: 16611 at 221 nm 13113 at 295 nm Methanol : Water = 1 : 99, pH 7.2: 26485 at 217 nm 9861 at 294 nm Methanol : HCl : Water = 1 : 10 : 89, pH 1.0: 29557 at 218 nm 14288 at 295 nm Methanol : NaOH : Water = 1 : 10 : 89, pH 12.5: 12107 at 224 nm 9977 at 295 nm	

3.2 Residue Chemistry: Use Pattern and Residues

In support of the MRL application to EFSA, the EMS submitted four residue trials conducted in 2009-2010 in Germany, according to the proposed Good Agricultural Practice (GAP)rate *(2x800 g/ha; PHI 10 days)*. EFSA concluded that the submitted supervised residue trials are sufficient to derive an MRL of 100 ppm for the proposed use on hops. Furthermore, the processing study showed dilution of residues in beer. As part of OPP's pilot, HED has reviewed and agreed with the submitted EFSA review of the submitted data in support of the amended use rate for hop and recommends for a tolerance level which is harmonized with the established EFSA MRL (of 100 ppm).

4.0 HAZARD CHARACTERIZATION AND EXPOSURE ASSESSMENT

Ametoctradin was subject of a global review in 2010-2011. The registrant submitted a complete acute battery for the ametoctradin technical grade active ingredient which were reviewed by USEPA. All the non-acute studies were primarily reviewed by Australia and secondarily reviewed by USEPA and other member countries for the joint-review.

No single dose or repeated dose study performed by any route of exposure produced a significant toxic effect up to or near enough to the limit dose (1000 mg/kg/day). This includes the studies performed with the ametoctradin metabolites. There was also no evidence of carcinogenicity or mutagenicity and therefore ametoctradin is considered "Not Likely to Be Carcinogenic to Humans."

Based on a review of the available ametoctradin toxicological studies, no toxicological points of departure where selected for ametoctradin and thus, an additional Food Quality Protection Act (FQPA) safety factor to protect children is not needed. As a result, no dietary, residential, occupational, or aggregate exposure assessments are required at this time.

References

1. MRID 49978301, (author: Anonymous), "Reasoned Opinion on the Modification of the Existing MRL for Ametoctradin in Hops - European Food Safety Authority (EFSA), Parma, Italy", 10/22/2014.
2. MRID 50202401, S. Richter, S. Djedovic, "Validation of BASF analytical method L0117/02 for the determination of BAS 650 F (Ametoctradin) in dried hops", BASF Study ID: 772934, 10/6/2016.
3. MRID 50202402, Thomas Link, "Independent laboratory validation (ILV) of an analytical method for the determination of BAS 650 F (Ametoctradin) in dried hops", SGS INSTITUT FRESENIUS Study No. IF-16/03810955, BASF Study ID: 772935, 11/22/2016.