REASONED OPINION

Reasoned opinion on the setting of an import tolerance for didecyldimethylammonium chloride (DDAC) in citrus[1]

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ABSTRACT

In accordance with Article 6 of Regulation (EC) No 396/2005, The Netherlands, hereafter referred to as the evaluating Member State (EMS), received an application from Exponent International Ltd (on behalf of ICA International Chemicals (PTY) Ltd) to set an import tolerance in citrus from South Africa for the active substance didecyldimethylammonium chloride (DDAC) at the level of 6 mg/kg. The Netherlands drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA. According to EFSA, the data require the setting of an import tolerance of 6 mg/kg for citrus. However, additional information on the typical South African post-harvest treatment practice should be provided to decide whether the submitted trials are representative of the authorised GAP. A sufficiently validated analytical method to enforce the proposed MRL of DDAC on citrus is available. EFSA concludes that the consumer risk assessment did not identify a consumer health risk resulting from the post harvest uses of DDAC on citrus fruits. However it should be noted that the risk assessment is affected by a high degree of uncertainties which result from data gaps identified in the dossier. Finally, EFSA concludes that risk managers have to decide whether the setting of an import tolerance of 6 mg/kg is acceptable since the MRL currently into force for citrus in South Africa is 2 mg/kg only.

KEY WORDS

didecyldimethylammonium chloride (DDAC), citrus, MRL application, Regulation (EC) No 396/2005, consumer risk assessment, alkyl-quaternary ammonium .

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SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, The Netherlands, hereafter referred to as the evaluating Member State (EMS), received an application from Exponent International Ltd (on behalf of ICA International Chemicals (PTY) Ltd) to set an import tolerance in citrus from South Africa for the active substance didecyldimethylammonium chloride (DDAC) at the level of 6 mg/kg. The Netherlands drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA on 03 April 2012.

EFSA bases its assessment on the evaluation report submitted by the EMS, the Draft Assessment Report (DAR) (and its addendum/addenda) prepared under Council Directive 91/414/EEC, the Commission Review Report on DDAC and the conclusion on the peer review of the pesticide risk assessment of the active substance DDAC.

Studies on mammalian toxicity were provided and discussed in the course of the peer review under Directive 91/414/EEC. However, no specifications could be established and confirmation could not be given that the batches used in the toxicological studies were of the same composition as the technical materiel. Taking into account the supported uses limited to ornamentals, dietary toxicological reference values were finally not proposed for DDAC. The toxicological studies were therefore reconsidered by the EMS in the framework of this MRL application and an ADI of 0.1 mg/kg bw per day and an ARfD of 0.61 mg/kg bw were proposed. Although not formally peer reviewed, these toxicological values were confirmed by the experts on mammalian toxicology during the Pesticides Peer Review expert meeting 103, held in Parma in May 2013. **However, these ADI and ARfD proposals should be considered as indicative only, as long as the concerns on the specifications of the active substance have not been solved.** As a first approach, EFSA proposes to use these ADI and ARfD values to conducted the consumer risk assessment in this MRL application.

The metabolism of DDAC in primary crops was not investigated in the course of the peer review. Metabolism study on citrus was submitted and assessed in the framework of this MRL application and the EMS proposed to define the residue for enforcement and risk assessment as DDAC. However, this metabolism covers a period of 7 days only while treated citrus might be stored over a much longer period and data covering a storage period of several months would be desirable. As a first approach, EFSA proposes to use the residue definitions proposed by the EMS to set the MRL value in this MRL application.

EFSA concluded that the submitted supervised residue trials require the setting of an import tolerance proposal of 6 mg/kg for citrus. However, additional information on the typical South African post-harvest treatment practice should be provided to decide whether the submitted trials are representative for the authorised GAP. In particular, it should be specified if the first application of DDAC by dipping might be followed by a second dipping or spray treatment with other pesticides. The QuEChERS method has been validated to analyse DDAC on high acid content matrices and therefore, an analytical method to enforce the proposed MRL of DDAC on citrus is available.

Studies investigating the nature of DDAC residues under standard hydrolysis conditions were not submitted. Several processing studies were provided and the data were sufficient to derive the following processing factors.

- Whole citrus/Peeled citrus: 0.1
- Orange/Orange juice: 0.3
- Orange/Wet pomace: 1.2
- Orange/Dry pomace 7.6

Since the proposed uses of DDAC is on imported crops and refers to post-harvest applications, investigations of residues in rotational crops are not required.

No data were submitted to assess the residue behaviour of DDAC in livestock animals, the applicant arguing that citrus treated with DDAC in South Africa and imported into Europe will predominantly be used as fresh fruit. Therefore, citrus pomace containing DDAC residues will not be available in Europe for use as an animal feedstuff. As it cannot be excluded that imported citrus will be processed, **EFSA is of the opinion that in accordance with the current EU data requirements data on the nature and magnitude of DDAC residues in livestock should be provided.**

The consumer risk assessment was performed with the revision 2 of the EFSA Pesticides Residues Intake Model (PRIMo). The calculation of chronic consumer exposure was estimated using the median residue level observed in the edible part of the citrus (flesh) and the default residue concentration of 0.5 mg/kg for all other food commodities as proposed in the EU guidelines (European Commission, 2012). Other sources of exposure are not taken into account. No long-term consumer intake concerns were identified for any of the European diets included in the EFSA PRIMo model, the highest calculated intake accounting for 34% (FR Toddler) of the ADI proposed at 0.1 mg/kg bw per day. The individual contribution of citrus fruits to the total consumer exposure was low, accounting for less than 1% of the ADI.

No acute consumer risk was identified in relation to the MRL proposal for citrus. The calculated maximum exposure in percentage of the ARfD was 22 % for orange (UK, infant) and 4% for orange juice (DE, child).

EFSA concludes that the consumer risk assessment did not identify a consumer health risk resulting from the post harvest uses of DDAC on citrus fruits. However it should be noted that the risk assessment is affected by a high degree of uncertainties which result from data gaps identified in the dossier in particular for the following issues:

- the deficiencies in the toxicological data referring to the specifications of the active substance,
- the representativeness of the residue trials,
- the possible residues in the products of animal origin,
- other possible sources of exposure, especially those resulting of the use of DDAC as biocide.

Finally and as reported in the summary table below, EFSA concludes that the risk managers have to decide whether the setting of an import tolerance of 6 mg/kg is acceptable, since the MRL value currently into force on citrus in South Africa is 2 mg/kg only.

Summary table

Code number[(a)]	**Commodity**	**Existing EU MRL** (mg/kg)	**Proposed Import** (mg/kg)	**Justification for the proposal**
Enforcement residue definition: DDAC				
110000	Citrus fruit	0.01*	6	The import tolerance proposal is supported by a sufficient number of trials, but further information on the post harvest treatment practices in South Africa are required. No risk was identified for consumers when the assessment is performed using the indicative toxicological reference values proposed for DDAC. The risk managers have to decide whether the setting of an import tolerance of 6 mg/kg is acceptable since the MRL currently into force on citrus in South Africa is 2 mg/kg only.

(a): According to Annex I of Regulation (EC) No 396/2005.
(*): Indicates that the MRL is set at the limit of analytical quantification.

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BACKGROUND

Regulation (EC) No 396/2005[3] 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[4], repealed by Regulation (EC) No 1107/2009[5], shall submit to a Member State, when appropriate, an application to set an import tolerance in accordance with the provisions of Article 7 of that Regulation.

The Netherlands, hereafter referred to as the evaluating Member State (EMS), received from the company Exponent International Ltd[6] (on the behalf of the company ICA International Chemicals (PTY) Ltd, South Africa) an application to set an import tolerance for the active substance didecyldimethylammonium chloride (DDAC) in citrus. This application was notified to the European Commission and EFSA, and was 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 03 April 2012.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2012-00480 and the following subject:

Didecyldimethylammonium chloride (DDAC) – Application to modify the existing MRL in citrus fruits

The Netherlands proposed to raise the existing MRL of DDAC in citrus from the limit of quantification (default value of 0.01* mg/kg) to 6 mg/kg.

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.

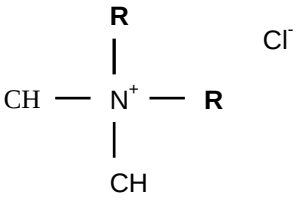
In accordance with Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within three months (which may be extended to six months where more detailed evaluations need to be carried out) from the date of receipt of the application. Where EFSA requests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

In this particular case, considering that a detailed evaluation have to be carried out with regard to the toxicological reference values and the residue definitions, EFSA proposed a 6 months evaluation period. Therefore the deadline for providing the reasoned opinion was calculated to be 3 October 2012.

[3] Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005. OJ L 70, 16.03.2005, p. 1-16.
[4] Council Directive 91/414/EEC of 15 July 1991. OJ L 230, 19.08.1991, p. 1-32.
[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] Exponent International Ltd, Hornbeam Park, The Lenz, HG2 8RE, Harrogate, UK.

THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Didecyldimethylammonium chloride (DDAC) has no ISO common name and a unique IUPAC name cannot be allocated as DDAC is a mixture of alkyl-quaternary ammonium salts with typical alkyl chain lengths of C8, C10 and C12.



R = alkyl chain with typical lengths of C8, C10 and C12

DDAC belongs to the class of alkyl-quaternary ammonium compounds. It is a non-systemic broad-spectrum fungicide, bactericide and herbicide (algicide). DDAC inhibits the growth and kills phytopathogenic fungi, phytopathogenic bacteria and algae in hydroponic systems, on hard surfaces, glasshouse walls and pavements, and equipments. Uses as post harvest treatment on citrus fruits, pome fruits and some fruiting vegetables are also reported.

DDAC was evaluated in the framework of Council Directive 91/414/EEC with The Netherlands designated as rapporteur Member State (RMS). It was included in Annex I of this Directive by Directive 2009/70/EC[7] which entered into force on 01 January 2010. According to this directive, only indoor uses for ornamental plants as bactericide, fungicide, herbicide and algaecide may be authorised. The minimum purity of the technical concentrate was defined in this directive as ≥70%; more than 90% of the alkyl-chains are expected to be C10. Directive 2009/70/EC also specifies that the notifier has to submit further confirmatory data on the specification of the active substance. In accordance with Commission Implementing Regulation (EU) No 540/2011[8] DDAC was approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC. Recently, the decision to withdraw the approval for DDAC was taken (Regulation (EU) No 175/2013[9]) since the notifier failed to provide the confirmatory information specified in Directive 2009/70/EC.

The Draft Assessment Report (DAR) of DDAC has been peer reviewed by EFSA (EFSA, 2008). The representative uses evaluated were disinfection of horticulture vessels, equipments (e.g. knives) and surfaces. In the EFSA conclusion a series of data gaps were identified, many of them linked to the lack of information on the exact composition of the active substance, necessary to derive a specification and a minimum purity for the technical DDAC. Since clear specifications could not be established and as the representative uses were referring to non-edible crops, it was concluded that the setting of toxicological reference values is not necessary.

According to Article 18(1)(b) of Regulation (EC) No 396/2005, the default LOQ of 0.01*mg/kg is applicable for DDAC at EU level. However, in 2012, the European Commission has been informed by food business operators and several Member States that various food products were found containing levels of DDAC higher than the default level of 0.01*mg/kg. The origin of these residues was not clearly identified; possible sources were, among others, the use of DDAC in biocidal products or as co-formulant in plant protection products. On 2 July 2012, the German Federal Institute for consumer protection and food safety (BfR), issued a statement declaring that based on the findings so far and assuming a (average) residue level of 1 ppm for bananas, citrus and fresh herbs, and for all other an average level of 0.1 mg/kg no long term or short term risk for any consumer group is to be expected. In the Standing Committee on Food Chain and Animal Health held in July 2012 an exchange of views on the available information and on the results of the risk assessment provided by the BfR took place. It was agreed that Member States should carry out investigations on the causes of the contamination and put in place a monitoring programme with a view to have a clear understanding of the levels of

[7] Commission Directive 2009/70/EC of 25 June 2009, OJ L 164, 26.06.2009, p. 59-63.
[8] Commission Implementing Regulation (EU) No 540/2011 of 23 May 2011. OJ L 153, 11.06.2011, p. 1-186.
[9] Commission Implementing Regulation (EU) No 175/2013 of 27 February 2013. OJ L56, 28.2.2013, p. 4-5.

DDAC in food and feed. In addition, it was agreed that food and feed with a level of DDAC higher than 0.5 mg/kg should not be placed on the market and be withdrawn from the market and safely disposed of. In October 2012 the guidelines were slightly modified to avoid ambiguities in enforcement (European Commission, 2012).

DDAC has not been reviewed by JMPR and therefore, no CXLs are established at Codex level. In South Africa, the MRL for citrus is set at the level of 2 mg/kg[10].

The application refers to a single post harvest treatment on citrus in South Africa by dipping at a dose rate of 12 g a.s./hl. Details of the authorised GAP are given in Appendix A. It should be noted that the dipping time foreseen in the South African post harvest practices has not been specified.

[10] Regulations governing the maximum limits for pesticide residues that may be present in foodstuffs, South Africa, Ministry of heath, 17 June 2010; available at http://www.doh.gov.za/docs/foodcontrol/drugs/2010/pesticides3.pdf

ASSESSMENT

EFSA bases its assessment on the evaluation report submitted by the EMS (The Netherlands, 2012), the Draft Assessment Report (DAR) (and its addendum/addenda) prepared under Council Directive 91/414/EEC (The Netherlands, 2007), the Commission Review Report on DDAC (EC, 2009), the conclusion on the peer review of the pesticide risk assessment of the active substance DDAC (EFSA, 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[11] 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).

1. Method of analysis

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

Analytical methods for the determination of DDAC residues in plant commodities were not assessed during the peer review under Directive 91/414/EEC (EFSA, 2009), considering the restricted uses as disinfectant of surfaces, equipments in ornamental plant productions.

The description of an enforcement method for DDAC and its validation data have not been submitted in the framework of this MRL application. The evaluation report details only ILV data for a LC-MS/MS method achieving a limit of quantification (LOQ) of 0.1 mg/kg for whole orange.

The EU Reference Laboratory (EURL) on single residue methods, has developed a method for the analysis of DDAC by applying the extraction procedure of the QuEChERS method described in the European Standard EN 15662:2008 and using LC-MS/MS determination. According to the validation data reported by the EURL-SRM, DDAC can be determined in plant matrices with high water and high acid content with a LOQ of 0.1 mg/kg (EURL, 2012).

Since citrus belongs to the crop group with high acid content, EFSA concludes that sufficiently validated methods should be available to enforce MRLs of DDAC on citrus.

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 provided. Pending the outcomes of the information requested on the fate of DDAC in livestock animals (see section 3.2), data on analytical methods to enforce DDAC in animal matrices might be requested.

2. Mammalian toxicology

No specifications could be established for DDAC in the course of the peer review under Directive 91/414/EEC (EFSA, 2009). The toxicological studies provided in the dossier were performed with alcoholic/aqueous solutions containing 50 to 80% of DDAC but the applicant could not provide a confirmation that the material used in these studies has the same composition as the technical material in the plant protection products. Consequently, considering the limited validity of the toxicological data and considering that the supported uses as disinfectant of surfaces, equipments in ornamental productions will not result in a consumer exposure to DDAC residues, the experts in the peer review decided not to propose dietary toxicological reference values for DDAC.

The EMS, in the framework of this MRL application, has reconsidered the toxicological data initially presented in the DAR and has derived chronic and acute reference values for DDAC. Although not

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

formally peer reviewed, these proposals were discussed in the Pesticides Peer Review expert meeting 103, held in Parma in May 2013. The experts on mammalian toxicology confirmed the values proposed by the EMS and concluded on an ADI of 0.1 mg/kg bw per day and an ARfD of 0.61 mg/kg bw. It should however be highlighted that the concerns raised on the specification of the active substance and on the representativeness of the test material used in toxicological studies still remain.

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

Due to its highly ionic nature DDAC is poorly absorbed from the gastrointestinal tract (1.2 to 2.5% based on urine excretion, tissues and residual carcass). It is widely distributed and extensively excreted mainly via faeces.

2.2. Acute toxicity

The oral LD_{50} of DDAC is 256 mg/kg bw. The acute dermal toxicity is >4000 and <6400 mg/kg bw. Due to the corrosive potential of DDAC an eye irritation test was not performed, nor an acute inhalation toxicity due to the low volatility of the a.s.. A valid skin sensitisation study is not available.

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
Acute oral Rat	P 0151 (50% DDAC) Lot no L-3183	LD_{50} (mg/kg bw) 256	Yes	Ullmann, L., 1983 (NL, 2007)
Acute dermal Rat	E-72-4 2/1/80 or Bardac 2280 (80% DDAC), Lot no. unknown	LD_{50} (mg/kg bw) > 4000 and < 6400	Yes	Nitka, S., 1980
Skin irritation Rabbit	P4289 (DDAC), Lot no. Q/90/154 GB-E, purity 96.4%	Corrosive	Yes	Allen, D.J., 1995
Skin sensitisation Guinea pig	Bardac 22 (50% DDAC), Batch no. unknown	skin sensitisation in 3 animals	No	Clement, C., 1992

2.3. Short term toxicity

Repeated subchronic oral exposures in rats and dogs resulted in NOAELs of 60.7 mg/kg bw per day and 10 mg/kg bw per day, respectively, with decreased body weight (gain) and food consumption and secondary haematological effects. A dermal study resulted in erythema, oedema, and increased incidence of exfoliation at the application site from 6 mg/kg bw per day. An inhalation repeated toxicity study is unnecessary, since the active substance is not volatile.

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

Type of test/ Species (purity test substance)	**Dose levels** (mg/kg bw per day)	**NOAEL** (mg/kg bw per day	**Effects at LOAEL and higher doses** (mg/kg bw per day	**Accepta -bility of the study**	**Reference**
13 weeks Rat (80.8%)	Males: 0, 6.2, 18.5, 36.8, 60.7 and 175 Females: and 0, 7.5, 22.3, 44.4, 74.3 and 226	60.7 males 74.3 females	Mortality, reduced food consumption, effects on body weight gain, clinical signs, haematology, clinical chemistry, effects observed at necropsy and histopathology	Yes	Van Miller, J.P., 1988

Type of test/ Species (purity test substance)	Dose levels (mg/kg bw per day)	NOAEL (mg/kg bw per day	Effects at LOAEL and higher doses (mg/kg bw per day	Accepta -bility of the study	Reference
1-year Dog (80.8%)	0, 3, 10, 30/20	10	Decreased body weight gain and decreased erythrocyte, haemoglobin and haematocrit in both sexes, decreased albumin and total protein in males and increased liver weight in females.	Yes	Schulze, G.E., 1991
Dermal 13 weeks Rabbit (80.8%)	0, 0.1, 0.3 and 0.6% (w/w) equal to 0, 2, 6 and 12 mg/kg bw/day	Local: <2 (0.1% DDAC) Systemic: ≥12 (0.6% DDAC)	Local: epidermitis No systemic toxicity	Yes	Gill, M.W. & Van Miller, J.P., 1988

2.4. Genotoxicity

DDAC was non-mutagenic in *in vitro* and *in vivo* tests.

Table 2-3: Summary of the genotoxicity studies

Test substance (batch and purity)	Test system	Concentrations/dose	Results	Accepta-bility of the study	Reference
In vitro studies					
Bardac 22 (50% DDAC), batch nr. DEGE030167	*S. typhimurium:* TA 1535, TA 1537, TA 98, TA 100, TA 102.	Exp. 1 and 2: -S9: 0.05, 0.15, 0.5, 1.5, 5, 15 µg/pl +S9: 0.15, 0.5, 1.5, 5, 15, 50 µg/pl	Neg	Yes	Thompson, P.W., 2001
P0151 (50% DDAC), batch nr. E 06130085	Chromosome aberration Chinese hamster ovary (CHO) cells	Exp: -S9 (treatment and harvest 24 h): 1, 2, 4, 8 µg/ml +S9 (treatment 6 h and harvest 24 h): 2, 4, 8 µg/ml	Neg	Yes	Holmstrom, M., Leftwich, D.J., Leddy, I.A., 1986
Bardac 2280 (80% DDAC), batch nr. B-1889	Gene mutations (HGPRT) Chinese hamster ovary (CHO) cells	DRF 1 (-S9): 5 to 5000 µg/ml DRF 2 (-S9): 0.1 to 8 µg/ml DRF 3 (-S9): 0.05 to 50 µg/ml DRF 1 (+S9): 5 to 5000 µg/ml Exp 1: (-S9) 3, 4, 5, 6, 7, 8 µg/ml (+S9) 5, 13, 15, 18, 20, 25 µg/ml Exp 2: (-S9) 3, 4, 5, 6, 7, 8, 10 µg/ml (+S9) 1, 5, 10, 15, 18, 20, 22 µg/ml	Neg	Yes	Young, R.R.,1988
In vivo studies					
P0151 (50% DDAC), batch nr. E 06130085	Chromosomal Aberration (bone marrow) Rat, Sprague-Dawley 5/sex/dose	DRF 1: 200, 400, 600, 800, 1000 mg/kg bw DRF 2: 600, 800, 1000, 1200 mg/kg bw Main: 600 mg/kg bw	Neg	Yes	Allen, J. A., Proudlock, R.J., Brooker, P.C., 1987

2.5. Long term toxicity

In the 2-year rat study, the relevant NOAEL is 32 mg/kg bw per day based on decreased bodyweight gain in females, and histological changes in bile ducts and mesenteric lymph nodes in both sexes. In the 78-week mouse study, the NOAEL of 76.3 mg/kg bw per day is based on reduced bodyweight gain in both sexes. No other treatment-related findings were observed. No oncogenic potential was observed in rats or mice.

Table 2-4: Summary of the long term toxicity studies

Type of test/ Species (purity test substance)	**Dose levels** (mg/kg bw per day)	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Accepta-bility of the study**	**Reference**
2-year oral Rat Bardac 2280 (DDAC) Lot no. B-1889 purity 80.8%	Males 0, 13, 32 and 64 Females 0, 16, 41 and 83	32 male 41 female	Reduced body weight gain and food consumption, morphological changes in bile ducts and mesenteric lymph nodes. No oncogenic potential was observed	Yes	Gill, M.W., Chun, J.S. and Wagner, C.L., 1991
18 months Mouse Bardac 2280 (DDAC) Lot no. B-1889 purity 80.8%	Males 0, 15.0, 76.3 and 156 Females: 0, 18.6, 93.1 and 193	76.3 male 93.1 female	Reduced body weight gain No oncogenic potential was observed	Yes	Gill, M.W., Hermansky, S.J. and Wagner, C.L., 1991

2.6. Reproductive toxicity

In a rat two-generation study no adverse effects on fertility were observed. The parental and offspring NOAEL are 50 mg/kg bw per day based on decreased bodyweight gain (and food consumption for the parents), whereas the reproductive NOAEL was 100 mg/kg bw per day (highest dose tested).

In the rat teratogenicity study, based on clinical signs observed at 10 mg/kg bw per day, the maternal NOAEL is 1 mg/kg bw per day, also taking into account local effects. The developmental NOAEL is 20.0 mg/kg bw per day (highest dose tested, no treatment-related findings in foetuses). In the rabbit developmental study, taking into account local adverse effects, a maternal NOAEL of 1 mg/kg bw per day is based on clinical signs and decreased bodyweight gain. Based on reduced foetal weight and increased incidence of dead foetuses at 10 mg/kg bw per day, the NOAEL for developmental toxicity is at 3.0 mg/kg bw per day.

Table 2-5: Summary of the reproductive toxicity studies

Type of test/ Species (purity test substance)	**Dose levels** (mg/kg bw/day)	**NOAEL** (mg/kg bw per day)	**Effects at LOAEL and higher doses** (mg/kg bw per day)	**Accepta-bility of the study**	**Reference**
Multigenerational					
Two-generation Oral dietary, rat (80.8%)	0, 20, 50 and 100	- Parental: 50 - Offspring: 50 - Reproductive: 100	Reduced bodyweight gain and food consumption. No reproductive effects were observed.	Yes	Neeper-Bradley, T.L., 1991
Developmental					
Developmental toxicity Oral gavage, rat (80.8%)	0, 1, 10 and 20	- Maternal local: 1 - Maternal systemic: 20 - Developmental: 20	- No maternal systemic toxicity (clinical signs observed, are considered to be local and reduced food consumption secondary to the local effects)	Yes	Neeper-Bradley, T.L., 1991
Developmental toxicity Oral gavage, rabbit (80.8%)	0, 1, 3 and 10	- Maternal local: 1 - Maternal systemic: ≥10 - Developmental: 3	- audible respiration and reduced body weight gain in females at 3.0 mg - absence of systemic toxic effects - reduced foetal weight and an increased incidence of dead foetuses	Yes	Tyl, R.W., 1989

2.7. Neurotoxicity

No neurotoxicity studies were submitted. In the absence of clinical signs potentially indicative of neurotoxicity in any of the studies performed, no specific neurotoxicity studies were needed.

2.8. Further toxicological studies

None

2.9. Medical data

No adverse effects were reported in manufacturing personnel. Some case reports indicate reversible irritation to skin and mucous membranes.

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

Based on the toxicological studies summarized above, and following the discussions in the Pesticides Peer Review expert meeting 103 on mammalian toxicology, an ADI of 0.1 mg/kg bw per day and an ARfD of 0.61 mg/kg bw were proposed for DDAC (Table 2-6).

The ADI of 0.1 mg/kg bw per day is based on the relevant NOAEL from the 1-year study in dogs, applying an uncertainty factor (UF) of 100. The study used for the derivation of a long term trigger value is a subchronic assay, however based on the analysis of available data (subchronic and chronic exposure in rats, oral *vs.* gavage administration in relationship to health effects) it is not expected that a longer term study in dogs would result in a higher level of toxicity.

The ARfD of 0.61 mg/kg bw per day proposed by the EMS and confirmed during the Pesticides Peer Review expert meeting 103, is based on the relevant NOAEL of 60.7 mg/kg bw per day from the 13-week study in rats, applying an uncertainty factor (UF) of 100. Local effects were also observed in the developmental studies, triggering a maternal local NOAEL of 1 mg/kg bw per day for both rats and rabbits but were regarded as a no suitable basis to set an ARfD, as related to the administration via gavage of a corrosive active substance (unlikely condition for consumers, considering that

concentration of DDAC administered by gavage is higher than the concentration when administered by the diet)

Table 2-6: Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	UF
Didecyldimethylammonium chloride (DDAC)					
ADI	EMS and EFSA PPR meeting 103	2012	0.1 mg/kg bw per day	1-year dog	100
ARfD			0.61 mg/kg bw	13-week rat	100
ADI/ARfD	EFSA	2008	Not allocated due to the intended uses and gaps on the specifications of the a.s.		

These toxicological reference values should however be considered as indicative only since the concerns on the specifications of the active substance identified in the peer review have not been solved yet. As long as the following questions are not addressed satisfactorily, the ADI and ARfD values can be considered only as indicative:

- What was the purity of the active substance tested in the individual toxicological studies?
- What was the composition of the active substance tested with regard to the alkyl-chains?
- Does the alkyl-chain have a significant impact on the toxicity of the substance?
- Is the active substance used in the plant protection product used in South Africa comparable with the active substance tested in the toxicological studies?

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 DDAC in primary crops was not evaluated in the framework of the peer review under Directive 91/414/EEC, as the representative uses were referring to non edible crops. A metabolism study conducted on tomato, apple and lemon was submitted and assessed by the EMS in the framework of this MRL application. Tomato, apple and citrus fruits received an application by dipping into an aqueous solution of ^{14}C-DDAC at the nominal concentrations of 12 and 24 g/hl (1N and 2N rate respectively) for 5 and 10 minutes. Samples were taken 1, 24, 72 and 168 hours after treatment. The overview of the 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** g a.s./hl	**No/ Interval**	**Sampling**	**Remarks**
Fruits and Fruiting vegetables	Tomato Apple Lemon	^{14}C on one of the didecyl chain	Dipping (5 and 10 min)	12 (1N) and 24 (2N)	1	1, 24, 72 &168 hours after dipping	

(a): Outdoor/field application (F) or glasshouse/protected crops/indoor application (G)

After treatment, TRRs in fruits were in the range of 0.84 to 3.17 mg/kg in the 1N dose level and 1.05 to 3.19 mg/kg in the 2N dose level for the 5 min dipping. A slight increase of the residue levels (*ca.* 10

to 20%) was observed for the 10 min dipping. At all sampling times and in all fruits, the majority of radioactivity was located at the surface or in the peel and identified to be mostly composed of DDAC (97 to 99% TRR). Although unidentified residues were exceeding the trigger value of 0.05 mg/kg for identification in whole lemon, the unidentified residue in the consumable part (flesh) was only 0.006 mg/kg which is below the trigger for identification or characterisation.

The period of 7 days covered by the metabolism study was considered acceptable by the RMS, assuming that the breakdown of DDAC will result in non toxicological relevant metabolites like linear fatty acids and amino compounds. The residue definitions for risk assessment and monitoring were therefore proposed as DDAC only. **However, since citrus might be stored over a much longer period, EFSA is of the opinion that data covering a storage over several months would be desirable**. As a first approach, EFSA proposes to use the residue definitions proposed by the EMS to derive the MRL value in the framework of this MRL application.

No specific residue definition has been set in Regulation (EC) No 396/2005. A default enforcement level of 0.5 mg/kg has been proposed for DDAC on food en feed commodities on a temporary basis (European Commission, 2012).

3.1.1.2. Magnitude of residues

In support of the MRL application, eight residue trials conducted in South Africa in 2009 and 2010 were submitted. Orange, mandarin and clementine fruits were treated by dipping for 5 minutes at dose rates of 6, 12 and 24 g/hl (0.5N, 1N and 2N). After this treatment, fruits were dried prior receiving an additional treatment by dipping for 40 seconds in a fungicide solution. Finally, oranges were coated with wax and dried before a first sampling for analyses. Remaining fruits were stored at +3°C until a second sampling 30 days after the treatment with DDAC.

An additional trial conducted in Australia in 2007 was submitted where oranges were treated by dipping in a DDAC solution at a dose rate of 12 g/hl for 3 minutes. Following this first treatment, a fungicide application was done by spraying. In all trials, fruits were analysed for pulp and peel separately and residue levels in whole fruit were derived by calculation.

EFSA is of the opinion that the experimental design of the South African trials is questionable, since the DDAC application was followed by a second dipping treatment in a fungicide solution which might have washed off DDAC to a certain extent from the treated fruits. Thus, in cases where citrus fruits do not undergo a second dipping treatment, the actual residues might be higher than the residues observed in the trials submitted. The doubts regarding the representativeness of these trials are underpinned by the fact that the residue levels in the South African trials (1.2 to 2.0 mg/kg) are much lower than those observed in the Australian trial (4.1 mg/kg) where the second application was done, not by dipping, but by spraying. **EFSA therefore concludes that additional information on the typical South African post harvest treatment practices has to be provided to decide whether the submitted trials are representative for the critical authorised GAPs.** In particular, it should be specified if the first application of DDAC by dipping might be, in some locations, followed by a second treatment by spraying. The duration of the dipping should also be reported.

The following assessment was performed under the assumption that the trials are valid and reflect the South African GAP. No significant differences were observed in the residue levels measured in orange or mandarin and clementine (U-test, 5%) and the data corresponding to the treatment at 12 g/hl were grouped together to derive an import tolerance proposal of 6 mg/kg for citrus.

Considering the South African trials, it is noted that an increase of the concentrations of DDAC in the dipping solution results in a non-proportional increase of the residue levels in fruits, as the mean levels in whole fruits were 1.1, 1.6 and 1.8 mg/kg for the respective dipping doses of 6, 12 and 24 g/hl.

The results of the residue trials, the related risk assessment input values (highest residue, median residue), and the import tolerance proposal are summarised in Table 3-2.

The storage stability of DDAC in primary crops was not investigated in the DAR under Directive 91/414/EEC, as this information was not required considering the uses supported in the peer review. Storage stability studies of incurred residues were therefore provided and assessed by the EMS in the framework of this MRL application. Residues of DDAC were found to be stable in orange flesh and peel samples for at least 9 months when stored frozen at -18°C. As the residue trial samples were stored under conditions for which integrity of the samples was demonstrated for a maximum period of 9 months, it is concluded that the residue data are valid with regard to storage stability.

According to the EMS, the analytical methods used to analyse the supervised residue trial samples have been sufficiently validated and were proven to be fit for purpose (The Netherlands, 2012).

Considering the available data, EFSA derives a MRL proposal of 6 mg/kg for the reported South African GAP for DDAC on citrus.

It should be highlighted that the current MRL into force for DDAC in citrus in South Africa is 2 mg/kg only. The requirement of an import tolerance of 6 mg/kg is therefore not consistent with the MRL value currently into force in South Africa.

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	Risk assessment					
Enforcement and risk assessment residue definition: DDAC									
Orange, mandarin and clementine	South Africa (8 trials) and Australia (1 trial)	Indoor (post-harvest)	**Whole fruit:** 1.2; 1.2; 1.6(f); 1.7(f); 1.8(f); 1.9(f); 2.0; 2.3(f); 4.1(g)	-	1.8	4.1	**6**	-	R_{ber}= 4.3 R_{max}= 4.6 MRL_{OECD} = 5.9/6.0
			Flesh: 0.09; 0.12; 0.04(f); 0.27(f); 0.32(f); 0.09(f); 0.50; 0.22(f); 1.00(g) (values in flesh sorted as for whole fruit)	-	0.22	1.0	-	-	

(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.
(c): 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): Residue level measured after a storage at *ca.* +3°C of 30 days (since higher than at day 0, just after at the dip-application).
(g): Australian trial with 1 dipping application of DDAC, followed by a spray application with a fungicide.

3.1.1.3. Effect of industrial processing and/or household preparation

The nature of DDAC residues under standard hydrolysis conditions was not investigated during the peer review and no information was provided in the framework of this application. The applicant refers to other compounds of similar structure such as chlormequat or mepiquat where no hydrolysis at high temperatures was observed. In addition it was argued that in case a hydrolysis would occur, the potential degradation products of DDAC would be free fatty acids and dimethyl-ammonium. These substances are considered of no toxicological concern since they may also evolve in the primary metabolism of DDAC (the Netherlands, 2012).

Studies to assess the magnitude of DDAC residues during the processing of citrus were provided. In addition, as samples from the residue studies were analysed for residues in pulp and peel separately, transfer factors were calculated for peel and pulp. The processing factors derived from these studies are summarised in the table 3-3 below.

Table 3-3: Overview of the available processing studies

Processed commodity	Number of studies	Median PF[(a)]	Median CF[(b)]	Comments
Enforcement residue definition: DDAC				
Whole citrus/peeled citrus	9	0.1	n.a.	9 studies but 39 individual values as different dose rates and sampling points were investigated in most of the studies.
Orange/juice	3	0.3	n.a.	3 studies with initial residue levels in whole fruit in the range of 2.1 to 3.9 mg/kg.
Orange/wet pomace	3	1.2	n.a.	
Orange/dry pomace	3	7.6	n.a.	

(a): The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.
(b): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

Transfer from whole fruit to flesh was derived from the entire dataset, considering the two different dose levels and the fruits collected 0 and 30 days after application, as no significant differences were observed. In particular, a similar distribution peel/flesh was observed at day 0 and after a storage period of 30 days (median PF 0.10 and 0.09 respectively). It can be therefore assumed that the storage period has no significant impact on the peel/flesh residue distribution.

3.1.2. Rotational crops

Since the current MRL application refers to the setting of an import tolerance and to a post-harvest use, investigations of residues in rotational crops are not required.

3.2. Nature and magnitude of residues in livestock

No data were submitted to assess the residue behaviour of DDAC in livestock animals, the applicant arguing that citrus treated with DDAC in South Africa and imported into Europe will predominantly be used as fresh fruit. Citrus pomace containing DDAC residues will therefore not be available for use as an animal feedstuff in Europe (the Netherlands, 2012).

According to EFSA it cannot be excluded that imported citrus are processed and the by-product (citrus pomace) used as animal feed. EFSA therefore calculated the livestock dietary exposure according to the agreed European methodology (EC, 1996), taking into account the expected residue concentration on citrus pomace. The calculated intakes exceeded the trigger value of 0.1 mg/kg DM for ruminants

(0.9 and 2.8 mg/kg DM for dairy and beef cattle, respectively), and therefore further data regarding the nature and magnitude of DDAC residues in livestock should be provided to finalise the overall assessment for the DDAC import tolerance request.

4. Consumer risk assessment

An indicative consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different sub-groups of the EU population [12] (EFSA, 2007).

For the calculation of the chronic exposure, EFSA used the median residue value derived for the edible part of the citrus (flesh) from the residue trials (see Table 3-2). For the other food commodities the enforcement level of 0.5 mg/kg defined in the EU guidelines (European Commission, 2012) was used as input value. Other sources of exposure are not taken into account.

The acute exposure assessment was performed with regard to the citrus fruits only, assuming the consumption of a large portion as reported in the national food surveys and considering the highest residue level observed in citrus flesh in residue trials. A variability factor accounting for the inhomogeneous distribution on the individual items consumed was included in the calculation (EFSA, 2007). For orange juice, a PF of 0.3 derived from the processing studies was included in the calculation (see table 3.3).

The input values used for the dietary exposure calculation are summarised in Table 4-1.

Table 4-1: Input values for the consumer dietary exposure assessment

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input value (mg/kg)	**Comment**	**Input value** (mg/kg)	**Comment**
Risk assessment residue definition: DDAC				
Citrus	0.22	Median residue in pulp	1.0	Highest residue in pulp
Orange juice	-	-	0.54 (1.8*0.3)	Median whole fruit * PF
Other commodities of plant and animal origin	0.5	Enforcement level according to EC guideline (EC, 2012)	The acute risk assessment was undertaken only with regard to the crops under consideration.	

The estimated exposure was then compared with the indicative toxicological reference values derived for DDAC (see Table 2-6). The results of the intake calculation are presented in Appendix B to this reasoned opinion.

According to the calculation of the expected long-term exposure, the exposure to DDAC residues via food does not exceed the indicative ADI derived on the basis of the available toxicological studies. The total calculated exposure accounted for up to 34% of the indicative ADI (FR toddler). The individual contribution of residues in citrus fruits to the total consumer exposure was low, accounting for less than 1% of the ADI.

[12] The calculation of the long-term exposure (chronic exposure) is based on the mean consumption data representative for 22 national diets collected from MS surveys plus 1 regional and 4 cluster diets from the WHO GEMS Food database; for the acute exposure assessment the most critical large portion consumption data from 19 national diets collected from MS surveys is used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007).

As regards the acute consumer exposure, the highest intake was identified for oranges (22% of the indicative ARfD for UK infants). For the other citrus fruits, the exposure (expressed in % of the indicative ARfD) ranged from 15% for grapefruit to 3% for limes. For orange juice the exposure amounted for 4% (DE, child).

EFSA concludes that the indicative consumer risk assessment did not identify a consumer health risk. However, this risk assessment is affected by a high degree of uncertainties which result from data gaps identified in the dossier. The following issues should be further addressed in order to reduce the overall uncertainty of the assessment:

- Deficiencies in the toxicological data provided which did not allow to derive definitive toxicological reference values (see section 2),
- Information on the authorised GAP in the country of origin (use of DDAC by dipping in combination with other dip or spray treatments and duration of the dipping),
- Information whether the residue trials provided with the application reflect the GAP in the country of origin (see also previous bullet point),
- Residue concentration in food of animal origin resulting from feed derived from citrus fruit treated with DDAC (see section 3.2),
- Residues on other food commodities resulting from the use of DDAC as biocide,
- Other possible sources of exposure.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Studies on mammalian toxicity were provided and discussed in the course of the peer review under Directive 91/414/EEC. However, no specifications could be established and confirmation could not be given that the batches used in the toxicological studies were of the same composition as the technical materiel. Taking into account the supported uses limited to ornamentals, dietary toxicological reference values were finally not proposed for DDAC. The toxicological studies were therefore reconsidered by the EMS in the framework of this MRL application and an ADI of 0.1 mg/kg bw per day and an ARfD of 0.61 mg/kg bw were proposed. Although not formally peer reviewed, these toxicological values were confirmed by the experts on mammalian toxicology during the Pesticides Peer Review expert meeting 103, held in Parma in May 2013. **However, these ADI and ARfD proposals should be considered as indicative only, as long as the concerns on the specifications of the active substance have not been solved**. As a first approach, EFSA proposes to use these ADI and ARfD values to conducted the consumer risk assessment in this MRL application.

The metabolism of DDAC in primary crops was not investigated in the course of the peer review. Metabolism study on citrus was submitted and assessed in the framework of this MRL application and the EMS proposed to define the residue for enforcement and risk assessment as DDAC. However, this metabolism covers a period of 7 days only while treated citrus might be stored over a much longer period and data covering a storage period of several months would be desirable. As a first approach, EFSA proposes to use the residue definitions proposed by the EMS to set the MRL value in this MRL application.

EFSA concluded that the submitted supervised residue trials require the setting of an import tolerance proposal of 6 mg/kg for citrus. However, additional information on the typical South African post-harvest treatment practice should be provided to decide whether the submitted trials are representative for the authorised GAP. In particular, it should be specified if the first application of DDAC by dipping might be followed by a second dipping or spray treatment with other pesticides. The QuEChERS method has been validated to analyse DDAC on high acid content matrices and therefore, an analytical method to enforce the proposed MRL of DDAC on citrus is available.

Studies investigating the nature of DDAC residues under standard hydrolysis conditions were not submitted. Several processing studies were provided and the data were sufficient to derive the following processing factors.

Whole citrus/Peeled citrus:	0.1
Orange/Orange juice:	0.3
Orange/Wet pomace:	1.2
Orange/Dry pomace	7.6

Since the proposed uses of DDAC is on imported crops and refers to post-harvest applications, investigations of residues in rotational crops are not required.

No data were submitted to assess the residue behaviour of DDAC in livestock animals, the applicant arguing that citrus treated with DDAC in South Africa and imported into Europe will predominantly be used as fresh fruit. Therefore, citrus pomace containing DDAC residues will not be available in Europe for use as an animal feedstuff. As it cannot be excluded that imported citrus will be processed, **EFSA is of the opinion that in accordance with the current EU data requirements data on the nature and magnitude of DDAC residues in livestock should be provided.**

The consumer risk assessment was performed with the revision 2 of the EFSA Pesticides Residues Intake Model (PRIMo). The calculation of chronic consumer exposure was estimated using the median residue level observed in the edible part of the citrus (flesh) and the default residue concentration of 0.5 mg/kg for all other food commodities as proposed in the EU guidelines (European Commission,

2012). Other sources of exposure are not taken into account. No long-term consumer intake concerns were identified for any of the European diets included in the EFSA PRIMo model, the highest calculated intake accounting for 34% (FR Toddler) of the ADI proposed at 0.1 mg/kg bw per day. The individual contribution of citrus fruits to the total consumer exposure was low, accounting for less than 1% of the ADI.

No acute consumer risk was identified in relation to the MRL proposal for citrus. The calculated maximum exposure in percentage of the ARfD was 22 % for orange (UK, infant) and 4% for orange juice (DE, child).

EFSA concludes that the consumer risk assessment did not identify a consumer health risk resulting from the post harvest uses of DDAC on citrus fruits. However it should be noted that the risk assessment is affected by a high degree of uncertainties which result from data gaps identified in the dossier in particular for the following issues:

- the deficiencies in the toxicological data referring to the specifications of the active substance,
- the representativeness of the residue trials,
- the possible residues in the products of animal origin,
- other possible sources of exposure, especially those resulting of the use of DDAC as biocide.

RECOMMENDATIONS

Code number[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed Import (mg/kg)	Justification for the proposal
Enforcement residue definition: DDAC				
110000	Citrus fruit	0.01*	6	The import tolerance proposal is supported by a sufficient number of trials, but further information on the post harvest treatment practices in South Africa are required. No risk was identified for consumers when the assessment is performed using the indicative toxicological reference values proposed for DDAC. The risk managers have to decide whether the setting of an import tolerance of 6 mg/kg is acceptable since the MRL currently into force on citrus in South Africa is 2 mg/kg only.

(a): According to Annex I of Regulation (EC) No 396/2005.
(*): Indicates that the MRL is set at the limit of analytical quantification.

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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	g as/hL min-max	Water L/ha min-max	kg a.s /ha min-max		
Citrus Fruits (Orange, Mandarin, Clementine)	South Africa	-	fungi and other microbes (green and blue mould, *Penicillium digitatum, Penicillium italicum Geotrichum candidum* including imazalil-resistant *Penicillium* populations)	SC	120 g/L	Dipping (post harvest application)	-	-	-	12 (120 ppm)	-	-	-	-

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. PESTICIDE RESIDUES INTAKE MODEL (PRIMO)

Didecyldimethylammonium chloride (DDAC)			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):		proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0.1**	ARfD (mg/kg bw):	**0.61**
Source of ADI:	**NL**	Source of ARfD:	**NL**
Year of evaluation:	**2012**	Year of evaluation:	**2012**

Prepare workbook for refined calculations

Undo refined calculations

Chronic risk assessment - refined calculations

TMDI (range) in % of ADI minimum - maximum	
5	34
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
34	FR toddler	22	PRODUCTS OF ANIMAL ORIGIN	9	VEGETABLES	1	CEREALS	
34	UK Infant	21	PRODUCTS OF ANIMAL ORIGIN	5	SUGAR PLANTS	3	VEGETABLES	
32	UK Toddler	12	PRODUCTS OF ANIMAL ORIGIN	11	SUGAR PLANTS	3	VEGETABLES	
30	NL child	16	PRODUCTS OF ANIMAL ORIGIN	6	VEGETABLES	3	Pome fruit	
27	DE child	12	PRODUCTS OF ANIMAL ORIGIN	6	Pome fruit	4	VEGETABLES	
27	FR infant	14	PRODUCTS OF ANIMAL ORIGIN	10	VEGETABLES	1	Pome fruit	
22	WHO Cluster diet B	7	VEGETABLES	6	CEREALS	4	PRODUCTS OF ANIMAL ORIGIN	
22	DK child	11	PRODUCTS OF ANIMAL ORIGIN	5	CEREALS	4	VEGETABLES	
18	SE general population 90th percentile	9	PRODUCTS OF ANIMAL ORIGIN	5	VEGETABLES	3	CEREALS	
16	ES child	9	PRODUCTS OF ANIMAL ORIGIN	3	CEREALS	2	VEGETABLES	
14	IE adult	5	VEGETABLES	3	CEREALS	3	PRODUCTS OF ANIMAL ORIGIN	
14	WHO cluster diet E	5	VEGETABLES	3	PRODUCTS OF ANIMAL ORIGIN	3	CEREALS	
14	WHO cluster diet D	5	VEGETABLES	4	CEREALS	4	PRODUCTS OF ANIMAL ORIGIN	
13	WHO regional European diet	5	PRODUCTS OF ANIMAL ORIGIN	5	VEGETABLES	2	CEREALS	
12	WHO Cluster diet F	4	PRODUCTS OF ANIMAL ORIGIN	4	VEGETABLES	3	CEREALS	
10	NL general	4	PRODUCTS OF ANIMAL ORIGIN	3	VEGETABLES	1	CEREALS	
9	ES adult	4	PRODUCTS OF ANIMAL ORIGIN	2	VEGETABLES	2	CEREALS	
9	UK vegetarian	2	SUGAR PLANTS	2	VEGETABLES	2	PRODUCTS OF ANIMAL ORIGIN	
9	FR all population	2	PRODUCTS OF ANIMAL ORIGIN	2	Berries & small fruit	2	VEGETABLES	
9	UK Adult	2	PRODUCTS OF ANIMAL ORIGIN	2	SUGAR PLANTS	2	VEGETABLES	
9	PT General population	3	VEGETABLES	3	CEREALS	1	Berries & small fruit	
8	DK adult	4	PRODUCTS OF ANIMAL ORIGIN	2	VEGETABLES	1	CEREALS	
8	LT adult	3	PRODUCTS OF ANIMAL ORIGIN	3	VEGETABLES	1	CEREALS	
8	IT kids/toddler	4	CEREALS	2	VEGETABLES	1	Pome fruit	
7	FI adult	3	PRODUCTS OF ANIMAL ORIGIN	1	VEGETABLES	1	CEREALS	
6	IT adult	3	CEREALS	2	VEGETABLES	1	Pome fruit	
5	PL general population	3	VEGETABLES	1	Pome fruit	0	Berries & small fruit	

Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.

A long-term intake of residues of Didecyldimethylammonium chloride (DDAC) is unlikely to present a public health concern.

	Acute risk assessment /children - refined calculations						Acute risk assessment / adults / general population - refined calculations					
	The acute risk assessment is based on the ARfD.											
	For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.											
	In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used. In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3.											
	Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**		---	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**		---
	IESTI 1	***)**	****)**	**IESTI 2**	***)**	****)**	**IESTI 1**	***)**	****)**	**IESTI 2**	***)**	**)
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	22	Oranges	1 / -	16	Oranges	1 / -	4	Oranges	1 / -	3	Oranges	1 / -
	15	Grapefruit	1 / -	15	Grapefruit	1 / -	3	Grapefruit	1 / -	2	Grapefruit	1 / -
	9	Mandarins	1 / -	7	Mandarins	1 / -	2	Mandarins	1 / -	2	Mandarins	1 / -
	6	Lemons	1 / -	4	Lemons	1 / -	1	Lemons	1 / -	1	Lemons	1 / -
	3	Limes	1 / -	2	Limes	1 / -	1	Limes	1 / -	1	Limes	1 / -
	No of critical MRLs (IESTI 1)			---			**No of critical MRLs (IESTI 2)**			---		
Processed commodities	**No of commodities for which ARfD/ADI is exceeded:**		---				**No of commodities for which ARfD/ADI is exceeded:**		---			
			*****)**						*****)**			
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)				Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)			
	4	Orange juice	0.54 / -				1	Orange juice	0.54 / -			
	*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported. **) pTMRL: provisional temporary MRL ***) pTMRL: provisional temporary MRL for unprocessed commodity											
	Conclusion: For Didecyldimethylammonium chloride (DDAC) IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available. No exceedance of the ARfD/ADI was identified for any unprocessed commodity. For processed commodities, no exceedance of the ARfD/ADI was identified.											

ABBREVIATIONS

ADI	acceptable daily intake
ARfD	acute reference dose
a.s.	active substance
BBCH	growth stages of mono- and dicotyledonous plants
BfR	Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment, *German*)
bw	body weight
CEN	European Committee for Standardisation (Comité Européen de Normalisation, *French*)
CF	conversion factor for enforcement residue definition to risk assessment definition
CIPAC	Collaborative International Pesticide Analytical Council
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DAR	Draft Assessment Report
DAT	days after treatment
DM	dry matter
EC	European Community
EFSA	European Food Safety Authority
EMS	evaluating Member State
EU	European Union
EURL	EU Reference Laboratory (former CRL)
FAO	Food and Agriculture Organisation of the United Nations
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (former GIFAP)
GS	growth stage
ha	hectare
hL	hectolitre
HR	highest residue
i.e.	that is (id est, *Latin*)
ILV	independent laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
kg	kilogram
L	litre
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observed adverse effect level
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States
MS/MS	tandem mass spectrometry
NOAEL	no observed adverse effect level

OECD	Organisation for Economic Co-operation and Development
PF	processing factor
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (method)
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
RAC	raw agricultural commodity
RD	residue definition
RMS	rapporteur Member State
SC	suspension concentrate
SCFCAH	Standing Committee on Food Chain and Animal Health
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organisation