European Food Safety Authority

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REASONED OPINION

Reasoned opinion on the modification of the existing MRL for tricyclazole in rice[1]

European Food Safety Authority[2,]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

In accordance with Article 6 of Regulation (EC) No 396/2005, Italy, herewith referred to as the evaluating Member State (EMS), received an application from Dow AgroScience to set an import tolerance for tricyclazole in rice to accommodate the authorized use in Brazil. Tricyclazole is a non-included active substance and no EU uses are currently authorized. Thus, the existing EU MRL of 1 mg/kg in rice should be lowered to the LOQ. The applicant requested to maintain the existing EU MRL to allow the import of rice treated with tricyclazole from third countries. The EMS confirmed that the MRL should be set provisionally at the level 1 mg/kg to accommodate the Brazilian GAP. EFSA is of the opinion that on the basis of the currently available studies, the toxicological reference values for tricyclazole cannot be set, since the genotoxic potential of tricyclazole could not be totally disregarded. In addition, uncertainties regarding the carcinogenic potential of tricyclazole were identified by EFSA. The submitted residue trials data were found to be insufficient to derive an MRL proposal which accommodates the use of tricyclazole on rice in Brazil. EFSA concludes that the import tolerance request for tricyclazole in rice is not sufficiently supported by data which are needed to justify maintaining the existing EU MRL of 1 mg/kg in rice.

KEY WORDS

Tricyclazole, rice, import tolerance, MRL application, Regulation (EC) No 396/2005, consumer risk assessment, fungicide

[1] On request from European Commission, Question No EFSA-Q-2012-00488, approved on 16 April 2013.

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SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005[3], Italy, herewith referred to as the evaluating Member State (EMS), received an application from Dow AgroScience to set an import tolerance for tricyclazole in rice to accommodate the authorized use in Brazil. Tricyclazole is a non-included active substance and no EU uses are currently authorized. Thus, the existing EU MRL of 1 mg/kg in rice should be lowered to the LOQ. The applicant requested to maintain the existing EU MRL to allow the import of rice treated with tricyclazole from third countries. The EMS confirmed that the MRL should be set provisionally at the level 1 mg/kg to accommodate the Brazilian GAP. The EMS drafted an evaluation report according to Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA on 3 April 2012.

On 17 April 2012 some data requirements were identified, which prevented EFSA to conclude on the legal validity of the submitted application. An updated evaluation report was submitted by the EMS on 24 September 2012. On 15 February 2013 the draft of the reasoned opinion was submitted for the Member State consultation. By the end of the commenting period, the comments were received from France and Italy and were further considered by EFSA for the finalisation of this reasoned opinion.

EFSA bases its assessment on the updated evaluation report submitted by the EMS Italy, the Draft Assessment Report (DAR) prepared under Council Directive 91/414/EEC[4] by the rapporteur Member State France and the Commission Review Report on tricyclazole.

The toxicological profile of tricyclazole was assessed by the RMS France in the framework of the peer review. The available data were insufficient to derive toxicological reference values. Because of these data gaps a decision on non-inclusion of tricyclazole in Annex I of Directive 91/414/EEC was taken. In a meanwhile, new toxicological studies have become available which were assessed by the EMS Italy in the framework of the current application. The EMS proposed an ADI of 0.05 mg/kg bw per day and an ARfD of 0.05 mg/kg bw, based on the rat developmental toxicity study. EFSA is of the opinion that on the basis of the currently available studies the setting of toxicological reference values is not appropriate since the genotoxic potential could not be totally disregarded. In addition, EFSA identified uncertainties regarding the carcinogenic potential of tricyclazole in rats where liver tumours were observed from the lowest dose level tested (4.2 mg/kg bw per day). In case the genotoxic potential of tricyclazole can be disproved, EFSA would propose to set the ADI at the level of 0.0042 mg/kg bw per day on the basis of the LOAEL of 4.2 mg/kg bw per day with an uncertainty factor (UF) of 1000; regarding the ARfD, EFSA would agree with the ARfD proposed by the EMS (0.05 mg/kg bw based on the NOAEL of 5 mg/kg bw per day observed in the rat developmental toxicity study (UF of 100)).

The metabolism of tricyclazole was evaluated in rice in the framework of the peer review using tricyclazole radiolabelled in the phenyl ring of the molecule. The compounds identified in rice grain, hulls and straw were parent tricyclazole and its alcohol metabolite. The major part of the radioactivity in grain was associated with glucose. The RMS provisionally proposed a residue definition for the risk assessment and enforcement as "tricyclazole and its alcohol metabolite". The enforcement residue definition in Regulation (EC) No 396/2005 is set as parent tricyclazole only. Taking into account the fact that the metabolism study labelled in the phenyl ring provided evidence of an extensive metabolism in rice, EFSA is of the opinion that an additional metabolism study in which tricyclazole is labelled in a second position of the molecule is indispensable to elucidate the metabolic behaviour in rice. EFSA concludes that the available rice metabolism studies are not sufficient to derive residue definitions for enforcement and risk assessment purposes.

Adequate analytical enforcement methods are available to control the residues of tricyclazole and tricyclazole alcohol metabolite in rice.

[3] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009. OJ L 309, 24.11.2009, p. 1-50.
[4] Council Directive 91/414/EEC of 15 July 1991. OJ L 230, 19.08.1991, p. 1-32.

The submitted residue trials data were found to be insufficient to derive an MRL proposal which accommodates the use of tricyclazole on rice in Brazil because the number of trials was not in line with the data requirements and because lacking information on the analytical method used and the storage period of samples prior to analysis does not allow to conclude on the validity of the residue trials.

The effect of processing on the nature of tricyclazole was investigated in a hydrolysis study. The results indicate that tricyclazole is stable under conditions representative for pasteurisation, boiling and sterilisation. Processing studies with rice demonstrated that the magnitude of tricyclazole residues is reduced in husked rice, polished rice and in rice bran. An increased residue concentration is only expected in husks.

The residues of tricyclazole in rotational crops are of no relevance for the import tolerance application.

Since rice and its by-products are not normally fed to livestock according to EU livestock diet, the nature and magnitude of tricyclazole residues in livestock was not assessed in the framework of this application.

EFSA was not able to perform the consumer risk assessment for tricyclazole as the available data did not allow to conclude on the following issues:

- residue definition for risk assessment
- mean residue concentration according to risk assessment residue definition derived from sufficient number of valid residue trials reflecting the critical GAP
- toxicological reference values

EFSA concludes that the import tolerance request for tricyclazole in rice is not sufficiently supported by data which are needed to justify maintaining the existing EU MRL of 1 mg/kg in rice.

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BACKGROUND

Regulation (EC) No 396/2005 establishes the rules governing the setting of pesticide MRLs at European Union level. Article 6 of that Regulation lays down that any party having a legitimate interest or requesting an authorisation for the use of a plant protection product in accordance with Council Directive 91/414/EEC, repealed by Regulation (EC) No 1107/2009[5], shall submit to a Member State, when appropriate, an application to set or to modify an MRL in accordance with the provisions of Article 7 of that Regulation.

Italy, hereafter referred to as the evaluating Member State (EMS), received an application from the company Dow AgroScience[6] to set an import tolerance for the active substance tricyclazole in rice. This application was notified to the European Commission and EFSA and subsequently evaluated by the EMS in accordance with Article 8 of the Regulation. After completion, the evaluation report was submitted to the European Commission who forwarded the application, the evaluation report and the supporting dossier to EFSA on 3 April 2012.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2012-00488 and the following subject:

Tricyclazole - Application to set the MRL in rice at 1 mg/kg.

On 17 April 2012 some data requirements were identified, which prevented EFSA to conclude on the legal validity of the submitted application. An updated evaluation report was submitted by the EMS on 24 September 2012 and taken into consideration by EFSA for finalization of this reasoned opinion. On 15 February 2013 the draft of the reasoned opinion was submitted for the Member State consultation. By the end of the commenting period, the comments were received from France and Italy and were further considered by EFSA for the finalisation of this reasoned opinion.

EFSA proceeded with the assessment of the application and the evaluation report as required by Article 10 of the Regulation.

TERMS OF REFERENCE

In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the evaluating Member State, provide a reasoned opinion on the risks to the consumer associated with the application.

In accordance with Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within three months (which may be extended to six months where more detailed evaluations need to be carried out) from the date of receipt of the application. Where EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

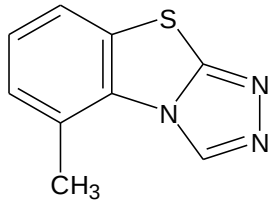
In this particular case the calculated deadline for providing the reasoned opinion is 12 March 2013.

[5] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009. OJ L 309, 24.11.2009, p. 1-50

[6] Dow AgroSciences S.A.S., Viale Masini 36, 40126, Bologna, Italy

THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Tricyclazole is the ISO common name for 5-methyl-1,2,4-triazolo[3,4-*b*][1,3]benzothiazole (IUPAC). The chemical structure of the compound is herewith reported.



Molecular weight: 189.24

Tricyclazole is a fungicide used on rice. It prevents the blast pathogen from penetrating the rice plant. Tricyclazole is rapidly absorbed by the rice leaf and translocated toward the tip. Within a few minutes after foliar application, absorption and translocation of tricyclazole to untreated sites starts. Translocation occurs via the water conducting xylem tissue and is regulated by the rate of transpiration from the leaf (France, 2007).

Tricyclazole was evaluated in the framework of Council Directive 91/414/EEC with France designated as rapporteur Member State (RMS). The representative use evaluated for the peer review was the foliar application on rice at a total seasonal application rate of 0.45 kg a.s./ha and a PHI interval of 49-56 days. Following the peer review, a decision on non-inclusion of tricyclazole in Annex I of Directive 91/414/EEC was taken by means of Commission Decision 2008/770/EC[7]. The reason for the non-inclusion was the lack of appropriate toxicological studies needed to set reliable toxicological reference values (i.e. ADI, ARfD and AOEL). It is noted that no EFSA conclusion is available for this active substance.

At EU level, authorisations of plant protection products containing tricyclazole had to be withdrawn by 30 March 2009. The period of grace expired on 30 March 2010. EFSA has been informed by the applicant that a new application for approval of tricyclazole as a new active substance (NAS) under Regulation (EC) No 1107/2009 is under preparation; the complete dossier was expected to be submitted to the new designated Rapporteur Member State Italy in December 2012. The new dossier was received in EFSA on 28 February 2013.

The EU MRLs for tricyclazole are established in Annex IIIA of Regulation (EC) No 396/2005 (Appendix B) and the existing EU MRL for rice is set at 1 mg/kg. Given that the use of tricyclazole is no longer authorised at EU level, the European Commission intended to lower this MRL to the LOQ. The applicant now submitted the request to maintain the MRL of 1 mg/kg in rice as an import tolerance. No CXLs have been established for tricyclazole.

The applicant reported several GAPs authorized in third countries for the use of tricyclazole on rice (India, Japan, South Korea, China, Malaysia, Thailand, Vietnam). As the critical GAP for which the import tolerance is requested, the applicant selected the Brazilian GAP. Details of this GAP are given in Appendix A. The applicant did not provide the information on the current MRL established in Brazil.

[7] Commission Decision 2008/770/EC of 30 September 2008, OJ L 263, 2.10.2008, p.16-17.

ASSESSMENT

EFSA bases its assessment on the updated evaluation report submitted by the EMS (RMS) Italy (Italy, 2012), the Draft Assessment Report (DAR) prepared under Council Directive 91/414/EEC (France, 2007) and the Commission Review Report on tricyclazole (EC, 2008). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011[8] and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (EC, 1996, 1997a, 1997b, 1997c, 1997d, 1997e, 1997f, 1997g, 2000, 2010a, 2010b, 2011; OECD, 2011).

It is noted that tricyclazole is currently not approved for use in the EU. The applicant recently submitted a new dossier for the approval of tricyclazole under Regulation (EC) No 1107/2009, thus the conclusions derived in this reasoned opinion might be reconsidered taking into account the additional information provided for the active substance in a new dossier.

1. Method of analysis

1.1. Methods for enforcement of residues in food of plant origin

Analytical methods for the determination of tricyclazole and tricyclazole alcohol metabolite[9] in rice were assessed in the DAR drafted for the peer review under Directive 91/414/EEC (France 2007). A GC-MS method was considered sufficiently validated for the determination of tricyclazole and its alcohol metabolite at an individual LOQ of 0.02 mg/kg in rice grain and at the individual LOQ of 0.05 mg/kg in rice green plant and straw. An ILV was also performed and confirmed the applicability of the analytical method for analysing both compounds in rice grain at the individual LOQ of 0.02 mg/kg.

The applicability of the multi-residue method DFG S 19 was also tested for the determination of tricyclazole in rice grain. It was concluded that the multi-residue method using GC-MS is fully validated for the determination of tricyclazole in rice grain at a LOQ of 0.02 mg/kg.

During the Member State consultation, the EMS Italy informed that QuEChERS multi-residue method (using HPLC- MS/MS) has been sufficiently validated for the determination of residues of tricyclazole and its alcohol metabolite in agricultural commodities representative of the four crop groupings and five animal matrices. The method was validated at the individual LOQ of 0.01 mg/kg. However, detailed validation data have not been provided.

EFSA concludes that adequate analytical enforcement methods are available to control tricyclazole residues in rice.

1.2. Methods for enforcement of residues in food of animal origin

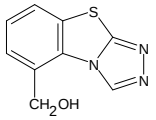
Analytical methods for the determination of residues in food of animal origin were not assessed in the current application, since rice is not fed to livestock in the EU and thus no residues are expected in commodities of animal origin.

2. Mammalian toxicology

EFSA bases it assessment on the evaluation report prepared by the EMS Italy (Italy, 2012) and on the draft assessment report prepared by the RMS France (France, 2007). In addition to toxicological

[8] Commission Regulation (EU) No 546/2011 of 10 June 2011. OJ L 155, 11.06.2011, p. 127-175.

[9] Tricyclazole alcohol metabolite: 5-methyl-1,2,4-triazolo[3,4-b][1,3]benzothiazole-5-methanol



studies available in the DAR (France, 2007), new studies have been evaluated by the EMS (Italy, 2012).

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Tricyclazole is rapidly absorbed, oral absorption being higher than 80%. Only 0.8-2.0% of the administered ^{14}C-tricyclazole remained in the tissues after 168 hours with some affinity for RBCs. It shows no potential for bioaccumulation. 92% of the radioactivity is excreted within 7 days, with 72% being excreted within 24 hours. Tricyclazole undergoes extensive metabolism characterized by conjugation with glutathione, with subsequent β-lyase cleavage to the corresponding thiol, followed by further conjugation with glucoronide or methylation. Benzyl oxidation was also observed.

2.2. Acute toxicity

Tricyclazole is of moderate acute toxicity to rats via oral routes and of low acute toxicity to rats via dermal and inhalation routes; it is not a skin or eye irritant nor a skin sensitiser.

Tricyclazole is classified with "H302 Harmful if swallowed" (category 4), according to the criteria in Regulation (EC) No 1272/2008[10].

Table 2-1: Summary of the acute toxicity studies

Type of test/ Species	Test substance/ Purity of test substance	Results	Acceptability of the study	Reference
Oral/gavage Rat/ male & female Wistar rats	Tricyclazole/ 99.4%	LD_{50} is 337.5 mg/kg (male) & 289.7 mg/kg (female) for batch: C53-C21-147 & 301.9 mg/kg (female) for batch B07-C1246	Supportive	Anonymous, no date (France, 2007; Italy, 2012).
Oral/gavage (Up/Down procedure) Rat/female Fischer 344	Tricyclazole/ 99.3%	Estimated LD_{50} is 237 mg/kg	Yes	Durando, J., 2005a (Italy, 2012).
Dermal/topical Rabbits/ male & female albino rabbits	Tricyclazole/ 99.4%	LD_{50} is > 2000 mg/kg	No	Anonymous, 1973 (France, 2007; Italy, 2012).
Dermal/topical (limit test) Rat/male & female Fischer 344	Tricyclazole/ 99.3%	LD_{50} is >5000 mg/kg	Yes	Durando, J., 2005b (Italy, 2012).

[10] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, OJ L 353, 31.12.2008, p.1-1979

Type of test/ Species	Test substance/ Purity of test substance	Results	Acceptability of the study	Reference
Inhalation/nose only Rat/ male & female Sprague-Dawley rats	Tricyclazole/ Batch purity: not mentioned	LC_{50} is >2.58 mg/L (highest technically achievable)	Supportive	Blagden, S.M., 1998 (France, 2007; Italy, 2012).
Inhalation/nose only Rat/male & female F344/DuCrl	Tricyclazole/ 99.3%	LC_{50} is >0.52 mg/L (highest technically achievable	Yes	Hotchkiss, J., 2006 (Italy, 2012).
Dermal/topical Rabbit/ male & female albino rabbits	Tricyclazole/ 99.4%	Not a skin irritant	No	Anonymous, 1973 (France, 2007; Italy, 2012).
Dermal/topical Rabbit/ male & female albino rabbits	Tricyclazole/ 99.3%	Not a skin irritant	Yes	Durando, J., 2005c (Italy, 2012).
Eye/instillation Rabbits/ male & female NZ albino rabbits	Tricyclazole/ 99.4%	Not an eye irritant	Yes	Anonymous, 1973 (France, 2007; Italy, 2012).
Eye/instillation Rabbits/NZ albino	Tricyclazole/ 99.3%	Not an eye irritant	Yes	Durando, J., 2005d (Italy, 2012).
Intradermal/ Topical Guinea pigs/ Dunkin Hartley albino guinea pigs (SPF)	Tricyclazole/ 96.7%	Not a skin sensitiser in the guinea pigs	No	Prinsen, M.K., 2003 (Italy, 2012).
Dermal/topical (LLNA) Female BALB/cAnNCrl mice[(a)]	Tricyclazole/ 99.3%	Not a skin sensitiser in the murine local lymph node assay	Yes	Woolhiser, M.R and Wiescinski, C.M., 2005 (Italy, 2012).

(a) Mouse strain differs from that recommended by OECD 429 (i.e. CBA mice).

2.3. Short term toxicity

Short-term toxicity has been studied with acceptable quality in one oral study in mice and one in dogs. The 90-day oral toxicity study in rats was considered supportive only. Tricyclazole showed a consistent profile of toxicity in all species after repeated oral administration, the dog being the most sensitive species. The primary target of toxicity was the liver. The relevant oral NOAEL is 5 mg/kg

bw per day from the 1-year dog study based on statistically significant lower hepatic p-nitroanisole O-demethylase activity and hepatic cytochrome P-450 content at 15 mg/kg bw per day (France, 2007).

According to EMS the NOAEL should be revised to 15 mg/kg bw per day based on an increase of absolute and relative liver and kidney weights at 45 mg/kg bw per day. Significant increase in both p-nitroanisole metabolism and P-450 content in males were considered of questionable significance (Italy, 2012). Despite the fact that p-nitroanisole metabolism and P-450 content are not normally measured in toxicological studies, EFSA considered that there is not sufficient evidence to disregard these effects as adverse.

Table 2-2: Summary of the short term toxicity studies

Type of test/ Species (purity of the test substance)	**Dose levels**	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Acceptability of the study**	**Reference**
Oral 90-day/ Wistar rats (M+F) (99.4%)	0, 282, 635 or 1,640 ppm (0, 20.5, 46.7, 153.3 mg/kg bw per day)	20.5 (282 ppm)	At 46.7 (635 ppm): death; lower body weight (-19% and -13%); lower weight gain (-24% and -12%); lower food consumption; lower food utilisation efficiency (-16% and -13%); higher hepatic p-nitroanisole degradation rate (+29% and +60%)	supportive	Howard, L.C. & Morton, D.M., 1978 (France, 2007; Italy, 2012).
Oral 1-year/ Beagle dogs (M+F) (96.58%)	0, 5, 15 or 45 mg/kg/bw per day (capsules)	5	At 15: 19% lower hepatic p-nitroanisole O-demethylase activity and 29% lower hepatic cytochrome P-450 content in males. At 45: 28% lower gain in females; 32% lower hepatic p-nitroanisole O-demethylase activity and 30% lower hepatic cytrocrome P-450 content in males; 25 and 59% higher absolute liver weight respectively in males an females.	Yes	Holzhousen, L.M., 1986 (France, 2007; Italy, 2012).
Oral 90-day/ ICR mice (M+F) (99.4%)	0, 400, 1,000, 2,500 or 3,600 ppm (0, 84.8, 264.8, 711.0, 1052.6 mg/kg bw per day)	84.8 (400 ppm)	At 264.8 (1000 ppm): Both sexes: 13% higher food intake. Males: deaths; thin appearance; 53% higher platelet count.	Yes	Howard, L.C. & Morton, D.M., 1978 (France, 2007; Italy, 2012).

Type of test/ Species (purity of the test substance)	**Dose levels**	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Acceptability of the study**	**Reference**
Oral 24 weeks, recovery period of 3 or 4 weeks/ ICR mice (M+F) (99.4%)	0, 310, 803 1900 or 3017 ppm	310 ppm	At 803 ppm: reversible higher absolute (+13% and +15%) and relative liver weights at 6 months; 12% (females) and 34% (males) higher rate of phase I metabolism (reversible after a 3-month recovery); reversible slight proliferation of small bile ducts at 6 months; lipocytes around portal spaces at 6 and 9 months	No	Howard L.C & Owen, N.V., 1979 (France, 2007; Italy, 2012).
Percutaneous 28-day/ Wistar rats (M+F) (95.2%)	0, 100, 300 or 1,000 mg/kg bw per day	300	At 1000: both sexes: higher absolute and relative liver weights; males: 25% lower food intake	Yes	Prinsen, M.K, 2003 (France, 2007; Italy, 2012).

M=Male
F=Female

2.4. Genotoxicity

Tricyclazole has been tested in an incomplete range of *in vitro* and *in vivo* genotoxicity assays. *In vitro*, tricyclazole did not induce gene mutations in the Ames test and in CHO-K1-B4 cells whereas a clear positive response was observed in mouse lymphoma cells with and without metabolic activation. An *in vitro* clastogenicity/aneugenicity test was not available (data requirement). *In vivo*, tricyclazole did not induce micronucleus (MN) in mice and the *in vivo* unscheduled DNA synthesis (UDS) test gave a negative response.

According to the EMS, tricyclazole is not considered a genotoxic compound. However, there are some uncertainties regarding the lack of an *in vitro* clastogenicity/aneugenicity test. Although the *in vivo* MN test gave a negative response, there was no evidence that the bone marrow was reached. The highest dose level (HDL) tested in the MN test appears to be low not reaching the MTD (i.e. the HDL was only 50% of the LD_{50}).

EFSA is of the opinion that due to the lack of *in vitro* clastogenicity/aneugenicity test and because of the lack of evidence of bone marrow exposure in the *in vivo* MN test, a definitive conclusion cannot be drawn regarding genotoxicity potential of tricyclazole. At least, an *in vitro* MN test should be done to clarify the clastogenic/aneugenic potential of tricyclazole. If positive, further *in vivo* genotoxicity testing should be done.

Table 2-3: Summary of the genotoxicity studies

Test substance (batch and purity)	**Test system**	**Concentrations /dose**	**Results**	**Acceptability of the study**	**Reference**
***In vitro* studies**					

Test substance (batch and purity)	**Test system**	**Concentrations /dose**	**Results**	**Acceptability of the study**	**Reference**
In vitro bacterial reverse mutation (98.8%)	*S. typhimurium* TA 98, TA 100, TA 102, TA 1535 and TA 1537.	12.8 to 1250µg/plate (± S9)	Negative(± S9)	Yes	Shukla, R. (2011) (Italy, 2012).
In vitro bacterial reverse mutation (97.1%)	*S. typhimurium* TA 98, TA 100, TA 1535, TA 1537, TA 1538, G46, C3076 and D3052. *Escherichia coli* WP2, WP2uvrA-	1000 to 100 µg/mL, 100 to 10 µg/mL, 10 to 1 µg/mL and 1 to 0.1 µg/mL (± S9)	NC [(a)]	No	Thomson CZ. (1981) (France, 2007; Italy, 2012).
In vitro bacterial reverse mutation (99.4%)	*S. typhimurium* TA 98, TA 100, TA 1535, TA 1537 and TA 1538. *Escherichia coli* WP2hcr-	10 to 5000 µg/plate (± S9)	Negative(± S9)	Supportive (low sensitivity, no certificate of analysis)	Shirasu Y, Moritani M, Sugiyama F (1978) (France, 2007; Italy, 2012).
In vitro bacterial rec-assay (99.4%)	*Bacillus subtilis* strains H17 and M45	20 to 2000 µg/disk	Positive	Supportive (no certificate of analysis)	Shirasu Y, Moritani M, Sugiyama F (1978) (France, 2007; Italy, 2012).
In vitro gene mutation (97.1%)	Mouse lymphoma cells L5178Y	4.2 to 810 µg/mL (-S9) 8.3 to 810 µg/mL (+S9) 15 to 400 µg/mL (-S9) 0.59 to 600 µg/mL (+S9)	Positive(± S9)	Yes	Steenwinkel M-J, ST (2003) (France, 2007; Italy, 2012).
In vitro gene mutation (99.3%)	Mouse lymphoma cells L5178Y	23 to 400 µg/mL (-S9) 0.15 to 600 µg/mL (+S9)	Positive(± S9)	Yes	Steenwinkel M-J, ST (2004) (France, 2007; Italy, 2012).
In vitro gene mutation (99.3%)	CHO-K1-B4 cells	7 to 900 µg/mL (±S9)	Negative(± S9)	Yes	Seidel SD, Schisler MR, Linscombe VA (2004) (France, 2007; Italy, 2012).
In vitro unscheduled DNA synthesis in hepatocytes (97.1%)	Hepatocytes from a male Fischer 344 rat	0.09 to 189.24 µg/mL	NC	No (low sensitivity, top-dose not validated)	Hill LE (1981) (France, 2007; Italy, 2012).
***In vivo* studies**					

Test substance (batch and purity)	Test system	Concentrations /dose	Results	Acceptability of the study	Reference
In vivo micronucleus test (97.1%)	Male and female CD-1 mice (micronucleu)	100 to 300 mg/kg bw (1 oral administration)	Negative	Supportive[(b)] (There was not evidence of tissue exposure)	Kehr CC, Parton JW, Garriott ML (1988) (France, 2007; Italy, 2012).
In vivo sister chromatid exchange in bone marrow cells (99.3%)	Female Chinese Hamster	21.25 to 170 mg/kg bw (1 IP injection)	Negative	Supportive (too low sensitivity)	Neal SB (1981) (France, 2007; Italy, 2012).
In vivo unscheduled DNA synthesis in hepatocytes (99.3%)	Male Fischer 344 rats	100 and 200 mg/kg bw (1 oral administration)	Negative	Yes	Cifone MA (2004) (France, 2007; Italy, 2012).
In vivo dominant lethal study in rat (99.6%)	Male Wistar rats	60 mg/kg bw (1 oral administration)	Negative	Supportive (too low sensitivity)	Worth HM, Markham JK, Owen NV *et al* (1977) (France, 2007; Italy, 2012).

(a): No definitive conclusion because of a too large number of deviations
(b): According to the RMS and EMS the study is considered acceptable.

2.5. Long term toxicity

The long-term toxicity and carcinogenicity of tricyclazole has been studied with acceptable quality in one study in rats and one study in mice. Tricyclazole showed the same toxicological profile as in short-term studies, the liver being the target organ. Non-specific effects, such as reduced body weight gain, were also observed. The relevant NOAELs from the long-term toxicity are 275 ppm (11 mg/kg bw per day) for rats and 75 ppm (7.98 mg/kg bw per day) for mice.

According to the EMS, no evidence of carcinogenicity was found in mice and rats (Italy, 2012). However, according to the results reported in the DAR, a slight increase in incidence of hepatocellular adenoma and carcinoma was observed in male and female rats from 100 and 275 ppm, respectively (France, 2007; Table 2-4). A clear dose-response was not observed and the results were not statistically significant, but the highest dose was only tested for 3 months not allowing a clear interpretation of the data. No historical control data appear to be available. The RMS France commented that on the assumption of a tumoral evolution of the liver starting from a hepatic hypertrophy with higher microsomal enzyme activity (observed in the 3 month rat study above 635 ppm) the relevance of this effect in humans could be questionable (France, 2007). However, EFSA is of the opinion that no mechanistic data are available to support this assumption and to assess the non-human relevance for liver tumours observed in rats.

Table 2-4: Summary of diagnoses of liver neoplasms in rats given tricyclazole in the diet for 2 years-study in studies R-764 and R-774 (combined)

Treatment-dose ppm (mg/kg bw per day)	hepatocellular adenoma	hepatocellular carcinoma	Total
0	0	0	0/240

100 (4.2)	1(M)	0	1/160
275 (11)	1(F)	1(M)	2/160
620 (26)	1 (M) + 1 (F)	0	2/160
1600 (106)*	1 (M) + 1 (F)	0	2/160

M=Male
F = female
* rats were administered tricyclazole during 3 months at the highest dose

EFSA is of the opinion that on the basis of the available studies a clear conclusion cannot be drawn regarding carcinogenicity potential in rats. In the absence of further data, the low dose level of 100 ppm (4.2 mg/kg bw per day) should be considered as the LOAEL.

Table 2-5: Summary of the long term toxicity studies

Type of test/ Species (purity of the test substance)	**Dose levels**	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Acceptability of the study**	**Reference**
3 or 24 months, dietary/ Wistar rats (M+F) (99.5% and 98.4%)	0, 100, 275, 620, 1600[(a)] ppm (0, 4.2, 11, 26 and 106 mg/kg bw per day)	LOAEL: 4.2	At 4.2: liver adenoma in males. At 11: liver adenoma in females and carcinoma in males. At 26: both sexes: liver adenomas, lower weight and weight gain (-12% to -15%) males: lower food consumption (-8% to -15%) females: food conversion efficiency (-11% to -15%)	Yes	Howard LC, Worth HM, Owen NV *et al* (1977) (France, 2007; Italy, 2012).
1-year toxicity, dietary/ ICR mice	0, 50, 140, 400 or 620 ppm	620 ppm	Not carcinogenic. No systemic toxicity at highest administered concentration	No	Howard, Jr.L.C. & Owen, N.V., (1979). (France, 2007; Italy, 2012).
2-year, dietary/ ICR mice	0, 50,140 and 400 ppm	400ppm	Not carcinogenic. No systemic toxicity at highest administered concentration	No	Howard, L.C., et al., 1977 (France, 2007; Italy, 2012).
22-month, dietary/ ICR mice	0, 25, 75, 250, 1000 ppm (0, 2.59, 7.98, 24.9, 101 mg/kg bw per day)	7.98 (75 ppm)	Not carcinogenic. At 250 ppm: histopathological liver findings	Yes	Harada T., 1985 (Italy, 2012).

M=Male
F=Female
(a): Rats were administered tricyclazole during 3 months at 190 mg/kg bw per d followed by 21 months on regular diet.

2.6. Reproductive toxicity

One acceptable two-generation study is available in rats. Parental and offspring toxicity was observed at 28.7 mg/kg bw per day where reduced body weight gain was observed. Delayed onset of preputial separation and vaginal opening was also observed at 28.7 mg/kg bw per day. No adverse effects were observed in the fertility parameters. The reproductive NOAEL is 28.7 mg/kg bw per day.

Two acceptable developmental studies are available. In rats, a delayed ossification was observed in pups in the presence of maternal toxicity. In rabbits, there was no evidence of teratogenicity. The relevant maternal and developmental NOAELs are 5 and 25 mg/kg bw per day in rats and rabbits respectively.

In one limited three-generation and one limited developmental study in mice, increased incidence of unilateral hydronephrosis and bilateral presence of 14 ribs was observed at 17 mg/kg bw per day in the absence of maternal toxicity. The results were outside historical control mean (no range was available).

The results of the submitted acceptable studies on reproductive toxicity and the respective criteria in Regulation (EC) No 1272/2008[11] suggest no classification and labelling for reproductive toxicity effects.

Table 2-6: Summary of the reproductive toxicity studies

Type of test/ Species (purity of the test substance)	**Dose levels**	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Acceptability of the study**	**Reference**
Multigenerational					
3-generations/ rat (99.6%)	0, 50 and 275 ppm (0, 2.5 and 14 mg/kg bw per day)	- Parental: 14 (275) - Offspring: 14 (275) - Reproductive: 14 (275)	Not applicable (highest administered dietary conc.)	No	Adams, E.R., *et al*., (1977) (France, 2007; Italy, 2012).
3-generations/ ICR mice (99.6%)	0, 50 and 275 ppm (0, 4 and 17 mg/kg bw per day)	- Parental: 17 (275) - Offspring: 4 (50). - Reproductive: 17 (275)	Parental: None. Offspring: 17 (275 ppm). Increased incidence of unilateral hydronephrosis.	Limited.	Adams, E.R., *et al*., (1977) (France, 2007; Italy, 2012).

[11] EFSA notes that tricyclazole is only classified in Annex VI to Regulation 1278/2008 with H302 (Acute Tox. 4).

Type of test/ Species (purity of the test substance)	**Dose levels**	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Acceptability of the study**	**Reference**
2-generations/ Wistar rats (M+F) (95.2%)	0, 30, 100 and 400 ppm (0, 2.1, 7.1 and 28.7 mg/kg bw per day).	- Parental: 7.1 (100 ppm). - Offspring: 7.1 (100 ppm) - Reproductive: 28.7 (400 ppm)	- Parental: At 28.7 (400 ppm): lower total body weight gain during the pre-mating period in F0 and F1 rats (up to -15% for males and -10% for females). - Offspring: At 28.7 (400 ppm): lower weight gains of males and females on days 14-21 (-13% in F0 and -18% in F1), delayed onset of preputial separation (+ 2.0 days) and vaginal opening (+ 5.4 days) in F1. - Reproductive: None.	Yes	Wolterbeek A (2004) (France, 2007; Italy, 2012).
Developmental					
Oral (gavage)/ Wistar rats (95.2 %)	0, 5, 20 and 50 mg/kg bw per day	- Maternal: 5 - Developmental: 5	- Maternal: 25% lower body weight gain during the first half of treatment; lower food consumption at 20. - Developmental: incomplete ossification of nasal and inter parietal bones at 20.	Yes	Wolterbeek, A.P.M. (2004) (France, 2007; Italy, 2012).
Oral (dietary)/ Wistar rats (99.5 and 99.6%)	0, 50 and 275 ppm (0, 3.5 and 16.2 mg/kg bw per day)	- Maternal: 16.2 (275). - Developmental: 16.2 (275)	Not applicable (highest administered dietary conc.)	No	Markham, J.K., 1977 (France, 2007; Italy, 2012).
Oral (dietary)/ ICR mice (99.5 and 99.6%)	0, 50 and 275 ppm (0, 4 and 17 mg/kg bw per day)	- Maternal: 17 (275) - Developmental: 4 (50).	-Maternal: None. -Developmental: At 17 (275 ppm):increased bilateral presence of 14 ribs.	Limited.	Markham, J.K., 1977 (France, 2007; Italy, 2012).
Oral (gavage)/ Dutch belted female rabbits (99.5%)	0, 2, 10, 50 mg/kg bw per day	- Maternal: 50 - Developmental: 50	Not applicable (highest administered dietary conc.)	No	Worth, H.M., *et al*., 1977 (France, 2007; Italy, 2012).

Type of test/ Species (purity of the test substance)	**Dose levels**	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Acceptability of the study**	**Reference**
Oral (gavage)/ New Zealand White rabbits (99.3%)	0, 7.5, 25, 75 mg/kg bw per day	- Maternal: 25 - Developmental: 25	-Maternal: reduced body weight gain and food consumption. Increased liver weight. -Developmental: reduced body weight.	Yes	Knapp, J. 2009 (Italy, 2012).

M=Male
F=Female

2.7. Neurotoxicity

No signs on neurotoxicity occurred according to the available studies. No data on delayed neurotoxicity are available, but they are not required since tricyclazole does not contain chemical groups common to organophosphates.

2.8. Further toxicological studies

No toxicity studies on the metabolites of tricyclazole have been submitted.

2.9. Medical data

No relevant information had been submitted.

2.10. Acceptable daily intake (ADI) and acute reference dose (ARfD)

The toxicological profile of the active substance tricyclazole was assessed by the RMS France (2007) and the EMS Italy (2012). The EMS proposed an ADI of 0.05 mg/kg bw per day and an ARfD of 0.05 mg/kg bw, both on the basis of the NOAEL of 5 mg/kg bw per day observed in the rat developmental toxicity study. An uncertainty factor (UF) of 100 was applied.

However, EFSA is of the opinion that on the basis of the currently available studies the setting of toxicological reference values is not appropriate since the genotoxic potential could not be totally disregarded due to the lack of *in vitro* clastogenicity/aneugenicity test and because lack of evidence of bone marrow exposure in the *in vivo* MN test. In addition, EFSA identified uncertainties regarding the carcinogenic potential of tricyclazole in rats where liver tumours were observed from the lowest dose level tested (4.2 mg/kg bw per day).

In case the applicant will provide additional studies which will allow to exclude the genotoxic potential of tricyclazole, EFSA would propose to set the ADI on the basis of the LOAEL of 4.2 mg/kg bw per day. To derive the ADI value the standard UF of 100 plus an additional UF of 10 should be applied resulting in an ADI of 0.0042 mg/kg bw per day. There would be a margin of safety (MOS) of 1000 with regard to the single incidence of adenoma in male rats.

Provided that the genotoxic potential can be excluded, EFSA would agree to set the ARfD of 0.05 mg/kg bw based on the NOAEL of 5 mg/kg bw per day observed in the rat developmental toxicity study (UF of 100).

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

3.1.1.1. Nature of residues

The metabolism of tricyclazole rice was evaluated in the DAR submitted for peer review under Directive 91/414/EEC (France, 2007). Further clarifications on the design and results of metabolism study were provided by the EMS Italy during the Member State consultation. The overview of the metabolism study designs is presented in the table below.

Table 3-1: Summary of available metabolism studies in plants

Group	Crop	Label position	Application details				
			Method, F or G[(a)]	Rate (kg a.s./ha)	No/ Interval	Sampling	Remarks
Cereals	Rice	Phenyl ring	Foliar	*Plot I:* 0.49 + 0.979	*Plot I:* 2x/35 d (BBCH 23 and BBCH 50-52)	*Plot I:* Immature crop: 0, 14, 30 days after 1st appl. and 0, 14 DALA; Mature crop: 82 DALA	GLP study (2003)
				Plot II: 0.927	*Plot II:* 1 x at BBCH 52	*Plot II:* Immature crop: 0, 14 DAT Mature crop: 82 DAT	

Plot I

On the day of the first application, immature rice plant contained 9.84 mg eq./kg of the TRR and 14 days later the majority of the TRR had decreased to 3.34 mg eq./kg. Samples of immature plant (forage) taken 30 days after the first treatment (30 DAT) contained 1.27 mg eq./kg of the TRR when radioactivity was extracted with acetone as organic solvent (sample 1) and 1.53 mg eq./kg TRR, when sample was re-analysed two years later using acetonitrile as organic solvent and acid hydrolysis (sample 2). The radioactivity of sample 2 contained 54% (0.83 mg/kg) tricyclazole with lower amounts of tricyclazole alcohol (7.5% TRR; 0.12 mg/kg).

On the day of the second application, the TRR in the immature plant accounted for 25.31 mg eq./kg and decreased to 13.06 mg eq./kg 14 days later. The characterisation of the TRR indicated that parent tricyclazole is a major component in rice plant and 14 days after the second application accounted for 69.6% TRR (9.08 mg/kg). Tricyclazole alcohol in the same sample accounted for 2.2% TRR (0.29 mg/kg) with other compounds being below 2% TRR.

At harvest (82 DALA), the TRR in mature rice grain (sample 1) was 0.33 mg/eq./kg, in rice hulls (sample 1) 4.19 mg eq./kg and in straw (sample 1) 21.46 mg eq./kg. Residues were extracted using acetone as organic solvent. Parent tricyclazole exceeded 10% TRR only in hulls (26% TRR; 1.07 mg/kg) and straw (27% TRR; 5.9 mg/kg) and in grain accounted for 7.3% TRR (0.02 mg/kg). Tricyclazole alcohol was identified at *ca.* 8 %TRR in straw and hulls.

The duplicate samples of immature plant (sample 2), grain (sample 2) and straw (sample 2) were re-analysed 2 years later using acetonitrile as organic solvent and acid hydrolysis. The TRR in the grain (sample 2) accounted for 0.36 mg eq./kg The TRR in grain consisted of parent tricyclazole (8.3% TRR

(0.03 mg/kg). 22% TRR (0.077 mg eq./kg) in organic extract and 56% TRR (0.2 mg eq./kg) in acid hydrolysate eluted in region 4 of the HPLC (in total 77.7% TRR; 0.277 mg eq./kg) and further attempts were made to characterise it. In total 67% (0.218 mg eq./kg) of this fraction and 61% of the total TRR in grain sample 2 was characterised as ^{14}C-glucose.

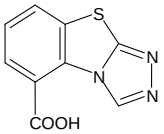
In the re-analysed straw sample (sample 2) the radioactivity was twice the amount (45.72 mg eq./kg) identified in the sample at first analysis (21.46 mg eq./kg). The characterisation of the TRR identified that parent tricyclazole accounts for 34% (15.6 mg/kg), tricyclazole alcohol for 17% (7.8 mg/kg). Since the duplicate samples of hull were not available, new hull (sample 2) and grain samples (sample 3) were derived from the stored grain. The samples were also subject to extraction both with organic solvent (acetonitrile) and acid hydrolysis. These grain and hull samples contained 0.21 mg eq./kg and 4.9 mg eq./kg TRR, respectively. Results indicated that tricyclazole accounts for 6% TRR (0.013 mg/kg) in mature grain and for 25% TRR in hulls (1.22 mg/kg). Tricyclazole alcohol metabolite was identified in hulls (6.7% TRR; 0.33 mg/kg), but not in grain. In grain the majority of the radioactivity eluted in region 4, accounting for 74% TRR (0.16 mg/kg), with less amounts of it in hulls (13.7% TRR; 0.67 mg/kg). Further attempts were performed to characterise it and in grain 87% of this region (0.14 mg eq./kg) was associated with ^{14}C-glucose, which accounted for above 80% of the total extracted radioactivity in rice grain (0.175 mg eq./kg).

TLC analysis was also performed, but only for forage sample 2, grain samples 1 and 3, hull sample 2 and straw sample 2. Detailed results of the TLC analysis have not been provided to EFSA. According to the conclusions of the RMS in the DAR, tricyclazole was the main residue in forage (61.8% region of interest (ROI)), straw (47.4% ROI), and hulls (55% ROI) but was <3% ROI in grain (sample1). The alcohol metabolite of tricyclazole was identified in forage (6.7%), hulls (9.6%) and straw (21.3%), but not in the grain sample 1. In the grain sample 3 parent tricyclazole was identified at 6.4%. In straw a third compound, an acid metabolite of tricyclazole[12], was identified at 5% TRR, which has not been identified previously. In grain (sample 3) an unidentified compound accounted for 81.86% ROI but was further not characterized. The RMS assumed that this compound could be compared with a substance which eluted as a region 4 in the HPLC analysis (France, 2007).

The non-extractable residues which accounted for 20.7% TRR (0.32 mg eq./kg) in forage (sample 2), 33.4% TRR (1.63 mg eq./kg) in hull (sample 2) and 27.9% TRR (12.8 mg eq./kg) in straw (sample 2), were subject to further characterisation to determine to which extent radioactivity was incorporated into natural products. In hulls 18.5% TRR was recovered in lignin and 5.7% TRR in cellulose. In straw, the residues were mainly found in lignin (18.5% TRR) and cellulose (12.9% TRR). In forage 14.6% of the radioactivity was associated with lignin and 6.9% with cellulose.

Plot II

The TRR in immature plant shortly after the application (0 day) was 17.54 mg eq./kg and decreased to 9.94 mg eq./kg 14 days later. At harvest, the TRR accounted for 0.22 mg eq./kg in mature rice grain, 4.02 mg eq./kg in hulls and 13.83 mg eq./kg in straw. The radioactivity of the samples was extracted using acetone as an organic solvent and no acid hydrolysis was performed. Results indicated that in forage 14 DAT the main component of the TRR was parent (78.2% TRR; 7.77 mg/kg) and no other component individually exceeded 5% TRR. Tricyclazole was the major component in mature grain (12% TRR; 0.026 mg/kg), hulls (30.6% TRR; 1.23 mg/kg) and straw (33.6% TRR; 4.64 mg/kg). The alcohol metabolite of tricyclazole was present at 4.7% TRR (0.01 mg/kg) in grain, 7.2% TRR (0.29 mg/kg) in hulls and 8% TRR (1.1 mg/kg) in the straw.



[12] Tricyclazole acid metabolite: 5-methyl-1,2,4-triazolo[3,4-*b*][1,3]benzothiazole-5-carboxylic acid

Generally, either using organic solvent or acid hydrolysis for the extraction of radioactivity, both procedures produced similar results. The studies indicate that tricyclazole is extensively metabolised with the major part of the radiolabelled material being incorporated in mature plant tissues. The compounds identified in rice grain, hulls and straw were parent tricyclazole and its alcohol metabolite. The major part of the radioactivity in grain was associated with glucose.

The RMS provisionally proposed a residue definition for the risk assessment and enforcement as "tricyclazole and its alcohol metabolite". The enforcement residue definition in Regulation (EC) No 396/2005 is set as parent tricyclazole only.

Taking into account the fact that the metabolism study labelled in the phenyl ring provided evidence of an extensive metabolism in rice, EFSA is of the opinion that an additional metabolism study which is labelled in a second position of the molecule is indispensable to elucidate the metabolic behaviour in rice. EFSA concludes that the available rice metabolism studies do not allow to confirm that the current residue definition established in Regulation (EC) No 396/2005 is appropriate. Furthermore the data are not sufficient to derive a residue definition for risk assessment.

3.1.1.2. Magnitude of residues

In support of the import tolerance request, the applicant submitted in total 16 residue trials on rice (8 were performed with the authorised application rate and 8 were performed with double the authorized rate). Trials have been performed in Brazil over growing seasons of 1993, 1996, 2003 and 2007. The eight overdosed trials and the one residue trial with incompliant PHI interval (17 days) were disregarded. It is noted that apart from foliar treatments, in four residue trials the seeds have been treated with tricyclazole (0.225 kg a.s./100 kg seed) 2-3 months before planting. The seed treatment was not considered to contribute significantly to the final residue levels in rice. It is noted, however, that the metabolism of tricyclazole in rice after seed treatment has not been investigated.

Samples were analysed for parent tricyclazole. In one trial the results were provided for polished rice only and in one trial no information was provided which part of the sample/fraction of the rice was analysed (polished rice, brown rice, paddy rice). These trials are of a limited validity since the MRLs should be set for whole grains/brown rice. Finally, five residue trials were considered by EFSA as compliant with the authorized GAP in Brazil. The results of the residue trials as reported by the applicant are summarised in Table 3-2.

The storage stability of tricyclazole and its alcohol metabolite was investigated in rice in the framework of the peer review under Directive 91/414/EEC (France, 2007). Residues of tricyclazole and its metabolite in rice were found to be stable at ≤ -18°C for up to 6 months. No information was provided the by the EMS on the storage intervals of residue trial samples prior to analysis. Detailed information on the applicability and validity of analytical methods used to analyse residue trial samples has not been provided either.

EFSA concludes that currently no MRL proposal can be derived for the following reasons:

- The data are not sufficient to derive residue definitions for enforcement and for risk assessment;
- The number of trials reflecting the critical GAP is not sufficient (3 additional residue trials on rice are required);
- The validity of the residue trials cannot be assessed since information on storage period of samples prior to analysis has not been provided;
- The validity of the analytical methods used to analyse the samples of the residue trials has not been demonstrated.

Table 3-2: Overview of the available residues trials data

Commodity	Residue region (a)	Outdoor /Indoor	Individual trial results (mg/kg)		Median residue (mg/kg) (b)	Highest residue (mg/kg) (c)	MRL proposal (mg/kg)	Median CF (d)	Comments (e)
			Enforcement (tricyclazole) (Reg. (EC) No. 396/2005)	**Risk assessment** Not sufficient data to derive residue definition for risk assessment					
Rice	Import (BR)	Outdoor	Major deficiencies were identified in the submitted residue trials (see page 20). Results as reported by the EMS: Polished rice: 0.01 Grain: 0.08[h] Grain without husk: 2 x <0.01[f]; 0.03[g]; 0.12[fg]; 0.19[fg]	-	-	-	-	-	Data not sufficient to derive MRL proposal and risk assessment values.

(a): NEU (Northern and Central Europe), SEU (Southern Europe and Mediterranean), EU (*i.e.* outdoor use) or Import (country code) (EC, 2011).
(b): Median value of the individual trial results according to the enforcement residue definition.
©: Highest value of the individual trial results according to the enforcement residue definition.
(d): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors for each residue trial.
(e): Statistical estimation of MRLs according to the EU methodology (R_{ber}, R_{max}; EC, 1997g) and unrounded/rounded values according to the OECD methodology (OECD, 2011).
(f): Seeds during storage had been treated with tricyclazole.
(g): Residue within a trial higher at a longer PHI interval of 40-41 days
(h): Not specified whether polished grain or brown grain or paddy rice was analysed.

3.1.1.3. Effect of industrial processing and/or household preparation

The effect of processing on the nature of tricyclazole has not been investigated in the framework of the peer review. During the Member State consultation, the EMS submitted a new study where the effects of processing on the nature of tricyclazole was investigated in a hydrolysis study simulating baking/brewing/boiling, pasteurisation, and sterilisation (20 minutes at 90°C, pH 4; 60 minutes at 100°C pH 5; 20 minutes at 120°C, pH 6) (G. Crabtree *et al*., 2012). The results indicate that tricyclazole is stable under all these processing conditions and no degradation occurs. Thus, in processed commodities parent tricyclazole is the main residue.

In the peer review the effect of husking, polishing and milling on the magnitude of tricyclazole residues in rice was investigated (France, 2007). One balance and 3 follow-up studies were performed. Paddy rice was de-husked and brown rice and husk were obtained. Brown/husked rice was then polished, obtaining three fractions: polished rice, bran flour and germ. The individual fractions were analysed for tricyclazole and tricyclazole alcohol metabolite. Paddy rice (raw agricultural commodity) contained 0.2 mg/kg of tricyclazole and 0.05 mg/kg of tricyclazole alcohol metabolite. Residues were below the LOQ in husked (brown rice), polished rice and bran. An increased tricyclazole concentration was observed in the husk.

Since the toxicological assessment of tricyclazole could not be finalized and no conclusions were derived concerning the nature and magnitude of tricyclazole residues in rice, no processing factors were derived.

3.1.2. Rotational crops

The residues of tricyclazole in rotational crops are of no relevance for the import tolerance application.

3.2. Nature and magnitude of residues in livestock

Since rice and its by-products are normally not fed to livestock according to the EU livestock diet, the nature and magnitude of tricyclazole residues in livestock was not assessed in the framework of this application.

4. Consumer risk assessment

EFSA was not able to perform the consumer risk assessment for tricyclazole residues in food as the available data did not allow to conclude on the following issues:

- Residue definition for risk assessment (see section 3.1.1.1)
- Mean residue concentration according to risk assessment residue definition derived from sufficient number of valid residue trials reflecting the critical GAP (see section 3.1.1.2)
- Toxicological reference values (see section 2.9).

EFSA concludes that the import tolerance request for tricyclazole in rice is not sufficiently supported by data which are needed to justify maintaining the existing EU MRL of 1 mg/kg in rice.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

The toxicological profile of tricyclazole was assessed by the RMS France in the framework of the peer review. The available data were insufficient to derive toxicological reference values. Because of these data gaps a decision on non-inclusion of tricyclazole in Annex I of Directive 91/414/EEC was taken. In a meanwhile, new toxicological studies have become available which were assessed by the EMS Italy in the framework of the current application. The EMS proposed an ADI of 0.05 mg/kg bw per day and an ArfD of 0.05 mg/kg bw, based on the rat developmental toxicity study. EFSA is of the opinion that on the basis of the currently available studies the setting of toxicological reference values is not appropriate since the genotoxic potential could not be totally disregarded. In addition, EFSA identified uncertainties regarding the carcinogenic potential of tricyclazole in rats where liver tumours were observed from the lowest dose level tested (4.2 mg/kg bw per day). In case the genotoxic potential of tricyclazole can be disproved, EFSA would propose to set the ADI at the level of 0.0042 mg/kg bw per day on the basis of the LOAEL of 4.2 mg/kg bw per day with an uncertainty factor (UF) of 1000; regarding the ArfD, EFSA would agree with the ArfD proposed by the EMS (0.05 mg/kg bw based on the NOAEL of 5 mg/kg bw per day observed in the rat developmental toxicity study (UF of 100)).

The metabolism of tricyclazole was evaluated in rice in the framework of the peer review using tricyclazole radiolabelled in the phenyl ring of the molecule. The compounds identified in rice grain, hulls and straw were parent tricyclazole and its alcohol metabolite. The major part of the radioactivity in grain was associated with glucose. The RMS provisionally proposed a residue definition for the risk assessment and enforcement as "tricyclazole and its alcohol metabolite". The enforcement residue definition in Regulation (EC) No 396/2005 is set as parent tricyclazole only. Taking into account the fact that the metabolism study labelled in the phenyl ring provided evidence of an extensive metabolism in rice, EFSA is of the opinion that an additional metabolism study in which tricyclazole is labelled in a second position of the molecule is indispensable to elucidate the metabolic behaviour in rice. EFSA concludes that the available rice metabolism studies are not sufficient to derive residue definitions for enforcement and risk assessment purposes.

Adequate analytical enforcement methods are available to control the residues of tricyclazole and tricyclazole alcohol metabolite in rice.

The submitted residue trials data were found to be insufficient to derive an MRL proposal which accommodates the use of tricyclazole on rice in Brazil because the number of trials was not in line with the data requirements and because lacking information on the analytical method used and the storage period of samples prior to analysis does not allow to conclude on the validity of the residue trials.

The effect of processing on the nature of tricyclazole was investigated in a hydrolysis study. The results indicate that tricyclazole is stable under conditions representative for pasteurisation, boiling and sterilisation. Processing studies with rice demonstrated that the magnitude of tricyclazole residues is reduced in husked rice, polished rice and in rice bran. An increased residue concentration is only expected in husks.

The residues of tricyclazole in rotational crops are of no relevance for the import tolerance application.

Since rice and its by-products are not normally fed to livestock according to EU livestock diet, the nature and magnitude of tricyclazole residues in livestock was not assessed in the framework of this application.

EFSA was not able to perform the consumer risk assessment for tricyclazole as the available data did not allow to conclude on the following issues:

- residue definition for risk assessment
- mean residue concentration according to risk assessment residue definition derived from sufficient number of valid residue trials reflecting the critical GAP
- toxicological reference values

EFSA concludes that the import tolerance request for tricyclazole in rice is not sufficiently supported by data which are needed to justify maintaining the existing EU MRL of 1 mg/kg in rice.

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APPENDICES

A. GOOD AGRICULTURAL PRACTICE (GAPS)

Crop and/or situation (a)	Member State or Country	F G or I (b)	Pest or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
				type (d – f)	conc. Of a.s. (i)	method kind (f – h)	growth stage & season (j)	number min max (k)	interval min max	kg as/hL min max	water L/ha min max	kg a.s./ha min max		
Rice	Brazil	F	*Pyricularia oryzae*	WP in WSB	750 g/kg	Direct foliar application	At complete tillering	1-2	10-15 days			0.15-0.225	30	

Remarks:
(a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Technical Monograph No 2, 4th Ed., 1999 or other codes, e.g. OECD/CIPAC, should be used
(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 plants – type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (Growth stages of mono-and dicotyledonous plants. BBCH Monograph, 2nd Ed., 2001), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI – minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions (*i.e.* feeding, grazing)

B. EXISTING EU MAXIMUM RESIDUE LEVELS (MRLS)

(Pesticides – Web Version – EU MRLs (File created on 07/02/2013 10:02))

Code number	Groups and examples of individual products to which the MRLs apply	Tricyclazole
100000	1. FRUIT FRESH OR FROZEN; NUTS	0,05*
110000	(i) Citrus fruit	0,05*
110010	Grapefruit (Shaddocks, pomelos, sweeties, tangelo, ugli and other hybrids)	0,05*
110020	Oranges (Bergamot, bitter orange, chinotto and other hybrids)	0,05*
110030	Lemons (Citron, lemon)	0,05*
110040	Limes	0,05*
110050	Mandarins (Clementine, tangerine and other hybrids)	0,05*
110990	Others	0,05*
120000	(ii) Tree nuts (shelled or unshelled)	0,05*
120010	Almonds	0,05*
120020	Brazil nuts	0,05*
120030	Cashew nuts	0,05*
120040	Chestnuts	0,05*
120050	Coconuts	0,05*
120060	Hazelnuts (Filbert)	0,05*
120070	Macadamia	0,05*
120080	Pecans	0,05*
120090	Pine nuts	0,05*
120100	Pistachios	0,05*
120110	Walnuts	0,05*
120990	Others	0,05*
130000	(iii) Pome fruit	0,05*
130010	Apples (Crab apple)	0,05*
130020	Pears (Oriental pear)	0,05*
130030	Quinces	0,05*
130040	Medlar	0,05*
130050	Loquat	0,05*
130990	Others	0,05*
140000	(iv) Stone fruit	0,05*
140010	Apricots	0,05*
140020	Cherries (sweet cherries, sour cherries)	0,05*
140030	Peaches (Nectarines and similar hybrids)	0,05*
140040	Plums (Damson, greengage, 27apporteu)	0,05*
140990	Others	0,05*
150000	(v) Berries & small fruit	0,05*
151000	(a) Table and wine grapes	0,05*
151010	Table grapes	0,05*
151020	Wine grapes	0,05*
152000	(b) Strawberries	0,05*
153000	© Cane fruit	0,05*
153010	Blackberries	0,05*
153020	Dewberries (Loganberries, Boysenberries, and cloudberries)	0,05*
153030	Raspberries (Wineberries)	0,05*
153990	Others	0,05*
154000	(d) Other small fruit & berries	0,05*
154010	Blueberries (Bilberries cowberries (red bilberries))	0,05*
154020	Cranberries	0,05*
154030	Currants (red, black and white)	0,05*
154040	Gooseberries (Including hybrids with other ribes species)	0,05*
154050	Rose hips	0,05*
154060	Mulberries (arbutus berry)	0,05*
154070	Azarole (27apporteur27an medlar)	0,05*
154080	Elderberries (Black chokeberry (appleberry), mountain ash, azarole, buckthorn (sea sallowthorn), hawthorn, service berries, and other treeberries)	0,05*
154990	Others	0,05*
160000	(vi) Miscellaneous fruit	0,05*
161000	(a) Edible peel	0,05*
161010	Dates	0,05*
161020	Figs	0,05*
161030	Table olives	0,05*
161040	Kumquats (Marumi kumquats, nagami kumquats)	0,05*
161050	Carambola (Bilimbi)	0,05*
161060	Persimmon	0,05*
161070	Jambolan (java plum) (Java apple (water apple), pomerac, rose apple, Brazilean cherry (grumichama), Surinam cherry)	0,05*
161990	Others	0,05*
162000	(b) Inedible peel, small	0,05*
162010	Kiwi	0,05*
162020	Lychee (Litchi) (Pulasan, rambutan (hairy litchi))	0,05*
162030	Passion fruit	0,05*
162040	Prickly pear (cactus fruit)	0,05*
162050	Star apple	0,05*
162060	American persimmon (Virginia kaki) (Black sapote, white sapote, green sapote, canistel (yellow sapote), and mammey sapote)	0,05*
162990	Others	0,05*
163000	© Inedible peel, large	0,05*
163010	Avocados	0,05*
163020	Bananas (Dwarf banana, plantain, apple banana)	0,05*
163030	Mangoes	0,05*
163040	Papaya	0,05*
163050	Pomegranate	0,05*
163060	Cherimoya (Custard apple, sugar apple (sweetsop) , llama and other medium sized Annonaceae)	0,05*
163070	Guava	0,05*
163080	Pineapples	0,05*
163090	Bread fruit (Jackfruit)	0,05*
163100	Durian	0,05*
163110	Soursop (guanabana)	0,05*
163990	Others	0,05*
200000	2. VEGETABLES FRESH OR FROZEN	0,05*
210000	(i) Root and tuber vegetables	0,05*
211000	(a) Potatoes	0,05*
212000	(b) Tropical root and tuber vegetables	0,05*
212010	Cassava (Dasheen, eddoe (Japanese taro), tannia)	0,05*
212020	Sweet potatoes	0,05*
212030	Yams (Potato bean (yam bean), Mexican yam bean)	0,05*
212040	Arrowroot	0,05*
212990	Others	0,05*
213000	© Other root and tuber vegetables except sugar beet	0,05*
213010	Beetroot	0,05*
213020	Carrots	0,05*
213030	Celeriac	0,05*
213040	Horseradish	0,05*
213050	Jerusalem artichokes	0,05*
213060	Parsnips	0,05*
213070	Parsley root	0,05*
213080	Radishes (Black radish, Japanese radish, small radish and similar varieties)	0,05*
213090	Salsify (Scorzonera, Spanish salsify (Spanish oysterplant))	0,05*
213100	Swedes	0,05*
213110	Turnips	0,05*
213990	Others	0,05*
220000	(ii) Bulb vegetables	0,05*
220010	Garlic	0,05*
220020	Onions (Silverskin onions)	0,05*
220030	Shallots	0,05*
220040	Spring onions (Welsh onion and similar varieties)	0,05*
220990	Others	0,05*
230000	(iii) Fruiting vegetables	0,05*
231000	(a) Solanacea	0,05*
231010	Tomatoes (Cherry tomatoes,)	0,05*
231020	Peppers (Chilli peppers)	0,05*
231030	Aubergines (egg plants) (Pepino)	0,05*
231040	Okra, lady's fingers	0,05*
231990	Others	0,05*
232000	(b) Cucurbits – edible peel	0,05*
232010	Cucumbers	0,05*
232020	Gherkins	0,05*
232030	Courgettes (Summer squash, marrow (patisson))	0,05*
232990	Others	0,05*
233000	© Cucurbits-inedible peel	0,05*
233010	Melons (Kiwano)	0,05*
233020	Pumpkins (Winter squash)	0,05*
233030	Watermelons	0,05*
233990	Others	0,05*
234000	(d) Sweet corn	0,05*
239000	(e) Other fruiting vegetables	0,05*
240000	(iv) Brassica vegetables	0,05*
241000	(a) Flowering brassica	0,05*
241010	Broccoli (Calabrese, Chinese broccoli, Broccoli raab)	0,05*
241020	Cauliflower	0,05*

Code number	Groups and examples of individual products to which the MRLs apply	Tricyclazole
241990	Others	0,05*
242000	(b) Head brassica	0,05*
242010	Brussels sprouts	0,05*
242020	Head cabbage (Pointed head cabbage, red cabbage, savoy cabbage, white cabbage)	0,05*
242990	Others	0,05*
243000	© Leafy brassica	0,05*
243010	Chinese cabbage (Indian (Chinese) mustard, pak choi, Chinese flat cabbage (tai goo choi), peking cabbage (pe-tsai), cow cabbage)	0,05*
243020	Kale (Borecole (curly kale), collards)	0,05*
243990	Others	0,05*
244000	(d) Kohlrabi	0,05*
250000	(v) Leaf vegetables & fresh herbs	0,05*
251000	(a) Lettuce and other salad plants including Brassicacea	0,05*
251010	Lamb´s lettuce (Italian comsalad)	0,05*
251020	Lettuce (Head lettuce, lollo rosso (cutting lettuce), iceberg lettuce, romaine (cos) lettuce)	0,05*
251030	Scarole (broad-leaf endive) (Wild chicory, red-leaved chicory, radicchio, curld leave endive, sugar loaf)	0,05*
251040	Cress	0,05*
251050	Land cress	0,05*
251060	Rocket, Rucola (Wild rocket)	0,05*
251070	Red mustard	0,05*
251080	Leaves and sprouts of Brassica spp (Mizuna)	0,05*
251990	Others	0,05*
252000	(b) Spinach & similar (leaves)	0,05*
252010	Spinach (New Zealand spinach, turnip greens (turnip tops))	0,05*
252020	Purslane (Winter purslane (miner's lettuce), garden purslane, common purslane, sorrel, glassworth)	0,05*
252030	Beet leaves (chard) (Leaves of beetroot)	0,05*
252990	Others	0,05*
253000	© Vine leaves (grape leaves)	0,05*
254000	(d) Water cress	0,05*
255000	(e) Witloof	0,05*
256000	(f) Herbs	0,05*
256010	Chervil	0,05*
256020	Chives	0,05*
256030	Celery leaves (fennel leaves , Coriander leaves, dill leaves, Caraway leaves, lovage, angelica, sweet cisely and other Apiacea)	0,05*
256040	Parsley	0,05*
256050	Sage (Winter savory, summer savory,)	0,05*
256060	Rosemary	0,05*
256070	Thyme (marjoram, oregano)	0,05*
256080	Basil (Balm leaves, mint, peppermint)	0,05*
256090	Bay leaves (laurel)	0,05*
256100	Tarragon (Hyssop)	0,05*
256990	Others	0,05*
260000	(vi) Legume vegetables (fresh)	0,05*
260010	Beans (with pods) (Green bean (28appor beans, snap beans), scarlet runner bean, slicing bean, yardlong beans)	0,05*
260020	Beans (without pods) (Broad beans, Flageolets, jack bean, lima bean, cowpea)	0,05*
260030	Peas (with pods) (Mangetout (sugar peas))	0,05*
260040	Peas (without pods) (Garden pea, green pea, chickpea)	0,05*
260050	Lentils	0,05*
260990	Others	0,05*
270000	(vii) Stem vegetables (fresh)	0,05*
270010	Asparagus	0,05*
270020	Cardoons	0,05*
270030	Celery	0,05*
270040	Fennel	0,05*
270050	Globe artichokes	0,05*
270060	Leek	0,05*
270070	Rhubarb	0,05*
270080	Bamboo shoots	0,05*
270090	Palm hearts	0,05*
270990	Others	0,05*
280000	(viii) Fungi	0,05*
280010	Cultivated (Common mushroom, Oyster mushroom, Shi-take)	0,05*
280020	Wild (Chanterelle, Truffle, Morel ,)	0,05*
280990	Others	0,05*
290000	(ix) Sea weeds	0,05*
300000	3. PULSES, DRY	0,05*
300010	Beans (Broad beans, navy beans, flageolets, jack beans, lima beans, field beans, cowpeas)	0,05*
300020	Lentils	0,05*
300030	Peas (Chickpeas, field peas, chickling vetch)	0,05*
300040	Lupins	0,05*
300990	Others	0,05*
400000	4. OILSEEDS AND OILFRUITS	0,05*
401000	(i) Oilseeds	0,05*
401010	Linseed	0,05*
401020	Peanuts	0,05*
401030	Poppy seed	0,05*
401040	Sesame seed	0,05*
401050	Sunflower seed	0,05*
401060	Rape seed (Bird rapeseed, turnip rape)	0,05*
401070	Soya bean	0,05*
401080	Mustard seed	0,05*
401090	Cotton seed	0,05*
401100	Pumpkin seeds	0,05*
401110	Safflower	0,05*
401120	Borage	0,05*
401130	Gold of pleasure	0,05*
401140	Hempseed	0,05*
401150	Castor bean	0,05*
401990	Others	0,05*
402000	(ii) Oilfruits	0,05*
402010	Olives for oil production	0,05*
402020	Palm nuts (palmoil kernels)	0,05*
402030	Palmfruit	0,05*
402040	Kapok	0,05*
402990	Others	0,05*
500000	5. CEREALS	
500010	Barley	0,05*
500020	Buckwheat	0,05*
500030	Maize	0,05*
500040	Millet (Foxtail millet, teff)	0,05*
500050	Oats	0,05*
500060	Rice	1
500070	Rye	0,05*
500080	Sorghum	0,05*
500090	Wheat (Spelt Triticale)	0,05*
500990	Others	0,05*
600000	6. TEA, COFFEE, HERBAL INFUSIONS AND COCOA	0,05*
610000	(i) Tea (dried leaves and stalks, fermented or otherwise of Camellia sinensis)	0,05*
620000	(ii) Coffee beans	0,05*
630000	(iii) Herbal infusions (dried)	0,05*
631000	(a) Flowers	0,05*
631010	Camomille flowers	0,05*
631020	Hybiscus flowers	0,05*
631030	Rose petals	0,05*
631040	Jasmine flowers	0,05*
631050	Lime (linden)	0,05*
631990	Others	0,05*
632000	(b) Leaves	0,05*
632010	Strawberry leaves	0,05*
632020	Rooibos leaves	0,05*
632030	Maté	0,05*
632990	Others	0,05*
633000	© Roots	0,05*
633010	Valerian root	0,05*
633020	Ginseng root	0,05*
633990	Others	0,05*
639000	(d) Other herbal infusions	0,05*
640000	(iv) Cocoa (fermented beans)	0,05*
650000	(v) Carob (st johns bread)	0,05*
700000	7. HOPS (dried) , including hop pellets and unconcentrated powder	0,05*
800000	8. SPICES	0,05*
810000	(i) Seeds	0,05*
810010	Anise	0,05*
810020	Black caraway	0,05*
810030	Celery seed (Lovage seed)	0,05*
810040	Coriander seed	0,05*
810050	Cumin seed	0,05*
810060	Dill seed	0,05*
810070	Fennel seed	0,05*
810080	Fenugreek	0,05*
810090	Nutmeg	0,05*
810990	Others	0,05*
820000	(ii) Fruits and berries	0,05*
820010	Allspice	0,05*
820020	Anise pepper (Japan pepper)	0,05*
820030	Caraway	0,05*
820040	Cardamom	0,05*
820050	Juniper berries	0,05*
820060	Pepper, black and white (Long pepper, pink pepper)	0,05*
820070	Vanilla pods	0,05*
820080	Tamarind	0,05*
820990	Others	0,05*

Code number	Groups and examples of individual products to which the MRLs apply	Tricyclazole
830000	(iii) Bark	0,05*
830010	Cinnamon (Cassia)	0,05*
830990	Others	0,05*
840000	(iv) Roots or rhizome	0,05*
840010	Liquorice	0,05*
840020	Ginger	0,05*
840030	Turmeric (Curcuma)	0,05*
840040	Horseradish	0,05*
840990	Others	0,05*
850000	(v) Buds	0,05*
850010	Cloves	0,05*
850020	Capers	0,05*
850990	Others	0,05*
860000	(vi) Flower stigma	0,05*
860010	Saffron	0,05*
860990	Others	0,05*
870000	(vii) Aril	0,05*
870010	Mace	0,05*
870990	Others	0,05*
900000	9. SUGAR PLANTS	0,05*
900010	Sugar beet (root)	0,05*
900020	Sugar cane	0,05*
900030	Chicory roots	0,05*
900990	Others	0,05*
1000000	10. PRODUCTS OF ANIMAL ORIGIN- TERRESTRIAL ANIMALS	0,05*
1010000	(i) Meat, preparations of meat, offals, blood, animal fats fresh chilled or frozen, salted, in brine, dried or smoked or processed as flours or meals other processed products such as sausages and food preparations based on these	0,05*
1011000	(a) Swine	0,05*
1011010	Meat	0,05*
1011020	Fat free of lean meat	0,05*
1011030	Liver	0,05*
1011040	Kidney	0,05*
1011050	Edible offal	0,05*
1011990	Others	0,05*
1012000	(b) Bovine	0,05*
1012010	Meat	0,05*
1012020	Fat	0,05*
1012030	Liver	0,05*
1012040	Kidney	0,05*
1012050	Edible offal	0,05*
1012990	Others	0,05*
1013000	© Sheep	0,05*
1013010	Meat	0,05*
1013020	Fat	0,05*
1013030	Liver	0,05*
1013040	Kidney	0,05*
1013050	Edible offal	0,05*
1013990	Others	0,05*
1014000	(d) Goat	0,05*
1014010	Meat	0,05*
1014020	Fat	0,05*
1014030	Liver	0,05*
1014040	Kidney	0,05*
1014050	Edible offal	0,05*
1014990	Others	0,05*
1015000	(e) Horses, asses, mules or hinnies	0,05*
1015010	Meat	0,05*
1015020	Fat	0,05*
1015030	Liver	0,05*
1015040	Kidney	0,05*
1015050	Edible offal	0,05*
1015990	Others	0,05*
1016000	(f) Poultry –chicken, geese, duck, turkey and Guinea fowl-, ostrich, pigeon	0,05*
1016010	Meat	0,05*
1016020	Fat	0,05*
1016030	Liver	0,05*
1016040	Kidney	0,05*
1016050	Edible offal	0,05*
1016990	Others	0,05*
1017000	(g) Other farm animals (Rabbit, Kangaroo)	0,05*
1017010	Meat	0,05*
1017020	Fat	0,05*
1017030	Liver	0,05*
1017040	Kidney	0,05*
1017050	Edible offal	0,05*
1017990	Others	0,05*
1020000	(ii) Milk and cream, not concentrated, nor containing added sugar or sweetening matter, butter and other fats derived from milk, cheese and curd	0,05*
1020010	Cattle	0,05*
1020020	Sheep	0,05*
1020030	Goat	0,05*
1020040	Horse	0,05*
1020990	Others	0,05*
1030000	(iii) Birds' eggs, fresh preserved or cooked Shelled eggs and egg yolks fresh, dried, cooked by steaming or boiling in water, moulded, frozen or otherwise preserved whether or not containing added sugar or sweetening matter	0,05*
1030010	Chicken	0,05*
1030020	Duck	0,05*
1030030	Goose	0,05*
1030040	Quail	0,05*
1030990	Others	0,05*
1040000	(iv) Honey (Royal jelly, pollen)	
1050000	(v) Amphibians and reptiles (Frog legs, crocodiles)	
1060000	(vi) Snails	
1070000	(vii) Other terrestrial animal products	

(*) Indicates lower limit of analytical determination

ABBREVIATIONS

ADI	acceptable daily intake
ArfD	acute reference dose
a.s.	active substance
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CF	conversion factor for enforcement residue definition to risk assessment residue definition
CIPAC	Collaborative International Pesticide Analytical Council
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DALA	days after last application
DAR	Draft Assessment Report
DAT	days after treatment
EC	European Community
EFSA	European Food Safety Authority
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (former GIFAP)
GLP	Good Laboratory Practice
GS	growth stage
ha	hectare
HDL	highest dose level
hL	hectolitre
ILV	independent laboratory validation
IPCS	International Programme of Chemical Safety
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
L	litre
LOAEL	lowest observed adverse effect level
LOQ	limit of quantification
MN	micronucleus

MSD	mass spectrometry detector
MS/MS	tandem mass spectrometry
MTD	maximum tolerable dose
MW	molecular weight
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PHI	pre-harvest interval
RBCs	red blood cells
R_{ber}	statistical calculation of the MRL by using a non-parametric method
R_{max}	statistical calculation of the MRL by using a parametric method
RMS	rapporteur Member State
ROI	region of interest
TLC	thin-layer chromatography
TRR	total radioactive residue
UDS	unscheduled DNA synthesis
UF	uncertainty factor
WP	wettable powder
WSB	water soluble bags/packets