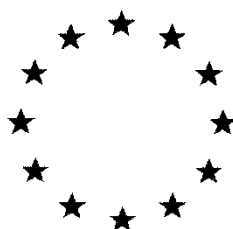


European Commission

**Second Programme for the Renewal of the Inclusion of Active Substances
in Annex I of Council Directive 91/414/EEC**



**Draft Renewal Assessment Report prepared according to the Commission
Regulation (EU) N° 1141/2010**

Amitrole

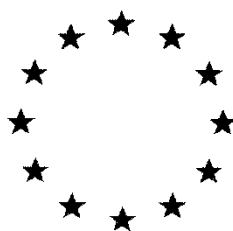
**Rapporteur Member State: France
Co-Rapporteur Member State: Hungary**

January 2013

Ministère de l'Agriculture, de l'Agroalimentaire et de la Forêt
Direction Générale de l'Alimentation
251, rue de Vaugirard
75732 PARIS Cedex 15
France

European Commission

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in Annex I of Council Directive 91/414/EEC**



**Draft Renewal Assessment Report prepared according to the Commission
Regulation (EU) N° 1141/2010**

Amitrole

Volume 1

**Rapporteur Member State: France
Co-Rapporteur Member State: Hungary**

January 2013

**Ministère de l'Agriculture, de l'Agroalimentaire et de la Forêt
Direction Générale de l'Alimentation
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France**

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Level 1

Amitrole

January 2012

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

1. STATEMENT OF SUBJECT MATTER AND PURPOSE FOR WHICH THE MONOGRAPH WAS PREPARED

1.1. PURPOSE FOR WHICH THE MONOGRAPH WAS PREPARED

1.2. SUMMARY AND ASSESSMENT OF INFORMATION RELATIVE TO THE COLLECTIVE PROVISION OF DOSSIERS

1.3. IDENTITY OF THE ACTIVE SUBSTANCE (ANNEX IIA 1)

1.3.1. Name and address of applicant(s) for inclusion in Annex I (Annex IIA 1.1)

NUFARM SAS
28, boulevard Camelinat
92230 Gennevilliers
FRANCE

Person to contact:

[REDACTED]

Phone:

Fax :

E-mail :

1.3.2. Common name and synonyms (Annex IIA 1.3)

ISO common name (approved or proposed): Amitrole

Synonyms: Aminotriazole

1.3.3. Chemical name (Annex IIA 1.4)

IUPAC: 1-H-1,2,4-triazol-3-ylamine

CA: 1-H-1,2,4-triazol-3-amine

1.3.4. Manufacturer's development code number (Annex IIA 1.5)

Code: CA0027

1.3.5. CAS, EEC and CIPAC numbers (Annex IIA 1.6)

CAS: 61-82-5

ENEICS: 200-521-5

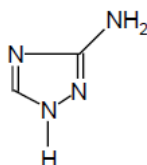
EU index: 613-011-00-6

CIPAC: 90

1.3.6. Molecular and structural formula, molecular mass (Annex IIA 1.7)

Molecular formula: C₂H₄N₄

Structural formula:



Molecular mass: 84.08 g/mol

1.3.7. Manufacturer or manufacturers of the active substance (Annex IIA 1.2)

[REDACTED]

Person to contact:

Stéphanie [REDACTED]

Phone: [REDACTED]

Fax : [REDACTED]

E-mail : Stephanie. [REDACTED]

1.3.8. Method or methods of manufacture (annex IIA 1.8)

Please refer to Volume 4, confidential part.

1.3.9. Specification of purity of the active substance (annex IIA 1.9)

The minimum content of pure active substance is ≥ 910 g/kg.

1.3.10. Identity of inactive isomers, impurities and additives (annex IIA 1.10)

Please refer to Volume 4, confidential part.

1.3.11. Analytical profile of batches (annex IIA 1.11)

Please refer to Volume 4, confidential part.

1.4. IDENTITY OF THE PLANT PROTECTION PRODUCT (ANNEX IIIA 1.1)

1.4.1. Current, former and proposed trade names and development code numbers (Annex IIIA 1.3)

Trade Name: WEEDAZOL TL

Company Code Number: CA2735

1.4.2. Manufacturer of the preparation (annexe IIIA 1.2)

[REDACTED]

1.4.3. Type of preparation and code (annex IIIA 1.5)

Soluble Concentrate (SL)

1.4.4. Function (annex IIA 3.1, annex III 1.6)

Herbicide

1.4.5. Compositions of the preparations (annex IIIA 1.4)

Please refer to Volume 4, confidential part.

1.5. USES OF THE PLANT PROTECTION PRODUCT

1.5.1. Field of use (Annex IIA 3.3 Annex IIIA 3.1)

Both agricultural (orchards, olive and vineyard) and non-agricultural (railways, roadsides, etc.)

1.5.2. Effects on harmful organisms (Annex IIA 3.2; Annex IIIA 3.2)

Non selective weed control.

Amitrole is systemic. It is rapidly absorbed by the leaves (mainly), but can be absorbed to a lesser extent by the roots. Once in the plants, it is translocated by both the xylem (apoplastic) and the phloem (symplastic). Weeds once treated with amitrole appear as whitening.

1.5.3. Summary of intended uses*

Crop and/or situation (a)	Member State	Product Name	F G I (b)	Pests or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	Kg a.i./ha min max (g/ha)	Water l/ha min max	Kg a.i./ha min max (*) (g/ha)		
Orchards (citrus fruits, pome and stone fruits, assorted fruits-edible or inedible peel, tree nuts)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	94-75	1 (or several splitted applications)	2-3 months	0.24-1	300 to 500	1.2-3	35	CA2735 is applied either once per year at 2977 gai/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Grapes (table and vine)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	92-79	1 (or several splitted applications)	2-3 months	0.24-1	300 to 500	1.2-3	42	CA2735 is applied either once per year at 2977 gai/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Olives	South EU MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	Spring and autumn	1-2 (or several splitted applications)	2-3 months	0.18-0.5	300 to 500	0.9-1.375	35	CA2735 is applied either once or twice per year at 1375 gai/ha (ie 6 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Non crop uses (impermeable and permeable surfaces: road, railways)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	Not applicable	1 (or several splitted applications)	2-3 months	0.36-1	300 to 500	1.8-3	-	CA2735 is applied either once per year at 2977 gai/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.

- * For uses where the column „Remarks“ in marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
- (a) For crops, the EU and Codex classification (both) should be taken into account ; where relevant, the use situation should be described (e.g. fumigation of a structure)
- (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
- (c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds
- (d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
- (e) GCPF Codes – GIFAP Technical Monograph N° 2, 1989
- (f) All abbreviations used must be explained
- (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant – type of equipment used must be indicated
- (i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypryr). **In certain cases, where only one variant synthesised, it is more appropriate to give the rate for the variant (e.g. benthialvalicarb-isopropyl).**
- (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
- (k) Indicate the minimum and maximum number of application possible under practical conditions of use
- (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)
- (m) PHI - minimum pre-harvest interval

Level 2

Amitrole

XXX 2012

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2. RESONED STATEMENT OF THE OVERALL CONCLUSIONS DRAWN BY THE RAPPORTEUR MEMBER STATE

2.1. IDENTITY

The manufacturing process has not changed. Nevertheless, regarding toxicological evaluation based on two batches, the previous specifications provided for the 1st inclusion of Amitrole can't be considered as acceptable. According to the new 5-batch analysis provided, new specifications based on the thumb rule mean $\pm 3SD$ can be proposed. The minimum purity of Amitrole is specified at 910 g/kg. Specifications are considered acceptable except for two impurities (impurity 1 and impurity 2) for which additional information (another *in vitro* genotoxicity test) is needed.

2.2. PHYSICAL AND CHEMICAL PROPERTIES

ACTIVE SUBSTANCE

Pure Amitrole is a colourless and odourless crystal. It has a melting point of 157 - 159 °C. It has no thermal decomposition. It has a relative density of 1.138 at 20°C. Its vapour pressure ($3.3 \cdot 10^{-5}$ Pa at 20 °C) indicates that it has a very low possibility to volatilize from soil to air. Its volatility ($1.76 \cdot 10^{-8}$ Pa.m³.mol⁻¹) indicates that it has a very low possibility to volatilize from water to air. It is highly soluble in water and from low to moderately soluble in solvents (from < 0.01 g/L in n-hexane to 27 g/L in isopropanol). It has a Log P_{ow} of - 0.969 in neutral conditions indicating that it should not be expected to bioaccumulate in the environment. It is stable to hydrolysis at pH 5, 7 and 9 and water photolysis. Degradation in the atmosphere has been evaluated with a DT₅₀ of 4.8 hours. Its dissociation constant is pKa1 = 4.14 and pKa2 = 10.69 at 20°C. Amitrole was not found to have flammable, explosive or oxidizing properties.

PLANT PROTECTION PRODUCT

The formulation WEEDAZOL TL is a dark brown fluid liquid, odourless soluble concentrate, containing 229 g/L of Amitrole and 215 g/L of ammonium thiocyanate. This formulation does not present explosive and oxidising properties. It is not highly flammable (no flash point was observed up to 108°C), and not auto-flammable (no self ignition observed up to 652 °C) at ambient temperature. The pH of a 1% solution at 20 °C is 6.17. The dynamic viscosity is < 10 mPa.s at 20°C. The surface tension is > 60 mN/m indicating that formulation is not surface active. Its relative density is 1.1171 at 20 °C. There is no effect of high and low temperature on the stability of the formulation, after 14 days at 54 °C and 7 days at 0 °C, neither the active ingredient content nor the technical properties were changed. The content of active substance is unchanged after 2 years of storage at ambient temperature in the previous formulation CA2210 demonstrating an acceptable 2 years shelf life for the product in commercial packaging (plastic flask). The 2-year stability study in CA2735 formulation is on-going. After 1 minute, 0 mL of persistent foam remained, indicating that the formulation is not a foaming product. The dilution stability is acceptable.

Under recommended use, no particular problems should be expected due to technical characteristics or physico-chemical properties.

2.3. METHODS OF ANALYSIS

2.3.1. Methods of analysis for determination of the active substance as manufactured

Analytical methods for the determination of active substance, significant/relevant impurities in the active substance as manufactured

Analytical method C-ORGANIQUE-00383-E-TA (based on CIPAC method 90/TC/(M)-) for the determination of Amitrole in technical material is considered as validated.

Analytical methods C-ORGANIQUE-00383-C-TA, C-ORGANIQUE-00467-C-TA and CIPAC MT 30.5 for the determination of impurities in technical material are considered as validated.

Analytical methods for the determination of active substance and significant/relevant impurities in the plant protection product

An analytical method based on CIPAC method 90/TC/(M)- for the determination of Amitrole in formulation CA2735 is considered as validated.

An HPLC/UV method based on CIPAC method 90/SL/M for the determination of Amitrole in the preparation CA2735 is considered as validated.

There are no toxicologically, environmentally or ecotoxicologically relevant impurities present in the preparation CA2735. Therefore, analytical methods for the determination of impurities of concern are not required. Nevertheless, an analytical method for the determination of the synergist ammonium thiocyanate in the preparation CA2735 has been submitted and considered as validated.

2.3.2. Analytical methods for determination of residues

Analytical methods for residue determination in plants

The residue definition for monitoring in plant is Amitrole.

An analytical method (Gemrot, F. 2011a and 2011b, Amic, S. 2012) and its ILV (Ivanov, E. 2012) using LC-MS/MS are considered as validated for the determination of Amitrole and its metabolites triazolylalanine and aminotriazolylalanine in plants (grapes, olives, apples) with **LOQ = 0.01 mg/kg** for each analyte.

The applicability of the DFG S19 multi-residue method has not been demonstrated and is required. (December 2012: Nufarm stated that a study is ongoing and that the final report will be available by March 2013)

Analytical methods for residue determination in food of animal origin

Studies on nature or magnitude of residues in commodities of animal origin are not available, or required. Following the estimation of the dietary burden arising from the authorised uses of Amitrole, MRLs for livestock products are not required because livestock is not expected to be exposed to significant levels of Amitrole residues.

So, no analytical method is necessary.

Analytical methods for residue determination in soil

The residue definition for monitoring in soil is Amitrole.

An analytical method (Amic, S. 2012) using LC-LC--MS/MS is considered as validated for the determination of Amitrole in soil with **LOQ = 0.01 mg/kg**.

Analytical methods for residue determination in water

The residue definition for monitoring in water is Amitrole.

An analytical method (Amic, S. 2012) using LC-LC-MS/MS is considered as validated for the determination of Amitrole in drinking and surface water with **LOQ = 0.05 µg/L**.

Analytical methods for residue determination in air

The residue definition for monitoring in air is Amitrole.

An analytical method fully validated is required according to guidance document SANCO/825/00 rev 8.1 (December 2012: Nufarm stated that the validation is ongoing and that the final report will be provided by Q2 2013.)

Analytical methods for residue determination in body fluids and tissues

An analytical method (Gemrot, F., 2011c) using LC-MS/MS is considered as validated for the determination of Amitrole in body fluids (urine) with **LOQ = 5 µg/L**.

2.4. CLASSIFICATION AND LABELLING

Active substance classification and labelling requirements

Classification of the active substance

Under Council Directive 67/548/EEC:

Hazard symbols: Xn Repr Cat 3



Risk phrases: R63 R48/22

Safety phrases: S36/37

Under Regulation (EC) No 1272/2008:



Warning

STOT RE 2 (H373), Repr. 2 (H361D)

Environment:

	According to directive 67/548	According to regulation 1272/2008
Identification of Danger	Dangerous for the environment (N) 	Warning, GHS09
Risk phrases	R51/53, Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	Aquatic chronic 2, H411: Toxic to aquatic life with long lasting effects

Safety phrases	S60, S61	P273, P391, P501
----------------	----------	------------------

Preparation classification and labelling requirements proposed by the rapporteur

Classification of the preparation CA2735

Under Council Directive 99/45/EC:

Hazard symbols: Xn Repr Cat 3



Risk phrases: R63 R48/22 R36

Safety phrases: S36/37

Under Regulation (EC) No 1272/2008:



Warning

STOT RE 2 (H373), Repr. 2 (H361d), Eye Irrit. 2 (H319)

Environment:

	According to directive 67/548	According to regulation 1272/2008
Identification of Danger	No signal word No pictogram	No signal word No pictogram
Risk phrases	R52/53, Harmful to aquatic life, may cause long-term adverse effects in the aquatic environment.	Aquatic chronic 3, H412: Harmful to aquatic life with long lasting effects
Safety phrases	S60	P273, P501

2.5. IMPACT ON HUMAN AND ANIMAL HEALTH

2.5.1. Effects having relevance to human and animal health arising from exposure to the active substance or to impurities contained in the active substance or their transformation products

2.5.1.1. Toxicokinetics and metabolism

Absorption, distribution, metabolism and excretion

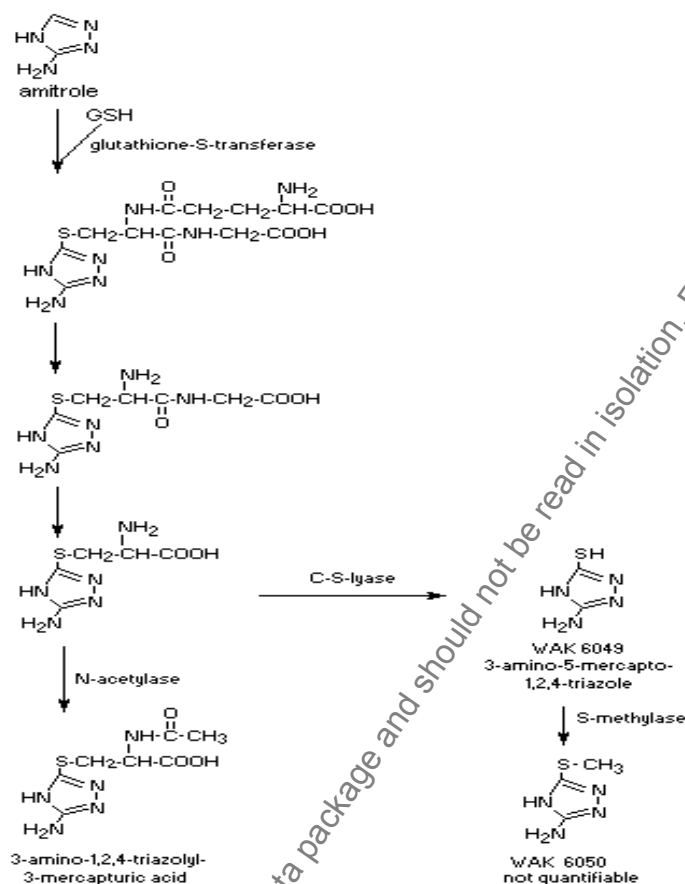
Pharmacokinetic studies were conducted in male and female mice, rats and rabbits.

Following oral administration, amitrole is readily absorbed from the gastro-intestinal tract of mammals. It is rapidly excreted from the body mainly as the parent compound. The main route of excretion in humans and laboratory animals is via the urine and the majority of excretion takes place during the first 24h.

This molecule is a polar molecule which is mostly excreted unchanged in urine. Phase II reactions can occur and consist in conjugation to glutathione through the glutathione transferase. Other enzymes like N-acetylase or CS lyase are also involved. N-acetylase leads to the formation of 3-amino-1,2,4-triazolyl-5-mercaptopuric acid in mammals whereas the CS lyase action gives rise to 3-amino-5-mercapto-1,2,4-triazole.

The reactions are shown in figure 1.

Figure 1. Proposed metabolic pathway of amitrole in rats



2.5.1.2. Acute toxicity

Technical amitrole is of low oral and dermal toxicity in rats ($\text{LD}_{50} > 5000 \text{ mg/kg b.w}$ and $> 2500 \text{ mg/kg b.w}$, respectively).

The acute toxicity was also very low when administered by intravenous route in rats and mice.

Acute inhalative exposure to the highest technically producible aerosol concentration (439 mg/m^3) was tolerated by rats without any adverse effect. The 4-hour LC_{50} was set to be greater than 0.439 mg/L (highest attainable concentration).

Technical amitrole is not irritant to the skin and slightly irritant to the eyes. Amitrole was shown not to be a skin sensitizer in a Magnusson and Kligmann test.

2.5.1.3. Short-term toxicity

Repeated oral administration of amitrole results mainly in effects on thyroid. It is currently well known that thyroid toxicity of amitrole is due to inhibition of thyroid peroxidase. Consequently rats treated with amitrole have low serum T4 and T3 levels with a parallel increase in TSH levels. Amitrole interferes with the production of thyroid hormones thus leading to hypertrophy and hyperplasia of the follicular cells of the thyroid. This can result in tumours of this gland in rodents after a prolonged administration. Evidence for reversibility of the thyroid effect in the rat was observed when the exposure was of short duration.

After 4 weeks of administration by oral route, thyroid effects are observed at levels greater than 1.5 mg/kg bw/d in rats (LOAEL of 5 mg/kg bw/d).

Three short-term studies were conducted in rats (one 10-week study and two 90-day studies), two one-year studies were carried out in dogs and a 90-day study was performed in monkeys.

In the 10-week study, the NOAEL was set at 1.5 mg/kg bw/d in females and less than 1.5 mg/kg bw/d in males, based on increase of TSH levels, follicular cell hypertrophy, small vesicles and increase vascularity observed from 12 mg/kg bw/d in females and 1.5 mg/kg bw/d in males. In the two 90-day studies (one performed in males only and the other in females only), the NOAEL were set at 0.1 mg/kg bw/d in males and females, based on thyroid effects (histological changes in the thyroid regarding appearance of follicular cells, content of colloid and capillary density in males; in females: increased iodine uptake shortly after injection, increased thyroid weight and histopathological changes of the thyroid).

Although no thyroid effects were observed in a 1-year dog study (NOAEL of 12.5 mg/kg bw/d, the highest dose level where only pale coloured pancreas was noted), thyroid parameters were affected from the LOAEL of 13 mg/kg bw/d in the other 1-year dog study. This consisted in enlarged thyroid, increased absolute and relative thyroid weight and follicular cells hyperplasia. The NOAEL was established at 0.3 mg/kg bw/d in this study.

A 90-day toxicity study was performed in cynomolgus monkey by oral route. The NOAEL were set at less than 30 mg/kg bw/d in males and at 100 mg/kg bw/d in females, based on thyroid effects observed from 30 mg/kg bw/d in males and 330 mg/kg bw/d in females.

Overall a NOAEL of 0.1 mg/kg bw/d for thyroid effects by oral route can be considered in the short-term studies.

By dermal route a NOAEL of 100 mg/kg bw/day was established in a 28-day study in rats based on thyroid effects (slightly higher TSH level and slightly decreased T3 and T4 levels, higher mean absolute and relative thyroid weight, morphological indication of gland hyperactivity) observed at 500 mg/kg bw/day. In rabbits no adverse effect was reported until the dose of 100 mg/kg bw/day.

By inhalation, a NOEC of 0.1 mg/L was established in a 28-day study in rats based on thyroid effects (decreased T3 and T4 level, thyroid hyperplasia and elevated thyroid weight) observed at 0.32 mg/L. However this NOEC was established based on the aerosol concentration in the inhalation chamber. The particle size distribution was not evaluated so that no information is given regarding the respirable fraction. Therefore the fraction of the aerosol concentration that was effectively inhaled cannot be determined in order to derive a systemic NOEL.

2.5.1.4. Genotoxicity

Amitrole has been extensively tested in *in vitro* and *in vivo* genotoxicity studies. If positive results were obtained in some *in vitro* tests, no genotoxicity was found *in vivo*.

By weight of evidence, amitrole is not a genotoxic compound. This was confirmed by recent *in vitro* gene mutation and chromosomal aberration tests.

2.5.1.5. Long-term toxicity

Long term and/or carcinogenicity studies have been performed in rats, mice and golden hamsters.

A first 2-year oral toxicity and carcinogenicity in the rat was considered as informative; it was indeed difficult to assess it because of several changes in dosing regimen. Nevertheless, thyroid appeared as the target organ (thyroid hyperplasia were seen in all treated groups, increased incidence of thyroid tumours (mainly follicular adenomas)).

In a carcinogenicity study in rats fed with dose levels of 0, 1, 10 and 100 ppm, a slight decrease in survival time, an increase in the incidence of (benign and malignant) thyroid tumours, and an increase of the incidence of (mainly benign) pituitary gland tumours was observed at 100 ppm. In this study a thyroid function was also performed in a small number of animals. At 100 ppm (5 mg/kg bw/d) thyroid weight was increased during the whole study period as was the percentage of accumulation of radioiodine in the thyroid. The NOAEL was set at 10 ppm (equivalent to 0.5 mg/kg bw/d).

In a 18-month carcinogenicity study in mice at level of 0, 1, 10 and 100 ppm in the diet, increased incidence of tumours was not observed. In this study a thyroid function was also performed in a small number of animals. At 100 ppm (15 mg/kg bw/d) an increase in thyroid weight and in iodine accumulation in the thyroid was observed. The NOAEL was set at 10 ppm (equivalent to 1.5 mg/kg bw/d).

In a 18-month carcinogenicity study in Syrian hamsters at level of 0, 1, 10 and 100 ppm in the diet, the NOAEL was set at 10 ppm (equivalent to 1 mg/kg bw/d) based on decreased body weight gain at 10 mg/kg bw/d. No effect on thyroid was observed. There was no evidence of carcinogenic potential.

The Scientific Committee on Plants evaluated amitrole in 2000 in the context of the inclusion of amitrole in Annex I to council directive 91/414/EEC (SCP/AMITR/002-Final, 13 July 2000) and concluded that:

“In conclusion, since

- a. the thyroid carcinogenic effect of amitrole appears to be mediated through thyroid-pituitary disruption to which humans are less sensitive*
 - b. there does not seem to be a role for increased TSH in human thyroid carcinogenicity,*
- the thyroid tumours observed in rats after long term amitrole treatment appear to be of little or no relevance for humans.”*

Corroborating this opinion, IARC Overall evaluation (2001) downgraded amitrole to Group 3 (not classifiable as to its carcinogenicity to humans) with supporting evidence from relevant data.

It was concluded that the thyroid tumours observed in rats were not considered relevant for human and that amitrole does not need to be classified for carcinogenicity.

2.5.1.6. Reproductive toxicity

In two generations studies it was shown that amitrole was not toxic to F0 and F1 generation up to 2 ppm and did not induce any effects on the reproductive performance of F0 and F1, nor impaired the development of F1 and F2 offspring up to 15 ppm. The dose of 15 ppm was slightly toxic for the F0 (males only) and F1 parental animals as shown by minimal increase of thyroid activity. The 112.5 ppm dose level was severely toxic for the F0 and F1 parents, impaired their fertility and disturbed the development of F1 and F2 litters. Nevertheless all findings on reproduction correlated with severe systemic parental toxicity, so that a primary effect on reproduction was excluded.

A NOAEL was set at 15 ppm (0.9 mg/kg bw/d) for reproductive toxicity and at 2 ppm (0.12 mg/kg bw/d) for parental toxicity.

Teratogenicity studies were conducted in rats (by oral route) and rabbits (by oral and dermal routes).

In rats exposed by gavage to dose levels of 0, 100, 500 and 1000 mg/kg bw/d, slight maternotoxicity was observed at 500 and 1000 mg/kg bw/d (reduced body weight gain and food consumption, increased thyroid weight). Reduced fetal body weight/litter and reduced skeletal ossifications were observed in the high-dose group. Increased incidences of enlarged and/or dark thyroids were seen in foetuses at 500 and 1000 mg/kg bw/d. The NOAEL for maternotoxicity and embryo/fetotoxicity was set at 100 mg/kg bw/d. Amitrole was considered not to be teratogenic in rats at doses levels up to 1000 mg/kg bw/d.

In rabbits exposed by gavage to dose levels of 0, 4, 40 and 400 mg/kg bw/d, a dose related increased incidence

of abortions was observed in all treated groups. Decrease body weight gain during the gestation period was observed at 40 and 400 mg/kg bw/d and increased liver weight at 400 mg/kg bw/d. Embryo/foetotoxicity were observed at 40 and 400 mg/kg bw/d. Increased incidences of irreversible structural changes were also found at these dose levels, which involved mainly the head and limbs. The NOAEL for maternotoxicity, embryo-foetotoxicity and teratogenicity was set at 4 mg/kg bw/d.

Based on this study, the classification of amitrole as reprotoxic category 3 (**Xn, Repr. Cat. 3 R63**) was agreed at European level by a specialised experts group (ECBI/59/00 – Add. 1 – Rev.2). Amitrole was thus classified reprotoxic category 2 according to the criteria of the regulation (EC) n°1272/2008 (**H361d: Suspected of damaging the unborn child**).

In a more recent study rabbits were exposed by gavage to dose levels of 0, 5, 20 and 80 mg/kg bw/d from gestation day 6 to 18. All dams were sacrificed on day 29. There was no treatment-related maternal death. In the 80 mg/kg bw/d group, the body weight gain, the feed consumption and water intake were reduced during the first week of treatment so that the NOAEL for maternal toxicity was set at 20 mg/kg bw/d. No teratogenic effect was observed.

The same dose levels were used in a special study to further characterize the toxicity in pregnant rabbits. The NOAEL for maternal toxicity was 5 mg/kg bw/d based on decreased absolute and relative liver weights and statistically significantly decreased albumin and protein levels seen at 20 and 80 mg/kg bw/d. At 80 mg/kg bw/d, there were reductions in food consumption, increased creatine kinase levels, decreased triiodothyronine and thyroxine levels and thyroid follicular cell hypertrophy.

A study to further investigate maternotoxicity in pregnant rabbits was performed in 2000. In this study rabbits received the test substance as an aqueous solution, by oral gavage, at 0, 3, 15 or 75 mg/kg bw/d from day 6 to 18 *post-coitum*. At the highest dose level of 75 mg/kg bw/d, effects observed in dams were: reduced body weight gains, food consumption and water intake, decreased T3, T4 and cholesterol levels and morphological changes indicative of thyroid hyperactivity, which were also evident at 15 mg/kg bw/d. The NOAEL for maternal toxicity was thus set at 3 mg/kg bw/d. At 75 mg/kg bw/d, 3/66 fetuses from 2 different litters displayed a domed-head, probably related to dilatation of cerebral ventricles/hydrocephaly. A relationship to treatment with the test substance cannot be ruled out. The developmental NOAEL could thus be set at 15 mg/kg bw/d. This finding supports the classification as Xn, Repr Cat 3 R63 proposed before this study report termination.

In a dermal teratogenicity study in rabbits at dose levels of 0, 1000, 1500 and 2000 mg/kg bw/d, maternotoxicity (decreased body weight and food consumption, thin appearance and anorexia) was observed at 2000 mg/kg bw/d. At this level, irreversible structural changes (anencephaly and microphthalmia) were observed. The NOAEL for maternotoxicity, embryo/foetotoxicity and teratogenicity after dermal exposure was 1500 mg/kg bw/d.

Based on thyroid effects observed in several species, amitrole is classified as **Xn, R48/22** (Harmful: danger of serious damage to health by prolonged exposure if swallowed) and **H373** (May cause damage to thyroid through prolonged or repeated exposure, STOT-RE Cat. 2) in the regulation (EC) n°1272/2008.

Mode of action and mechanism of action leading to toxicity

Amitrole acts on thyroid by blocking the iodide uptake and inhibiting thyroid peroxidase.

The inorganic form of iodine, iodide, is quickly and efficiently absorbed from the gastrointestinal tract and enters the follicular cells through the basal membrane. This uptake is rapidly followed by an oxidation reaction catalyzed by Thyroid Peroxidase (TPO) resulting in synthesis of DIT (diiodotyrosine) and MIT (monoiodotyrosine). Within the protein thyroglobulin, iodine tyrosyl moieties (DIT and MIT) are combined to form the thyroid hormones T3 and T4 (cf figure 2).

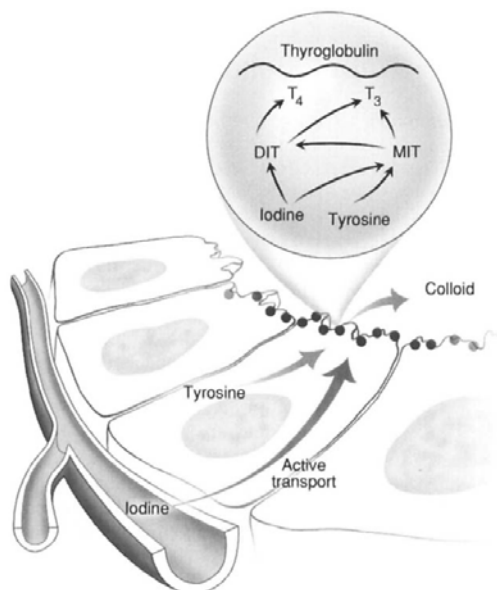


Figure 2: Uptake of iodide into the follicular cell by NIS (Sodium Iodide Symporter). Oxidation reaction (catalysed by Thyroid Peroxidase) resulting in synthesis of DIT = diiodotyrosine; MIT = monoiodotyrosine; T3 = triiodothyronine; T4 = thyroxine (from Clifton-Bligh and Delbridge 2005).

By blocking the iodine uptake and inhibiting thyroid peroxidase, amitrole inhibits the thyroid hormone synthesis which results in a decrease in T3 and T4 blood levels and causes an increase in TSH (Thyroid Stimulating Hormone) production in pituitary gland. This hormone imbalance leads to cell hypertrophy/hyperplasia and can lead to thyroid tumour formation.

Literature review

The applicant provided a literature review report on the toxicology of amitrole.

From the registration of amitrole, none of the published papers gives new/unknown information compared to data provided in the first monograph.

2.5.2. Acceptable Daily Intake (ADI)

As already agreed (Review report (6839/VI/97-final 22 Marc 2001)), the ADI is set at 0.001 mg/kg bw/day based on thyroid effects observed in the 90-day rat studies and by using a safety factor of 100.

2.5.3. Acute Reference Dose (ARfD)

The most relevant study to derive an ARfD is the 28-day rat study, in which the NOAEL is 1.5 mg/kg bw/day, based on decreased body weight and food consumption and decreased T3/T4 levels. By using a safety factor of 100, an ARfD of 0.015 mg/kg bw can be derived.

2.5.4. Acceptable Operator Exposure Level (AOEL)

As already agreed (Review report (6839/VI/97-final 22 Marc 2001)), the AOEL is set at 0.001 mg/kg bw/day based on thyroid effects observed in the 90-day rat studies and by using a safety factor of 100.

2.5.5. Proposal for a maximum allowable concentration (MAC) in drinking water / drinking water limit (DWL)

The maximum admissible concentration of a pesticide active substance is 0.1 µg/L, as established by Dir. EC 98/83.

2.5.6. Impact on human and animal health arising from exposure to the active substance or impurities contained in it

2.5.6.1. Operator exposure

The risk to operators using a tractor-mounted/trailed boom sprayer is not acceptable in vineyards, orchards and olive groves. Uses of a lance or a hand-held sprayer are not considered by the applicant and should be dealt at Member State level.

In absence of data provided by the applicant, the risk to operator cannot be finalised for non crop areas and should be addressed at Member State level.

2.5.6.2. Bystander exposure

The risk to a bystander incidentally exposed to CA2735 is acceptable in orchards, vineyards and olive groves.

In absence of data provided by the applicant, the risk to bystander cannot be finalised for non crop areas and should be addressed at Member State level.

2.5.6.3. Worker re-entry exposure

There is no unacceptable risk anticipated from amitrole for the worker wearing PPE (long-sleeved shirt and trousers), when re-entering vineyards, orchards and olive groves treated with CA2735.

In absence of data provided by the applicant, the risk to worker cannot be finalised for non crop areas and should be addressed at Member State level.

None of the intended uses are considered to lead to an acceptable risk for the operator.

2.6. RESIDUE

2.6.1. Definition of residues relevant to MRLs

2.6.1.1. Definition of residues in plant

Following new data provided in the context of this addendum, it is not necessary to change the residue definition for enforcement in plants already set as amitrole, parent compound only.

2.6.1.2. Definition of residues in animal products

Livestock is not expected to be exposed to amitrole residues. Therefore, no residue definition in products of animal origin is required.

2.6.2. Residue trials

Since the first inclusion, new trials were provided on apple, grape and olive. They demonstrate that residue levels are below the LOQ in fruits.

Regarding to the no residue situation in those crops and the possibility for extrapolation given in guideline appendix D rev.9, sufficient numbers of residue trials are available to support all intended GAPs for amitrole on orchards, grapes and olives.

In addition, new residue results were also provided on metabolites triazolylalanine and aminotriazolylalanine in olives and grapes where a no residue situation was also shown. Consequently, the need to include these metabolites in the residue definition is not considered necessary with regard to the intended uses.

2.6.3. Livestock feeding studies

Since the first inclusion, studies on the nature or magnitude of residues in commodities of animal origin are neither available nor required since livestock is not expected to be exposed to amitrole residues. Residue definitions and MRLs for livestock products are consequently not required.

2.6.4. Effects of processing

As quantifiable residues of amitrole are not expected in the treated crops, there is no need to investigate the effect of industrial and/or household processing. Although not required, one study investigating the magnitude of residues in grapes, juice, must and wine (white and red) was provided. Nevertheless, no robust processing factors could be derived since residues were below the LOQ in both raw and processed commodities.

2.6.5. Residues in succeeding crops

Orchards, grapes and olives are not expected to be grown in rotation. Further investigation of residues in rotational crops is therefore not required with regard to the intended uses. Nevertheless further information would be required in future if additional uses are intended and rotated and when, at EU level, a harmonized approach on how to consider triazoles derivatives metabolites in the risk assessment will be available.

2.6.6. Proposed MRL

No MRL exceedance will result from the intended uses. This assessment goes on the same way than the EFSA reasoned opinion about the review of the existing maximum residue levels (MRLs) for amitrole according to Article 12 of Regulation (EC) No 396/2005.

2.6.7. Estimation of the exposure through diet and other means

Chronic and acute consumer exposures resulting from the uses proposed in the framework of this application were calculated. Based on EFSA PRIMo (rev2), acute and chronic exposures were considered as acceptable for all groups of consumers as no ARfD nor ADI exceedances are expected.

2.7. FATE AND BEHAVIOUR IN THE ENVIRONMENT

2.7.1. Fate and behaviour in soil

Route of degradation in soil

The route of degradation of Amitrole under aerobic laboratory conditions was investigated in 3 studies. Two of them (Hawkins *et al.*, 1982 and Scholz *et al.*, 1988) had already been submitted in the original DAR. Both studies had been accepted although they presented some deviations. An additional study (Hall, 1995), not reported in the original DAR is considered acceptable. This study confirms the degradation pathway that had been proposed in the original DAR.

Amitrole is rapidly degraded by microbial activity into CO₂. Depending on the studies, mineralisation reaches 20-60% AR after 7 days (Hawkins *et al.*, 1982) or 44.5% AR after 91 days (Hall, 1994). Non extractable residues are also important, reaching 20-50% after 7 days (Hawkins *et al.*, 1982) or 40.89% AR after 91 days. No major metabolites were quantified. Degradation should proceed via 5-hydroxyaminotriazole rapidly degraded to cyanamide then urea. A secondary pathway leads to urazole. Only urazole, cyanamide, urea and aminoguanidine bicarbonate are found in trace amounts in soil. RMS noted that some unidentified radioactivity reaches levels above 10% on some occasions in the study of Hall (1994). RMS highlights that the HPLC reference standard of 1,2,4-triazole was used in the study, therefore it is not expected that this unknown radioactivity corresponds to 1,2,4-triazole. This should be confirmed by the applicant. **The applicant should also clarify whether the unidentified radioactivity is formed by several compounds or not and whether each compound exceeds 5% AR or not.** The applicant indicated at the end of December 2012 that this point was currently being checked.

Under sterile conditions, amitrole degrades at slower rate. Mineralisation is negligible (*ca* 1% AR after 365 days) and bound residues are formed (50.6% AR after 7 days in Hawkins *et al.*, 1982 and 41.8% AR after 91 days in Hall, 1994).

No new study on degradation of amitrole under anaerobic conditions was provided. Amitrole is degraded at a slower rate than under aerobic conditions, and still represents 28.5% AR after 112 days (19.8% AR after 364 days). Non-extractable residues reached a maximum of 61.4% AR after 112 days (65.7% AR after 224 days) and volatiles were negligible (<0.6% AR after 112 days). Amitrole was the major compound identified in the extractable radioactivity, other components were minor (one reached a maximum of 6.2% AR after 28 days, others did not exceed 5% AR).

Among the 2 studies provided in the original DAR to investigate photodegradation, only one (Das, 1990) was considered as reliable. Amitrole was more degraded in the irradiated samples (Xenon lamp, 360-800 nm, 500 Watt/m², 12 h photoperiod) than in dark controls: after 30 days irradiation, amitrole represented 66.4% AR against 88.7% in dark controls. The rate of degradation of amitrole under irradiated conditions was estimated by linear first-order regression to 73 days. The only degradation product was 1,2,4-triazole, exceeding 5% from day 3 and increasing up to 9.9% at the end of the experiment (30 days). In dark controls, 1,2,4-triazole was detected at each sampling date, and reached a maximum of 4.1% AR after 21 days.

1,2,4-triazole was included in the risk assessment for soil, surface water and groundwater by the applicant for all intended uses. RMS notes that according to the sustained GAP for agricultural uses (application period), photodegradation is not expected to be a major route of degradation of amitrole in soil and therefore 1,2,4-triazole is not expected to be formed in significant amounts. Therefore, to the RMS opinion, a risk assessment was not strictly required. However, RMS considers that if further agricultural uses occurring when photodegradation may be important would be sustained, it should be discussed whether 1,2,4-triazole may need to be included in the risk assessment or not. It is highlighted that photodegradation and microbial degradation will be concomitant and concurrent processes. Therefore, if photodegradation occurs in field, the maximum occurrence reached is expected to be lower than 9.9%.

Rates of degradation in soil

The rates of degradation of Amitrole under laboratory aerobic conditions and field conditions have been updated according to FOCUS Kinetics (2006). In addition, DT50 from additional studies compared to the original DAR are available. Amitrole follows single first-order degradation. In laboratory under aerobic conditions, DT50 ranged between 3.4 days to 23.8 days (n=4). Normalised DT50 to 20°C and pF 2 ranged between 4.1 to 20.8 days (geometric mean: 7.4 days). Values from 3 field sites (one in UK, 2 in US) are also available. They ranged between 7.6 and 17.1 days.

For 1,2,4-triazole, common agreed endpoints were specified during PRAPeR 12 (2007). These endpoints were recently updated by CRD in the following document: "Triazole Derived Metabolite: 1,2,4-Triazole - Proposed revision to DT50 - Summary, Scientific Evaluation and Assessment - July 2011, revised September 2011 (after comments from MS and EFSA)". These new endpoints are used in the risk assessment.

Mobility in soil

Adsorption of Amitrole was investigated in 3 batch adsorption studies (2 studies provided in the original DAR and one new study) that give reliable adsorption parameters for 9 soils covering a range of pH values (5.3-7.4), organic carbon content (0.5-3.4%) and clay content (2-42.7%). K_{oc} of Amitrole ranged between 20 and 202 mL/g, with 1/n between 0.65 and 0.87. According to McCall classification, Amitrole exhibits medium to very high mobility in soil.

Adsorption parameters of 1,2,4-triazole were agreed in PRAPeR 12. They were investigated on 4 soils. K_{oc} ranged between 43 and 120 mL/g, with 1/n between 0.83 and 1.02. According to McCall classification, 1,2,4-triazole exhibits high to very high mobility in soil.

Mobility of Amitrole was also studied on 2 soils in a column leaching study, provided in the original DAR. Radioactivity in the leachates reached 24-31% AR in the first soil, and was <0.8% in the second soil. In the first-soil, most of the radioactivity in the leachates corresponded to the parent Amitrole.

PEC_{soil} calculations

PEC_{soil} were calculated for amitrole and 1,2,4-triazole for the worst-case use: 1 application at 2977 g/ha, considering no interception. The maximal PEC_{soil} are 3.969 mg/kg and 0.323 mg/kg for amitrole and 1,2,4-triazole, respectively. With the new endpoints, 1,2,4-triazole can be considered as persistent in soil. A plateau concentration of 0.494 mg/kg, reached after 8 years, was calculated.

2.7.2. Fate and behaviour in water

Route and rate of degradation in water

No new study on the fate and behavior of Amitrole in water was provided, except a water/sediment study under anaerobic conditions. Amitrole is hydrolytically stable at 25°C and pH 5, 7 and 9 and at 90°C and pH 4, 7 and 9. Amitrole is photolytically stable at 25°C and pH 5, 7 and 9. It shows no light absorption above 290 nm. Amitrole is not readily biodegradable.

In dark aerobic water/sediment systems, Amitrole is slowly degraded in total system: 41.3-46.9% AR remain as amitrole after 91 days. In the water phase, it still represents 32.8-43.7% AR at the end of incubation (91 days). Adsorption on sediment is low (maximum 5.9-14% AR after 0-7 days). Non extractable residues reach 26.4-40.1% AR after 91 days. Mineralisation represents 10.3-18.7% AR after 91 days. No major metabolites are identified. Minor metabolites are quantified, among which triazole and urea are identified, always below 2.5% AR.

The rates of degradation/dissipation of Amitrole in water/sediment systems were updated according to the guidance document FOCUS Kinetics (2006). In total system, DT50 ranged between 83.6 and 88.7 days (SFO kinetics). Dissipation rates in water ranged between 67.6 and 87.6 days. Dissipation rates in sediment ranged between 116.8 and 124.8 days.

In dark anaerobic water/sediment systems, Amitrole is very slowly degraded: it still represents 91.4-93.7% AR after 91 days (75.9-84.6% AR after 364 days) in total system. Adsorption on sediment is low (maximum 17.8-20.8% AR after 273 days). No major metabolites were identified. Bound residues represent 6.3-8.4% AR after 182-273 days. Mineralisation is negligible.

PECgw calculations

PECgw were calculated for Amitrole and 1,2,4-triazole. For agricultural uses, PECgw were calculated with the model FOCUS PELMO 4.4.3, for the worst-case application rate of 2977 g/ha, corrected by 1/3 to take into account the banded application, with no interception. PECgw for Amitrole are < 0.001 µg/L for all scenarios and all uses. For 1,2,4-triazole, PECgw exceed 0.1 µg/L for all scenarios and all uses. However, it is highlighted that PECgw for 1,2,4-triazole are expected to be overestimated. As explained above, according to the sustained GAP, photodegradation is not expected to be a major route of degradation of amitrole in soil and therefore 1,2,4-triazole is not expected to be formed in significant amounts. In addition, photodegradation and microbial degradation will be concomitant and concurrent processes. Therefore, if photodegradation occurs in field, the maximum occurrence reached is expected to be lower than 9.9%. **Refined PECgw for metabolite 1,2,4-triazole shall be submitted by the applicant to show that a safe use can be identified.** Although it is difficult to predict whether 1,2,4-triazole will be formed in significant amount or not according to the proposed GAP, it is noted that even if it is formed in small amount, the exceedance of the the drinking water limit could not be excluded because of the high applied dose of the parent.

No specific calculations were performed for non crop uses on permeable surfaces, however the same conclusions as for agricultural uses are expected. For non crop uses on impermeable surfaces, no risk of groundwater contamination is expected.

For the specific uses on railways, the model HardSPEC v. 1.4.2 was used. PECgw for Amitrole ranged between 0.0038 to 0.0835 µg/L. PECgw for 1,2,4-triazole ranged between 0.0257 and 0.0657 µg/L. Therefore, no risk of groundwater contamination is expected.

PECsw calculations

For agricultural uses, the calculations initially provided by the applicant for PECsw for Amitrole were not considered acceptable. The applicant was asked to provide new PECsw calculations, taking into account the specificities of the sustained uses (crop interception of 0%, considering the full dose for the drift entries and a lower dose (1/3) for the drainage and run-off entries, correcting the drift entries to take into account that amitrole is applied on the ground and not on foliage, as recommended by FOCUS SW guidance document).

The additional calculations provided by the applicant do not address the RMS request's and cannot be validated by RMS. **Therefore, the applicant is asked to provide new PECsw calculations for Amitrole. In absence of validated PECsw, the exposure to surface water cannot be finalized.** An additional study on PECsw calculations was finally provided by the applicant at the end of December 2012. However, since it was too late in

the evaluation and the DAR had already been sent for comments to co-RMS, the study was not summarized nor assessed by RMS.

For 1,2,4-triazole, PEC_{sw} were calculated using FOCUS Step 1. PEC_{sw} ranged between 25.02 to 32.22 µg/L.

For non agricultural uses on permeable surfaces, no specific calculations were provided by the applicant for amitrole, although requested by RMS. **Therefore, the applicant is asked to provide PEC_{sw} calculations for Amitrole.** For 1,2,4-triazole, PEC_{sw} were calculated using FOCUS Step 1 and are estimated to 27.18 µg/L.

For non agricultural uses on impermeable surfaces, PEC_{sw} were calculated using HardSPEC. Depending on the scenarios considered, PEC_{sw} ranged between 7.821 and 453.782 µg/L for Amitrole, and between 0.636 and 37.615 µg/L for 1,2,4-triazole.

2.7.3. Fate and behaviour in air

No new study on the fate and behavior of Amitrole in air was provided. Based on the vapour pressure of Amitrole of $3.3 \cdot 10^{-5}$ Pa at 20°C, it can be concluded that significant volatilisation from soil is not to be expected. However, volatilization from plant surfaces may occur, according to the FOCUS Air criteria. This is confirmed by laboratory experiments, in which volatilization from soil was negligible after 24 hours and volatilization from plant surface was estimated to 11% AR after 24 hours.

The chemical lifetime of Amitrole in the troposphere was calculated to be 4.8 hours, assuming an OH concentration of $5 \cdot 10^5$ /cm³ over 24 hours. Therefore, an accumulation of Amitrole in the air is not to be expected.

2.8. EFFECTS ON NON-TARGET SPECIES

2.8.1. Effects on terrestrial vertebrates

2.8.1.1. Birds

The risk assessments for birds were conducted in accordance to EFSA guidance (European Food Safety Authority; Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009; 7(12): 1438).

Endpoints for the risk assessment are acute LD₅₀ > 2150 mg/kg b.w. and dietary LD₅₀ > 829 mg/kg b.w./d. The one-generation reproduction test on mallard duck (NOEC=12.1 mg a.s./kg b.w./day) is not sufficient for assessing potential effects on development and reproduction due to endocrine disrupting properties of the active substance. This is due to the fact that the one-generation avian reproduction study does not include exposure during all relevant stages of the bird's development. These potential consequences on development and reproduction are studied with the 2-generation study in birds (Mallard duck).

No NOEC could be established as there were impacts upon thyroid gland size (higher size than in the control) at all concentrations tested in F0 and F1. An amendment to the final study report was submitted at the end of December 2012. In this amendment, it is reported that at collection of thyroids for potential histopathology from selected (up to two per pen) F2 hatchlings and untreated 14-day old survivors, thyroids appeared comparable in size to the control group. However, no measured data were submitted to the RMS. In these conditions, due to this uncertainty no NOEC based on effects on thyroid can be set.

In conclusion, a NOEC based on reproductive performance parameters can be set at 95 ppm. However, no overall NOEC can be set. In F0 and F1 there are impacts upon thyroid gland size at all tested concentrations. It is well known that increase or decrease of thyroid gland size may influence vertebrates behaviour. There is therefore an uncertainty on the impact of such effects on wild animals at population level in natural conditions (e.g. parental care, nesting behaviour, territoriality and mounting behaviour). The value of 95 ppm a.s. corresponding to 16 mg/kg bw/day should therefore be considered as a LOEC. Therefore, long term risk assessment for birds could not be finalized.

A bibliographic search was conducted by the notifier in order to try to find a relationship between an increase of thyroid size and an impact on parental care, nesting behaviour, territoriality and mounting behavior. A list of

references was submitted at the end of December 2012, but no summary of these papers was done by the notifier. The notifier concludes that nothing could be found. However, considering the late submission of this bibliography, it was not possible for the RMS to check. Moreover, even if nothing could be found, it doesn't mean that there are no uncertainties about such effect on thyroid gland size.

Therefore, as there is an uncertainty, long term risk assessment for birds cannot be finalized.

In a first screening step risk assessment, the acute TER value is higher than the trigger value of 10 for insectivorous and omnivorous birds in orchards and vineyard, respectively.

Long term TER for birds were calculated by the applicant based on the one-generation NOEL of 12.1 mg/kg b.w./day but as no overall NOEC could be established from the two-generation bird study, long term risk assessment for birds couldn't be finalized.

Concerning risk from drinking water, the TER_{acute} is above the trigger of 5.

Due to the low log K_{OW} (< 3) of amitrole, the risk to birds through secondary poisoning had not to be assessed. The application of CA2735, therefore, does not raise concerns regarding an accumulation in the food chain or secondary poisoning.

The use of CA2735 in accordance to the recommended uses is acceptable to birds.

2.8.1.2. Mammals

The risk assessments for mammals were conducted in accordance to EFSA guidance (European Food Safety Authority; Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009; 7(12): 1438).

The relevant endpoints for the risk assessment for mammals are $LD_{50} = 5000$ mg/kg b.w. and NOEL of 0.9 mg/kg b.w./d.

In a first screening step risk assessment, the acute TER value is higher than the trigger value of 10 for small herbivorous mammals for orchards and vineyard.

In a first screening step and Tier 1 risk assessment, the long-term TER values are lower than the trigger value of 5 for small herbivorous, large herbivorous, small insectivorous and omnivorous mammals.

Therefore a higher tier risk assessment is conducted. The following refinement parameters are taken into account:

The focal species for the relevant feeding guilds, proportion of time spent in the treated field (PT factor) and proportions of food items obtained from the treated area (PD factor):

In vineyard, the focal species was the woodmouse and this species was therefore considered in the higher tier risk with a refined PT value of 0.41. PT and PD were not refined for other species.

In orchard, the focal species was the vole and this species was therefore considered in the higher tier risk. This species is the same as the generic focal species for screening and Tier 1 calculation. PT and PD were not refined.

Moreover, the evaluation was refined taking into consideration the maximum residue concentrations determined in a study conducted under realistic conditions. The different scenarios considered are presented in the following table:

Diet Composition & Portion of Diet	Maximum measured Residue		
	Scenario 1	Scenario 2	Scenario 3
Animal matter	0.61 ^a	3.09 ^b	0.67 ^c
Plant matter	0.08 ^d	0.08 ^d	0.08 ^d

^a Soil Dwelling Arthropods (Vortis sampling) R_{max}

^b Crop & Soil dwelling Arthropods (Earwig traps) R_{max}

^c Soil dwelling Arthropods (Pitfall traps) Mean R_{max}

^d Short vegetation R_{max}

Thus, based on the combined application of the two main refinement parameters (PT and realistic RUD values), all TERs are above the trigger of 5 for herbivorous and omnivorous mammals. TER for small insectivorous are lower than the trigger of 5. However for this species all other parameters (PT and PD) used in the calculation are default parameters. Risk assessment for insectivorous mammals should be further refined.

TER values for Vineyard are:

Species	Wood mouse (focal species)	Vole (generic focal species)	Lagomorph (generic focal species)	Shrew (generic focal species)
Diet Guild	Omnivorous	Small herbivorous	Large herbivorous	Small insectivorous
TER	18.4 to 72.2	16	54.4	1 to 5.1

TER values for Orchards are:

Species	Vole (focal species)	Wood mouse (generic focal species)	Lagomorph (generic focal species)	Shrew (generic focal species)
Diet Guild	Small herbivorous	Omnivorous	Large herbivorous	Small insectivorous
TER	16	7.6 to 29.6	42.5	1 to 5.1

Concerning risk from drinking water, the TER_{acute} and TER_{repro} are above the trigger of 5 indicating an acceptable risk.

Due to the low $\log K_{OW}$ (< 3) of amitrole, the risk to birds through secondary poisoning had not to be assessed. The application of CA2735, therefore, does not raise concerns regarding an accumulation in the food chain or secondary poisoning.

The use of CA2735 in accordance to the recommended uses is acceptable to mammals.

2.8.2. Effects on aquatic organisms

2.8.2.1. Toxicity to aquatic organisms

The risk assessments for aquatic organisms (fish, aquatic invertebrates, algae and aquatic plants) were conducted in accordance to SANCO/3268/2001 rev. 4 final (Guidance Document on Aquatic Ecotoxicology).

For agricultural uses (pome fruit, citrus, olives and vineyard) and non-crop areas (grass), the initial PEC_{sw} calculations provided were not considered acceptable. Additional calculations were asked to the applicant, but the new calculations provided still did not address RMS' request and therefore could not be accepted. The applicant finally provided additional calculations at the end of December 2012. However, since it was too late in the evaluation, they were not taken into account. (see vol. 1_2.7.2)

For impermeable non-cropped areas (uses on road and railways), PEC_{sw} were calculated in vol. 3.B.8 according to HardSpec. The risk assessment for the active substance and the metabolites was conducted with the HardSpec PEC_{sw}.

For uses on railway, TER calculated for the active substance and the metabolite are higher than the trigger values for all aquatic organisms but the long term risk for fish could not be finalized.

The literature review report brings some information about the mechanism of action of amitrole in fish metabolism and confirms thyroid disruption. Amitrole did not block the production of THs in rare minnow but alterations of Thyroid Hormones-related genes expressions in liver and brain were noted at 10 to 10000 ng/L. The chronic test on juvenile fish (NOEC=100 mg a.s./L) is not relevant for assessing potential effects on development and reproduction due to endocrine disrupting properties. These potential consequences on development and reproduction *in vivo* should have been addressed with the fish full life-cycle test in fish

(Medaka). Available data from this new study were not reliable to conclude on the potential impact of amitrole on hatchability of eggs in the F1 generation (from parental exposure). The notifier informed the RMS late in december 2012 that a new experimental phase is being conducted in order to conclude on potential effects on hatchability of eggs. Moreover, no data were available to conclude on potential impact in the F2 generation. In these conditions, it was concluded that data were not enough to address completely the question of thyroid mediated effects during long term exposures. No endpoint (NOEC) can be derived from this study. Therefore, as there is an uncertainty concerning potential effects on development and reproduction, long term risk assessment for fish cannot be finalized.

For uses on road, long term risk assessment for fish cannot be finalized for the same reasons.

No risk assessment is required for sediment dwelling organisms and aquatic rooted plants as amitrole is not expected to adsorb strongly on sediment. Moreover, it can be considered that toxicity data from *daphnia* and *Lemna* are sufficient to cover other aquatic invertebrates as sediment dwelling organisms and other aquatic plant as aquatic rooted plant, respectively.

Concerning other organisms, TER calculated for the active substance and the metabolite are higher than the trigger values for fish and gastropod molluscs for acute exposure. For *daphnia*, aquatic crustaceans, algae and aquatic plants, TER are lower than the trigger values for some scenarios (or for all scenario depending on the species).

Acute risk assessment for *Daphnia* and *Mysidopsis bahia* is refined based on the hypothesis of the possible renewal of populations following degradation of the active substance few days after application of the product compensating the mortality at initial predicted surface water concentrations. As endpoints are based on acute effects, the risk assessment might only be based on initial exposure, and should not take into account a possible degradation of the active substance. Acute risk assessment based on mortality has therefore to be conducted based on initial predicted surface water concentrations. Considering these comments, a new refined risk assessment has been asked. The risk assessment for the urban, major road and domestic streams scenario has not been further refined and should be considered at member state level.

Long term risk assessment for *Daphnia* is refined based on the same hypothesis of the possible renewal of populations following degradation of the active substance. Long term risk assessment has to be conducted based on initial predicted surface water concentrations as degradation of the active substance in surface water may not be appropriate for use with endocrine disrupting compound. Moreover, even if the NOEC of 320 µg a.s/L is based on effects on growth at the LOEC of 560 µg a.s/L and therefore risk assessment could eventually be refined with PEC_{twa} (twa duration depending on the time-to-onset-of-effects), effects on reproduction have been observed in this study at the LOEC of 1000 µg a.s/L concluding to a NOEC reproduction of 560 µg a.s/L that would be used with initial predicted surface water concentrations. Considering these comments, a new refined risk assessment has been asked. The risk assessment for the urban, major road and domestic streams scenario has not been further refined and should be considered at member state level.

Risk assessment for *Algae* and *Lemna gibba* is refined based on the same hypothesis of the possible renewal of populations following degradation of the active substance few days after application of the product compensating the inhibition of growth at initial predicted surface water concentrations. As endpoints are based on growth effects and considering that the active substance was stable in the tests, risk assessment could be refined on two exposure (two duration depending on the time-to-onset-of-effects) but it hasn't been done as no PEC_{twa} are available in vol 3 B.8. Otherwise a higher tier *Selenastrum capricornutum* and *Lemna* studies could be conducted in order to mimic a realistic worst-case exposure profile based on the proposed use of amitrole and PEC surface water modelling. The aim of the study would be to assess the effects under a more realistic exposure regime and also demonstrate recovery of *Selenastrum capricornutum* and *Lemna* for initial concentrations (able to cover those expected from modelling) to conclude that any effect on *Selenastrum capricornutum* and *Lemna* will be reversible and populations of algae and aquatic plants have potential for recovery. The submission of these studies or further refinement should be considered at member state level.

2.8.2.2. Bioaccumulation of substance name along aquatic food chain

Amitrole has a log P_{ow} below 3. Therefore, no risk of bioaccumulation exists. However, a BCF of 2.38 (whole fish) in 7 days was determined, please refer to review report SANCO/ 6839/VI/97-final, 22/03/2001.

2.8.3. Effects on bees and other arthropods species

2.8.3.1. Effects on bees

The risk assessment for bees was conducted in accordance with SANCO/10329/2002 rev. 2 final (Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (2002)).

Hazard Quotients for both acute oral and acute contact exposure were calculated to be <20 and <30 respectively. These values are below the relevant trigger of 50 as defined in Commission Regulation (EU) No 546/2011 indicating an acceptable risk to bees. When considering the formulated product, the Hazard Quotients for both acute oral and acute contact exposure are lower than 73. However, CA2735 is applied under the row and the spray is directed to the foot of trees and vine plants. Therefore, the actual dose rate applied represents only 1/3 of the nominal rate of 13 L/ha. On this basis, the Hazard Quotients are therefore lower than 24 indicating a low risk to bees of CA2735.

The use of CA2735 in accordance to the recommended uses is acceptable to bees.

2.8.3.2. Effects on other arthropods

The risk assessment for non-target arthropods other than bees was conducted in accordance to ESCORT 2 (Candolfi et al. 2000: Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods) and SANCO/10329/2002 rev. 2 final (Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (2002)).

Based on the results in the Tier 2 extended laboratory studies with the standard species *A. rhopalosiphi* and *T. pyri*, only the in-field HQ for *Typhlodromus pyri* is above the trigger of 1 (corresponding to ≥50% effect at the predicted in-field exposure) and needs to be refined. The off-field HQ is below the trigger of 1 (corresponding to <50% effect at the predicted off-field exposure) indicating an acceptable off-field risk with respect to a no spray buffer zone of 75 meters.

A potential risk has been identified in-field and off-field for *T. pyri*, the representative species for mites. According to ESCORT 2, a refined in-field risk assessment has to be provided, based on a higher tier study (aged residue study or field study for example). The two standard species (*Aphidius rhopalosiphi* and *Typhlodromus pyri*) are used in risk assessment (HQ calculation) as they cover risk assessment for other non target arthropods. Therefore, even if *Typhlodromus pyri* might be considered not relevant in field in relation with the GAPs, the endpoint from the test conducted with this species has to be used in risk assessment in-field and off-field in order to cover all other non target arthropods. Off field risk is acceptable with respect to a no spray buffer zone of 75 meters. A field study to evaluate the effects of CA2735 on predatory mite population development in a vineyard in southern France was performed and submitted in December 2012. It is reported by the notifier that amitrole application has no impact on the population of *Typhlodromus pyri*. Considering the late submission of this study (December 2012), it was not possible for RMS to assess it. This study should be submitted at national level (level 4).

On the other hand, the most exposed species (soil-dwelling species) are far less sensitive and no significant was observed on several species such as *Pardosa sp.*, *Aleochara bilineata* and *Poecilus cupreus* at higher doses than recommended application rate. No in-field and therefore off-field risk is indicated *Pardosa sp.*, *Aleochara bilineata* and *Poecilus cupreus* with effect levels of below 50%.

2.8.4. Effects on earthworms and other soil macro-organisms

2.8.4.1. Effects on earthworms

The risk assessment for earthworms was conducted in accordance to SANCO/10329/2002 rev. 2 final (Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (2002)).

Under the conservative assumptions of a Tier 1 assessment and underlying the most conservative PEC_{soil}, the acute TER for earthworms exposed to amitrole is above the trigger of 10, as defined in Commission Regulation (EU) No 546/2011 indicating acceptable risk to earthworms. As amitrole is not persistent in soil and no high risk is indicated for acute risk, reproductive testing is not necessary.

The metabolite 1,2,4-triazole (photodegradation metabolite with a maximum occurrence in soil of 9.9%) was included in the risk assessment for soil organisms by the applicant. The acute TER for earthworms exposed to 1,2,4-triazole is above the trigger of 10 indicating acceptable acute risk to earthworms. The long term TER for earthworms exposed to 1,2,4-triazole is below the trigger of 5 indicating necessary for refinement. However, RMS notes that according to the sustained GAP, photodegradation is not expected to be a major route of degradation of amitrole in soil and therefore 1,2,4-triazole is not expected to be formed in significant amounts (<9.9%). RMS considers that if further uses occurring when photodegradation may be important would be sustained, it should be discussed whether 1,2,4-triazole may need to be included in the risk assessment or not.

The use of CA2735 in accordance to the recommended uses is acceptable to earthworms.

2.8.4.2. Effects on other soil macro-organisms

The risk assessments for other soil macro-organisms were conducted in accordance to SANCO/10329/2002 rev. 2 final (Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (2002)).

For amitrole, the results indicate no persistence in soil (see vol 3 B.8.). Moreover, there is a low toxicity to soil-dwelling arthropods and earthworms. Therefore, no study on other non-target organisms was considered to be necessary.

The long term TER for soil macro-organisms *Folsomia candida* exposed to 1,2,4-triazole is below the trigger of 5 indicating necessary for refinement. However, RMS notes that according to the sustained GAP, photodegradation is not expected to be a major route of degradation of amitrole in soil and therefore 1,2,4-triazole is not expected to be formed in significant amounts (<9.9%). RMS considers that if further uses occurring when photodegradation may be important would be sustained, it should be discussed whether 1,2,4-triazole may need to be included in the risk assessment or not.

The use of CA2735 in accordance to the recommended uses is acceptable to soil macro-organisms other than earthworms.

2.8.5. Effects on soil micro-organisms

The risk assessment for soil micro-organisms was conducted in accordance to SANCO/10329/2002 rev. 2 final (Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (2002)).

Amitrole, even when tested at higher soil concentrations than the maximum PEC_{soil} did not result in effects above $\pm 25\%$ on the nitrogen transformation and respiration of soil microorganisms as defined in Commission Regulation (EU) No 546/2011.

For 1,2,4-triazole, no effects on nitrogen and carbon mineralisation after 28 days at up to 0.353 mg/kg soil. On the basis of the recommended GAP, one single application of 13 L/ha, the PEC plateau was calculated: 0.494 mg/kg. However, RMS notes that according to the sustained GAP, photodegradation is not expected to be a major route of degradation of amitrole in soil and therefore 1,2,4-triazole is not expected to be formed in significant amounts (<9.9%). Moreover, there are no effects in the test at the maximum tested dose of 0.353 mg/kg soil. RMS considers that if further uses occurring when photodegradation may be important would be sustained, it should be discussed whether 1,2,4-triazole may need to be included in the risk assessment or not.

The use of CA2735 in accordance to the recommended uses is acceptable to soil microorganisms and their functions.

2.8.6. Effects on other non-target organisms (flora and fauna)

2.8.6.1. Effects on non-target plants

The risk assessment for terrestrial non-target plants was conducted in accordance to SANCO/10329/2002 rev. 2 final (Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC (2002)).

Underlying the most conservative effect endpoints obtained from seedling emergence and vegetative vigour tests for plants treated with amitrole, TERs exceed the trigger value of 5 at distances of 5 m.

The use of CA2735 in accordance to the recommended uses is acceptable to non-target plants with mitigation measure (5 m buffer zone).

2.8.7. Effects on biological methods of sewage treatment

The effect of amitrole on the respiration rate of micro-organisms contained in activated sludge after a contact time of 3h was assessed. Amitrole was tested at 10, 31,6, 100, 316 and 1000 mg/L with 3,5 dichlorophenol as a reference. No decrease in oxygen consumption was observed at any tested level. The EC50 > 1000 mg/L.

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APPENDIX 1

Standard terms and abbreviations

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Standard Terms and Abbreviations

ADI	acceptable daily intake
a.s.	active substance
ARfD	acute reference dose
BCF	bioconcentration factor
BOD	biological oxygen demand
BOC	biological oxygen consumption
bw	body weight
°C	degree celsius
ca	approximately
CEC	cation exchange capacity
cm	centimeter
COD	chemical oxygen demand
CV	coefficient of variation
d	day
DAR	draft assessment report
DL	detection limit
DOC	dissolved organic carbon
DT ₅₀	Degradation half-life
DT ₉₀	Time to achieve 90% of degradation
EC ₀	effect concentration at which 0% of the organisms are affected
EC ₁₀	effect concentration at which 10% of the organisms are affected
EC ₅₀	effect concentration at which 50% of the organisms are affected
EC ₁₀₀	effect concentration at which 100% of the organisms are affected
EC	European Commission
ECD	electron capture detection
EFSA	European Food Safety Agency
Eq	equivalent
EU	European Union
g	gram
GAP	good agricultural practice
GC	gas chromatography
GLC	gas liquid chromatography
GLP	good laboratory practice
h	hour(s)
ha	hectare
HPLC	high pressure liquid chromatography or high performance liquid chromatography
IC ₅₀	effect concentration or 50% growth inhibition
i.e.	namely
k	kilo
kg	kilogram
Kd	Adsorption value
Koc	Adsorption value on organic content
L	litre
LC	lethal concentration
LC ₅₀	lethal concentration at which 50% died
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level

LOQ	limit of quantification
LSC	liquid scintillation counting or counter
m	metre
µg	microgram
µm	micrometre
mg	milligram
min	minute(s)
ml	millilitre
mm	millimetre
MRL	maximum residue limit
MS	mass spectrometry
NA	not analysed
NER	non-extractable residues
No.	number
NOEC	no observed effect concentration
NOEL	no observed effect level
NOAEL	no observed adverse effect level
P	Pure substance
Pa	Pascal
PEC	predicted environmental concentration
pH	pH-value
Pow	partition coefficient between n-octanol and water
ppb	parts per billion (1×10^{-9})
ppm	parts per million (1×10^{-6})
PRIMo	pesticide residue intake model
rad	radioactivity
RMS	Rapporteur Member State
s	second
SD	standard deviation
T	technical substance
TCAS	technical compound active substance
TLC	thin layer chromatography
UV	ultraviolet
v/v	volume ratio (volume per volume)
VIS	visual
w/w	weight ratio (weight per weight)
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to
±	plus / minus

APPENDIX 2

Specific terms and abbreviations

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Code	Description	Definition
AB	Grain bait	Special forms of bait
AE	Aerosol dispenser	A container-held preparation which is dispersed generally by a propellant as fine droplets/particles upon actuation of a valve.
AL	Other liquids to be applied undiluted	Self defining
BB	Block baits	Special forms of bait.
BR	Briquette	Solid block designed for controlled of active ingredient into water
CB	Bait concentrate	A solid or liquid intended for dilution before use a bait
CG	Encapsulated granule	A granule with a protective or release controlling coating.
CS	Capsule suspension	A stable suspension of capsules in a fluid normally intended for dilution with water before use.
DC	Dispersible concentrate	A liquid homogeneous preparation to be applied as a solid dispersion after dilution in water
DP	Dustable powder	A free-flowing powder suitable for dusting
DS	Powder for dry seed treatment	A powder for application in the dry state directly to seed.
EC	Emulsifiable concentrate	A liquid homogenous preparation to be applied as an emulsion after dilution in water.
ED	Electrochargeable liquid	Special liquid preparation for electrostatic (electrodynamic) spraying.
EO	Emulsion, water in oil	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticide in water in a continuous organic liquid phase.
ES	Emulsion for seed treatment	A stable emulsion for application to the seed either directly or after dilution.
EW	Emulsion, oil in water	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticides in an organic liquid in a continuous water phase.
FD	Smoke tin	Special form of smoke generator.
FG	Fine granule	A granule in the particle size range from 300 to 2500 μ .
FK	Smoke candle	A smoke generator in the form of a candle.
FP	Smoke cartridge	Special form of smoke generator.
FR	Smoke rodlet	Special form of smoke generator
FS	Flowable concentrate for seed treatment	A stable suspension for application to the seed either directly or after dilution
FT	Smoke tablet	Special form of smoke generator.
FW	Smoke generator	A combustible preparation generally solid, which upon ignition releases the active substance in the form of a smoke
FW	Smoke pellet	Special form of smoke generator

Code	Description	Definition
GA	Gas	A gas packed in pressure bottle or pressure tank.
GB	Granular bait	Special form of bait.
GE	Gas generating product	A preparation which generates a gas by chemical reaction.
GG	Macrogranule	A granule in the particle size range from 2000 to 6000 µ.
GP	Flo-dust	Very fine dustable powder for pneumatic application in glass-houses.
GR	Granule	A free-flowing solid preparation of a defined granule size range ready for use.
GS	Grease	Very viscous preparation based on oil or fat.
HN	Hot fogging concentrate	A preparation suitable for application by fogging equipment either directly or after dilution.
KN	Cold fogging concentrate	A preparation suitable for application by cold fogging equipment, either or after dilution.
LA	Lacquer	A solvent based film-forming preparation.
LS	Solution for seed treatment	A solution for application to the seed either directly or after dilution.
MG	Microgranule	A granule in the particle size range from 100 to 600 µ.
OF	Oil miscible flowable (=oil active substances in a miscible suspension)	A stable suspension of concentrate fluid intended for dilution in an organic liquid before use.
OL	Oil miscible liquid	A liquid, homogenous preparation to be applied as a homogenous liquid after dilution in an organic liquid.
OP	Oil dispersible powder	A powder preparation to be applied as a suspension after dispersion in an organic liquid
PA	Paste	A water based film forming preparation.
PB	Plate bait	Special forms of bait.
PC	Gel or paste concentrate	A solid preparation to be applied as a gel or a paste after dilution with water.
PR	Plant rodlet	A small rodlet, usually a few centimeters in length and a few millimeters in diameter containing active substance.
PS	Seed coated with a pesticide	Self defining.
RB	Bait (ready for use)	A preparation designed to attract and be eaten by the target species.
SB	Scrap bait	Special forms of bait.
SC	Suspension concentrate (= flowable concentrate)	A stable suspension of active substance(s) in a fluid intended for dilution with water before use.
SE	Suspo-emulsion	A fluid, heterogeneous preparation consisting of a stable dispersion of active substance(s) in the form of solid particles and of fine globules in a continuous water phase.

Code	Description	Definition
SG	Water soluble granules	A preparation consisting of granules to be applied as a true solution of active substance after dissolution in water but may contain insoluble inert ingredients.
SL	Soluble concentrate	A liquid homogenous preparation to be applied as a true solution of the active substance after dilution with water.
SO	Spreading oil	A preparation designed to form a surface layer on application to water.
SP	Water soluble powder	A powder preparation to be applied as a true solution of the active substance after solution in water but which may contain insoluble inert ingredients.
SS	Water soluble powder for seed treatment	A powder to be dissolved in water before application to the seed.
SU	Ultra low volume (ULV) suspension	A suspension ready for use through ULV equipment.
TB	Tablet	Solid preparation in the form of small, flat plates for dissolution in water.
TP	Tracking powder	A rodenticidal contact preparation in powder form.
UL	Ultra low volume (ULV) liquid	A homogenous liquid ready for use through ULV equipment.
VP	Vapour releasing product	A preparation containing one or more volatile ingredients, the vapours of which are realised into the air. Evaporation rate normally is controlled by using suitable preparations and/or dispensers.
WG	Water dispersible	A preparation granule consisting of granules to be applied after disintegration and dispersion in water.
WP	Wettable powder	A powder preparation to be applied as a suspension after dispersion in water.
WS	Water dispersible powder for slurry seed treatment	A powder to be dispersed at high concentration in water before application as a slurry to the seed.
XX	Others.	

APPENDIX 3

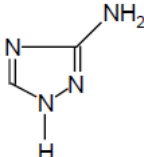
Listing of end points

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis**Identity, Physical and Chemical Properties, Details of Uses, Further Information**

Active substance (ISO Common Name) ‡	Amitrole
Function (<i>e.g.</i> fungicide)	Herbicide
Rapporteur Member State	France
Co-rapporteur Member State	Hungary

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	1-H-1,2,4-triazol-3-ylamine
Chemical name (CA) ‡	1-H-1,2,4-triazol-3-amine
CIPAC No ‡	90
CAS No ‡	61-82-5
EC No (EINECS or ELINCS) ‡	200-521-5
FAO Specification (including year of publication) ‡	FAO Specifications 90/TC/S/P (1998)
Minimum purity of the active substance as manufactured ‡	910 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	C ₂ H ₄ N ₄
Molecular mass ‡	84.08 g/mol
Structural formula ‡	

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis**Physical and chemical properties (Annex IIA, point 2)**

Melting point (state purity) ‡	157 - 159 °C
Boiling point (state purity) ‡	Not applicable
Temperature of decomposition (state purity)	-
Appearance (state purity) ‡	Colourless crystals
Vapour pressure (state temperature, state purity) ‡	$3.3 \cdot 10^{-5}$ Pa at 20 °C
Henry's law constant ‡	$1.76 \cdot 10^{-8}$ Pa.m ³ .mol ⁻¹ at 20°C
Solubility in water (state temperature, state purity and pH) ‡	280 g/L at 23 °C; pH not specified 264 g/L at pH 7, 261 g/L at pH 10
Solubility in organic solvents ‡ (state temperature, state purity)	isopropanol : 27 g/l at 20°C toluene : 0.02 g/l at 20°C dichloromethane : 0.10 g/l at 20°C n-hexane : < 0.01 g/l at 20°C
Surface tension ‡ (state concentration and temperature, state purity)	-
Partition co-efficient ‡ (state temperature, pH and purity)	- 0.969 at pH 7 at 23°C
Dissociation constant (state purity) ‡	pK ₁ 4.14 at 20°C pK ₂ 10.7 at 20°C
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	UV _{max} 198 nm ; ε 4947 L.mol ⁻¹ .cm ⁻¹
Flammability ‡ (state purity)	Brief ignition and rapid extinction
Explosive properties ‡ (state purity)	Lower explosion limit = Ca.500 g/m ³ No sensitive to impact
Oxidising properties ‡ (state purity)	-

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**RMS = FR
Co-RMS = HU**January 2013****Amitrole****Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis****Summary of representative uses evaluated (name of active substance or the respective variant)***

Crop and/or situation (a)	Member State	Product Name	F G I (b)	Pests or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc of a.i. g/kg (i)	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Interval between applications (min)	Kg a.i./hl min max (g/hl)	Water l/ha min max	Kg a.i./ha min max (*) (g/ha)		
Orchards (citrus fruits, pome and stone fruits, assorted fruits-edible or inedible peel, tree nuts)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	94-75	1 (or several splitted applications)	2-3 months	0.24-1	300 to 500	1.2-3	35	CA2735 is applied either once per year at 2977 gai/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Grapes (table and vine)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	92-79	1 (or several splitted applications)	2-3 months	0.24-1	300 to 500	1.2-3	42	CA2735 is applied either once per year at 2977 gai/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Olives	South EU MS	CA 2735	F	Non selective control of annual and perennial monocotyledones and dicotyledones weeds (growth stage 40-60)	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on localized areas with tractor mounted boom	Spring and autumn	1-2 (or several splitted applications)	2-3 months	0.18-0.5	300 to 500	0.9-1.375	35	CA2735 is applied either once or twice per year at 1375 gai/ha (ie 6 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000 gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
Non crop uses (impermeable and permeable surfaces: road, railways)	All MS	CA 2735	F	Non selective control of annual and perennial monocotyledones	Soluble concentrate (SL)	229 g:L (HPLC)	broadcast spraying under the row or on	Not applicable	1 (or several splitted applications)	2-3 months	0.36-1	300 to 500	1.8-3	-	CA2735 is applied either once per year at 2977 gai/ha (ie 13 L product/ha) or several times at lower rates but respecting the maximum application rate /year of 3000

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**RMS = FR
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				and dicotyledones weeds (growth stage 40-60)			localized areas with tractor mounted boom									gai/ha/year. A split application technique is possible at lower rates especially in case of mixture with foliar or residual herbicide according to the crop.
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* For uses where the column „Remarks“ in marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).

- (a) For crops, the EU and Codex classification (both) should be taken into account ; where relevant, the use situation should be described (e.g. fumigation of a structure)
- (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
- (c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds
- (d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
- (e) GCPF Codes – GIFAP Technical Monograph N° 2, 1989
- (f) All abbreviations used must be explained
- (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant – type of equipment used must be indicated

- (i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxyppyr). **In certain cases, where only one variant synthesised, it is more appropriate to give the rate for the variant (e.g. benthialdicarb-isopropyl).**
- (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
- (k) Indicate the minimum and maximum number of application possible under practical conditions of use
- (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)
- (m) PHI - minimum pre-harvest interval

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	HPLC/UV (215 nm)
Impurities in technical as (analytical technique)	HPLC/UV (215 nm) and ion chromatography
Plant protection product (analytical technique)	HPLC/UV (215 nm)

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Amitrole
Food of animal origin	Not relevant
Soil	Amitrole
Water surface	Amitrole
drinking/ground	Amitrole
Air	Amitrole

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS LOQ = 0.01 mg/kg (grape, olive, apple) DFG S19 method required
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant
Soil (analytical technique and LOQ)	LC-LC-MS/MS LOQ = 0.01 mg/kg
Water (analytical technique and LOQ)	LC-LC-MS/MS LOQ = 0.05 µg/L (surface and drinking water)
Air (analytical technique and LOQ)	method required
Body fluids and tissues (analytical technique and LOQ)	LC-MS/MS LOQ = 5 µg/L (urine)

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	-

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Mammalian toxicology**Impact on Human and Animal Health****Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)**

Rate and extent of oral absorption ‡	Almost completely absorbed; oral; rat <1d (70-95%)
Distribution ‡	Rapid to all tissues; liver highest level
Potential for accumulation ‡	No potential for accumulation
Rate and extent of excretion ‡	Eliminated within 2 days; urine (60-90%)
Metabolism in animals ‡	Minor metabolites through glutathione-S-transferase. Presence of mercapturic acid metabolite
Toxicologically relevant compounds ‡ (animals and plants)	Amitrole
Toxicologically relevant compounds ‡ (environment)	Amitrole and 1,2,4-triazole

Acute toxicity (Annex IIA, point 5.2)

Rat LD ₅₀ oral ‡	>5000 mg/kg bw	
Rat LD ₅₀ dermal ‡	>2500 mg/kg bw	
Rat LC ₅₀ inhalation ‡	>0.439 mg/L (highest attainable concentration)	
Skin irritation ‡	Not irritant	
Eye irritation ‡	Slightly irritant	
Skin sensitisation ‡	Not sensitiser (M & K)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Thyroid effects; several species	R48/22
Relevant oral NOAEL ‡	0.1 mg/kg bw/d – 90-d rat 0.3 mg/kg bw/d – 1-y dog	
Relevant dermal NOAEL ‡	100 mg/kg bw/d – 28-d rat	
Relevant inhalation NOAEL ‡	0.1 mg/L (NOEC) – 28-d rat	

Genotoxicity ‡ (Annex IIA, point 5.4)

Not genotoxic by weight of evidence	
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Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Thyroid effects	R48/22
Relevant NOAEL ‡	0.5 mg/kg bw/d – 2-y rat	
Carcinogenicity ‡	Thyroid tumours (not relevant for humans)	

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Mammalian toxicology**Reproductive toxicity (Annex IIA, point 5.6)****Reproduction toxicity**

Reproduction target / critical effect ‡

Relevant parental NOAEL ‡

Relevant reproductive NOAEL ‡

Relevant offspring NOAEL ‡

Thyroid effects	R48/22
0.12 mg/kg bw/d – 2-generation rat	
0.9 mg/kg bw/d – 2-generation rat	
0.9 mg/kg bw/d – 2-generation rat	

Developmental toxicity

Developmental target / critical effect ‡

Relevant maternal NOAEL ‡

Relevant developmental NOAEL ‡

Thyroid effects, malformations of the head and limbs, visceral and skeletal variants	R48/22, Repr Cat 3 R63
5 mg/kg bw/d - rabbit	
5 mg/kg bw/d - rabbit	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡

Repeated neurotoxicity ‡

Delayed neurotoxicity ‡

Not relevant	
Not relevant	
Not relevant	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡

Studies performed on metabolites or impurities ‡

Not relevant
Not relevant

Medical data ‡ (Annex IIA, point 5.9)

The applicant reported two worker accidents in manufacturing plant. No major effects reported.

Summary (Annex IIA, point 5.10)

ADI ‡

AOEL ‡

ARfD ‡

Value	Study	Safety factor
0.001 mg/kg bw/d	90-d rat studies	100
0.001 mg/kg bw/d	90-d rat studies	100
0.015 mg/kg bw	28-d rat study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (CA2735, 229 g/L SL)

Undiluted: 1%
Spray dilutions: 10%
In vitro study on human skin

Exposure scenarios (Annex IIIA, point 7.2)

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Mammalian toxicology

Operator

Orchards, grapes, olives:
UK-POEM with PPE: 11975%
BBA with PPE: 1380%
Field study: >100% AOEL

Non crop uses: no data, to be addressed at Member State level

No acceptable use identified

Workers

Orchards, grapes, olives: 50% with PPE

Non crop uses: no data, to be addressed at Member State level

Bystanders

Orchards, grapes, olives: 82%

Non crop uses: no data, to be addressed at Member State level

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

Substance classified

Amitrole

Classification according to Council Directive 67/548/EEC / Regulation (EC) No 1272/2008:

Harmonised classification and labelling:
Xn, Repr Cat 3 R63 R48/22
STOT RE 2 (H373) Repr. 2 (H361d)

Peer review proposal*

Under Council Directive 67/548/EEC¹
Xn
Repr Cat 3 R63
R48/22

Under Regulation (EC) No 1272/2008²
STOT RE 2 (H373)
Repr. 2 (H361d)

* It should be noted that classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals.

¹ OJ No 196, 16.08.1967, p. 001-0098

² OJ No L 353, 31.12.2008, p. 0001-1355

Rapporteur Member State	Month and year	Active Substance (Name)
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Residues**Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)**

Plant groups covered	Fruits and fruiting vegetables
Rotational crops	Not relevant, applied on perennial crops
Metabolism in rotational crops similar to metabolism in primary crops?	-
Processed commodities	Not relevant, no residue situation
Residue pattern in processed commodities similar to residue pattern in raw commodities?	-
Plant residue definition for monitoring	Amitrole
Plant residue definition for risk assessment	Amitrole
Conversion factor (monitoring to risk assessment)	-

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Not relevant
Time needed to reach a plateau concentration in milk and eggs	-
Animal residue definition for monitoring	Not relevant
Animal residue definition for risk assessment	Not relevant
Conversion factor (monitoring to risk assessment)	Not relevant
Metabolism in rat and ruminant similar (yes/no)	-
Fat soluble residue: (yes/no)	No

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

Not relevant

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Crop	Characteristics of the crop group	Acceptable Maximum Storage duration
Apple	Crop with high water content	16 months for amitrole
Grape	Crop with acid content	8 months for amitrole 6.5 months for triazolyalanine 6.5 months for aminotriazolyalanine
Olive	Crop with high lipid content	6.5 months for amitrole 6.5 months for triazolyalanine 6.5 months for aminotriazolyalanine
Animal Products		

Rapporteur Member State	Month and year	Active Substance (Name)
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Residues

Not relevant

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)

Potential for accumulation (yes/no)

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)

Muscle

Liver

Kidney

Fat

Milk

Eggs

Ruminant	Poultry	Pig
Conditions of requirement of feeding studies		
Not relevant		
Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Not relevant		

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Residues**Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)**

Zone	Number of trials supporting the GAP	Residues (mg/kg)	STMR	HR	Comments	
Enforcement and risk assessment residue definition : amitrole						
Orchards						
GAP : 1 x 1.2-3kg a.i/ha – 35 day PHI						
Northern EU	6	Apples and pear	<0.01x4; <0.02 x 2	0.01	0.01	Dataset on apples(5) and pear(1) with 1-2 application (total application comprised between 8-10kg/ha) PHI comprised between 4 and 42 days 13 others trials : dataset on apples (9), pears(4) in north with 1-4 application (total application comprised between 5.8-15kg/ha) PHI comprised between 49 and 111 days and <LOQ
Southern EU	9	Apples and pear and peach	<0.01 x 9	0.01	0.01	Combined dataset on apples(4), pear(1); and peaches(4) with 1-4 application (total application comprised between 5.8-11.7kg/ha) PHI comprised between 37 and 111 days
Grapes						
GAP : 1 x 1.2-3kg a.i/ha – 42 day PHI						
Northern EU	11	Fruit	<0.01 x 5; <0.02 x 6	0.01	0.01	with 1-2 application (total application comprised between 3.6-8kg/ha) PHI comprised between 28 and 43 days
Southern EU	9	Fruit	<0.01 x 5; <0.025 x 4	0.01	0.01	with 1 application (total application comprised between 2.9-3.7kg/ha) PHI comprised between 15 and 30 days
Olives						
GAP : 1 x 0.9-3kg a.i/ha – 35 day PHI						
Southern EU	5	Fruit	<0.01 x 5	0.01	0.01	with 1 application (total application comprised between 1.9-2.1kg/ha) PHI comprised between 6 and 35 days

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
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Fate and behaviour in the environment**Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)**

ADI	0.001 mg/kg b.w./day
TMDI (% ADI) according to WHO European diet	20%
NEDI (% ADI)	-
Factors included in IEDI and NEDI	-
ARfD	0.015 mg/kg b.w.
IENTI (%ARfD)	9%
NESTI (% ARfD) according to national (to be specified) large portion consumption data	-
Factors included in IESTI and NESTI	-

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Not relevant				

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

See EFSA reasoned opinion about the review of the existing maximum residue levels (MRLs) for amitrole according to Article 12 of the Regulation (EC) No 396/2005.

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment**Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)**

Mineralization after 100 days ‡

20.3-61.1 % after 7 d, [5-¹⁴C]-label (n³=2)
 36.1-59.9 % after 7 d, [3,5-¹⁴C]-label (n=2)
 44.5 % after 91 d, [3-¹⁴C]-label (n= 1)
 Sterile conditions: ca 1 % after 365 d (n= 1)

Non-extractable residues after 100 days ‡

28.4-41 % after 7 d, [5-¹⁴C]-label (n=1)
 23.7-50.8 % after 7 d, [3,5-¹⁴C]-label (n= 2)
 40.9 % after 91 d, [3-¹⁴C]-label (n= 1)

Metabolites requiring further consideration ‡
 - name and/or code, % of applied (range and maximum)

None

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days

<0.6 % after 112 d, [3,5¹⁴C]-label (n= 1)

Non-extractable residues after 100 days

61.4 % after 112 d, [3,5¹⁴C]-label (n= 1)

Metabolites that may require further consideration
 for risk assessment - name and/or code, % of
 applied (range and maximum)

None.

Soil photolysis ‡

Metabolites that may require further consideration
 for risk assessment - name and/or code, % of
 applied (range and maximum)

Conditions: Xenon lamp (300-800 nm, 500 W/m², 12h photoperiod)
 Amitrole: 66.4% AR after 30 days in irradiated samples, 88.7% AR in dark controls
 Metabolite 1,2,4-triazole: 9.9 % at 30 d (n= 1) (minor non transient)

³ n corresponds to the number of soils.

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Fate and behaviour in the environment**Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)**

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X ⁴	pH	t. °C / % MWHC	DT ₅₀ /DT ₉₀ (d)	DT ₅₀ (d) 20 °C pF2/10kPa	St. (r ²)	Method of calculation
Sand		6.2	22°C / 75% pF2	23.8/79.1	20.8	6.7	SFO
Standard 2.1		6.5	22°C / nr	3.4/11.2	4.1	17.6	SFO
Standard 2.2		6.1	22°C / nr	3.6/11.9	4.3	11.3	SFO
Standard 2.3		5.5	22°C / nr	6.8/22.5	8.2	4.3	SFO
Sand		6.2	7°C / 75% pF2	87.2/289.7	-	4.8	SFO
Geometric mean/median					7.4		

Laboratory studies

1,2,4-triazole (applied as parent)	Aerobic conditions						
Soil type	X ⁵	pH	t. °C / % MWHC	DT ₅₀ fast phase/DT ₅₀ slow phase(d)/g	DT ₅₀ (d) 20°C pF2/10kPa	St. (r ²)	Method of calculation
Sandy loam		6.4	20 °C / 40 %	0.9/59.2/ 0.683			DFOP
Loamy sand		5.8	20 °C / 40 %	1.5/247.6/0.5 80			DFOP
Silt loam		6.7	20 °C / 40 %	0.8/20.6/ 0.443			DFOP
Geometric mean/median				1.0/67.1/ 0.569			DFOP

⁴ X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

⁵ X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

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Fate and behaviour in the environment

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X ¹	pH	Depth (cm)	DT ₅₀ (d) actual	DT ₉₀ (d) actual	St. (χ ²)	DT ₅₀ (d) Norm.	Method of calculation
Loam (cropped)	Oregon (USA)		5.8	90	16.1	53.4	16.5		SFO
Loam (cropped)	Washington (USA)		6.8	90	7.7	25.4	26.0	-	SFO
Loam (bare)	Huntington (UK)		7.6	40	16.8	55.8	5.3	-	SFO
Geometric mean/median								-	

Field studies ‡

1,2,4-triazole (applied as parent)	Aerobic conditions, kinetics calculated for ambient conditions . Bare soil with grass sown immediately after application (with exception of Spain site where no grass sown).								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X ¹	pH	Depth (cm)	DT ₅₀ (d) actual	DT ₉₀ (d) actual	St. (χ ²)	DT ₅₀ (d) Norm.	Method of calculation
Silt loam	Germany		6.4	0-30	7.8	366.7	15.2		FOMC
Silty clay loam	Italy		7.6	0-40	21.2	207.4	10.7		DFOP
Sandy loam	UK		7.4	0-40	6.8	109.3	17.8		DFOP
Loam	Spain		5.8	0-30	28.1	717.6	13.3		DFOP
Geometric mean/median									
1,2,4-triazole (applied as parent)	Aerobic conditions, kinetics calculated timestep normalised to 20°C and pF2 moisture . Bare soil with grass sown immediately after application (with exception of Spain site where no grass sown).								
Soil type	Location		pH	Depth (cm)	DT ₅₀ (d) Fast phase	DT ₅₀ (d) Slow phase	'g'	St. (χ ²)	Method of calculation
Silt loam	Germany		6.4	0-30	2.5	70.7	0.655	18.8	DFOP
Silty clay loam	Italy		7.6	0-40	1.4	59.8	0.364	10.6	DFOP
Sandy loam	UK		7.4	0-40	0.5	25.1	0.458	18.1	DFOP
Loam	Spain		5.8	0-30	4.6	126.0	0.489	12.7	DFOP
Geometric mean ('g' value is arithmetic mean)					1.68	60.5	0.489		DFOP

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR

Co-RMS = HU

January 2013

Amitrole

Fate and behaviour in the environment

pH dependence ‡

(yes / no) (if yes type of dependence)

No

Soil accumulation and plateau concentration ‡

No accumulation expected for amitrole.

A plateau concentration is calculated for 1,2,4-triazole
(see PECsoil)

Laboratory studies ‡

Parent

Anaerobic conditions

Degradation slower than under aerobic conditions (47.6% AR remains as amitrole after 56 days)

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	K _d (mL/g)	K _{oc} (mL/g)	K _f (mL/g)	K _{foc} (mL/g)	1/n
Sandy loam	1.74	6.1 (un)			3.52	202	0.65
Silt loam	3.42	6.8 (un)			3.79	111	0.77
Silty clay loam	2.9	7.0 (un)			1.57	54	0.86
Sand	0.46	5.6 (un)			0.685	149	0.80
Silty clay	0.64	7.4 (CaCl ₂)			0.714	112	0.77
Sandy loam	0.75	6.8 (CaCl ₂)			0.223	30	0.85
Sand	0.75	5.6 (CaCl ₂)			0.152	20	0.87
Silt	1.8	5.3 (CaCl ₂)			0.921	51	0.86
Clay	1.64	7.2 (CaCl ₂)			1.9	114	0.81
Arithmetic mean/median					1.50/0.92	94/111	0.80/0.81
pH dependence, Yes or No				No			

(un): matrix of pH measurement unknown

Metabolite 1,2,4-triazole							
Soil Type	OC %	Soil pH (CaCl ₂)	K _d (mL/g)	K _{oc} (mL/g)	K _f (mL/g)	K _{foc} (mL/g)	1/n
Silty clay	0.70	8.8			0.83	120	0.897
Clay loam	1.74	6.9			0.75	43	0.827
Silty clay loam	0.70	7.0			0.72	104	0.922

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment

Sandy loam	0.81	6.9			0.72	89	1.016
Arithmetic mean/median					0.76	89	0.92
pH dependence (yes or no)				No			

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡

Elution (mm): 200 mm

Time period (d): 2 d

Leachate:

24-31 % AR in leachate, mainly Amitrole in standard soil 2.1 (6.8% silt + clay, 0.6% OC, pH6)

0.8 % AR in leachate in agricultural soil (32.4% silt + clay, 2.9% OC, pH5.5)

Aged residues leaching ‡

No reliable data (ageing time too long), not required.

Lysimeter/ field leaching studies ‡

No reliable data (LOD too high – 10 µg/L), not required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Amitrole

Method of calculation

DT₅₀ (d): 28.6 days (the longest laboratory DT₅₀ of 23.8 days measured at 22°C is normalized to 20°C using a Q10 of 2.58, resulting in a DT50 value of 28.6 days at 20°C)

Kinetics: SFO

Field or Lab: representative worst case from laboratory studies (at 20°C).

Application data

Crop: orchards, grapes, olives, non crop uses

Depth of soil layer: 5cm

Soil bulk density: 1.5g/cm³

% plant interception: No interception

Number of applications: 1

Interval (d): -

Application rate(s): 2977 g as/ha

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment

PEC _(s) (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	3.969		-	
Short term 24h	3.874	3.922	-	-
2d	3.782	3.875	-	-
4d	3.603	3.783	-	-
Long term 7d	3.350	3.651	-	-
21 d	2.386	3.111	-	-
28d	2.014	2.882	-	-
50d	1.182	2.301	-	-
100d	0.352	1.493	-	-
Plateau concentration	No accumulation expected			

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Fate and behaviour in the environment

Metabolite 1,2,4-triazole

Method of calculation

Molecular weight relative to the parent: 69.1/84.08
 DT₅₀ (d): 28.1 days
 Kinetics: DFOP (parameters: $k_1 = 0,002 \text{ day}^{-1}$, $k_2 = 0,0632 \text{ day}^{-1}$, $g = 0,573$)
 Field or Lab: representative worst case from field studies.

Application data

Application rate assumed: 242 g as/ha (assumed 1,2,4-triazole is formed at a maximum of 9.9 % of the applied dose and molecular ratio of 69.1/84.08)

PEC_(s)
(mg/kg)

	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.323		-	
Short term 24h	0.314	0.318	-	-
2d	0.306	0.314	-	-
4d	0.290	0.306	-	-
Long term 7d	0.271	0.295	-	-
21 d	0.214	0.257	-	-
28d	0.198	0.244	-	-
50d	0.173	0.218	-	-
100d	0.152	0.189	-	-
Plateau concentration	0.494 mg/kg after 8 yrs (in 5 cm)			

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡

Stable at pH 5, 7, 9 and 25°C.
 Stable at pH 4, 7, 9 and 90°C.

Photolytic degradation of active substance and metabolites above 10 % ‡

Stable at pH 5, 7, 9 and 25°C

Quantum yield of direct phototransformation in water at $\Sigma > 290 \text{ nm}$

No light absorption above 290 nm.

Readily biodegradable ‡
(yes/no)

No

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Fate and behaviour in the environment**Degradation in water / sediment**

Parent	Distribution (eg max in water 86.8-87.4 % after 0 d. Max. sed 5.9-14.0 % after 0-7 d)									
Water / sediment system	pH water phase	pH sed (CaCl ₂)	t. °C	DT ₅₀ -DT ₉₀ whole sys.	St. (χ ²)	DissT ₅₀ -DissT ₉₀ water	St. (χ ²)	DissT ₅₀ -DissT ₉₀ sed	St. (χ ²)	Method of calculation
Pond	8.6	6.9	20	88.7-294.5	3.0	87.6-291.1	3.1	116.8-388.2	1.6	SFO
Ditch	8.3	7.4	20	83.6-277.6	5.3	67.6-224.5	9.7	124.8-414.6	5.7	SFO
Geometric mean/median				86.1-285.9		77.0-255.6		120.7-401.2		

Metabolites	No major metabolite in water / sediment compartments
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Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. max x % after n d (end of the study)
Pond	8.6	6.9	18.7 % after 91 d	26.4 % after 91 d	26.4 % after 91 d
Ditch	8.3	7.4	10.3 % after 91 d	40.1 % after 91 d	40.1 % after 91 d

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)**For agricultural uses**

Parent

Parameters used in FOCUSsw step 1 and 2

Version control no. of FOCUS calculator: 1.1
Molecular weight (g/mol): 84.08
Water solubility (mg/L): 264 000
K_{OC}/K_{OM} (L/kg): 111 (median)
DT₅₀ soil (d): 7.4 days (normalised geomean from lab)
DT₅₀ water/sediment system (d): 86.1 (geomean)
DT₅₀ water (d): 86.1 (geomean from total system)
DT₅₀ sediment (d): 86.1 (geomean from total system)
Crop interception (%): No interception

Parameters used in FOCUSsw step 3 (if performed)

Version control no.'s of FOCUS software: SWASH 3.1
Vapour pressure: 3.3 10⁻⁵ (20°C)
K_{om}/K_{oc}: 111 (median)
1/n: 0.81 (median)
DT₅₀ water (d): 86.1 (geomean from total system)
DT₅₀ sediment (d): 1000 (conservative value)
Plant uptake: 0.5

Application rate

Crop: Pome fruits, Vines, Citrus, Olives
Crop interception: no interception

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment

Number of applications: 1
Interval (d): -
Application rate(s): Amitrole is intended to be used as a banded application, 2977 g as/ha for drift entries, 992 g/ha for run-off/drainage entries
Drift should be corrected for groundspray application
Application window: Oct-Feb for Step 1-2, 15 Oct-15 Nov / 15 Feb-15 Mar for Step 3

No PEC_{sw} for amitrole could be validated by RMS for agricultural uses. Input parameters to be used are reported above for information. Data gap for the applicant.

Metabolite 1,2,4-triazole

Parameters used in FOCUS_{sw} step 1 and 2

Molecular weight: 69.1
Water solubility (mg/L): 730 000
Soil or water metabolite: Soil
Koc/Kom (L/kg): 89
DT₅₀ soil (d): not needed (Step 1 only)
DT₅₀ water/sediment system (d): 1000 (conservative value)
DT₅₀ water (d): not needed (Step 1 only)
DT₅₀ sediment (d): not needed (Step 1 only)
Crop interception (%): No interception

Parameters used in FOCUS_{sw} step 3 (if performed)

Application rate

Not performed
Crop: pome/stone fruits (early & late), citrus, vines (early), olives
Number of applications: 1
Interval (d): -
Application rate(s): 81.5 g as/ha (2977 g/ha corrected by 1/3 for banded application, by maximum occurrence in soil of 9.9% and by molecular ratio of 69.1/84.08)
Application window: Oct-Feb

Main routes of entry

Run-off / drainage

FOCUS STEP 1 Scenario	Day after overall maximum	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg)	
		Actual	TWA	Actual	TWA
Pome fruits, early	0h	32.22		21.61	
Pome fruits late, citrus, olives	0h	28.56		21.61	
Vines, early	0h	25.02		21.61	

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment**For non crop uses, impermeable surfaces**

Method of calculation

Model(s) used: HardSPEC 1.4.2 Crop: non crop uses, impermeable surfaces
Parent: Water solubility : 264 g/L (20°C) Specific gravity: 1.138 Soil DT _{50lab} 7.4 d (geomean) K _{OC} : median 111 mL/g DT ₅₀ water (d): 86.2 (geomean from total system) DT ₅₀ sediment (d): 86.2 (geomean from total system)
Metabolite 1,2,4-triazole: simulated with a pseudo-application Water solubility: 730 g/L (20°C) Specific gravity: 1.138 (same as parent) Geometric mean DT _{50field} 60.5 d (geomean from DFOP slow phase) K _{OC} : mean 89 mL/g DT ₅₀ water (d): 1000 (conservative value) DT ₅₀ sediment (d): 1000 (conservative value)
Application rate for parent: 2977 g/ha Application rate for metabolite (pseudo-application): 242 g/ha (2977 g/ha corrected for max. occurrence of 9.9% and molecular ratio 69.1/84.08) No. of applications: 1

Application rate

	Acute (24 hrs) concentration		Application day PEC _{sw} from spray drift (mg l ⁻¹)
	Water phase (µg / L)	Sediment phase (µg / kg)	
Urban stream	453.782	503.335	27.309
Urban pond	42.733	47.350	0.172
Major road stream	233.210	258.863	19.399
Domestic stream	76.356	84.755	0.000
Railway ditch leaching	7.821	0.877	7.821
Railway ditch runoff	7.821	3.616	7.821

	Acute (24 hrs) concentration		Application day PEC _{sw} from spray drift (mg l ⁻¹)
	Water phase (µg / L)	Sediment phase (µg / kg)	
Urban stream	37.615	33.454	2.220
Urban pond	3.589	3.202	0.014
Major road stream	19.570	17.417	1.577
Domestic stream	8.922	7.940	0.000
Railway ditch leaching	0.636	0.128	0.636
Railway ditch runoff	0.636	0.454	0.636

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment**For non crop uses, permeable surfaces**

No PEC_{sw} for amitrole could be validated by RMS. Data gap for the applicant.

Metabolite 1,2,4-triazole

Parameters used in FOCUS_{sw} step 1 and 2

Molecular weight: 69.1
 Water solubility (mg/L): 730 000
 Soil or water metabolite: Soil
 Koc/Kom (L/kg): 89
 DT₅₀ soil (d): not needed (Step 1 only)
 DT₅₀ water/sediment system (d): 1000 (conservative value)
 DT₅₀ water (d): not needed (Step 1 only)
 DT₅₀ sediment (d): not needed (Step 1 only)
 Crop interception (%): No interception

Parameters used in FOCUS_{sw} step 3 (if performed)

Application rate

Not performed
 Crop: grass
 Number of applications: 1
 Interval (d): -
 Application rate(s): 88.5 g as/ha (2977 g/ha corrected by 0.3 for banded application, by maximum occurrence in soil of 9.9% and by molecular ratio of 69.1/84.08)
 Application window: Oct-Feb

Main routes of entry

Run-off / drainage

FOCUS STEP 1 Scenario	Day after overall maximum	PEC _{sw} (µg/L)		PEC _{sed} (µg/kg)	
		Actual	TWA	Actual	TWA
Grass	0h	27.18		23.47	

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment**PEC (ground water) (Annex IIIA, point 9.2.1)****For agricultural uses**

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)

For FOCUS gw modelling, values used –
Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance.
Model(s) used: PELMO 4.4.3
Scenarios (list of names): all relevant scenarios
Crop: apples, vines, citrus

Parent:
Vapour pressure: $3.3 \cdot 10^{-5}$ Pa (20°C), $1.32 \cdot 10^{-4}$ Pa (30°C)
Water solubility : 264 g/L (20°C), 528 g/L (30°C)
Geometric mean DT_{50lab} 7.4 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58).
 K_{OC} : median 111 mL/g, $1/n = 0.81$.
Plant uptake: 0.5

Metabolite 1,2,4-triazole: simulated with a pseudo-application
Vapour pressure: 10^{-10} Pa (20°C), $4 \cdot 10^{-10}$ Pa (30°C) (conservative values)
Water solubility : 730 g/L (20°C), 1460 g/L (30°C)
Geometric mean $DT_{50field}$ DFOP kinetics 1.68 d for fast phase, 60.5 d for slow phase, $g = 0.489$ (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58).
 K_{OC} : mean 89 mL/g, $1/n = 0.92$.
Plant uptake: 0

Application rate

Application rate for parent: 992 g/ha (2977 g/ha corrected by 1/3 for banded application).
Application rate for metabolite (pseudo-application): 80.7 g/ha (992g/ha corrected for max. occurrence of 9.9% and molecular ratio 69.1/84.08)⁶
No. of applications: 1
Time of application (month or season): 15 March and 15 October

⁶ Recommendations of the FOCUS kinetic guidance document were followed to implement the DFOP kinetic of metabolite 1,2,4-triazole. 2 simulations were conducted: the first for the fast-phase, with an application rate corrected by g , the 2nd for the slow phase, with an application rate corrected by (1- g). The concentrations were then summed to get the final concentrations. Since 1/ n of 1,2,4-triazole differs from 1, the application rate was doubled, and the final concentrations were divided by 2.

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Fate and behaviour in the environment**PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)**

PELMO 4.4.3 / Apples	Scenario	15 March		15 October	
		Parent (µg/L)	1,2,4-triazole (µg/L)	Parent (µg/L)	1,2,4-triazole (µg/L)
	Chateaudun	<0.001	0.622	<0.001	0.624
	Hamburg	<0.001	0.503	<0.001	0.813
	Jokioinen	<0.001	0.255	<0.001	0.375
	Kremsmunster	<0.001	0.444	<0.001	0.549
	Okehampton	<0.001	0.606	<0.001	0.889
	Piacenza	<0.001	0.522	<0.001	0.699
	Porto	<0.001	0.301	<0.001	0.633
	Sevilla	<0.001	0.361	<0.001	0.335
	Thiva	<0.001	0.358	<0.001	0.530

PELMO 4.4.3 / Vines	Scenario	15 March		15 October	
		Parent (µg/L)	1,2,4-triazole (µg/L)	Parent (µg/L)	1,2,4-triazole (µg/L)
	Chateaudun	<0.001	0.463	<0.001	0.517
	Hamburg	<0.001	0.429	<0.001	0.671
	Kremsmunster	<0.001	0.391	<0.001	0.474
	Piacenza	<0.001	0.419	<0.001	0.619
	Porto	<0.001	0.262	<0.001	0.614
	Sevilla	<0.001	0.169	<0.001	0.168
	Thiva	<0.001	0.184	<0.001	0.403

PELMO 4.4.3 / Citrus	Scenario	15 March		15 October	
		Parent (µg/L)	1,2,4-triazole (µg/L)	Parent (µg/L)	1,2,4-triazole (µg/L)
	Piacenza	<0.001	0.355	<0.001	0.608
	Porto	<0.001	0.222	<0.001	0.555
	Sevilla	<0.001	0.142	<0.001	0.324
	Thiva	<0.001	0.172	<0.001	0.547

For non crop uses on railways

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)

For FOCUS gw modelling, values used –
Modelling using HardSPEC.

Model(s) used: HardSPEC 1.4.2

Crop: non crop, railway

Parent:

Water solubility : 264 g/L (20°C)

Specific gravity: 1.138

Soil DT_{50lab} 23 d (median)⁷

K_{OC}: median 114 mL/g⁸

Metabolite 1,2,4-triazole: simulated with a pseudo-application

Water solubility : 730 g/L (20°C)

Specific gravity: 1.138 (same as parent)

Geometric mean DT_{50field} 60.5 d (geomean from DFOP slow phase)

K_{OC}: mean 89 mL/g

Application rate

Application rate for parent: 2977 g/ha

Application rate for metabolite (pseudo-application): 242 g/ha
2977 g/ha corrected for max. occurrence of 9.9% and molecular ratio 69.1/84.08)

No. of applications: 1

Amitrole**Railway over Groundwater**

Average annual concentration at the base of the railway formation (mg / L)	0.64		
Exposure at the abstraction well-head	Chalk	Limestone	Sandstone
Maximum concentration in well (µg / L)	0.0835	0.0038	0.0042
Period when plume > 0.1 µg / L in well (days)	0.0	0.0	0.0

1,2,4-triazole**Railway over Groundwater**

Average annual concentration at the base of the railway formation (mg / L)	0.08		
Exposure at the abstraction well-head	Chalk	Limestone	Sandstone
Maximum concentration in well (µg / L)	0.0657	0.0263	0.0257
Period when plume > 0.1 µg / L in well (days)	0.0	0.0	0.0

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡

No data, not required.

Quantum yield of direct phototransformation

No data, not required.

Photochemical oxidative degradation in air ‡

DT₅₀ of 4.8 hours derived by the Atkinson model.

OH (24 h) concentration assumed = 5x10⁵ cm⁻³

⁷ It is noted that the correct value to be used is 7.4 days. However, calculations performed are conservative and so were not performed again.

⁸ It is noted that the correct value to be used is 111 mL/g.

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Fate and behaviour in the environment

Volatilisation ‡

from plant surfaces (BBA guideline): 11 % after 24 hours
from soil surfaces (BBA guideline): negligible after 24 hours

PEC (air)

Method of calculation

Expert judgement, based on vapour pressure (3.3×10^{-5} Pa at 20°C), Henry's Law Constant (1.76×10^{-8} Pa.m³.mol⁻¹) and information on volatilisation from plants and soil.

PEC_(a)

Maximum concentration

Negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).

Soil:	Amitrole, 1,2,4-triazole
Surface Water:	Amitrole, 1,2,4-triazole
Sediment:	Amitrole
Ground water:	Amitrole, 1,2,4-triazole
Air:	Amitrole

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)

No data

Surface water (indicate location and type of study)

No data

Ground water (indicate location and type of study)

Provided data are difficult to interpret. No conclusion can be delivered.

Air (indicate location and type of study)

No data

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Candidate for R53

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Ecotoxicology**Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)**

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Bird ‡				
<i>Bobwhite quail</i>	a.s.	Acute	> 2150 mg/kg b.w.	
<i>Mallard duck</i>	a.s.	Short-term (5d)	> 829 mg a.s./kg b.w./day	> 5000 ppm a.s.
<i>Mallard duck</i>	a.s.	Long-term_1 generation (22 weeks)*	NOEC = 12.1 mg a.s./kg b.w./day	NOEC = 100 ppm a.s.
<i>Mallard duck</i>	a.s.	Long-term_2 generations (15 months)	NOEC reproductive = 95 ppm a.s., equivalent to ca. 16 mg a.s./kg b.w./day At all necropsy intervals, impacts upon thyroid size were noted at all concentrations. Overall LOEC = 95 ppm a.s., equivalent to ca. 16 mg a.s./kg b.w./day Overall NOEC: none	-
Mammals ‡				
<i>rat</i>	a.s.	Acute	5000 mg a.s./kg b.w.	-
<i>rat</i>	a.s.	Long-term_2 generations	NOAEL = 0.9 mg a.s./kg b.w./d	-
Additional higher tier studies ‡				
-				

* Toxicity data not sufficient for assessing potential effects on development and reproduction due to endocrine disrupting properties of the active substance

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Long term DDD and TER for birds were calculated by the applicant based on the one-generation NOEL of 12.1 mg/kg b.w./day but as no overall NOEC could be established from the two-generation bird study, long term risk assessment for birds couldn't be finalized.

Vineyard: 1 × 0.993 kg Amitrole/ha (1/3 of the full dose rate due to the application made under the row)

Indicator species	Time scale	DDD	TER ¹	Annex VI Trigger
BIRDS				
Screening step				
Small omnivorous bird	Acute	94.63	22.7	10
	Long-term	-	-	5
MAMMALS				

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Ecotoxicology

Screening step				
Small herbivorous mammal	Acute	121.4	41	10
	Long-term	38.05	0.02	5
Tier 1 (Mammals)				
Large herbivorous mammal “lagomorph”	Long-term	5.24	0.2	5
Small herbivorous mammal "vole		34.1	0.03	
Small insectivorous mammal “shrew”		2.25	0.4	
Wood mouse (<i>Apodemus sylvaticus</i>): 25% weeds / 50% weed seeds / 25% ground arthropods		3.68	0.2	
Higher tier refinement (Mammals)_based on focal species and refined PT value and/or measured RUDs (worst case values)				
Large herbivorous mammal “lagomorph”	Long-term	0.0164	54.4	5
Small herbivorous mammal "vole		0.0564	16.0	
Small insectivorous mammal “shrew”		0.901	1.0	
Wood mouse (<i>Apodemus sylvaticus</i>)_focal species		0.0489	18.4	

¹ in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)

Orchards: 1 × 0.993 kg Amitrole/ha (1/3 of the full dose rate due to the application made under the row)

Indicator species	Time scale	DDD	TER ¹	Annex VI Trigger
BIRDS				
Screening step				
Small insectivorous bird	Acute	41.65	46.3	10
	Long-term	-	-	5
MAMMALS				
Screening step				
Small herbivorous mammal	Acute	121.4	41	10
	Long-term	38.05	0.02	5
Tier 1 (Mammals)				
Small insectivorous mammal "shrew"	Long-term	1	0.9	5
Small herbivorous mammal "vole"		34.1	0.03	
Large herbivorous mammal "lagomorph"		11.32	0.1	
Wood mouse (<i>Apodemus</i>)		3.68	0.2	

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Ecotoxicology

<i>sylvaticus</i>): 25% weeds / 50% weed seeds / 25% ground arthropods				
Higher tier refinement (Mammals)_based on focal species and refined PT value and/or measured RUDs (worst case values)				
Small insectivorous mammal "shrew"	Long-term	0.9007	1.0	5
Small herbivorous mammal "vole_focal species"		0.0564	16.0	
Large herbivorous mammal "lagomorph"		0.0212	42.5	
Wood mouse (<i>Apodemus sylvaticus</i>): 25% weeds / 50% weed seeds / 25% ground arthropods		0.119	7.6	

¹ in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group (species)	Test substance	Time scale	Endpoint	Value (mg a.s./L)	Expressed as *
Fish					
Fish (<i>O. mykiss</i>)	a.s.	Acute (static) 96H	LC ₅₀	>1000	Nominal
Fish (<i>O. mykiss</i>)	a.s.	Chronic (static) ¹ 21d	NOEC	100	Nominal
Fish (<i>O. mykiss</i>)	preparation	Acute (static) 96H	LC ₅₀	>100 mg preparation/L (>22.15 mg a.s/L)	Nominal
Fish (<i>O. mykiss</i>)	1,2,4-triazole	Acute (static) 96H	LC ₅₀	498**	Nominal
Fish (<i>O. mykiss</i>)	1,2,4-triazole	Chronic (semi-static) 28d	NOEC	>100 (mortality) 3.2 (sub lethal effects)	Nominal
Aquatic invertebrate					
Invertebrate (<i>D. magna</i>)	a.s.	Acute (static) 48H	EC ₅₀	6.1	Nominal
Invertebrate (<i>Mysidopsis bahia</i>)	a.s.	Acute (static) 96H	EC ₅₀	2.8	Mean measured
Invertebrate (<i>D. magna</i>)	a.s.	Chronic (static) 21d	NOEC	0.32	Nominal

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Ecotoxicology

Invertebrate (<i>D. magna</i>)	preparation	Acute 48H (static)	EC ₅₀	12 mg preparation/L (2.66 mg a.s/L)	Nominal
Invertebrate (<i>D. magna</i>)	1,2,4- triazole	Acute 48H (static)	EC ₅₀	>100	Nominal
Aquatic molluscs					
Aquatic molluscs (<i>Crassostrea virginica</i>)	a.s.	Acute 96 h	EC ₅₀	>110	Mean measured
Algae					
Algae (<i>Scenedesmus subspicatus</i>)	a.s.	72H growth test	EC ₅₀	2.3	Nominal
Algae (<i>Anabaena flos-aquae</i>)	a.s.	120H growth test (static)	E _b C ₅₀ EC _{r50}	3.9*** >4.8	Nominal
Algae (<i>Selenastrum capricornutum</i>)	a.s.	5d growth test	EC _{b50} EC _{r50}	2.3 >5.1	Mean measured
Algae (<i>Selenastrum capricornutum</i>)	a.s.	8d growth test	EC _{b50} /EC _{r50} NOEC	> 6 6	Nominal
Algae (<i>Skeletonema costatum</i>)	a.s.	5d growth test	EC _{b50} EC _{r50}	2.1 >5.1	Mean measured
Algae (<i>Navicula pelliculosa</i>)	a.s.	5d growth test	EC _{b50} EC _{r50}	2.1 >3.1	Mean measured
Algae (<i>Selenastrum capricornutum</i>)	preparation	72H growth test	EC _{b50} EC _{r50}	126 mg preparation/L (27.91 mg a.s/L) >200 mg preparation/L (>44.3 mg a.s/L)	Nominal
Algae (<i>Selenastrum capricornutum</i>)	1,2,4- triazole	72H growth test	EC _{b50} EC _{r50}	13 >31	Nominal
Algae (<i>Selenastrum capricornutum</i>)	1,2,4- triazole	72H growth test	EC _{b50} EC _{r50}	8.2 22.5*****	Nominal
Aquatic plant					
Aquatic plant (<i>Lemna gibba</i>)	a.s.	14d growth test (static)	EC ₅₀	2.5	Measured (initial concentration)

1 Toxicity data not sufficient for assessing potential effects on development and reproduction due to endocrine disrupting properties of the active substance

* RMS comment: endpoint expressed in term of mean measured concentration could be expressed in term of nominal concentration as amitrole was very stable during these tests

** value set during the expert meeting 43 (march 2008)

*** RMS comment: There is a mistake in the review report (EC₅₀ of 2.5 mg a.s/L has been reported whereas this value corresponded to the NOEC_b in the addendum to monograph)

**** value set during the expert meeting 13 (january 2007)

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

For agricultural uses (pome fruit, citrus, olives and vineyard) and permeable non-crop areas (grass), in absence of validated PEC_{sw} for amitrole (see environmental section), the exposure to surface water cannot be finalized. Therefore, risk assessment for aquatic organism cannot be finalized. (Data gap for the applicant)

For impermeable non-cropped areas (uses on road and railways), PEC_{sw} for amitrole were calculated in Environmental section according to HardSpec

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Ecotoxicology**FOCUS Step 1****Agricultural uses (pome fruit, citrus, olives and vineyard) and permeable non-crop areas (grass)**

Test substance	Organism	Toxicity end point (µg/L)	Time scale	Worst case scenario	PEC	TER	Annex VI Trigger
a.s.	Fish	LC ₅₀ > 1000000	Acute	-	N.A	N.A	100
a.s.	Fish	NOEC: N.A	Chronic	-	N.A	N.A	10
a.s.	Fish	The chronic test on juvenile fish (NOEC=100 mg a.s/L) is not sufficient for assessing potential effects on development and reproduction due to endocrine disrupting properties. These potential consequences on development and reproduction <i>in vivo</i> should have been addressed with the fish full life-cycle test in fish (Medaka) but this study is not considered valid. Therefore, as there is an uncertainty concerning potential effects on development and reproduction, long term risk assessment for fish cannot be finalized.					
a.s.	Aquatic invertebrates (<i>D. magna</i>)	EC ₅₀ = 6100	Acute	-	Not finalised	N.A	100
a.s.	Aquatic invertebrates (<i>D. magna</i>)	NOEC = 320	Chronic	-	Not finalised	N.A	10
a.s.	Aquatic invertebrates (<i>Mysidopsis bahia</i>)	EC ₅₀ = 2800	Acute	-	N.A	N.A	100
a.s.	Algae	E _b C ₅₀ = 2100 (lowest EC ₅₀)	Chronic	-	N.A	N.A	10
a.s.	Higher plants	E _b C ₅₀ = 2500	Chronic	-	N.A	N.A	10
1,2,4-triazole	Fish	LC ₅₀ = 498000	Acute	orchards	32.22	≥ 14991	100
1,2,4-triazole	Fish	NOEC = 3200	Chronic	orchards	32.22	≥ 96	10
1,2,4-triazole	Aquatic invertebrates	EC ₅₀ > 100000	Acute	orchards	32.22	>3103	100
1,2,4-triazole	Algae	E _b C ₅₀ = 8200	Chronic	orchards	32.22	≥254	10

Hardspec**For impermeable non crop uses (uses on road and railways)**

Test substance	Organism	Toxicity end point (µg/L)	Time scale	Worst case scenario	PEC (µg/L)	TER	Annex VI Trigger ¹
a.s.	Fish	LC ₅₀ > 1000000	Acute	Urban stream	454	>2202	100
a.s.	Fish	NOEC : N.A	Chronic	Urban stream	454	N.A	10
a.s.	Fish	The chronic test on juvenile fish (NOEC=100 mg a.s/L) is not sufficient for assessing potential effects on development and reproduction due to endocrine disrupting properties.					

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Ecotoxicology

		These potential consequences on development and reproduction <i>in vivo</i> should have been addressed with the fish full life-cycle test in fish (Medaka) but this study is not considered valid. Therefore, as there is an uncertainty concerning potential effects on development and reproduction, long term risk assessment for fish cannot be finalized.					
a.s.	Aquatic invertebrates (<i>D. magna</i>)	EC ₅₀ = 6100	Acute	Urban stream	454	14	100
				Urban pond	43	142	
				Major road stream	233	26	
				Domestic stream	77	79	
				Railway ditch leaching	8	763	
				Railway ditch runoff	8	763	
a.s.	Aquatic invertebrates (<i>D. magna</i>)	NOEC = 320	Chronic	Urban stream	454	0.7	10
				Urban pond	43	7.5	
				Major road stream	233	1.4	
				Domestic stream	77	4.1	
				Railway ditch leaching	8	40	
				Railway ditch runoff	8	40	
a.s.	Aquatic invertebrates (<i>Mysidopsis bahia</i>)	EC ₅₀ = 2800	Acute	Urban stream	454	6	100
				Urban pond	43	65	
				Major road stream	233	12	
				Domestic stream	77	36	
				Railway ditch leaching	8	350	
				Railway ditch runoff	8	350	
a.s	Aquatic molluscs (<i>Crassostrea virginica</i>)	EC ₅₀ > 100000	acute	Urban stream	454	>221	100
a.s.	Algae	E _b C ₅₀ = 2100 (lowest EC ₅₀)	Chronic	Urban stream	454	5	10
				Urban pond	43	49	
				Major road stream	233	9	
				Domestic stream	77	27	
				Railway ditch leaching	8	262	
				Railway ditch runoff	8	262	
a.s.	Higher plants	E _b C ₅₀ = 2500	Chronic	Urban stream	454	6	10
				Urban pond	43	58	

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Ecotoxicology

				Major road stream	233	11	
				Domestic stream	77	32	
				Railway ditch leaching	8	312	
				Railway ditch runoff	8	312	
1,2,4-triazole	Fish	LC ₅₀ = 498000	Acute	Urban stream	37.615	13239	100
1,2,4-triazole	Fish	NOEC = 3200	Chronic	Urban stream	37.615	≥ 85	10
1,2,4-triazole	Aquatic invertebrates	EC ₅₀ > 100000	Acute	Urban stream	37.615	> 2658	100
1,2,4-triazole	Algae	E _b C ₅₀ = 8200	Acute	Urban stream	37.615	> 217	10

	Active substance
logP _{O/W}	-0.969 (pH7;23°C)
Bioconcentration factor (BCF) ¹ ‡	2.38 (whole fish)
Annex VI Trigger for the bioconcentration factor	-
Clearance time (days) (CT ₅₀)	Not available, not triggered
(CT ₉₀)	Not available, not triggered
Level and nature of residues (%) in organisms after the 14 day depuration phase	Not available, not triggered

¹ only required if log P_{O/W} > 3.

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD ₅₀ µg/bee)	Acute contact toxicity (LD ₅₀ µg/bee)
a.s. ‡	LD ₅₀ > 152 µg a.s./bee	LD ₅₀ > 100 µg a.s./bee
Preparation ¹	LD ₅₀ > 200 µg preparation/bee (> 42 µg a.s./bee)	LD ₅₀ > 200 µg preparation/bee (> 42 µg a.s./bee)

¹ for preparations indicate whether end point is expressed in units of a.s. or preparation

Hazard quotients for honey bees (Annex IIIA, point 10.4)**Crop and application rate**

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	<30	50
a.s.	oral	<20	50

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Ecotoxicology**Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)**

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect ¹
<i>Aphidius colemani</i> (adults; lab. test)	(4.72 kg as/ha; Amitrole SL 236 g a.s./L)	Mortality	Effect (mortality): 80%
<i>Typhlodromus pyri</i> (protonymphs; lab. test)	(4.72 kg as/ha; Amitrole SL 236 g a.s./L)	Mortality	Effect (mortality): 100%
<i>Orius insidiosus</i> (nymphs, 2nd stage; lab. test)	(4.72 kg as/ha; Amitrole SL 236 g a.s./L)	Mortality	Effect (mortality): 100%
<i>Poecilus cupreus</i> (adults; lab. test)	(4.72 kg as/ha; Amitrole SL 236 g a.s./L)	Mortality	Effect (mortality): 3.7%
<i>Poecilus cupreus</i> (adults; lab. test)	(14.6 kg a.s./ha; Amitrole WP 50% w/w a.s.)	Mortality Food consumption	Effect (mortality): 0% Effect (food consumption) = 1.18 (ratio treated/control)
<i>Pardosa armentata</i> (adults)	(4.9 kg a.s./ha; Amitrole WP 50% w/w a.s.)	Mortality	Effect (mortality): 100%
<i>Aleochara bilineata</i> (adults; lab. test)	(5.0 kg a.s./ha; Amitrole WP 50% w/w a.s.)	Mortality Reproduction	Effect (mortality): 0% Effect (reproduction) = 0.01 (ratio treated/control)
<i>Aleochara bilineata</i> (adults; lab. test)	(5.0 kg a.s./ha; Amitrole WP 50% w/w a.s.)	Mortality Fecundity	Effect (mortality): 11.7% Effect (fecundity) = 1.0 (ratio treated/control)

¹ positive percentages relate to adverse effects or not

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (L preparation/ha)	End point	% effect ¹	Trigger value
<i>Aphidius rhopalosiphii</i>	Adults	Amitrole SL 236 g a.s./L	20 L preparation/ha	Mortality Reproduction ability	Corrected mortality: 45.71% Reproduction ability: 0.1469	50 %
<i>Aphidius rhopalosiphii</i>	Adults	Amitrole SL 229 g a.s./L	Up to 45 L preparation/ha	LR50 ER50	LR ₅₀ : > 45000 mL preparation/ha ER ₅₀ : > 45000 mL preparation/ha	50 %

‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**RMS = FR
Co-RMS = HU

January 2013

Amitrole

Ecotoxicology

Species	Life stage	Test substance, substrate and duration	Dose (L preparation/ha)	End point	% effect ¹	Trigger value
<i>Typhlodromus pyri</i>	Proto-nymphs	Amitrole SL 229 g a.s./L	up to 0.015 L preparation/ha	LR50 ER50	LR ₅₀ : 3.6 mL preparation/ha ER ₅₀ : > 3.75 mL preparation/ha (highest tested dose in the reproduction phase)	50 %
<i>Pardosa sp.</i>	Adults	Amitrole SL 229 g a.s./L	15 L preparation/ha	Mortality Feeding capacity	Effect (mortality): 21.2% at 15000 mL/ha Effect (feeding capacity): none up to 15000 mL/ha	50 %
<i>Orius insidiosus</i>	Nymphs	Amitrole SL 236 g a.s./L	20 L preparation/ha	Mortality	Effect (mortality): 100%	50 %
<i>Chrysoperla carnea</i>	Adults	Amitrole SL 229 g a.s./L	9 L preparation/ha	LR50 ER50	LR ₅₀ : > 9000 mL prod./ha ER ₅₀ : > 9000 mL prod./ha (2nd assessment)	50 %

¹ positive percentages relate to adverse effects or not**Agricultural uses : 13 L preparation/ha**

Test substance	Species	Effect (LR ₅₀ mL/ha)	Exposure in field (mL/ha)	Exposure off-field ¹ (mL/ha)	Exposure off-field (mL/ha) taking into account VDF ¹ and SCF ²	Trigger
Amitrole SL 229 g a.s./L	<i>Typhlodromus pyri</i>	3.6	13000	1m: 360 50m: 7.8 75m: 5.2	1m: 180 50m: 3.9 75m: 2.6	50%
Amitrole SL 229 g a.s./L	<i>Aphidius rhopalosiphii</i>	> 45000	13000	Not necessary (risk acceptable in-field)	Not necessary (risk acceptable in-field)	50%

¹ vegetation distribution factor of 10 was considered to be appropriate for 2D extended lab studies with *T.pyri* and of 5 for 3D extended lab study with *Aphidius rhopalosiphii*.² species safety factor of 5, covers differences in sensitivity between different species**Field or semi-field tests**

A field study to evaluate the effects of CA2735 on predatory mite population development in a vineyard in southern France is on-going. The study plan has been submitted and the draft final report should be available in December 2012. This study should be submitted at member state level to conclude on the risk in-field.

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5, Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point
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‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR Co-RMS = HU	January 2013	Amitrole
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Ecotoxicology

Test organism	Test substance	Time scale	End point
Earthworms			
	a.s. ‡	Acute 14 days	LC ₅₀ >448 mg a.s./kg d.w.soil
	a.s. ‡	Chronic 8 weeks	-
	Preparation	Acute	>1000 mg formulation/kg soil dry weight (equivalent to >221.5 mg a.s./ kg soil dry weight)
	Preparation	Chronic	-
	1,2,4 triazole	Acute	>1000
	1,2,4 triazole	Chronic	1
Other soil macro-organisms			
Soil mite	a.s. ‡	-	-
	Preparation	-	-
	1,2,4 triazole	-	-
Collembola			
	a.s. ‡	-	-
	Preparation	-	-
	1,2,4 triazole	Chronic	NOEC= 1.8 mg a.i./kg d.w.soil
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		transient retardation of nitrification processes, recovery after 42 days (up to 20 mg a.s/kg soil)
	1,2,4 triazole		no effects on nitrogen and carbon mineralisation after 28 days at up to 0.353 mg/kg soil (highest dose tested)
Carbon mineralisation	a.s. ‡		No effect on carbon mineralisation up to 20 mg/kg soil.
	1,2,4 triazole		no effects on nitrogen and carbon mineralisation after 28 days at up to 0.353 mg/kg soil (highest dose tested)
Field studies			
not required			

Toxicity/exposure ratios for soil organisms**Group and application rate**

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
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‡ End point identified by the EU-Commission as relevant for Member State when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Ecotoxicology

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s. ‡	Acute	3.967 ¹	>113	10
	1,2,4 triazole	Acute	0.494 ²	>2024	10
	1,2,4 triazole	Chronic	0.494 ²	2*	5
Other soil macro-organisms					
Collembola	1,2,4 triazole		0.494 ²	3.64 ³	5

¹ initial PEC soil was used (e.g. plateau PEC)² plateau PEC soil was used (after 8 years)

* RMS notes that according to the sustained GAP, photodegradation is not expected to be a major route of degradation of amitrole in soil and therefore 1,2,4-triazole is not expected to be formed in significant amounts (<9.9%) and does not need to be assessed (see volume 3 B.8). RMS considers that if further uses occurring when photodegradation may be important would be sustained, it should be discussed whether 1,2,4-triazole may need to be included in the risk assessment or not.

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Laboratory dose response tests

Most sensitive species	Test substance	EC ₅₀ (kg/ha) vegetative vigour	EC ₅₀ (kg/ha) emergence
Cabbage (for emergence) and sunflower (vegetative vigour)	Active substance	0.1345 kg a.s./ha	0.616 kg a.s./ha

Application rate (kg a.s./ha)	Crop	Test	Buffer distance (m)	TER	Annex VI Trigger
Based on lowest EC ₅₀ = 0.1345 kg a.s./ha (Tier 1)					
1 x 2.977	Agricultural uses	Vegetative vigour	1 (default)	1.63	5
			5	7.9	5

Additional studies (e.g. semi-field or field studies)

Not necessary

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge	EC ₅₀ > 1000 mg/L

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Amitrole, 1,2,4 triazole
water	Amitrole, 1,2,4 triazole
sediment	-

Rapporteur Member State	Month and year	Active Substance (Name)
RMS = FR Co-RMS = HU	January 2013	Amitrole

Ecotoxicology

groundwater	Amitrole, 1,2,4 triazole
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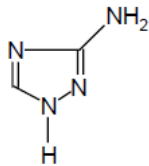
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

Active substance

RMS/peer review proposal
Classification acc. to Dir. 67/549/EEC: Proposed Label: Symbol: N Indication of danger: Dangerous for the environment Risk phrases: R51/53 Safety phrases: S60, S61 Classification acc. to Reg. 1272/2008: Proposed Label: Symbol: Warning, GHS09 Indication of danger: Aquatic chronic 2 Risk phrases: H411 Safety phrases: P273, P391, P501

Preparation

RMS/peer review proposal
Classification acc. to Dir. 67/549/EEC: Proposed Label: Symbol: No signal word Indication of danger: No signal word Risk phrases: R52/53 Safety phrases: S60 Classification acc. to Reg. 1272/2008: Proposed Label: Symbol: No signal word Indication of danger: No signal word Risk phrases: H412 Safety phrases: P273, P501

Code/Trivial name	Chemical name	Structural formula
Amitrole	IUPAC: 1-H-1,2,4-triazol-3-ylamine CA: 1-H-1,2,4-triazol-3-amine	

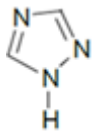
Rapporteur Member State**Month and year****Active Substance (Name)**

RMS = FR
Co-RMS = HU

January 2013

Amitrole

Ecotoxicology

1,2,4 triazole	1-H-1,2,4-triazole	
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Level 3

Amitrole

SUMMARY AND CONSIDERATION WITH RESPECT TO THE APPROVAL CRITERIA OF REGULATION (EC) No 1107/2009

IDENTIFICATION OF DATA GAPS, PROPOSED CONDITIONS, RISK MANAGEMENT MEASURES, ISSUES THAT COULD NOT BE FINALISED AND CRITICAL AREAS OF CONCERN

PROPOSED DECISION

January 2013

3. PROPOSED DECISION WITH RESPECT TO THE APPLICATION

3.1. BACKGROUND TO THE PROPOSED DECISION

3.1.1. Proposal on acceptability against the decision making criteria – Article 4 and annex II of regulation (EC) No 1107/2009

3.1.1.1. Article 4			
		Yes	No
i)	It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically the RMS considers that authorisation in at least one Member State is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses.		X
3.1.1.2. Submission of further information			
		Yes	No
i)	It is considered that a complete dossier has been submitted	X	
ii)	It is considered that in the absence of a full dossier the active substance may be approved even though certain information is still to be submitted because: (a) the data requirements have been amended or refined after the submission of the dossier; or (b) the information is considered to be confirmatory in nature, as required to increase confidence in the decision.		
3.1.1.3. Restrictions on approval			
		Yes	No
	It is considered that in line with Article 6 of Regulation (EC) No 1107/2009 approval should be subject to conditions and restrictions.	X	
3.1.1.4. Criteria for the approval of an active substance			
Dossier			
		Yes	No
	It is considered the dossier contains the information needed to establish, where relevant, Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD).	X	
	It is considered that the dossier contains the information necessary to carry out a risk assessment and for enforcement purposes (relevant for	X	

substances for which one or more representative uses includes use on feed or food crops or leads indirectly to residues in food or feed). In particular it is considered that the dossier: (a) permits any residue of concern to be defined; (b) reliably predicts the residues in food and feed, including succeeding crops (c) reliably predicts, where relevant, the corresponding residue level reflecting the effects of processing and/or mixing; (d) permits a maximum residue level to be defined and to be determined by appropriate methods in general use for the commodity and, where appropriate, for products of animal origin where the commodity or parts of it is fed to animals; (e) permits, where relevant, concentration or dilution factors due to processing and/or mixing to be defined.		The toxicological profile of amitrole was evaluated at EU level for the first inclusion. Since this time new considerations are proposed in the context of AIR II to define an ARfD. An ARfD should be set based on the lowest NOAEL observed in the short-term and teratology toxicity studies. With a safety factor of 100 an ARfD is proposed at 0.015 mg/kg bw. Primary crop metabolism of amitrole was investigated in apple to define residue for enforcement and risk assessment in crops under consideration. New metabolism studies are not deemed necessary with regard to intended uses on orchards, grapes and considering the same mode of application on the soil in early season. Additionally a different consideration for the use on olive is not deemed necessary since the log P_{ow} of amitrole is very low and in all likelihood with poor affinity with high lipid content matrix. Since the first inclusion, new trials were provided on apple, grape and olive. Previously, stability was sufficiently demonstrated in high water, high acid and high lipid content matrices under frozen condition. Trials were mainly realized in the presence of the synergist ammonium thiocyanate and demonstrated that residue levels are below the LOQ in fruits. This confirms that no MRL exceedance will result from the intended uses. This assessment goes on the same way than the EFSA reasoned opinion about the review of the existing maximum residue levels (MRLs) for amitrole according to Article 12 of the Regulation (EC) No 396/2005. Therefore, regarding to the no residue situation in those crops and the possibility for extrapolation given in guideline appendix D rev.9, sufficient number of residue trials are available to support all intended GAPs for amitrole on orchards, grapes and olives. In addition, new residue results were also provided on metabolites triazolylalanine and aminotriazolylalanine in olives and grapes where a no residue situation was also shown. Consequently, the need to include these metabolites in the residue definition is not considered necessary with regard to the intended uses. The residue definition in plants for monitoring and risk assessment remains the parent amitrole. As quantifiable residues of amitrole are not expected in the treated crops, there is no need to investigate the effect of industrial and/or household processing. Although not required, one study investigating the magnitude of residues in grapes, juice, must and wine (white and red) was provided. Nevertheless no robust processing factors could be derived since residues
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				were below the LOQ in both raw and processed commodities. Orchards, grapes and olives are not expected to be grown in rotation. Further investigation of residues in rotational crops is therefore not required with regard to the intended uses. Nevertheless further information would be required in future if additional uses are intended and rotated and when, at EU level, a full assessment report about triazoles derivatives metabolites will be available. Since the first inclusion, studies on the nature or magnitude of residues in commodities of animal origin are not available nor required since livestock is not expected to be exposed to amitrole residues. Residue definitions and MRLs for livestock products are consequently not required. Chronic and acute consumer exposures resulting from the uses proposed in the framework of this application were calculated. Based on EFSA PRIMo (rev2), acute and chronic exposures were considered as acceptable for all groups of consumers as no ARfD nor ADI exceedances are expected. This overall conclusion applies to all the representative uses (i.e.: grapes, pome fruits, stone fruits, citrus, nuts and olives)
	It is considered that the dossier submitted is sufficient to permit, where relevant, an estimate of the fate and distribution of the active substance in the environment, and its impact on non-target species.		X	The information provided is sufficient to describe the fate and behaviour of Amitrole in soil, water and air, and to estimate the exposure in soil, groundwater and air for all sustained uses. However, the exposure in surface water could not be finalised for agricultural uses and non crop uses (permeable surfaces). It is noted that the exposure in groundwater for 1,2,4-triazole is over-estimated for agricultural uses and non crop uses (permeable surfaces). Moreover, there is a lack of data for birds and fish to complete the assessment of potential endocrine disrupting properties. Additional data are requested.
Efficacy				
		Yes	No	
	It is considered that it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective.	X		The efficacy was not assessed for the Annex-I renewal process of amitrole. CA2735 is currently registered on the representative uses in some MS. Products containing amitrole will be re-assessed following the re-inclusion of amitrole.
Relevance of metabolites				
		Yes	No	
	It is considered that the documentation submitted is sufficient to	X		The main identified metabolite is 1,2,4-triazole for which enough relevant

	permit the establishment of the toxicological, ecotoxicological or environmental relevance of metabolites.			information is available.
Composition				
		Yes	No	
	It is considered that the specification defines the minimum degree of purity, the identity and maximum content of impurities and, where relevant, of isomers/diastereo-isomers and additives, and the content of impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.	X		The minimum purity of Amitrole is specified at 910 g/kg. Specifications are considered acceptable except for two impurities (impurity 1 and impurity 2) for which additional information (another <i>in vitro</i> genotoxicity test) is needed. None of the manufacturing impurities considered are, on the basis of information currently available, of toxicological or environmental concern.
	It is considered that the specification is in compliance with the relevant Food and Agriculture Organisation specification, where such specification exists.	X		The specification of 910 g/kg for Amitrole is in accordance with the FAO Specifications 90/TC/S/P (1998), where it is indicated that the Amitrole content shall be declared not less than 900 g/kg..
	It is considered for reasons of protection of human or animal health or the environment, stricter specifications than that provided for by the FAO specification should be adopted		X	Not relevant
Methods of analysis				
		Yes	No	
	It is considered that the methods of analysis of the active substance, safener or synergist as manufactured and of determination of impurities of toxicological, ecotoxicological or environmental concern or which are present in quantities greater than 1 g/kg in the active substance, safener or synergist as manufactured, have been validated and shown to be sufficiently specific, correctly calibrated, accurate and precise.	X		In the technical material, the determination of the active substance is done by HPLC with UV detection (215 nm). The method is fully validated and considered as acceptable. For the significant impurities please refer to Volume 4, confidential part. In the formulation, the determination of the active substance is done by HPLC with UV detection (215 nm). The method is fully validated and considered as acceptable.
	It is considered that the methods of residue analysis for the active substance and relevant metabolites in plant, animal and environmental matrices and drinking water, as appropriate, shall have been validated and shown to be sufficiently sensitive with respect to the levels of concern.		X	<u>Analytical methods for residue determination in food of plant origin</u> An analytical method (Gemrot, F. 2011a and 2011b, Amic, S. 2012) and its ILV (Ivanov, E. 2012) using LC-MS/MS are considered as validated for the determination of Amitrole and its metabolites triazolyalanine and aminotriazolyalanine in plants (grapes, olives, apples) with LOQ = 0.01 mg/kg for each analyte. The applicability of the DFG method S19 multi-residue method has not been demonstrated and is required. (December 2012: Nufarm stated that a study is ongoing and that the final report will be available by March 2013.)

				<u>Analytical methods for residue determination in soil</u> An analytical method (Amic, S. 2012) using LC-LC-MS/MS is considered as validated for the determination of Amitrole in soil with LOQ = 0.01 mg/kg. <u>Analytical methods for residue determination in water</u> An analytical method (Amic, S. 2012) using LC-LC-MS/MS is considered as validated for the determination of Amitrole in drinking and surface water with LOQ = 0.05 µg/L. <u>Analytical methods for residue determination in air</u> An analytical method fully validated is required according to guidance document SANCO/825/00 rev 8.1. (December 2012: Nufarm stated that the validation is ongoing and that the final report will be provided by Q2 2013.) <u>Analytical methods for residue determination in body fluids</u> An analytical method (Gemrot, F., 2011c) using LC-MS/MS is considered as validated for the determination of Amitrole in body fluids (urine) with LOQ = 5 µg/L.
	It is confirmed that the evaluation has been carried out in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		
Impact on human health				
Impact on human health - ADI, AOEL, ARfD				
		Yes	No	
	It is confirmed that (where relevant) an ADI, AOEL and ARfD can be established with an appropriate safety margin of at least 100 taking into account the type and severity of effects and the vulnerability of specific groups of the population.	X		The ADI and the AOEL were not changed since the first inclusion of active substance (see Review Report (6839/VI/97-final 22 march 2001). Although no ARfD was set for the first approval of amitrole, an ARfD of 0.015 mg/kg bw is now proposed. It is based on the 28-day rat toxicity study, by using a safety factor of 100.
Impact on human health – proposed genotoxicity classification				
		Yes	No	
	It is considered that, on the basis of assessment of higher tier genotoxicity testing carried out in accordance with the data requirements and other available data and information, including a review of the scientific literature, reviewed by the Authority, the substance SHOULD BE classified or proposed for classification, in		X	Amitrole has been extensively tested in <i>in vitro</i> and <i>in vivo</i> genotoxicity studies. By weight of evidence, amitrole is not a genotoxic compound. This was confirmed by recent <i>in vitro</i> gene mutation and chromosomal aberration tests.

	accordance with the provisions of Regulation (EC) No 1272/2008, as mutagen category 1A or 1B.			
Impact on human health – proposed carcinogenicity classification				
		Yes	No	
i)	It is considered that, on the basis of assessment of the carcinogenicity testing carried out in accordance with the data requirements for the active substances, safener or synergist and other available data and information, including a review of the scientific literature, reviewed by the Authority, the substance SHOULD BE classified or proposed for classification , in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogen category 1A or 1B.		X	Thyroid tumours are observed in rats. Nevertheless, they were not considered relevant for human and amitrole does not need to be classified carcinogen cat 1A or 1B (see level 2.5.2.5).
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
Impact on human health – proposed reproductive toxicity classification				
		Yes	No	
i)	It is considered that, on the basis of assessment of the reproductive toxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature, reviewed by the Authority, the substance SHOULD BE classified or proposed for classification , in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 1A or 1B.		X	The harmonized and accepted classification of amitrole is reprotoxic category 2 according to the criteria of Regulation (EC) n°1272/2008 (see level 2.5.2.6).
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in			

	accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
Impact on human health – proposed endocrine disrupting properties classification				
		Yes	No	
i)	It is considered that the substance SHOULD BE classified or proposed for classification in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogenic category 2 and toxic for reproduction category 2 and on that basis shall be considered to have endocrine disrupting properties		X	
ii)	It is considered that the substance SHOULD BE classified or proposed for classification in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 2 and in addition the RMS considers the substance has toxic effects on the endocrine organs and on that basis shall be considered to have endocrine disrupting properties	X		Amitrole is classified as toxic for reproduction category 2. In addition, thyroid effects were observed in several species (rat, mouse, dog, monkey and rabbit) after oral, inhalation and dermal exposure (see level 2.5).
iii)	Linked to either i) or ii) immediately above. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.		X	
Fate and behaviour in the environment				
Persistent organic pollutant (POP)				
		Yes	No	
	It is considered that the active substance FULFILLS the criteria of a persistent organic pollutant (POP) as laid out in Regulation 1107/2009 Annex II Section 3.7.1.		X	Considering the degradation rates of Amitrole in soil and water/sediment system (see Level 2), Amitrole is not considered as a persistent substance. In addition, there is no concern for long-range transport.
Persistent, bioaccumulative and toxic substance (PBT)				
		Yes	No	
	It is considered that the active substance FULFILLS the criteria of a persistent, bioaccumulative and toxic (PBT) substance as laid out in Regulation 1107/2009 Annex II Section 3.7.2.		X	Considering the degradation rates of Amitrole in soil and water/sediment system (see Level 2), Amitrole is not considered as a persistent substance. Considering the Bioconcentration Factor of Amitrole in fish (see Level 2), Amitrole is not considered as a bioaccumulative substance.

				Considering that the fish full life cycle test doesn't permit to conclude on potential endocrine effects on fish and consequently on potential impact on fish development or on their reproduction capacities, it is not possible to conclude on a NOEC for fish and therefore there is a data gap concerning the parameter "toxic" for ecotoxicology section.
Very persistent and very bioaccumulative substance (vPvB).				
		Yes	No	
	It is considered that the active substance FULFILS the criteria of a a very persistent and very bioaccumulative substance (vPvB) as laid out in Regulation 1107/2009 Annex II Section 3.7.3.		X	Considering the degradation rates of Amitrole in soil and water/sediment system (see Level 2), Amitrole is not considered as a persistent substance. Considering the Bioconcentration Factor of Amitrole in fish (see Level 2), Amitrole is not considered as a bioaccumulative substance.
Ecotoxicology				
		Yes	No	
	It is considered that the risk assessment demonstrates risks to be acceptable in accordance with the criteria laid down in the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) under realistic proposed conditions of use of a plant protection product containing the active substance, safener or synergist. The RMS is content that the assessment takes into account the severity of effects, the uncertainty of the data, and the number of organism groups which the active substance, safener or synergist is expected to affect adversely by the intended use.	X		The risk is acceptable for the intended uses for mammals, bees, earthworms and other soil macroorganisms, soil microorganisms and non target plants. No overall NOEC can be established from the two-generation bird study and therefore long term risk assessment for birds cannot be finalized. The risk assessment could not be finalised for aquatic organisms as no valid PEC values were available. The initial PEC _{sw} calculations provided were not considered acceptable. Additional calculations were asked to the applicant, but the new calculations provided still did not address RMS' request and therefore could not be accepted. The applicant finally provided additional calculations at the end of December 2012. However, since it was too late in the process, they were not taken into account. No conclusion can therefore be drawn on the acceptability of the risk for these organisms. Moreover, the fish full life cycle test was not valid and therefore long term risk assessment for fishes cannot be finalized. The in-field risk assessment could not be finalised for other non target arthropods. A higher tier study (field study) was performed and submitted in December 2012. It is reported by the notifier that amitrole application has no impact on the population of <i>Typhlodromus pyri</i> . Considering the late submission of this study (December 2012), it was not possible for RMS to

				assess it.
	It is considered that, on the basis of the assessment of Community or internationally agreed test guidelines, the substance HAS endocrine disrupting properties that may cause adverse effects on non-target organisms.	X		Effects on thyroid (higher size) have been observed in a two-generation study on birds at all tested doses. The lower size of the offspring individuals observed at the two highest doses over 3 can be related to these effects on thyroid weight. There is an uncertainty concerning potential thyroid mediated effects during chronic exposure. The lack of validity of the fish full life cycle test doesn't permit to conclude on potential endocrine effects on fish. Nevertheless, a literature review showed evidence of amitrole on thyroid hormones in fish. However, no data are available showing any impact neither on fish development, nor on their reproduction capacities. The notifier informed the RMS late in december 2012 that a new experimental phase is being conducted in order to conclude on potential effects on hatchability of eggs. Available data are not reliable to conclude on the potential impact of amitrole on hatchability of eggs in the F1 generation (from parental exposure). Moreover, no data are available to conclude on potential impact in the F2 generation. In these conditions, it is concluded that data are not enough to completely address the question of thyroid mediated effects during long term exposures. No endpoint (NOEC) can be derived from this study.
	Linked to the consideration of the endocrine properties immediately above. It is considered that the exposure of non-target organisms to the active substance in a plant protection product under realistic proposed conditions of use is negligible.		X	
	It is considered that it is established following an appropriate risk assessment on the basis of Community or internationally agreed test guidelines, that the use under the proposed conditions of use of plant protection products containing this active substance, safener or synergist: — will result in a negligible exposure of honeybees, or — has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honeybee larvae and honeybee behaviour.	X		The risks for bees were assessed according to the current guidance. Accounting for the intended uses, long term effects on bee colonies are not expected.
Residue definition				

	Yes	No	
It is considered that, where relevant, a residue definition can be established for the purposes of risk assessment and for enforcement purposes.	X		Following new data provided in the context this is not necessary to change the residue definition in plants for risk assessment and enforcement already set as: amitrole, parent compound only
Fate and behaviour concerning groundwater			
	Yes	No	
It is considered that it has been established for one or more representative uses, that consequently after application of the plant protection product consistent with realistic conditions on use, the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation 1107/2009.	X		PECgw for amitrole do not exceed 0.1 µg/L for all sustained uses. PECgw for 1,2,4-triazole do not exceed 0.1 µg/L for application on railways. For agricultural uses and non crop uses on permeable surfaces, an assessment expected to be conservative showed that PECgw of 1,2,4-triazole exceed 0.1 µg/L. Since PECgw were expected to be overestimated, the applicant must submit a refined exposure assessment to show that a safe use could be identified.

3.1.2. Proposal – Candidate for substitution

Candidate for substitution			
	Yes	No	
It is considered that the active substance shall be approved as a candidate for substitution		X	

3.1.3. Proposal – Low risk active substance

Low-risk active substances			
	Yes	No	
It is considered that the active substance shall be considered of low risk. In particular it is considered that the substance should NOT be classified or proposed for classification in accordance with		X	

	Regulation (EC) No 1272/2008 as at least one of the following: — carcinogenic, — mutagenic, — toxic to reproduction, — sensitising chemicals, — very toxic or toxic, — explosive, — corrosive. In addition it is considered that the substance is NOT: — persistent (half-life in soil more than 60 days), — has a bioconcentration factor higher than 100, — is deemed to be an endocrine disrupter, or — has neurotoxic or immunotoxic effects.			
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3.1.4. List of studies to be generated, still ongoing or available but not peer reviewed

Data gap	Relevance in relation to representative use(s)	Study status		
		No confirmation that study available or on-going.	Study on-going and anticipated date of completion	Study available but not peer-reviewed
3.1.4.1. Identity of the active substance or formulation				
Additional information (another <i>in vitro</i> genotoxicity test) is required for impurity 1 and impurity 2.		X (According to the applicant, “ <i>These tests will be conducted on a batch of amitrole technical compliant with the new</i>		

		specifications”)		
3.1.4.2. Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation				
Storage stability study in CA2735 formulation at ambient temperature during 2 years in the commercial packaging			X Study will be available in July 2013	
3.1.4.3. Data on uses and efficacy				
-	-	-	-	-
3.1.4.4. Data on handling, storage, transport, packaging and labelling				
-	-	-	-	-
3.1.4.5. Methods of analysis				
The applicability of the DFG S19 multi-residue method is required.		X		
An analytical method fully validated in air is required according to guidance document SANCO/825/00 rev 8.1.		X		
3.1.4.6. Toxicology and metabolism				
-	-	-	-	-
3.1.4.7. Residue data				
Additional residue results of amitrole, aminotriazolylalanine and triazolylalanine from a study realized in France in the end of 2012 with intended GAP on apples was provided but this report was not included in the addendum since not considered as a finalized report. Nevertheless similar new residue studies on grapes and olives were provided which demonstrate a non residue situation for amitrole,	Use on pome fruits		X Residue report with trials realized at the end of 2012 was not included in the addendum since it not fulfill the requirements to be considered as a finalized report	

aminotriazolylalanine and triazolylalanine in resulted fruits. Therefore, a same situation is highly presumed for the waited study on apple.				
3.1.4.8. Environmental fate and behaviour				
-	-	-	-	-
3.1.4.9. Ecotoxicology				
A field study to evaluate the effects of CA2735 on predatory mite population development in a vineyard in southern France was performed and submitted in December 2012. Considering the late submission of this study (December 2012), it was not assessed by RMS. This study should be submitted at national level (level 4).				X
Complementary information regarding the fish two generation study are requested. Additionnal information to conclude about the potential endocrine properties in birds might also be requested.		X		

3.1.5. Issues that could not be finalized

An issue is listed as an issue that could not be finalized where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) No 546/2011, and where the issue is of such importance that it could, when finalized, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

Area of the risk assessment that could not be finalised on the basis of the available data	Relevance in relation to representative use(s)
Environment: Risk of groundwater contamination by 1,2,4-triazole.	Relevant for agricultural uses and non crop uses on permeable surfaces.
Environment: PEC _{sw} calculations for Amitrole.	Relevant for agricultural uses and non crop uses on permeable surfaces. The initial PEC_{sw} calculations provided were not considered acceptable. Additional calculations were asked to the applicant, but the new calculations provided still did not comply with guidance document and therefore could not be accepted. The applicant finally provided additional calculations at the end of December 2012. However, since it was too late in the process, they were not taken into account.
Ecotoxicology: Long term risk assessment for birds and fish. In-field risk for non target arthropods	Relevant for agricultural uses and non crop uses.

3.1.6. Critical areas of concern

An issue is listed as a critical area of concern:

- (a) where the substance does not satisfy the criteria set out in points 3.6.3, 3.6.4, 3.6.5 or 3.8.2 of Annex II of Regulation (EC) No 1107/2009 and the applicant has not provided detailed evidence that the active substance is necessary to control a serious danger to plant health which cannot be contained by other available means including non-chemical methods, taking into account risk mitigation measures to ensure that exposure of humans and the environment is minimised, or
- (b) where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) 546/2011, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

Critical area of concern identified	Relevance in relation to representative use(s)
Operator exposure	No acceptable use
With the available data, a high potential of groundwater exposure by 1,2,4-triazole above 0.1 µg/L is predicted over a wide range of geoclimatic conditions.	Relevant for agricultural uses and non crop uses (permeable surfaces).
Ecotoxicology: Long term risk assessment for birds and fish. In-field risk for non target arthropods	Relevant for agricultural uses and non crop uses.

3.1.7. Overview table of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in 3.3.1, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

All columns are grey as the material tested in the toxicological studies has not been demonstrated to be representative of the technical specification.

Representative use		Use "A" (Orchards)	Use "B" (Grapes)	Use "C" (Olives)	Use "D" (Non crop uses)
Operator risk	Risk identified	X	X	X	
	Assessment not finalised				X
Worker risk	Risk identified				
	Assessment not finalised				X
Bystander risk	Risk identified				
	Assessment not finalised				X
Consumer risk	Risk identified				
	Assessment not finalised				
Risk to wild non target terrestrial vertebrates	Risk identified				
	Assessment not finalised	X	X	X	X
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	X	X	X	X
	Assessment not finalised	X	X	X	X
Risk to aquatic organisms	Risk identified				
	Assessment not finalised	X	X	X	X
Groundwater exposure active substance	Legal parametric value breached				
	Assessment not finalised				
Groundwater exposure		Legal parametric value breached			

metabolites	Parametric value of 10µg/L ^(a) breached				
	Assessment not finalised	X	X	X	X
Comments/Remarks					

The superscript numbers in this table relate to the numbered points indicated within chapter 3.1.5 and 3.1.6. Where there is no superscript number, see level 2 for more explanation.

(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

3.1.8. Area(s) where expert consultation is considered necessary

It is recommended to organize a consultation of experts on the following parts of the assessment report:

Area(s) where expert consultation is considered necessary	Justification
Risk to wild non target terrestrial vertebrates	Not finalized
Exposure and risk to aquatic organisms	Not finalized
Operator risk	No acceptable use
Risk of groundwater contamination by 1,2,4-triazole.	Not finalized

3.1.9. Critical issues on which the Co RMS did not agree with the assessment by the RMS

Points on which the co-rapporteur Member State did not agree with the assessment by the rapporteur member state. Only the points relevant for the decision making process should be listed.

Issue on which Co-RMS disagrees with RMS	Opinion of Co-RMS	Opinion of RMS
B.6.8.2 Position paper on the relevance of potential endocrine disrupting properties of amitrole for humans	HU: Humans are known to be less sensitive to thyroid effects than rodents, but harmful effects at higher doses can not be excluded. The endocrine disrupting properties of amitrole can not be assessed without clear regulatory criteria, especially cut off values.	Pending the provision of regulatory criteria for the determination of endocrine disrupting properties (scheduled for December 2013), it is considered that default cut-off criteria laid down in Regulation (EC) No 1107/2009 apply. In fact, substances that are classified as toxic for reproduction category 2 in accordance to Regulation (EC) No

		1272/2008 and which have toxic effects on the endocrine organs may be considered to have endocrine disrupting properties. This is the case of amitrole which has an harmonized classification as Xn, Repr Cat 3 R63 or Toxic for reproduction Category 2 (H361d) and which showed effects on thyroid of several species.
B.6.10.3 Acceptable operator exposure level (AOEL)	HU: Setting the AOEL on the NOAEL of a rat study, where thyroid effects were observed in the next higher dose, is very conservative. Humans are supposed to be less sensitive to thyroid effects of amitrole than rodents. Setting the AOEL on the 90 day monkey study might be less conservative and still appropriate, with the use of a safety factor of 300 to 1000.	The AOEL was set during the first peer-review of the active substance (see Review Report 6839/VI/97-final 22 march 2001). In absence of new data/study available which could have an impact on the AOEL setting (e. g. short-term study), it is not considered necessary to reassess this value.
B.6.14.1.2 Measurement of operator exposure	HU: The co-RMS considers the field study acceptable in spite of some limitations. The bio-monitoring data seems to be more useful than that of the passive dosimetry. For 30 operators the 75th centile of the data can be used as the toxic effect (basis of the NOAEL for the AOEL setting) has been observed in a repeated exposure study, the population is large enough and exposure shows a log-normal distribution. The 75th centile of exposure values of 0.000263 mg/kg bw/day, and the 90th centile value of 0.000434 mg/kg bw/day (all operators monitored) are below the proposed AOEL of 0.001 mg/kg bw/day. Exclusion of operator 34 from the evaluation is justified. It is not likely that big tank leakage might occur during normal mixing and loading operations. On the other hand operator 34 stopped working, so his exposure could not be taken into account.	Even if all the subjects from the three different sites are considered all together, it remains operators that showed systemic exposure greater than 100% of the AOEL of amitrole. In the case of a biomonitoring study which directly reflects the systemic exposure of operators, it is considered that all individual measured systemic values should be less than 100% of the AOEL of the active substance.

3.2. PROPOSED DECISION

It is proposed that:

Amitrole [REDACTED] under Regulation (EC) No 1107/2009

3.3. RATIONAL FOR THE CONDITIONS AND RESTRICTIONS TO BE ASSOCIATED WITH THE APPROVAL OR AUTHORISATION(S), AS APPROPRIATE

3.3.1. Particular conditions proposed to be taken into account to manage the risks identified

Proposed condition/risk mitigation measure	Relevance in relation to representative use(s)
-	-

3.4. APPENDICES

GUIDANCE DOCUMENTS USED IN THIS ASSESSEMENT

[List of Guidance documents used in the conduct of the evaluation and risk assessment.]

Section physico-chemistry and analytical methods

Technical Material and Preparations: Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414 - SANCO/3030/99 rev.4, 11/07/00

Guidance document on pesticide residue analytical methods - SANCO/825/00 rev. 8.1, 16/11/2010

Residues: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414 - SANCO/3029/99 rev.4, 11/07/00

Manual on development and use of FAO and WHO specifications for pesticides - November 2010 - second revision of the First Edition

Technical Monograph n° 17 - Guidelines for Specifying the Shelf Life of Plant Protection Products - May 1993 (and 2nd edition June 2009)

Section toxicology

European Commission, 2004. Guidance Document on Dermal Absorption. SANCO/222/2000 rev. 7, 19 March 2004.

EFSA Panel on Plant Protection Products and their Residues (PPR); Guidance on Dermal Absorption. EFSA Journal 2012;10(4):2665. [30 pp.] doi:10.2903/j.efsa.2012.2665

European Commission, 2011. Guidance Document on the Assessment of the Equivalence of Technical Materials of Substances Regulated under Regulation (EC) No 1107/2009. SANCO/10597/2003 – rev. 9, 17 June 2011.

Section residues

EC (European Commission), 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev.3.

EC (European Commission), 1997b. Appendix B. General recommendations for the design, preparation and realization of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/VI/95-rev.6.

EC (European Commission), 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev.2.

EC (European Commission), 1997d. Appendix E. Processing studies. 7035/VI/95-rev.5.

EC (European Commission), 1997f. Appendix H. Storage stability of residue samples. 7032/VI/95-rev.5.

EC (European Commission), 1997g. Appendix I. Calculation of maximum residue level and safety intervals. 7039/VI/95. As amended by the document: classes to be used for the setting of EU pesticide maximum residue levels (MRLs). SANCO 10634/2010.

EC (European Commission), 2000. Residue analytical methods. For pre-registration data requirement for Annex II (part A, section 4) and Annex III (part A, section 5 of Directive 91/414. SANCO/3029/99-rev.4.

EC (European Commission), 2004. Residue analytical methods. For post-registration control. SANCO/825/00-rev.7.

EC (European Commission), 2010. Classes to be used for the setting of EU pesticide Maximum Residue Levels (MRLs). SANCO 10634/2010 Rev. 0, finalized in the Standing Committee on the Food Chain and Animal Health at its meeting of 23-24 March 2010.

EC (European Commission), 2011. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev.9.

Section fate & behavior in the environment

FOCUS (2006) "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp

FOCUS. (1996). Soil Persistence Models and EU Registration, European Commission Document No. 7617/VI/96.

FOCUS. (2000). FOCUS Groundwater Scenarios in the EU Review of Active Substances. Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference Sanco/321/2000 rev.2, 202 pp.

FOCUS. (2002). Generic Guidance for FOCUS groundwater scenarios. Version 1.1

FOCUS. (2009). Assessing Potential for Movement of Active Substances and their Metabolites to Ground Water in the EU. Report of the FOCUS Ground Water Work Group, EC Document Reference Sanco/13144/2010 version 1, 604 pp.

Sanco/221/2000 rev.10. 25 February 2003. Guidance document on the assessment of the relevance of metabolites in Groundwater of substance regulated under Council Directive 91/414/EEC

FOCUS. (2003). FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC Review of Active Substances. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference Sanco/4802/2001 rev.2, 245 pp.

FOCUS (2007a). "Landscape And Mitigation Factors In Aquatic Risk Assessment. Volume 1. Extended Summary and Recommendations". Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment, EC Document Reference SANCO/10422/2005 v2.0. 169 pp.

FOCUS (2007b). "Landscape And Mitigation Factors In Aquatic Risk Assessment. Volume 2. Detailed Technical Reviews". Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment, EC Document Reference SANCO/10422/2005 v2.0. 436 pp.

Section ecotoxicology

EFSA guidance (European Food Safety Authority; Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009; 7(12): 1438).

SANCO/3268/2001 rev. 4 final Guidance Document on Aquatic Ecotoxicology

SANCO/10329/2002 rev. 2 final Guidance Document on Terrestrial Ecotoxicology

ESCORT 2 (Candolfi et al. 2000: Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods)

3.5. REFERENCE LIST

List [in the conventional format] any references specifically cited in Volume 1 (i.e references to underpinning documents such as PPR-Panel Opinions, EFSA conclusions, national documents etc.).

Section toxicology

European Commission, 2001. Review report for the active substance amitrole. Finalised in the Standing Committee on Plant Health at its meeting on 12 December 2000 in view of the inclusion of amitrole in Annex I of Directive 91/414/EEC. 6839/VI/97 - final, 22 March 2001.

European Commission – European Chemicals Bureau, 2001. Summary record, Commission Group of Specialised Experts in the fields of Carcinogenicity, Mutagenicity and Reprotoxicity. Meeting in Arona, 06-08 September 2000, ECBI/59/00 – Add. 1 – Rev. 2, 11.04.2001.

European Commission – Scientific Committee on plants, 2000. Opinion of the Scientific Committee on Plants regarding the inclusion of amitrole (aminotriazole) in Annex I to Council Directive 91/414/EEC concerning the placing of plant protection products on the market. SCP/AMITR/002-Final, 13 July 2000.

Section residues

EC (European Commission), 2001. Review report for the active substance amitrole. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 12 December 2000 in view of the inclusion of amitrole in Annex I of Council Directive 91/414/EEC. SANCO 6839/VI/97 Final, 22 March 2001.

EFSA (European Food Safety Authority), 2012. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for amitrole according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2012;10(06):2763. [35 pp.] doi:10.2903/j.efsa.2012.2763.

FAO (Food and Agriculture Organisation of the United Nations), 1998. Amitrole. In: Pesticide residues in food – 1998. Evaluations. Part I. Residues. FAO Plant Production and Protection Paper 079.

France, 1996. Draft assessment report on the active substance amitrole prepared by the Rapporteur Member State France in the framework of Council Directive 91/414/EEC, June 1996.

France, 2000. Addendum to the draft assessment report on the active substance amitrole prepared by the rapporteur Member State France in the framework of Council Directive 91/414/EEC, March 2000.

Carter, M. C. 1965. Studies on the metabolic activity of 3-amino-1,2,4-triazole. *Physiol. Plant.* 1965. 18, 1054.

Massini, P. *Acta Bot Nederl.* 1963. 12, 64.

Donnalley, W.F. 1934. Studies on the herbicidal enhancement of 3-amino-1,2,4-triazole by ammonium thiocyanate with *agropyron repens*. 65-1728.

Babiker, A.G.T and Duncan, H.J. 1975. Penetration of bracken fronds by amitrole as influenced by pre-spraying conditions, surfactants and other additives. *Weed research.* vol15, 123-127.

Donnalley, W.F & Ries, S.K. 1964 Jul 31. Amitrole translocation in *agropyron repens* increased by the addition of ammonium thiocyanate. *Science.* 145 (3631) : 497-8

Cook, G.T & Duncan, H.J. 1979. Mode of action of thiocyanates and iodides in amitrole formulations. *Pestic. Sci.* 281-290

Level 4

Amitrole

January 2013

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

4. FURTHER INFORMATION TO PERMIT A DECISION TO BE MADE, OR TO SUPPORT A REVIEW OF THE CONDITIONS AND RESTRICTIONS ASSOCIATED WITH THE PROPOSED INCLUSION IN ANNEX I

4.1. IDENTITY OF THE ACTIVE SUBSTANCE AND FORMULATION

ACTIVE SUBSTANCE :

Additional information (another *in vitro* genotoxicity test) is required for impurity 1 and impurity 2. (December 2012: Nufarm stated that these tests will be conducted on a batch of Amitrole technical compliant with the new specifications)

FORMULATION :

The 2-year stability study in CA2735 formulation is required.

4.2. PHYSICAL AND CHEMICAL PROPERTIES

ACTIVE SUBSTANCE :

No further information is required.

FORMULATION :

No further information is required.

4.3. DATA ON APPLICATION AND FURTHER INFORMATION

4.4. CLASSIFICATION, PACKAGING AND LABELLING

No further information is required.

4.5. METHODS OF ANALYSIS

4.5.1. Analytical methods for active substance analysis

No further information is required.

4.5.2. Analytical methods for formulation analysis

No further information is required.

4.5.3. Analytical methods for determination of residues

The applicability of the DFG S19 multi-residue method is required. (December 2012: Nufarm stated that a study is ongoing and that the final report will be available by March 2013.)

An analytical method fully validated in air is required according to guidance document SANCO/825/00 rev 8.1. (December 2012: Nufarm stated that the validation is ongoing and that the final report will be provided by Q2 2013.)

4.6. TOXICOLOGY

4.6.1. Absorption, distribution, excretion and metabolism in mammals (toxicokinetics)

No further information is required.

4.6.2. Acute toxicity

No further information is required.

4.6.3. Short-term toxicity

No further information is required.

4.6.4. Long term toxicity and carcinogenicity

No further information is required.

4.6.5. Genotoxicity

No further information is required.

4.7. RESIDUE DATA

The additional ongoing residue study on apple would be appreciated

4.8. FATE AND BEHAVIOUR IN THE ENVIRONMENT

The following data gaps are identified:

- It should be clarified whether the unidentified radioactivity in the study of Hall (1994) on the route of degradation of Amitrole in soil is formed by several compounds or not and whether each compound exceeds 5% AR or not. The applicant indicated at the end of December 2012 that this point was currently being checked.
- A refined assessment of the risk of groundwater contamination by 1,2,4-triazole is needed for agricultural uses and non crop uses on permeable surfaces.
- PECsw calculations for Amitrole for agricultural uses and non crop uses (permeable soils) are needed. It is highlighted that an additional study on PECsw calculations was provided by the applicant at the end of December 2012. However, considering the late submission of the study (December 2012), it was not summarized nor assessed by RMS. The study may address this data gap.

4.9. ECOTOXICOLOGY

- No overall NOEC can be established from the two-generation bird study and therefore long term risk assessment for birds cannot be finalized. Supplemental data might be provided.
- For agricultural uses (pome fruit, citrus, olives and vineyard) and permeable non cropped areas (permeable soils), in absence of validated PECsw (see 4.8), the exposure to surface water cannot be finalized. Therefore, risk assessment for aquatic organism cannot be finalized.
- The lack of validity of the fish full life cycle test doesn't permit to conclude on potential endocrine effects on fish for all uses. Supplemental data to conclude on the impact on hatchability and effects on a second generation are requested.
- The risk assessment for the non cropped areas (impermeable soil) and more precisely for urban (pond and/or stream), major road stream and domestic stream scenario has not been further refined for aquatic invertebrates and should be considered at member state level. The risk assessment for urban stream

and/or major road stream scenario has not been further refined for algae and aquatic plants and should be considered at member state level.

- A potential risk has been identified in-field for *T.pyri*, the representative species for mites. According to ESCORT 2, a refined in-field risk assessment has to be provided, based on a higher tier study (aged residue study or field study for example). A field study to evaluate the effects of CA2735 on predatory mite population development in a vineyard in southern France was performed and submitted in December 2012. Considering the late submission of this study (December 2012), it was not assessed by RMS. This study should be submitted at national level (level 4) to conclude on risk in-field.

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