REASONED OPINION

EFSA Journal

ADOPTED: 9 November 2021

doi: 10.2903/j.efsa.2021.6950

Modification of the existing maximum residue levels for dodine in citrus fruits

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Arysta LifeScience (ALS) Benelux SPRL submitted a request to the competent national authority in Spain to modify the existing maximum residue level (MRL) for the active substance dodine in citrus fruits. The data submitted in support of the request were found to be sufficient to derive MRL proposals for the group of citrus fruits. Adequate analytical methods for enforcement are available to control the residues of dodine in the commodities under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg. In animal matrices, no enforcement method is available for fat, muscle and milk whereby in liver and kidney dodine can be enforced at the LOQ of 0.01 mg/kg however an interlaboratory validation (ILV) is still required. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the uses of dodine according to the reported agricultural practices is unlikely to present a risk to consumer health.

Keywords: dodine, citrus fruits, fungicide, MRL, consumer risk assessment

Requestor: European Commission

Question number: EFSA-Q-2020-00387

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Acknowledgments: EFSA wishes to thank: Stathis Anagnos, Laszlo Bura, Aija Kazocina, Andrea Mioč, Marta Szot, Aikaterini Vlachou for the support provided to this scientific output.

Suggested citation: EFSA (European Food Safety Authority), Bellisai G, Bernasconi G, Brancato A, Carrasco Cabrera L, Ferreira L, Giner G, Greco L, Jarrah S, Leuschner R, Magrans JO, Miron I, Nave S, Pedersen R, Reich H, Ruocco S, Santos M, Scarlato AP, Theobald A, Vagenende B and Verani A, 2021. Reasoned Opinion on the modification of the existing maximum residue levels for dodine in citrus fruits. EFSA Journal 2021;19(11):6950, 26 pp. https://doi.org/10.2903/j.efsa.2021.6950

ISSN: 1831-4732

The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.

Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Arysta LifeScience (ALS) Benelux SPRL submitted an application to the competent national authority in Spain (evaluating Member State, EMS) to modify the existing maximum residue level (MRL) for the active substance dodine in citrus fruits. The EMS 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 the European Food Safety Authority (EFSA) on 14 May 2020. To accommodate for the intended uses of dodine, the EMS proposed to raise the existing MRL from the limit of quantification (LOQ) 0.01 to 1.5 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL Regulation. EFSA identified data gaps, for which information was requested from the EMS. On 30 August 2021 the EMS submitted a revised evaluation report, which replaced the previously submitted evaluation report.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC, the data evaluated under previous MRL assessment and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of dodine following foliar application was investigated in crops belonging to the group of fruit crops (apples, strawberries and pecans). Studies investigating the effect of processing on the nature of dodine (hydrolysis studies) demonstrated that dodine is stable. As the proposed uses of dodine are on permanent crops, an investigation of residues in rotational crops is not required.

Based on the metabolic pattern identified in metabolism studies and hydrolysis studies, the residue definitions for fruit crops were proposed as dodine for enforcement and risk assessment (tentative for nuts). These residue definitions are applicable to primary fruit crops and processed products.

EFSA concluded that for the crops assessed in this application, metabolism of dodine in primary crops and the possible degradation in processed products has been sufficiently addressed and that the previously derived residue definitions are applicable for citrus fruits.

Sufficiently validated analytical methods based on high-performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) are available to quantify residues in the commodities assessed in this application according to the enforcement residue definition. The methods enable quantification of dodine residues at or above the LOQ of 0.01 mg/kg in the commodities assessed (acidic matrix).

The available residue trials are sufficient to derive an MRL proposal of 1.5 mg/kg for the group of citrus fruits.

Processing factors (PF) for the crops under assessment were derived from processing studies provided and are recommended to be included in Annex VI of Regulation (EC) No 396/2005 as follows:

- Orange/pulp: 0.17
- Orange/peel: 3.0
- Orange/dried slices: 2.66
- Orange/juice: 0.69
- Orange/wet pomace: 0.69
- Mandarin/pulp: 0.18
- Mandarin/peel: 2.63
- Orange/marmalade: 0.06
- Orange/orange oil: 37.4

As a by-product of citrus fruits is used as feed item, a potential carry-over into food of animal origin was assessed. The calculated livestock dietary burden exceeded the trigger value of 0.1 mg/kg dry matter (DM) for all relevant animal species with exception of poultry.

The contribution of dodine residues in the commodities under consideration in this MRL application to the total livestock exposure was overall below the animal dietary burden of the previous assessment performed in the MRL review with exception of pigs where the trigger value was exceeded.

The nature and magnitude of dodine residues in livestock has been investigated during the MRL review and the residue definition for enforcement and risk assessment was proposed in ruminant commodities *by default* as dodine. In this assessment, these residue definitions were considered applicable for pigs by extrapolation because the metabolism of dodine in ruminants is similar to that in rats. A modification of the existing MRLs set at the LOQ of 0.01 mg/kg for commodities of animal origin was considered unnecessary.

It is to be noted that fully validated methods for enforcement of dodine in animal commodities are not available. No enforcement method is available for fat, muscle, and milk. In liver and kidney dodine can be enforced at the LOQ of 0.01 mg/kg, however an interlaboratory validation (ILV) is still required.

The toxicological profile of dodine was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.1 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.1 mg/kg bw.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo).

The consumer risk assessment did not identify concerns from acute exposure to dodine for grapefruits, oranges, lemons, limes and mandarins (with 12%; 21%; 5%; 3% and 9% of the ARfD, respectively). The total calculated chronic intake accounted for a maximum of 6% of the ADI (GEMS/ Food G08 diet) with the highest contribution of oranges (0.16% of the ADI), whereby the contributions of the other commodities belonging to citrus fruits was below 0.1%.

EFSA concluded that the proposed uses of dodine on citrus crops will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers' health.

EFSA proposes to amend the existing MRLs as reported in the summary table below.

Full details of all end points and the consumer risk assessment can be found in Appendices B to D.

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Dodine				
0110010	Grapefruits	0.01*	1.5	The submitted data are sufficient to derive MRL proposals for the SEU uses. Risk for consumers unlikely.
0110020	Oranges	0.01*	1.5	
0110030	Lemons	0.01*	1.5	
0110040	Limes	0.01*	1.5	
0110050	Mandarins	0.01*	1.5	
0110990	Other citrus fruits	0.01*	1.5	

MRL: maximum residue level; SEU: southern Europe.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.

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Assessment

The European Food Safety Authority (EFSA) received an application to modify the existing maximum residue level (MRL) for dodine in citrus fruits. The detailed description of the intended uses of dodine, which are the basis for the current MRL application, is reported in Appendix A.

Dodine is the ISO common name for 1-dodecylguanidinium acetate (IUPAC). The chemical structures of the active substance and its main metabolite are reported in Appendix E.

Dodine was evaluated in the framework of Directive 91/414/EEC[1] with Portugal designated as rapporteur Member State (RMS) for the representative uses as a foliar treatment on apples, pears, peaches and cherries. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (2010). Dodine was approved[2] for the use as fungicide on 1 June 2011.

The EU MRLs for dodine are established in Annexes II of Regulation (EC) No 396/2005[3]. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed (EFSA, 2015) and the proposed modifications have been implemented in the MRL legislation.[4]

In accordance with Article 6 of Regulation (EC) No 396/2005, Arysta LifeScience (ALS) Benelux SPRL submitted an application to the competent national authority in Spain (evaluating Member State, EMS) to modify the existing MRL for the active substance dodine in citrus fruits. The EMS 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 14 May 2020. To accommodate for the intended uses of dodine, the EMS proposed to raise the existing MRL from the limit of quantification (LOQ) of 0.01 to 1.5 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified data gaps, which were requested from the EMS. On 30 August 2021, the EMS submitted a revised evaluation report (Spain, 2020), which replaced the previously submitted evaluation report.

EFSA based its assessment on the evaluation report submitted by the EMS (Spain, 2020), the DAR and its addendum (Portugal, 2006, 2009) prepared under Council Directive 91/414/EEC, the Commission review report on dodine (European Commission, 2010c), the conclusion on the peer review of the pesticide risk assessment of the active substance dodine (EFSA, 2010), as well as the reasoned opinion on the review of the existing MRLs for dodine according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2015).

For this application, the data requirements established in Regulation (EU) No 544/2011[5] and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1996, 1997a–g, 2000, 2010a,b, 2017a,b; OECD, 2008, 2011, 2013). 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[6].

A selected list of end points of the studies assessed by EFSA in the framework of this MRL application including the end points of relevant studies assessed previously, is presented in Appendix B.

The evaluation report submitted by the EMS (Spain, 2020) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion.

[1] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32.

[2] Commission Directive 2011/9/EU of 1 February 2011 amending Council Directive 91/414/EEC to include dodine as active substance and amending Decision 2008/934/EC. OJ L 28, 2.2.2011, p. 36–39.

[3] Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

[4] For an overview of all MRL Regulations on this active substance, please consult: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=search.as

[5] Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.

[6] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.

1. Residues in plants

1.1. Nature of residues and methods of analysis in plants

1.1.1. Nature of residues in primary crops

The metabolism of dodine was investigated in the framework of the EU pesticides peer review under Directive 91/414/EEC (EFSA, 2010) and in the framework of the MRL review (EFSA, 2015). Metabolism of dodine in primary crops was investigated for foliar applications on fruits and fruiting vegetables (apples, strawberries, pecans) using ^{14}C-labelled dodine. While the metabolic pattern of dodine was shown to be similar, parent dodine was predominant in apples and strawberries, while in nutmeat, metabolite guanidine was the major compound recovered. Thus, the residue definition for monitoring and risk assessment was defined as dodine only, with exception of nuts (EFSA, 2010, 2015).

For the intended uses on citrus crops, the metabolic behaviour of dodine in primary crops is considered as sufficiently addressed.

1.1.2. Nature of residues in rotational crops

As the proposed uses of dodine are on permanent crops, an investigation of residues in rotational crops is not required.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of dodine was investigated in the framework of the EU pesticides peer review (EFSA, 2010). Dodine is hydrolytically stable under the representative processing conditions of pasteurisation, baking, brewing, boiling, and sterilisation.

1.1.4. Methods of analysis in plants

Analytical methods for the determination of dodine residues in plant commodities were assessed during the EU pesticides peer review under Directive 91/414/EEC (EFSA, 2010) and in the previously issued EFSA reasoned opinions (EFSA, 2013a,b, 2015).

The multi-residue QuEChERS method in combination with high-performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS), as described by CEN (2008), was reported for analysis of dodine in acidic commodities. However, recovery data of the method were provided by one laboratory only and were considered as too limited to conclude on the validity of this analytical method by the MRL review. Therefore, a data gap was set by the MRL review for a fully validated analytical enforcement method for dodine in high acid commodities (EFSA, 2015).

A new analytical HPLC–MS/MS method for the determination of dodine residues and its interlaboratory validation (ILV) was submitted with the current MRL application (Spain, 2020). The method monitors two mass transitions and is considered sufficiently validated for the analysis of dodine in citrus fruits (commodities under consideration) at or above the LOQ of 0.01 mg/kg.

EFSA concludes that the data gap identified during the MRL review was fully addressed. Mean recoveries for dodine of 82–86% were reported with an overall mean recovery for dodine being in the range of 70–110% and a relative standard deviation of less or equal to 20% (Spain, 2020). It is to be noted that the extraction efficiency for the analytical methods applied for enforcement and used for the residue trials is not proven according to the requirements of the extraction efficiency guidance (European Commission, 2017b). Further investigation on this matter would in principle be required. EFSA would therefore recommend reconsidering this point in the framework of the peer review for the renewal of approval of the active substance.

1.1.5. Storage stability of residues in plants

The storage stability of dodine in plants stored under frozen conditions was investigated in the framework of previous EFSA assessments (EFSA, 2010, 2013b). Dodine residues were shown to be stable for up to 18 months when stored frozen at –18°C in high water content matrices (apples, peaches, cherries) (EFSA, 2010). Moreover, storage stability of dodine was demonstrated for a period of 9 months at –20°C in high oil content commodities (peanuts) (EFSA, 2013b).

The MRL review noted that no storage stability data in high acid content commodities were available and it was concluded that the need for a storage stability study in acidic commodities was a minor data gap considering that the storage stability in plant commodities has been demonstrated for at least 9 months (EFSA, 2015).

With this application, an interim report covering 12 months of an ongoing 24 months storage stability study on dodine in orange peel, orange pulp, apples, dry beans, carrots and olives was provided which demonstrated that dodine is stable in all commodities studied at the set freezer temperature of –20°C (Spain, 2020).

EFSA concludes that the interim data are considered as sufficient to support stability of dodine in the frame of this application by noting a minor deficiency regarding two residue trials on mandarins which were stored for 14 months and the fact that the storage stability study covering 24 months is still ongoing. Therefore, a full study report while in principle still required is considered as desirable (see Section 1.2.1).

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in metabolism studies, the results of the hydrolysis studies, and the capabilities of enforcement analytical methods, the following residue definitions were proposed for fruit crops (EFSA, 2015):

- residue definition for risk assessment: dodine (for fruit crops; tentative for nuts).
- residue definition for enforcement: dodine (for fruit crops, tentative for nuts).

The same residue definitions are applicable to processed products.

The residue definition for enforcement set in Regulation (EC) No 396/2005 is identical with the above-mentioned residue definition. EFSA concluded that these residue definitions are appropriate for commodities of the group of citrus fruits.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

The intended Good Agricultural Practice (GAP) is on grapefruits, oranges, lemons, limes and mandarins: southern Europe (SEU) foliar use, 1–2 × 680 g a.s./ha, preharvest interval (PHI) 21 days (Appendix A).

In support of the intended SEU foliar use of dodine on citrus crops, the applicant submitted 17 GAP-compliant SEU trials on oranges (eight trials) and mandarins (nine trials) which were all performed in Italy and Spain from 2015 to 2018. Four residue trials on oranges of the 2015 (two trials), 2016 (one trial) and 2017 (one trial) growing seasons and four trials on mandarins of the 2015 (one trial), 2016 (one trial), 2017 (one trial) and 2018 (one trial) growing seasons represented decline trials. The residue data are summarised in Appendix B.1.2.1.

The samples were analysed for dodine according to the residue definitions for enforcement and risk assessment. According to the assessment of the EMS, the methods used were sufficiently validated and fit for purpose (Spain, 2020).

The samples of these residue trials were stored under conditions for which integrity of the samples has been demonstrated with exception of two residue trials on mandarins which were stored for 14 months, however since no degradation was observed for 12 months this is considered as a minor deficiency only (see also Section 1.1.5). Therefore, provision of the results of the full 24 months storage stability study upon finalisation is only desirable.

The applicant proposed to combine available residue data on oranges and on mandarins and to extrapolate to the whole group of citrus fruits. According to the EU guidance document (European Commission, 2017a), such an extrapolation is acceptable and is sufficiently supported by residue data. An MRL proposal of 1.5 mg/kg is thus derived for the whole group of citrus fruits.

1.2.2. Magnitude of residues in rotational crops

Citrus fruits represent permanent crops and are not expected to be grown in rotation with other plants. Therefore, no studies on the magnitude of residues of dodine in rotational crops are required in the framework of this application (OECD, 2007).

1.2.3. Magnitude of residues in processed commodities

Studies investigating the magnitude of dodine in processed oranges and mandarins were provided for this application (Spain, 2020).

Three processing studies on oranges covering dried orange slices, orange oil, pasteurised marmalade, pasteurised orange juice and wet pomace, compliant with the GAP of the intended use allowed deriving robust processing factors. Furthermore, data on dodine residues in oranges (8 GAP-compliant trials) and mandarins (9 GAP-compliant trials), on whole fruits, peel and pulp are provided which allow deriving robust peeling factors.

Processing studies demonstrated that pasteurisation and cooking (orange juice, marmalade and wet pomace) lead to a reduction, whereby drying (dried orange slices) and orange oil preparation lead to a concentration of the residues in the processed products (see Appendix B.1.2.3).

The number and quality of the processing studies is sufficient to derive robust peeling factors on oranges and mandarins and robust processing factors on orange juice, orange marmalade, orange wet pomace, dried oranges and orange oil which are recommended to be included in Annex VI of Regulation (EC) No 396/2005.

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for the commodities under evaluation (see Appendix B.1.2.1).

It is concluded that an MRL of 1.5 mg/kg in citrus fruits is appropriate to accommodate for the SEU uses of dodine on citrus crops.

In Section 3, EFSA assessed whether residues on citrus fruits resulting from the intended uses are likely to pose a consumer health risk.

2. Residues in livestock

The intended uses of dodine on citrus crops relate to citrus dried pulp, a feed item which might have an impact on the residues expected in food of animal origin. Hence, it was necessary to update the previous dietary burden calculation for livestock assessed during the MRL review (EFSA, 2015).

The input values for the exposure calculations for livestock are presented in Appendix D.1. The results of the dietary burden calculation demonstrated that the exposure of poultry did not exceed the trigger values defined in the relevant guidance document (European Commission, 1996). However, it exceeded the trigger values in meat and dairy ruminants and pigs (see Appendix B.2). Further investigation of residues is therefore only required in these groups of livestock.

It is to be noted that for meat and dairy ruminants the dietary burden remained below the calculations of the previous assessment in the MRL review (EFSA, 2015), whereby for pigs, dried citrus pulp as main contributor to the diet lead to an exceedance of the trigger value which was not the case in the previous assessment.

The nature of dodine residues in commodities of animal origin was investigated in the framework of the EU pesticides peer review under Directive 91/414/EEC (EFSA, 2010) and by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) (FAO, 2003). One metabolism study performed on lactating goats with ^{14}C-labelled dodine has been reported. The characteristics of this study are summarised in Appendix B.2.1.1.

Lactating goat was dosed with 0.4 mg/kg body weight (bw) per day of dodine, corresponding to approximately 20 times the calculated exposure of cattle which remains below the exposure derived in the previous EFSA assessment (EFSA, 2015). Considering the total radioactive residues (TRRs) calculated for the different goat matrices on a 1N dose rate basis, it was concluded previously by EFSA that the total residues in edible tissues of ruminants and milk are expected to be very low, and therefore no residue definitions and MRLs were proposed for products of animal origin (EFSA, 2010, 2015). This conclusion is considered also relevant for pigs by noting that an extrapolation from ruminant to pigs is possible, because the metabolism of dodine in ruminants is similar to rats and the calculated dietary burden is lower than that of cattle.

The data gap identified in the MRL review on the analytical methods in livestock commodities, is still open (EFSA, 2015). Namely, that dodine can be enforced in liver and kidney with an LOQ of 0.01 mg/kg, whereby an ILV of the method is missing and is still required. A fully validated analytical method for dodine in milk, fat, and muscle is missing and is required (EFSA, 2015).

It can be concluded that the conclusions reached in previous EFSA assessments are still valid in the context of this application.

3. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 3.1 of the EFSA PRIMo (EFSA, 2019). This exposure assessment model contains food consumption data for different sub-groups of the EU population and allows the acute and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (EFSA, 2018). The calculations were based on the highest residue (HR) or median residue values (STMR) derived from supervised field trials and the complete list of input values can be found in Appendix D.2. For citrus fruits, a median peeling factor of 0.17, derived from a combined data set on oranges and mandarins, was applied (see Appendix B.1.2.3).

The toxicological profile of dodine was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.1 mg/kg bw per day and an acute reference dose (ARfD) of 0.1 mg/kg bw (European Commission, 2010c).

The short-term exposure did not exceed the ARfD for any of the commodities assessed in this application (see Appendix B.3). The consumer risk assessment did not identify concerns from acute exposure to dodine for the commodities in the group of citrus fruits, namely grapefruits, oranges, lemons, limes and mandarins (12%; 21%; 5%; 3% and 9% of the ARfD, respectively).

For the calculation of the chronic exposure to dodine from citrus fruits (grapefruits, oranges, lemons, limes and mandarins, including other citrus fruits), EFSA used the STMR value for citrus fruits as derived by residue trials (combined dataset on oranges and mandarins) (see Sections 1.2.1 and B.1.2.1). For the remaining crops, the STMR values as reported by the MRL review were used as input values (EFSA, 2015) which included a review of the Codex MRLs implemented in the EU MRL legislation and the STMR values derived by JMPR were taken into account in the risk assessment process (FAO, 2003; EFSA, 2015). MRLs for blueberries, cranberries, currants, gooseberries and celery, which were lowered to the LOQ of 0.01 mg/kg in the Commission Regulation (EU) 2016/1002[7], were not considered in the calculations.

No concerns from long-term exposure to dodine were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated intake accounted for a maximum of 6% of the ADI (GEMS/Food G08 diet). The contribution of residues in grapefruits, oranges, lemons, limes and mandarins was low (0.03% of ADI for IE adult diet, 0.16% of ADI for DE child diet, 0.02% of ADI for GEMS/Food G11 diet, 0.002% of ADI for IE adult diet and 0.03% of ADI for FR toddler 2 diet, respectively).

EFSA concluded that the long-term intake of residues of dodine resulting from the existing and the intended uses is unlikely to present a risk to consumer health.

For further details on the exposure calculations, a screenshot of the Report sheet of the PRIMo is presented in Appendix C.

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found to be sufficient to derive an MRL proposal for the group of citrus fruits.

EFSA concluded that the proposed uses of dodine on citrus crops (grapefruits, oranges, lemons, limes, mandarins and other) will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers' health.

The MRL recommendations are summarised in Appendix B.4.

It is to be noted that:

- an intermediate report of the storage stability study (results at 12 months instead of 24 months) was submitted and deemed sufficient for the current assessment. However, the final report of this storage stability (results at 24 months) would be desirable for future applications;
- data gaps for the method of enforcement in animal commodities highlighted by the MRL review are still relevant.

[7] Commission Regulation (EU) 2016/1002 of 17 June 2016 amending Annexes II, III and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for AMTT, diquat, dodine, glufosinate and tritosulfuron in or on certain products. OJ L 167, 24.6.2016, p. 1–45.

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Abbreviations

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CAC	Codex Alimentarius Commission
CXL	Codex maximum residue limit
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{90}	period required for 90% dissipation (define method of estimation)
EMS	evaluating Member State
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GC-MS	gas chromatography with mass spectrometry
HPLC-MS/MS	high-performance liquid chromatography with tandem mass spectrometry
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
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
LC	liquid chromatography
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States
MS/MS	tandem mass spectrometry detector
MW	molecular weight
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PBI	plant-back interval
PF	processing factor
PHI	preharvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RA	risk assessment
RAC	raw agricultural commodity
RD	residue definition
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SC	suspension concentrate
SEU	southern Europe
STMR	supervised trials median residue
TRR	total radioactive residue
WHO	World Health Organization

Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

Crop and/or situation	NEU SEU, MS or country	F G or I[a]	Pests or group of pests controlled	Preparation		Application				Application rate per treatment				PHI (days)[d]	Remarks
				Type[b]	Conc. a.s.	Method kind	Range of growth stages and season[c]	Number min-max	Interval between application (days) min	g a.s./hL min–max	Water (L/ha) min–max	Rate	Unit		
Grapefruits	SEU	F	*Altenaria alternata* f. sp. *citri* [ALTEAC]	SC	544.0 g/L	Foliar treatment – broadcast spraying	53–81	2	14	–	1,000–2,500	680	g a.s./ha	21	Max application rate per season 1360 g a.s./ha (680 g a.s./ha × 2)*
Oranges	SEU	F	*Altenaria alternata* f. sp. *citri* [ALTEAC]	SC	544.0 g/L	Foliar treatment – broadcast spraying	53–81	2	14	–	1,000–2,500	680	g a.s./ha	21	Max application rate per season 1,360 g a.s./ha (680 g a.s./ha × 2)*
Lemons	SEU	F	*Altenaria alternata* f. sp. *citri* [ALTEAC]	SC	544.0 g/L	Foliar treatment – broadcast spraying	53–81	2	14	–	1,000–2,500	680	g a.s./ha	21	Max application rate per season 1,360 g a.s./ha (680 g a.s./ha × 2)*
Limes	SEU	F	*Altenaria alternata* f. sp. *citri* [ALTEAC]	SC	544.0 g/L	Foliar treatment – broadcast spraying	53–81	2	14	–	1,000–2,500	680	g a.s./ha	21	Max application rate per season 1,360 g a.s./ha (680 g a.s./ha × 2)*
Mandarins	SEU	F	*Altenaria alternata* f. sp. *citri* [ALTEAC]	SC	544.0 g/L	Foliar treatment – broadcast spraying	53–81	2	14	–	1,000–2,500	680	g a.s./ha	21	Max application rate per season 1,360 g a.s./ha (680 g a.s./ha × 2)*
Other citrus fruits	SEU	F	*Altenaria alternata* f. sp. *citri* [ALTEAC]	SC	544.0 g/L	Foliar treatment – broadcast spraying	53–81	2	14	–	1,000–2,500	680	g a.s./ha	21	Max application rate per season 1,360 g a.s./ha (680 g a.s./ha × 2)*

NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; SC; suspension concentrate.
*: GAP confirmed with EMS.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.

Appendix B – List of end points

B.1. Residues in plants

B.1.1. Nature of residues and methods of analysis in plants

B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

Primary crops (available studies)	**Crop groups**	**Crops**	**Applications**	**Sampling (DAT)**	**Comment/Source**
	Fruit crops	Apples	Foliar spray; 3 × 0.90 kg a.s./ha	7	Radiolabelled active substance: phenyl-UL-^{14}C-guanidine. Only fruits were sampled (EFSA, 2010).
		Strawberries	Foliar spray; 4 × 3 kg a.s./ha	14	Radiolabelled active substance: phenyl-UL-^{14}C-guanidine. Only fruits were sampled (EFSA, 2010).
		Pecans	Foliar spray; 3 × 5.7 kg a.s./ha	9	Radiolabelled active substance: phenyl-UL-^{14}C-guanidine. At maturity, only fruits (nuts) were sampled (EFSA, 2010).

Rotational crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**PBI (DAT)**	**Comment/Source**
	Crops under evaluation are not expected to be grown in rotation. Further investigation of residues in rotational crops is therefore not required. The MRL review outlined that according to the laboratory degradation studies evaluated in the framework of the peer review, DT_{90} values of dodine range between 10.6 and 27.2 days (EFSA, 2015). These results are far below the trigger value of 100 days (EFSA, 2010). Moreover, no relevant soil metabolites were identified. According to the European guidelines on rotational crops (European Commission, 1997c), further investigation of residues in rotational crops is not required and relevant residues in rotational crops are not expected.				

Processed commodities (hydrolysis study)	**Conditions**	**Stable?**	**Comment/Source**
	Pasteurisation (20 min, 90°C, pH 4)	Yes	EFSA (2010)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	Yes	
	Sterilisation (20 min, 120°C, pH 6)	Yes	

Can a general residue definition be proposed for primary crops?	No	EFSA (2010, 2015)
Rotational crop and primary crop metabolism similar?	Not triggered	Intended uses are on permanent crops (Spain, 2020)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes	EFSA (2010)
Plant residue definition for monitoring (RD-Mo)	Fruit crops: dodine (tentative for nuts) (EFSA, 2015)	

Plant residue definition for risk assessment (RD-RA)	Fruit crops: dodine (tentative for nuts) (EFSA, 2015)
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)	High acid content commodities: HPLC–MS/MS, LOQ: 0.01 mg/kg; monitoring two mass transitions, confirmatory method and ILV available (Spain, 2020); Multi-residue QuEChERS HPLC–MS/MS method (CEN, 2008) considered not sufficiently validated (EFSA, 2015). High water content commodities: GC-MSD (with derivatisation), LOQ 0.05 mg/kg; confirmatory method: LC–MS/MS, LOQ 0.05 mg/kg; ILV available (EFSA, 2010); High oil content commodities: LC–MS/MS, LOQ: 0.01 mg/kg; ILV available (EFSA, 2013a).

DAT: days after treatment; a.s.: active substance; PBI: plant-back interval; MRL: maximum residue level; DT_{90}: period required for 90% dissipation; HPLC-MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; GC–MS: gas chromatography with mass spectrometry; LC–MS/MS: liquid chromatography with tandem mass spectrometry.

B.1.1.2. Stability of residues in plants

Plant products (available studies)	**Category**	**Commodity**	**T (°C)**	**Stability period**		**Compounds covered**	**Comment/Source**
				Value	**Unit**		
	High water content	Apples	–18/–20	18	Months	Dodine	EFSA (2010)
		Peaches	–18/–20	18	Months	Dodine	
		Cherries	–18/–20	18	Months	Dodine	
		Apples	–20	12	Months	Dodine	Twelve-month interim results of 2 years (24 months) ongoing storage stability study (Spain, 2020).
		Carrots	–20	12	Months	Dodine	
	High oil content	Peanuts	–20	9	Months	Dodine	EFSA (2013b)
		Olives	–20	12	Months	Dodine	Twelve-month interim results of 2 years (24 months) ongoing storage stability study (Spain, 2020).
	High protein content	Beans, dry	–20	12	Months	Dodine	
	Dry/High starch	–	–	–	–	–	–
	High acid content	Orange, pulp	–20	12	Months	Dodine	Twelve-month interim results of 2 years (24 months) ongoing storage stability study (Spain, 2020).
	Processed products	Apple, juice	–18/–20	18	Months	Dodine	EFSA (2010)
		Apple, wet pomace	–18/–20	18	Months	Dodine	
	Others	Orange, peel	–20	12	Months	Dodine	Twelve-month interim results of 2 years (24 months) ongoing storage stability study (Spain, 2020).

B.1.2. Magnitude of residues in plants

B.1.2.1. Summary of residues data from the supervised residue trials

Commodity	Region[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)
Citrus fruits	SEU	0.10[d]; 0.13; 0.15; 0.17[d]; 0.2; 0.23; 0.23; 0.24; 0.24, 0.29, 0.35; 0.35; 0.39; 0.65; 0.68; 0.79; 0.91	Combined data set with residue trials on oranges (8) and mandarins (9) (underlined), all compliant with GAP. Extrapolation to the whole group of citrus fruits possible (Spain, 2020). MRL_{OECD} = 1.5 mg/kg	**1.5**	0.91	0.24

MRL: maximum residue level; SEU: southern European Union; GAP: Good Agricultural Practice.
(a): SEU: Outdoor trials conducted in southern Europe.
(b): Highest residue. The highest residue for risk assessment refers to the whole commodity and not to the edible portion.
(c): Supervised trials median residue. The median residue for risk assessment refers to the whole commodity and not to the edible portion.
(d): Samples were stored for 14 months.

B.1.2.2. Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined and field rotational crop studies?	Not triggered. The intended uses are on permanent crops.

B.1.2.3. Processing factors

Processed commodity	Number of valid studies[a]	Processing Factor (PF)		Comment/ Source
		Individual values	Median PF	
Peeled oranges (pulp/whole fruit)	8	0.03; 0.1; 0.15; 0.17; 0.17; 0.21; 0.22; 0.23	0.17	Spain (2020)
Peel of oranges (peel/whole fruit)	8	2.46; 2.48; 2.8; 2.89; 3.0; 3.05; 3.38; 3.62	3.0	
Peeled mandarines (pulp/whole fruit)	9	0.1; 0.1; 0.13; 0.17; 0.18; 0.2; 0.21; 0.22; 0.24	0.18	
Peel of mandarines (peel/whole fruit)	9	2.51; 2.58; 2.60; 2.62; 2.63; 2.67; 2.76; 2.9; 3.1	2.63	
Peeling factor for citrus fruits[b] (pulp/ whole fruit)	17	0.03; 0.1; 0.1; 0.1; 0.13; 0.15; 0.17; 0.17; 0.17; 0.18; 0.20; 0.21; 0.21; 0.22; 0.22; 0.23; 0.24	0.17	
Orange, wet pomace	3	0.29; 0.69; 1.1	0.69	
Orange, pasteurised juice	3	0.5; 0.69; 0.74	0.69	
Orange, zest (process marmalade)	3	2.7, 3.23, 3.83	3.23	
Orange, pasteurised marmalade	3	0.06; 0.06; 0.1	0.06	
Orange, dried	3	1.94; 2.66; 3.2	2.66	
Orange, zest (process oil)	3	2.31; 3.46; 3.6	3.46	
Orange, oil	3	19.43; 37.4; 42.69	37.40	

(a): Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).
(b): Combined dataset of PF derived from oranges and mandarins to derive a common PF for all citrus fruits.

B.2. Residues in livestock

Dietary burden calculation according to OECD, 2013. Calculations performed with Animal model 2017[8]

Relevant groups	Dietary burden expressed in				Most critical diet[(a)]	Most critical commodity[(b)]		Trigger exceeded (Yes/No)	Previous assessment (EFSA, 2015)
	mg/kg bw per day		mg/kg DM					0.10	Max burden
	Median	Maximum	Median	Maximum				mg/kg DM	mg/kg DM
Cattle (all diets)	0.020	0.020	0.53	0.53	Beef cattle	Citrus	Dried pulp	Yes	0.57
Cattle (dairy only)	0.020	0.020	0.53	0.53	Dairy cattle	Citrus	Dried pulp	Yes	1.7
Sheep (all diets)	0.005	0.005	0.12	0.12	Lamb	Apple	Pomace, wet	Yes	0.57
Sheep (ewe only)	0.004	0.004	0.12	0.12	Ram/Ewe	Apple	Pomace, wet	Yes	1.7
Swine (all diets)	0.009	0.009	0.40	0.40	Swine (breeding)	Citrus	Dried pulp	Yes	–
Poultry (all diets)	–	–	–	–	–	–	–	No	–
Poultry (layer only)	–	–	–	–	–	–	–	No	–

bw: body weight; DM: dry matter.
(a): When several diets are relevant (e.g. cattle, sheep and poultry 'all diets'), the most critical diet is identified from the maximum dietary burdens expressed as "mg/kg bw per day".
(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as 'mg/kg bw per day'.

B.2.1. Nature of residues and methods of analysis in livestock

B.2.1.1. Metabolism studies, methods of analysis and residue definitions in livestock

Livestock (available studies)	Animal	Dose (mg/kg bw per day)	Duration (days)	Comment/Source
	Laying hen	–	–	–
	Lactating ruminants	0.4	5	Lactating goat, ^{14}C-guanidine ring labelled dodine (EFSA, 2010)
	Pig	–	–	–
	Fish	–	–	–

[8] https://ec.europa.eu/food/plant/pesticides/max_residue_levels/guidelines_en

Time needed to reach a plateau concentration in milk and eggs (days)	Milk: 3–4 days	EFSA (2010)
	Eggs: –	Not relevant
Metabolism in rat and ruminant similar	Yes	EFSA (2010)
Can a general residue definition be proposed for animals?	No	EFSA (2015)
Animal residue definition for monitoring (RD-Mo)	For meat and dairy ruminants: dodine *by default* (EFSA, 2015) For pigs: dodine *by default* (current assessment based on EFSA (2015)) For poultry and poultry layers: not required (EFSA, 2015)	
Animal residue definition for risk assessment (RD-RA)	For meat and dairy ruminants: dodine *by default* (EFSA, 2015) For pigs: dodine *by default* (current assessment based on EFSA (2015)) For poultry and poultry layers: not required (EFSA, 2015)	
Fat soluble residues	No	EFSA (2010)
Methods of analysis for monitoring of residues (analytical technique, matrix, LOQs)	Milk, muscle, fat: no enforcement method available (EFSA, 2015) Liver and kidney: LC–MS/MS, LOQ: 0.01 mg/kg; validation data were provided for two transitions, the method is considered highly specific; ILV missing (EFSA, 2015).	

bw: body weight; LOQ: limit of quantification; LC–MS/MS: liquid chromatography with tandem mass spectrometry; ILV: independent laboratory validation.

B.3. Consumer risk assessment

ARfD	0.1 mg/kg bw (European Commission, 2010c)
Highest IESTI, according to EFSA PRIMo	Oranges: 21% of ARfD Grapefruits: 12% of ARfD Mandarins: 9% of ARfD Lemons: 5% of ARfD Limes: 3% of ARfD
Assumptions made for the calculations	The calculation is based on the highest residue levels according to the enforcement residue definition expected in whole citrus fruits as derived from the residue trials in the current assessment. For grapefruits, oranges, lemons, limes and mandarins, the derived peeling factor of 0.17 for the group of citrus fruits was applied. Calculations performed with PRIMo revision 3.1.

ADI	0.1 mg/kg bw per day (European Commission, 2010c)
Highest IEDI, according to EFSA PRIMo	6% of ADI (GEMS/FoodG08 diet) Contribution of crops assessed: Grapefruits: 0.03% of ADI (IE adult diet); Oranges: 0.16% of ADI (DE child diet); Lemons: 0.02% of ADI (GEMS/Food G11 diet); Limes: 0.002 of ADI (IE adult diet); Mandarins: 0.03% of ADI (FR toddler 2 diet)
Assumptions made for the calculations	The calculation is based on the median residue levels according to the enforcement residue definition expected in whole citrus fruits as derived from the residue trials in the current assessment, whereby for grapefruits, oranges, lemons, limes and mandarins the derived peeling factor of 0.17 for citrus fruits was applied. For the remaining commodities, the STMR values as derived in the MRL review (EFSA, 2015) were used as input values (whereby a peeling factor of 0.06 derived for bananas in a previous EFSA assessment was applied by the MRL review (EFSA, 2013a, 2015)), where the respective MRL recommendations were implemented in the legislation (Commission Regulation (EU) 2016/1002). For the remaining commodities, the MRL at the LOQ was used, where authorised uses were reported (EFSA, 2015). Calculations performed with PRIMo revision 3.1.

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; ADI: acceptable daily intake; IEDI: international estimated daily intake; STMR: supervised trials median residue; MRL: maximum residue level.

B.4. Recommended MRLs

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Dodine				
0110010	Grapefruits	0.01*	1.5	The submitted data are sufficient to derive MRL proposals for the SEU use. Risk for consumers unlikely.
0110020	Oranges	0.01*	1.5	
0110030	Lemons	0.01*	1.5	
0110040	Limes	0.01*	1.5	
0110050	Mandarins	0.01*	1.5	
0110990	Other citrus fruits	0.01*	1.5	

MRL: maximum residue level; SEU: southern Europe.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.

Appendix C – Pesticide Residue Intake Model (PRIMo)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Dodine

LOQs (mg/kg) range from: 0.01 to: 1.5

Toxicological reference values

ADI (mg/kg bw per day):	0.1	ARfD (mg/kg bw):	0.1
Source of ADI:	EC	Source of ARfD:	EC
Year of evaluation:	2010	Year of evaluation:	2010

Input values

Details – chronic risk assessment | Supplementary results – chronic risk assessment

Details – acute risk assessment/children | Details – acute risk assessment/adults

Comments:

Refined calculation mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	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	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	6%	GEMS/Food G08	6.11	5%	Olives for oil production	0.3%	Apples	0.3%	Table olives	0.1%	6%
	6%	ES child	5.91	5%	Olives for oil production	0.3%	Table olives	0.3%	Apples	0.2%	6%
	5%	NL toddler	4.99	3%	Apples	1%	Pears	0.6%	Milk: Cattle	0.6%	5%
	5%	DE child	4.61	3%	Apples	0.5%	Cherries (sweet)	0.3%	Olives for oil production	0.2%	5%
	3%	ES adult	3.49	3%	Olives for oil production	0.2%	Table olives	0.2%	Apples	0.1%	3%
	3%	GEMS/Food G06	3.17	2%	Olives for oil production	0.2%	Apples	0.2%	Table olives	0.0%	3%
	3%	GEMS/Food G10	3.13	2%	Olives for oil production	0.2%	Apples	0.1%	Table olives	0.1%	3%
	3%	GEMS/Food G07	2.68	2%	Olives for oil production	0.3%	Apples	0.2%	Table olives	0.1%	3%
	3%	NL child	2.54	1%	Apples	0.3%	Pears	0.3%	Olives for oil production	0.3%	3%
	3%	PT general	2.50	2%	Olives for oil production	0.4%	Table olives	0.3%	Apples		3%
	2%	GEMS/Food G11	2.35	2%	Olives for oil production	0.4%	Apples	0.2%	Table olives	0.1%	2%
	2%	GEMS/Food G15	2.12	1%	Olives for oil production	0.3%	Apples	0.2%	Table olives	0.1%	2%
	2%	FR child 3 15 yr	1.76	0.7%	Olives for oil production	0.4%	Apples	0.2%	Milk: Cattle	0.3%	2%
	2%	DE women 14-50 yr	1.72	0.6%	Apples	0.6%	Olives for oil production	0.2%	Cherries (sweet)	0.1%	2%
	2%	FR toddler 2 3 yr	1.68	0.8%	Apples	0.3%	Milk: Cattle	0.3%	Olives for oil production	0.3%	2%
	2%	DE general	1.61	0.6%	Apples	0.6%	Olives for oil production	0.1%	Milk: Cattle	0.1%	2%
	1%	UK infant	1.02	0.4%	Apples	0.4%	Milk: Cattle	0.1%	Cherries (sweet)	0.4%	1%
	1.0%	RO general	0.98	0.4%	Apples	0.2%	Table olives	0.2%	Cherries (sweet)	0.1%	1.0%
	1.0%	SE general	0.97	0.3%	Table olives	0.3%	Apples	0.1%	Milk: Cattle	0.2%	1.0%
	1.0%	DK child	0.97	0.6%	Apples	0.2%	Pears	0.1%	Milk: Cattle	0.2%	1.0%
	0.9%	IE adult	0.91	0.4%	Table olives	0.2%	Apples	0.1%	Pears	0.1%	0.9%
	0.8%	FR adult	0.85	0.4%	Olives for oil production	0.2%	Apples	0.0%	Milk: Cattle	0.1%	0.8%
	0.8%	UK toddler	0.81	0.4%	Apples	0.2%	Milk: Cattle	0.1%	Oranges	0.2%	0.8%
	0.8%	NL general	0.79	0.4%	Apples	0.1%	Olives for oil production	0.1%	Milk: Cattle	0.1%	0.8%
	0.8%	FR infant	0.76	0.4%	Apples	0.2%	Milk: Cattle	0.1%	Olives for oil production	0.2%	0.8%
	0.7%	PL general	0.70	0.5%	Apples	0.1%	Cherries (sweet)	0.1%	Pears		0.7%
	0.6%	LT adult	0.60	0.5%	Apples	0.0%	Pears	0.0%	Milk: Cattle	0.1%	0.6%
	0.6%	IT toddler	0.56	0.2%	Apples	0.1%	Cherries (sweet)	0.1%	Pears		0.6%
	0.5%	IT adult	0.50	0.2%	Apples	0.1%	Table olives	0.1%	Cherries (sweet)		0.5%
	0.5%	FI 3 yr	0.49	0.2%	Apples	0.1%	Table olives	0.1%	Olives for oil production		0.5%
	0.4%	DK adult	0.41	0.2%	Apples	0.1%	Pears	0.1%	Milk: Cattle	0.1%	0.4%
	0.3%	FI 6 yr	0.33	0.1%	Apples	0.1%	Olives for oil production	0.0%	Pears		0.3%
	0.3%	UK vegetarian	0.31	0.1%	Apples	0.0%	Table olives	0.0%	Oranges	0.0%	0.3%
	0.3%	FI adult	0.27	0.1%	Apples	0.1%	Table olives	0.0%	Oranges		0.3%
	0.2%	UK adult	0.21	0.1%	Apples	0.0%	Milk: Cattle	0.0%	Oranges	0.0%	0.2%
	0.1%	IE child	0.14	0.1%	Apples	0.0%	Milk: Cattle	0.0%	Cherries (sweet)	0.0%	0.1%

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Dodine is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

Acute risk assessment/children	Acute risk assessment/adults/general population
Details – acute risk assessment/children	Details – acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
66%	Pears	0.9/0.48	66
60%	Quinces	5/2.43	60
52%	Apples	0.9/0.48	52
38%	Table olives	20/11.2	38
34%	Medlar	5/2.43	34
26%	Cherries (sweet)	3/2.11	26
21%	Oranges	1.5/0.15	21
12%	Grapefruits	1.5/0.15	12
9%	Mandarins	1.5/0.15	9.2
8%	Olives for oil production	20/6.5	8.3
7%	Peaches	0.1/0.07	6.7
5%	Lemons	1.5/0.15	5.3
3%	Limes	1.5/0.15	3.1
2%	Apricots	0.1/0.07	2.4
2%	Bananas	0.5/0.02	1.5

Expand/collapse list

Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
37%	Quinces	5/2.43	37
21%	Cherries (sweet)	3/2.11	21
17%	Medlar	5/2.43	17
15%	Pears	0.9/0.48	15
13%	Apples	0.9/0.48	13
11%	Table olives	20/11.2	11
5%	Olives for oil production	20/6.5	5.0
5%	Oranges	1.5/0.15	4.7
3%	Mandarins	1.5/0.15	2.8
3%	Grapefruits	1.5/0.15	2.8
1%	Lemons	1.5/0.15	1.4
1%	Peaches	0.1/0.07	1.3
1%	Limes	1.5/0.15	1.1
0.8%	Apricots	0.1/0.07	0.76
0.4%	Milk: Cattle	0.01/0.01	0.39

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
14%	Apples/juice	0.9/0.25	14
13%	Oranges/juice	1.5/0.24	13
12%	Olives for oil production/oils	20/13	12
8%	Pears/juice	0.9/0.25	8.1
7%	Table olives/canned	20/6.5	7.3
5%	Quinces/jam	5/1.7	5.1
2%	Peaches/canned	0.1/0.07	1.8
0.8%	Peaches/juice	0.1/0.05	0.83
0.7%	Lemons/jam	1.5/0.24	0.73
0.0%	Limes/juice	1.5/0.24	0.02

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
8%	Apples/juice	0.9/0.25	8.3
8%	Table olives/canned	20/6.5	8.3
4%	Oranges/juice	1.5/0.24	3.6
3%	Grapefruits/juice	1.5/0.24	2.6
2%	Quinces/jam	5/1.7	2.1
0.6%	Peaches/canned	0.1/0.07	0.57
0.5%	Lemons/juice	1.5/0.24	0.46

Conclusion:
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short-term intake of residues of Dodine is unlikely to present a public health risk.
For processed commodities, no exceedance of the ARfD/ADI was identified.

Appendix D – Input values for the exposure calculations

D.1. Livestock dietary burden calculations

Feed commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: dodine				
Apple, wet pomace	0.66	STMR (0.25 mg/kg) × PF (2.63) (EFSA, 2015)	0.66	STMR (0.25 mg/kg) × PF (2.63) (EFSA, 2015)
Citrus, dried pulp	2.4	STMR × PF[(a)] (Appendix B.1.2.3)	2.4	STMR × PF[(a)] (Appendix B.1.2.3)

STMR: supervised trials median residue; PF: processing factor.
(a): The default processing factor of 10 was applied for citrus (dried pulp).

D.2. Consumer risk assessment

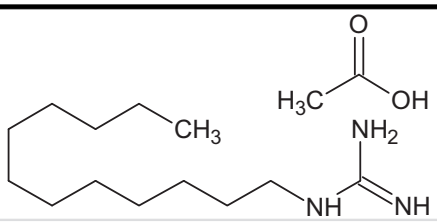
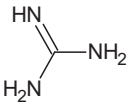
Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value (mg/kg)	Comment	Input value (mg/kg)	Comment[(a)]
Risk assessment residue definition: dodine						
Grapefruits	**1.5**	Proposed	0.04	STMR-RAC × PeF (0.17)	0.15	HR-RAC × PeF (0.17)
Oranges	**1.5**	Proposed	0.04	STMR-RAC × PeF (0.17)	0.15	HR-RAC × PeF (0.17)
Lemons	**1.5**	Proposed	0.04	STMR-RAC × PeF (0.17)	0.15	HR-RAC × PeF (0.17)
Limes	**1.5**	Proposed	0.04	STMR-RAC × PeF (0.17)	0.15	HR-RAC × PeF (0.17)
Mandarins	**1.5**	Proposed	0.04	STMR-RAC × PeF (0.17)	0.15	HR-RAC × PeF (0.17)
Other citrus fruits	**1.5**	Proposed	0.04	STMR-RAC × PeF (0.17)	–	–
Apples	0.9	EFSA (2015)	0.25	STMR-RAC	0.48	HR-RAC
Pears	0.9	EFSA (2015)	0.25	STMR-RAC	0.48	HR-RAC
Quinces	5	EFSA (2015)	1.7	STMR CXL (2005)	2.43	HR-RAC (CXL)
Medlar	5	EFSA (2015)	1.7	STMR CXL (2005)	2.43	HR-RAC (CXL)
Loquats/ Japanese medlars	5	EFSA (2015)	1.7	STMR CXL (2005)	2.43	HR-RAC (CXL)
Other pome fruits	0.9	EFSA (2015)	0.25	STMR-RAC	–	–
Apricots	0.1	EFSA (2015)	0.05	STMR-RAC	0.07	HR-RAC
Cherries (sweet)	3	EFSA (2015)	1.21	STMR CXL (2005)	2.11	HR-RAC (CXL)
Peaches	0.1	EFSA (2015)	0.05	STMR-RAC	0.07	HR-RAC
Table olives	20	EFSA (2015)	6.5	STMR-RAC	11.2	HR-RAC
Bananas	0.05	EFSA (2015)	0.0096	STMR-RAC × PeF (0.06)	0.0156	HR-RAC × PeF (0.06)
Olives for oil production's	20	EFSA (2015)	6.5	STMR-RAC	6.5	STMR-RAC

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value (mg/kg)	Comment	Input value (mg/kg)	Comment[(a)]
Swine: Muscle/ meat	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Swine: Fat tissue	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Swine: Liver	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Swine: Kidney	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Swine: Edible offals (other than liver and kidney)	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Swine: Other products	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Bovine: Muscle/ meat	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Bovine: Fat tissue	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Bovine: Liver	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Bovine: Kidney	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Bovine: Edible offals (other than liver and kidney)	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Bovine: Other products	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Sheep: Muscle/ meat	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Sheep: Fat tissue	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Sheep: Liver	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Sheep: Kidney	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Sheep: Edible offals (other than liver and kidney)	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Sheep: other products	0.01*	EFSA (2015)	0.01	LOQ	–	–
Goat: Muscle/ meat	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Goat: Fat tissue	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Goat: Liver	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Goat: Kidney	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Goat: Edible offals (other tha liver and kindey)	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Goat: other products	0.01*	EFSA (2015)	0.01	LOQ		
Equine: Muscle/ meat	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Equine: Fat tissue	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Equine: Liver	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Equine: Kidney	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ

Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value (mg/kg)	Comment	Input value (mg/kg)	Comment[(a)]
Equine: Edible offals (other than liver and kidney)	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Equine: Other products	0.01*	EFSA (2015)	0.01	LOQ	–	–
Other farmed animals: Muscle/ meat	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Other farmed animals: Fat tissue	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Other farmed animals: Liver	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Other farmed animals: Kidney	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Other farmed animals: Edible offals (other than liver and kidney)	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Other farmed animals: Other products	0.01*	EFSA (2015)	0.01	LOQ	–	–
Milk: Cattle	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Milk: Sheep	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Milk: Goat	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Milk: Horse	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ
Milk: Others	0.01*	EFSA (2015)	0.01	LOQ	0.01	LOQ

STMR-RAC: supervised trials median residue in raw agricultural commodity; HR-RAC: highest residue in raw agricultural commodity; PeF: Peeling factor; CXL: Codex maximum residue limit: LOQ: limit of quantification.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Input values for the commodities which are not under consideration for the acute risk assessment are reported in grey.

Appendix E – Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/ InChiKey[b]	Structural formula[c]
Dodine	1-dodecylguanidinium acetate CC(=O)O.N=C(N)NCCCCCCCCCCCC YIKWKLYQRFRGPM-UHFFFAOYSA-N	
Guanidine	guanidine N=C(N)N ZRALSGWEFCBTJO-UHFFFAOYSA-N	

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system; InChiKey: International Chemical Identifier Key.
(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2020.2.1 ACD/Labs 2020 Release (File version N15E41, Build 116563, 15 June 2020).
(c): ACD/ChemSketch 2020.2.1 ACD/Labs 2020 Release (File version C25H41, Build 121153, 22 March 2021).