CONCLUSION ON PESTICIDES PEER REVIEW

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Peer review of the pesticide risk assessment for the active substance dithianon in light of confirmatory data submitted

European Food Safety Authority (EFSA)

Abstract

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessment carried out by the competent authority of the rapporteur Member State Greece, for the pesticide active substance dithianon are reported. The context of the peer review was that requested by the European Commission following the submission and evaluation of confirmatory mammalian toxicology and residues data. The conclusions were reached on the basis of the evaluation of the representative uses of dithianon as a fungicide on table and wine grapes and pome fruit. The reliable endpoints concluded as being appropriate for use in regulatory risk assessment, derived from the available studies and literature in the dossier peer reviewed, are presented. Concerns are identified.

Key words: dithianon, peer review, confirmatory data, risk assessment, pesticide, fungicide

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Summary

Dithianon was included in Annex I to Directive 91/414/EEC on 1 June 2011 by Commission Directive 2011/41/EU, and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011. It was a specific provision of the approval that the applicant was required to submit to the European Commission further studies on the storage stability and the nature of residues in processed products, the aquatic and groundwater exposure assessment for phthalic acid and the risk assessment for aquatic organisms with respect to phthalic acid, phthalaldehyde and 1,2 benzenedimethanol by 31 May 2013.

In accordance with the specific provision, the applicant, BASF SE, submitted an updated dossier in May 2013, which was evaluated by the designated rapporteur Member State (RMS), Greece, in the form of an addendum to the draft assessment report. In compliance with guidance document SANCO 5634/2009 rev.4.5, the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 5 December 2013. The RMS collated all comments in the format of a reporting table, which was submitted to the European Commission in July 2014.

Following consideration of the comments received, the European Commission requested EFSA to organise a peer review of the RMS's evaluation of the confirmatory data submitted in relation to the nature of residues in processed products and the toxicological assessment of the processing metabolites and to deliver its conclusions.

A data gap has been identified to address the magnitude of residues of metabolites Reg. No. 4005234 (phthalic acid), Reg. No. 4107273, Reg. No. 31062 and Reg. No. 4110933 in processed commodities. Pending the outcome of this data gap, toxicological data may be needed to address the genotoxicity profile of metabolites Reg. No 4005234 and Reg. No 4107273 and the toxicity profile of the identified metabolites recovered at significant levels in processing studies.

Given the data gaps identified for storage stability data on dithianon residues in grape wine, and for the magnitude of the metabolites Reg. No. 4107273, Reg. No. 31062, Reg. No. 4005234 (phthalic acid) and Reg. No. 4110933 in apple and grapes processed commodities, the consumer exposure assessment could not be concluded on and was identified as a critical area of concern. An acute intake concern has already been identified for table grapes (149 % ARfD) in the previous EFSA conclusion.

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Background

Dithianon was included in Annex I to Directive 91/414/EEC[1] on 1 June 2011 by Commission Directive 2011/41/EU,[2] and has been deemed to be approved under Regulation (EC) No 1107/2009[3], in accordance with Commission Implementing Regulation (EU) No 540/2011[4], as amended by Commission Implementing Regulation (EU) No 541/2011[5]. EFSA previously finalised a Conclusion on this active substance on 15 November 2010 (EFSA, 2010).

It was a specific provision of the approval that the applicant was required to submit to the European Commission further studies on the storage stability and the nature of residues in processed products, the aquatic and groundwater exposure assessment for phthalic acid and the risk assessment for aquatic organisms with respect to phthalic acid, phthalaldehyde and 1,2 benzenedimethanol by 31 May 2013.

In accordance with the specific provision, the applicant, BASF SE, submitted an updated dossier in May 2013, which was evaluated by the designated rapporteur Member State (RMS), Greece, in the form of an addendum to the draft assessment report. In compliance with guidance document SANCO 5634/2009 rev.4.5 (European Commission, 2011), the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 5 December 2013. The RMS collated all comments in the format of a reporting table, which was submitted to the European Commission in July 2014.

Following consideration of the comments received, the European Commission requested EFSA to organise a peer review of the RMS's evaluation of the confirmatory data submitted in relation to the nature of residues in processed products and the toxicological assessment of the processing metabolites.

Following the commenting on the assessment of confirmatory data, the applicant provided substantial comments in the column 3 of the reporting table and the RMS prepared an updated addendum (Greece, 2014). In order to give Member States the opportunity to comment on this new information and assessment, a consultation took place with Member States via a written procedure in June – July 2015.

A final consultation on the conclusions arising from the peer review took place with Member States via a written procedure in September – October 2015.

The conclusions laid down in this report were reached on the basis of the peer review of the RMS's evaluation of the confirmatory data submitted in relation to the nature of residues in processed products and the toxicological assessment of the processing metabolites. A key supporting document to this conclusion is the peer review report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the compilation of comments in the reporting table to the conclusion. The peer review report (EFSA, 2015) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the reporting table (September 2015),
- the comments received on the revised addendum,
- the comments received on the draft EFSA conclusion.

[1] Council Directive 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 2011/41/EU of 11 April 2011 amending Council Directive 91/414/EEC to include dithianon as active substance and amending Commission Decision 2008/934/EC. OJ L 97, 12.4.2011, p. 38–40.

[3] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

[4] Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

[5] Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.

Given the importance of the addendum to the assessment report (Greece, 2014) and the peer review report, these documents are considered as background documents to this conclusion.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated to have regulatory access to the information on which this conclusion report is based.

The active substance and the formulated product

Dithianon is the ISO common name for 5,10-dihydro-5,10-dioxonaphtho[2,3-*b*]-1,4-dithiine-2,3-dicarbonitrile (IUPAC).

The representative formulated product for the evaluation was 'Delan 70 WG', a water dispersible granule (WG), containing 700 g/kg dithianon, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying on table and wine grapes and pome fruit against various fungal diseases. Full details of the GAP can be found in the list of end points in Appendix A.

Conclusions of the evaluation

Genotoxicity studies were provided on metabolites Reg. No. 31062, 4110904 and 4110933 indicating that these compounds are unlikely to be genotoxic. Metabolites Reg. No. 4005234 (Phthalic acid), Reg.No. 31062, Reg. No. 4107273 and Reg. No. 4110933 were found to be potentially relevant in processed commodities. Pending the outcome of the investigation on the magnitude of residues of these compounds in processed commodities, toxicological data may be needed to address the genotoxicity profile of metabolites Reg. No. 4005234 and Reg. No. 4107273 and the toxicity profile of the identified metabolites recovered at significant levels in processing studies.

Confirmatory data on storage stability

The submitted data demonstrated stability of dithianon residues under frozen conditions in apples for up to 24 months. Storage stability data on incurred residues of dithianon in grape wine were not provided. Although the processing studies demonstrated that dithianon residues above the limit of quantification (LOQ) (0.01 mg/kg) were not quantified in grape wine, the time interval between processing and analysis was one month from the processing trials and a fast degradation of the residues in grape wine samples cannot be excluded in view of the results of the previous storage stability data (recovery < 10% within 1 month). EFSA is therefore of the opinion that storage stability data on dithianon residues in grape wine are still needed.

Confirmatory data on the nature of residues in processed commodities

A processing study was submitted to address the nature of dithianon residues in processed commodities under hydrolysis conditions simulating the standard processing operations of pasteurization, baking/brewing/boiling and sterilisation in apple juice. Dithianon was the predominant compound of the total applied radioactivity (TAR) for pasteurization (up to 47.3 % TAR) whilst it was extensively degraded for the two other processes into Reg. No. 4107273 (up to 12.7 % TAR), Reg. No. 4110904 (up to 9.4 % TAR), Reg. No. 31062 (up to 10.5 % TAR) and to a lesser extent into Reg. No. 4005234 (Phthalic acid) and Reg. No. 4110933 (up to 2.2 % and 4.1 % TAR, respectively). Processing trials on apples and grapes showed a negligible transfer of dithianon and Reg. No. 4110904 residues in all processed commodities (< 0.01 mg/kg) except in apple dried pomace, in grape wet pomace and in raisins. EFSA notes that the magnitude of residues of the other metabolites of concern (Reg. No. 4107273, Reg. No. 31062, Reg. No. 4005234 (Phthalic acid) and Reg. No. 4110933) was not determined in apple and grapes processed commodities and should be addressed. If it turns out that these metabolites are recovered at significant levels in processed commodities (> 0.01 mg/kg), their toxicological profile should be assessed in order to derive sound residue definitions both for monitoring and risk assessment in processed commodities. The concept of the Threshold of Toxicological Concern (TTC) was applied for the evaluation of the toxicological relevance of metabolites Reg. No. 4110904 and Reg. No. 31062 only and not for the other relevant metabolites identified in the hydrolysis study. The way the approach was applied is considered inappropriate by EFSA. With regard to metabolite Reg. No. 4110904, considering the low residue levels of this compound compared to the residue levels of parent dithianon recovered in raisins, the low contribution of this food item to the consumer dietary intake and the non genotoxicity of Reg. No. 4110904, it can reasonably be concluded that no further toxicity data on this compound is required to conduct the consumer exposure for the representative uses on apples and grapes. This assessment should be reconsidered, if additional uses are envisaged in the future. On the other hand, the assumptions that were made to estimate the residue levels of metabolite Reg. No. 31062 in apple and grapes raw and processed commodities are not considered scientifically sound, and the way the

residue levels were derived is not reproducible. Other metabolites that were found in the study simulating processing conditions were not addressed. The EFSA Scientific Committee (2012) recommends that when the TTC approach is applied to substances with closely related structures and to which there is co-exposure, it may be appropriate to sum their exposures, as would be done in a cumulative risk assessment on substances with the same mode of action. A case considering to what extend this is applicable to the metabolites under consideration was not submitted.

EFSA therefore concludes that the TTC approach is not appropriate to assess the toxicological relevance of the metabolites identified in the hydrolysis study. The residue definition for enforcement and risk assessment in processed commodities as well as a robust consumer dietary risk assessment cannot be finalised based on these confirmatory data and will be reconsidered pending the outcome of the outstanding data on the magnitude and the toxicological profile of all the metabolites identified during processing under the standard hydrolysis conditions. It is noted that the RMS considered the TTC approach conducted on both compounds acceptable. An acute intake concern has already been identified for table grapes (149% ARfD) (EFSA, 2010).

Data gaps

This is a list of data gaps identified in the focussed peer review process of confirmatory data. Data gaps identified in the previously finalised EFSA Conclusion on this active substance (EFSA, 2010) that were not part of the focussed peer review process of confirmatory data remain unchanged.

- Pending the outcome of the investigation on the magnitude of residues of metabolites Reg. No. 4005234 (phthalic acid), Reg. No. 4107273, Reg. No. 31062 and Reg. No. 4110933 in processed commodities, toxicological data may be needed to address the genotoxicity profile of metabolites Reg. No. 4005234 and Reg. No. 4107273 and the toxicity profile of the identified metabolites recovered at significant levels in processing studies (relevant for all representative uses).
- Storage stability data on dithianon residues in grape wine (relevant for the representative use on wine grapes).
- The magnitude of residues of the metabolites Reg. No. 4107273, Reg. No. 31062, Reg. No. 4005234 (Phthalic acid) and Reg. No. 4110933 in apple and grapes processed commodities (relevant for all representative uses).

Concerns

1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[6], and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

None identified for the representative uses assessed.

2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active

[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.

substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

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

1. Given the data gaps identified for storage stability data on dithianon residues in grape wine, and for the magnitude of the metabolites Reg. No. 4107273, Reg. No. 31062, Reg. No. 4005234 (Phthalic acid) and Reg. No. 4110933 in apple and grapes processed commodities the consumer exposure assessment could not be concluded on. An acute intake concern has already been identified for table grapes (149 % ARfD) in the previous EFSA conclusion.

3. Overview of the concerns identified for each representative use considered

Table 1: Overview of concerns

Representative use		Table grapes	Wine grapes	Pome fruit
Consumer risk	Risk identified	X[1]	X[1]	X[1]
	Assessment not finalised			

Columns are grey, if no safe use can be identified. The superscript number in this table relates to the numbered points indicated in Sections 1 and 2.

References

EFSA (European Food Safety Authority), 2010. Conclusion on the peer review of the pesticide risk assessment of the active substance dithianon. EFSA Journal 2010;8(11):1904, 121 pp. doi:10.2903/j.efsa.2010.1904

EFSA Scientific Committee, 2012. Scientific Opinion on Exploring options for providing advice about possible human health risks based on the concept of Threshold of Toxicological Concern (TTC). EFSA Journal 2012;10(7):2750, 103 pp. doi:10.2903/j.efsa.2012.2750

EFSA (European Food Safety Authority), 2015. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance dithianon. Available online: www.efsa.europa.eu

European Commission, 2011. Guidance document on the procedures for submission and assessment of confirmatory data following inclusion of an active substance in Annex I of Council Directive 91/414/EEC. SANCO 5634/2009-rev. 4.5.

Greece, 2014. Addendum to the Draft Assessment Report (DAR) on the active substance dithianon prepared by the rapporteur Member State Greece in the framework of Directive 91/414/EEC, November 2013, revised in June 2014

Abbreviations

a.s.	active substance
ADI	acceptable daily intake
AR	applied radioactivity
ARfD	acute reference dose
bw	body weight
DAR	draft assessment report
GAP	good agricultural practice
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
LOQ	limit of quantification (determination)
MRL	maximum residue level
NESTI	national estimated short-term intake
NEU	northern European Union
PHI	pre-harvest interval
SEU	southern European Union
STMR	supervised trials median residue
TAR	total applied radioactivity
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TTC	threshold of toxicological concern
WG	water dispersible granule

Appendix A – List of end points for the active substance and the representative formulation

Summary of representative uses evaluated

Crop and/ or situation	Member State, Country or Region	Product name	F G or I	Pests or Group of pests controlled	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days)	Remarks
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL (l) min – max	water L/ha min – max	kg as/ha (l) min – max	(m)	
Pome fruit	EU (South& North)	Delan 70 WG (BAS 216 03F)	F	*Venturia inaequalis, Gloeosporium spp.Nectria galligena, Venturia pirina*	WG	700	High volume spraying	BBCH 10 - 79	1-12	7 – 12 days	0.0350 – 0.0525	1000 - 1500	0.525	21	Preventive treatment.
Grape (Table and Wine)	EU (South & North)	Delan 70 WG (BAS 216 03F)	F	*Plasmopara viticola*	WG	700	High volume spraying	BBCH 10 - 79	1 - 8	7 – 12 days	0.047 - 0.140	400 – 1200	0.560	42	Preventive treatment. Water volume is depending on the cropping.

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha

(m) PHI - minimum pre-harvest interval

Impact on Human and Animal Health

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	**7-day oral nephrotoxicity study, rat** NOAEL = 12 mg/kg bw per day Critical effect: pale kidneys, hydropic degeneration of the proximal tubular epithelial cells and electron microscopy changes on the mitochondria in the proximal tubular cells at 60 mg/kg bw per day **28-day oral nephrotoxicity study, rat** NOAEL = 12 mg/kg bw per day Critical effect: increase in tubular cell turnover rate at 60 mg/kg bw per day **7-day oral S-phase response study, rat** Males: Marginal exacerbation of basophilic tubules in kidney parenchyma (OSOM and cortex), cell proliferation in OSOM area and increased apoptosis in cortex area at all doses Females: Increased kidney weight, degenerative lesions in the kidney parenchyma and significant increase of cell proliferation in OSOM area of high-dose animals **28-day oral S-phase response study, rat** Males: Increased kidney and liver weight at all doses, marginal exacerbation of basophilic tubules at all doses, cell proliferation and secondary apoptosis in the OSOM area of kidney of high-dose animals. Females: Decreased body weight and increased relative kidney weight in high-dose animals. Multifocally distributed, vacuolar degeneration of tubular epithelial cells of the proximal tubules in the kidney parenchyma, significant increase of cell proliferation in the OSOM area of high-dose animals.
Studies performed on metabolites or impurities ‡	**D4 (Reg. No. 31062)** Ames test: negative (-) *In vivo* mouse micronucleus: (-) **Reg. No. 4110904** Ames test: (-) *In vitro* Gene mutation in mammalian cells: (-) *In vitro* clastogenicity in mammalian cells: positive (+) *In vitro* clastogenicity in mammalian cells: inconclusive *In vivo* micronucleus: (-) *In vivo* Comet assay: (-) **D8 (Reg. No. 4110933)** Ames test: (-) *In vivo* micronucleus: (-)

o-phthalic acid (Reg. No. 4005234)
common metabolite to picoxistrobin and phosmet
Survey of published literature (November 2000)
Acute oral LD_{50}, rat: 7500-8400 mg/kg bw
In vitro genotoxicity (Ames test & cytogenetic assay in CHO cells): (-)
Dominant lethal test: questionable positive test result involving reduced male fertility and abnormal sperm morphology
Non-carcinogenic in rats and mice according to NTP carcinogenicity programme
Reduced foetal body weight and retarded ossification in rats at maternal toxic doses

Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Fruits (apples, oranges), leafy crop (spinach), wheat (cereals) via foliar treatment
Rotational crops	Not required since intended to be used in permanent crops (pome fruits and grapes)
Metabolism in rotational crops similar to metabolism in primary crops?	Not required since intended to be used in permanent crops (pome fruits and grapes)
Processed commodities	Dithianon was the predominant compound of the total applied radioactivity (TAR) for pasteurization (up to 47.3 % TAR) whilst it was extensively degraded at baking/brewing/boiling and sterilisation into Reg. No 4107273 (up to 12.7 % TAR), Reg. No 4110904 (up to 9.4 % TAR), Reg. No 31062 (up to 10.5 % TAR) and to a lesser extent into Reg. No 4005234 (Phthalic acid) and Reg. No 4110933 (up to 2.2 % and 4.1 % TAR, respectively). Data gap: The magnitude of residues of the metabolites Reg. No. 4107273, Reg. No. 31062, Reg. No. 4005234 (Phthalic acid) and Reg. No. 4110933 in apple and grapes processed commodities is required.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No
Plant residue definition for monitoring	Dithianon Open for processed commodities
Plant residue definition for risk assessment	Dithianon Open for processed commodities
Conversion factor (monitoring to risk assessment)	Not applicable

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

Animals covered	Goat, hen
Time needed to reach a plateau concentration in milk and eggs	Goat: 1 - 2 days Hen: > 4 days (not relevant, since the target crops are not fed to poultry)
Animal residue definition for monitoring	Dithianon
Animal residue definition for risk assessment	Dithianon
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes (log P_{ow} > 3)

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

Not required since intended to be used in permanent crops (pome fruits and grapes)

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

-Pome fruit: Acceptable storage stability of dithianon incurred residues under frozen conditions in apples for up to 24 months. -Grapes: Incurred dithianon residues in wine grapes were shown to be stable under frozen conditions for up to 14 months covering the storage time interval of the samples from the residue trials. -Processed grapes products: Dithianon is stable under freezer storage conditions in grape must (24 months), grape juice (18 months), grape pomace (6 months). However, an almost complete and rapid degradation of dithianon residues was observed in grape wine (recovery rate below 10% within 1 month of storage). Data gap: Storage stability data on dithianon residues in grape wine are still required.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes 0.39 mg/kg (dairy) 1.12 mg/kg (beef)	No	No
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle Liver Kidney Fat Milk Eggs	no cow feeding study conducted metabolism results indicate that the residues will be far below the LOQ (milk, tissues 0.01 mg/kg)	no hen feeding study conducted metabolism results indicate that the residues will be far below the LOQ (eggs, tissues: 0.01 mg/kg)	no pig feeding study conducted; metabolism in rat and ruminant similar, residues will be below 0.01 mg/kg (LOQ).

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Apples	Northern	0.36, 2 x 0.48, 0.62, 0.76, 1.5, 1.7, 1.89 mg/kg	-	3.0 mg/kg(1)	1.89 mg/kg	0.62 mg/kg
Pears	Northern	0.19, 0.37, 0.39, 0.87 mg/kg				
Apples	Southern	0.43, 0.59, 0.86, 1.69, 1.73 mg/kg				
Grapes (Table and Wine)	Northern	0.57, 0.62, 0.62, 0.98, 1.01, 1.20, 1.27, 1.41, 1.91, 2.2, 2.65 mg/kg	-	3.0 mg/kg(1)	2.72 mg/kg	1.01 mg/kg
	Southern	0.38, 0.52, 0.59, 1.0, 1.1, 1.48, 2.72 mg/kg				

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17

(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use

(c) Highest residue

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.01 mg/kg bw per day
TMDI (% ADI) according to EFSA PRIMo Model rev.2A	419.4% ADI (German child)(1)
NEDI (specify diet) (% ADI)	92.3% ADI (German child)(1)
ARfD	0.12 mg/kg bw
IESTI (% ARfD) according to EFSA PRIMo Model rev.2A	Apples: 89.4% ARfD(1) Pears: 79% ARfD(1) Table grapes: 148.4% ARfD Wine grapes: 17.6% ARfD(1)
Factors included in IESTI	Factors included in IESTI calculation: -The NEU and SEU residue data set in pome fruit and grapes were respectively pooled as statistically supported. -Pome fruit: HR:1.89 mg/kg; VF: 3.8 (derived from the unit-to-unit variability residue study in apples) -Table/wine grapes: HR:2.72 mg/kg

(1) The residue definition for enforcement and risk assessment in processed commodities as well as a robust consumer dietary risk assessment will be reconsidered pending the outcome of the outstanding data on the magnitude of all the metabolites identified during processing under the standard hydrolytic conditions and potentially their toxicological profile. The stability of dithianon residues under frozen storage conditions in processed grape wine should also be considered.

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Apple/washed apples	7 trials	0.23 - 1.8(1)		
Apple/juice	10 trials	0.0045 - 0.1(1)		
Apple/wet pomace	10 trials	0.49 - 3.5(1)		
Apple/dry pomace	6 trials	0.43 - 0.77(1)		
Apple/sauce	8 trials	0.006 - 0.125(1)		
Apple/dried apples	2 trials	0.029, 0.033(1)		
Apple/canned apples	4 trials	0.033 - 0.125(1)		
Grapes/must	13 trials	0.01 - 0.33(1)		
Grapes/wine	13 trials	0.002 - 0.08(1)		
Grapes/juice	4 trials	0.002 - 0.003(1)		
Grapes/wet pomace	4 trials	0.19 - 2.18(1)		
Grapes/dry pomace	4 trials	0.08 - 0.28(1)		
Grapes/young wine	4 trials	0.002 - 0.003(1)		
Grapes/must deposit	1 trial	1.2(1)		
Grapes/lees	2 trials	0.002, 0.01(1)		

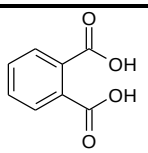
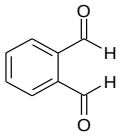
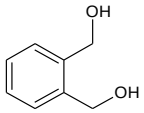
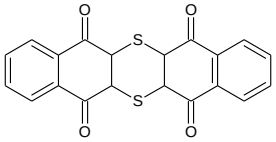
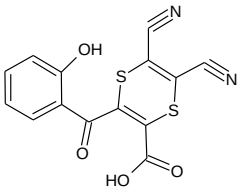
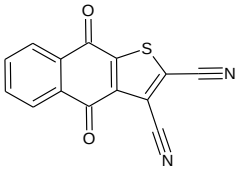
(1) The residue definition for enforcement and risk assessment in processed commodities as well as a robust consumer dietary risk assessment will be reconsidered pending the outcome of the outstanding data on the magnitude of all the metabolites identified during processing under the standard hydrolytic conditions and potentially their toxicological profile. The stability of dithianon residues under frozen storage conditions in processed grape wine should also be considered.

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

Pome fruits:	3.0 mg/kg(1)
Wine grapes:	3.0 mg/kg(1)

(1) The residue definition for enforcement and risk assessment in processed commodities as well as a robust consumer dietary risk assessment will be reconsidered pending the outcome of the outstanding data on the magnitude of all the metabolites identified during processing under the standard hydrolytic conditions and potentially their toxicological profile. The stability of dithianon residues under frozen storage conditions in processed grape wine should also be considered.

Appendix B – Used compound codes

Code/trivial name	Chemical name/SMILES notation	Structural formula
phthalic acid **o-phthalic acid** **Reg. No 4005234**	phthalic acid OC(=O)c1ccccc1C(=O)O	
phthalaldehyde	phthalaldehyde O=Cc1ccccc1C=O	
1,2-benzenedimethanol	1,2-phenylenedimethanol OCc1ccccc1CO	
D4 **Reg. No. 31062**	5a,6a,12a,13a-tetrahydrodibenzo[*b,i*]thianthrene-5,7,12,14-tetrone O=C2C1SC5C(SC1C(=O)c3ccccc23)C(=O)c4ccccc4C5=O	
Reg. No. 4110904 **CL 1017911**	5,6-dicyano-3-(2-hydroxybenzoyl)-1,4-dithiine-2-carboxylic acid OC(=O)C=2SC(C#N)=C(SC=2C(=O)c1ccccc1O)C#N	
D8 **Reg. No. 4110933**	4,9-dioxo-4,9-dihydronaphtho[2,3-*b*]thiophene-2,3-dicarbonitrile N#Cc1sc3c(c1C#N)C(=O)c2ccccc2C3=O	
D2 **Reg. No. 4107273**	1,4-naphthoquinone O=C2C=CC(=O)c1ccccc12