TECHNICAL REPORT

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Recommendations on the use of the proportionality approach in the framework of risk assessment for pesticide residues

European Food Safety Authority

Abstract

The technical report reflects the outcome of the discussions and agreements that were reached in the pesticides peer review meeting on residues and maximum residue levels regarding the principles and guidance for application of the proportionality concept in the risk assessment methodologies used at European level for the estimation of the maximum residue levels for pesticides. In addition, practical experiences on the use of the proportionality approach gained by EFSA have been included in this document. Specific cases that are not fully covered by the general principles of the proportionality concept outlined in the OECD guidance document and further recommendations are reported. This output does not preclude the production of other technical reports on this topic to clarify further aspects of the proportionality concept used in the context of the assessment of pesticide residues in food.

Key words: pesticides, active substance, plant protection product, proportionality

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Summary

The proportionality concept was discussed in the pesticides peer review meeting 158 on residues and maximum residue levels that took place from 3 to 5 May 2017.

The technical report reflects the outcome of the discussions and agreements that were reached in the pesticides peer review meeting on residues and maximum residue levels regarding the principles and guidance for application of the proportionality concept in the risk assessment methodologies used at European level for the estimation of the maximum residue levels for pesticides. The report has been prepared to share the views expressed by Member State and EFSA experts with all the Member States that could not attend the meeting in order to harmonise our approach when using the proportionality principle in the assessment of the residue trials and for MRLs setting. EFSA also acknowledged that further discussion is needed on some specific points to come to an agreement. This output does not therefore preclude the production of other technical reports on this topic to clarify further aspects of the proportionality concept used in the context of the assessment of pesticide residues in food.

The recommendations on the proportionality concept as defined at Codex level were adopted at EU level at the Standing Committee on the Food Chain and Animal Health Meeting in September 2015.

In September 2016, the OECD guidance document on crop field trials was published (ENV/JM/MONO(2011)50/REV1, September 2016), which also addressed and reconsidered some of the principles for the use of the proportionality concept in the framework of assessment of the residue trials and setting of maximum residue levels.

During the meeting the experts discussed specific cases that were not fully covered by the general principles of the proportionality concept described in the OECD guidance document or that lead to different interpretations among experts and several recommendations were agreed and included in this technical report.

After the expert meeting, EFSA identified further points that should be addressed in this document. Thus, additional recommendations derived on the basis of practical experiences were included in this document.

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1. Introduction

During the EFSA peer review of pesticide active substances under Regulation (EC) No 1107/2009[1] EFSA identified several general issues in the area of residues which deserved experts' consultation and agreement in order to enhance the harmonisation of the risk assessment of active substances.

To this purpose a general meeting was organised which took place in May 2017 (Pesticide Peer Review Meeting 158, 3-5 May 2017). Member States representatives with expertise in the peer review and MRL areas attended this meeting.

The proportionality concept developed by JMPR and OECD (OECD, 2016) was one of the topics identified where further discussions with Member States would be needed to ensure that Member States and EFSA have a common approach to apply the provisions for scaling of residue trials in a consistent manner.

In this report, the discussions and agreements derived in this meeting are summarised. This report represents the opinion of Member State and EFSA experts attending the meeting mentioned above and should be made available to all the Member States that could not attend the meeting in order to harmonise our approach when using the proportionality principle in the assessment of the residue trials and for MRLs setting. Additional recommendations derived on the basis of practical experiences of EFSA were also included in this document.

EFSA also acknowledged that further discussion is needed on some specific points to come to an agreement. This output does not therefore preclude the production of other technical reports on this subject in the future, if considered necessary to clarify further aspects of the proportionality principles used in the context of the assessment of pesticide residues in food.

2. Background

In order to derive maximum residue levels (MRLs) for pesticide residues in food, applicants are obliged to provide, among other data, supervised field trials compliant with the intended Good Agricultural Practice (GAP). The application rates tested in residue trials should not deviate by more than ±25% from the application rate defined in the Good Agricultural Practice. A deviation of the application rate within these boundaries is only acceptable, if no other parameters of the trials conditions deviate from the GAP, e.g. the pre-harvest interval (PHI), number of applications.

MacLachlan and Hamilton (2010) performed detailed analysis of side-by-side residue trials in which different application rates were tested to verify the hypothesis that there is a correlation between the application rates and the final residues in the crops.

Based on this analysis, JMPR derived the principles and guidance for application of the proportionality concept for the estimation of the maximum residue limits for pesticides. The recommendations were agreed at the 45th session of the Codex Committee on pesticide residues in 2013 and adopted at the 36th session of the Codex Alimentarius Commission (RPE13/PR, July 2013) and subsequently included in the Procedural Manual as an Annex to the Risk Analysis Principles applied by the Codex Committee on pesticides residues (REP13/PR, para. 91-99, Appendix VIII).

The recommendations on the proportionality concept as defined at Codex level were adopted at EU level at the Standing Committee on the Food Chain and Animal Health Meeting in September 2015.

In September 2016, the OECD guidance document on crop field trials was published (ENV/JM/MONO(2011)50/REV1, September 2016), which also addressed and reconsidered some of the principles for the use of the proportionality concept in the framework of assessment of the residue trials.

The following provisions were established in the OECD guidance document (OECD, 2016):

(The different cases described in the OECD guidance document presented below are illustrated in Figure 1 and 2; please note that the illustrations are not part of the OECD guidance document).

[1] 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.

- The use of the concept for soil, seed and foliar treatments has been confirmed by analysis of residue data. Active substances confirmed included insecticides, fungicides, herbicides, and plant growth regulators, except desiccants.
- The proportionality concept can be applied to residue data from field trials conducted within a dose rate range of between 0.3x and 4x the GAP dose rate (Figure 1, cases 1, 2, 3 and 4). This is only valid when quantifiable residues occur in the dataset. Where there are no quantifiable residues, i.e. residue values are lower than the limit of quantification; the residues may only be scaled down (Figure 1, case 7, results <LOQ are displayed as white diamonds)). It is unacceptable to scale up in this situation (Figure 2, case 3[2], (results <LOQ are displayed as white diamonds)).
- The variation associated with residue values derived using this approach can be considered to be comparable to using data selected according to the "± 25% rule" for the application rate.
- Scaling is only acceptable if the application rate is the only deviation from the critical GAP (cGAP) (See Case A – Appendix A). In agreement with JMPR practices, additional use of the ±25% rule for the other parameters such as PHI, number of applications is not acceptable. For additional uncertainties introduced, e.g. use of global residue data, scaling needs to be considered on a case-by-case basis so that the overall uncertainty of the residue estimate is not increased.
- Proportionality cannot be used for post-harvest situations at this time. It is also recommended that the concept is not used for hydroponic situations due to lack of data.
- The proportionality concept can be applied for both major and minor crops. The main difference between minor and major crops is the number of trials required by national/regional authorities (Figure 1, case 6 (small data set for minor crop)), which has no direct relevance to the proportionality of residue. If scaling is applied on representative commodities, there is no identified concern with extrapolation to other members of an entire commodity group or subgroup.
- Regarding processed commodities, it is assumed that the processing factor is constant within an application rate range and resulting residues in the commodity being processed. Therefore existing processing factors can also be used for scaled datasets.
- With respect to exposure assessment, no restrictions appear to be necessary. The approach may be used for distribution of residues in peel and pulp, provided the necessary information for scaling is available from each trial. Scaled datasets for feed items may also be used for dietary burden calculations for livestock.
- The approach may be used where the dataset is otherwise insufficient to make an MRL recommendation. This is where the concept provides the greatest benefit. The concept has been used by JMPR and different national authorities on a case-by-case basis and in some cases MRLs may be estimated from trials where all of the data (100%) has been scaled (Figure 1, cases 2, 3 and 4).
- Although the concept can be used on large datasets containing 100% scaled residue trials, at least 50% of the minimum required number of trials at or above (within the "±25% rule") the cGAP may be requested on a case-by-case basis depending for example on the range of scaling factors. In addition, some trials at GAP might be useful as confirmatory data to evaluate the outcome in cases where the uses result in residue levels leading to a significant dietary exposure.

Since some of the conditions give room for interpretation, in particular in the framework of the EU data requirements for residues, the need to discuss details on the implementation of the proportionality principles in risk assessment methodologies used at European level was identified. In addition, the implications of the proportionality approach on the current EU practice regarding the use of the "±25% rule" should be agreed.

[2] In case 3, Figure 2 the number of residue trials would not be sufficient to derive a MRL proposal.

3. Overall conclusions and recommendations

The experts discussed specific cases that were not fully covered by the general principles of the proportionality concept described in the OECD guidance document or that lead to different interpretation among experts. The following recommendations were derived.

- As a general principle, it was agreed that the use of the proportionality concept should be proposed by the applicant and/or the RMS/EMS. It is not the responsibility of the risk assessors to identify trials that would be suitable for scaling to complete an incomplete residue dataset.
- If sufficient residue trials are available that are compliant with the cGAP (within the "±25% rule") according to the current requirements (at least 8 trials for a major crop and at least 4 trials for a minor crop), the residue trials conducted at an application rate outside the "±25% rule" do not need to be considered (Figure 2, case 4[3], minor crop with 4 trials within the acceptable deviation of "±25%" and 4 additional trials with wider deviation outside the "±25%" rule). However, in certain circumstances it might not be suitable to disregard these additional trials (e.g. if markedly higher estimation of residues would be indicated if the scaling was applied to the additional trials conducted at an application rate outside the "±25% rule").
- In the evaluation reports submitted by the Evaluating Member States and in the EFSA outputs (List of end points of EFSA conclusions and EFSA reasoned opinions), for sake of transparency, the scaling process should be reported in three steps, which include the reporting of the "unscaled" residue values, the individual scaling factors and the "scaled" residue values resulting from the combination of data generated with different application rates.
- For complex residue definitions the scaling should be applied on the residue values reported as "calculated as" and not on the individual components of the residue definition, e.g. when scaling is used for a residue definition that includes metabolites (parent + metabolite A + its conjugates expressed as parent) it should be done on the residue values as normally reported as "calculated as", and not on the individual components of the residue definition. Up scaling is only applicable when all the individual components of the residue definitions have residues above the LOQ of the method.
- For residue trials in which the application rate is expressed as a concentration (i.e. kg a.s./hL), scaling can be applied. However, in this situation, the spray volume of the residue trials (i.e. water volume/ha) has to match with the cGAP.
- It was reiterated that, in accordance with the OECD guidance document, up- and down-scaling within one dataset (mixed approach) is acceptable (Figure 1, cases 1 and 2).
- Where there are no quantifiable residues, i.e. residue concentrations are reported as lower than the limit of quantification (<LOQ), scaling up is not applicable (Figure 2, case 3[4] (results <LOQ are displayed as white diamonds)). According to OECD, in this case, residues may only be scaled down (Figure 1, case 7). However, this will not have a major impact on the MRL proposal since MRLs are established at the LOQ of the method and not lower than the LOQ.
- Frequently, MRLs are derived from a combined data set of outdoor residue trials performed respectively in the NEU and SEU zones, if the following two conditions are fulfilled: a) the GAP is the same in the NEU and SEU zones and b) the statistical assessment demonstrates that the residue populations are not significantly different. If residue trials in one zone require scaling because the application rate deviates by more than 25% from the application rate defined in the GAP, residue trials in the second zone also have to be scaled if they do not match exactly the GAP (i.e. if they are all within ±25%). Thus, mixing of a scaled and an un-scaled data set from NEU and SEU is not acceptable (See Case A – Appendix A).

[3] For case 4 in Figure 2, the number of trials within the 25% deviation range would be sufficient to derive a MRL proposal.
[4] For case 3 in Figure 2 the number of trials would be insufficient to derive a MRL proposal.

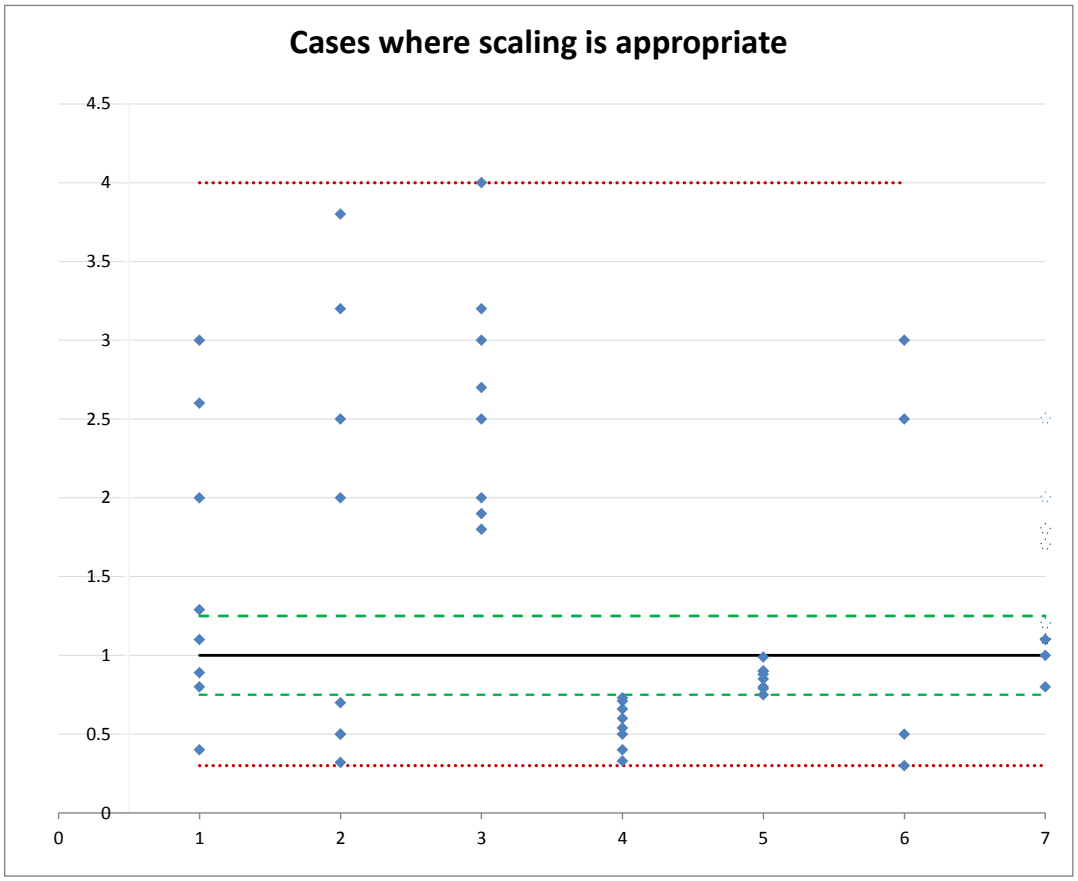
- In case of multiple applications, scaling is in principle applicable if the dose rate in the individual applications deviate from the application rate defined in the GAP by a constant factor. If this is not the case, the application of the proportionality principle might not be suitable. On a case-by-case basis the application of the proportionality to the seasonal application rate may be acceptable, but should be supported by a reasoned case, i.e. considering the persistence of the compound, its systemicity (based on metabolism data, decline residue trials), the time interval between applications and whether it can be demonstrated that the successive applications contribute significantly to the residues (residue transfer rates). If the last application is shown to contribute the most to the terminal residues, i.e. significant and rapid degradation of the residues along with the PHI after last application (decline residue trials), the scaling factor can be calculated on the basis of the dose rate at the last application only (See Case B – Appendix A).
- According to the OECD guidance document (OECD, 2016), MRLs may be derived from trials where all residue data (100%) have been scaled (Figure 1, cases 2, 3 and 4). However, under certain conditions, at least 50% of trials at the GAP may be requested, depending for example on the range of scaling factors. The experts attending the meeting were of the opinion that at least 50% of the minimum required number of trials should be conducted at the cGAP (within the "±25% rule") under the following conditions:
  - if the STMR/HR values derived from the scaled data set lead to a significant dietary exposure (e.g. acute exposure >75% of the ARfD, chronic exposure close to 100% of the ADI with a significant contribution of the commodity of concern);
  - if the scaled residue values show a high variability;
  - if the residue trials with lower application rate lead to higher residues than trials matching the cGAP.

  Commission supported the view that the risk assessors should have the flexibility to ask for up to 50% of the minimum required number of residue trials for a crop on a case-by-case basis (i.e. up to 4 residue trials for major crops and up to 2 residue trials for minor crops can be requested to comply with the target application rate (±25% deviation of the application rate).
- In case the residue dataset is constituted of overdosed and underdosed residue trials when the dose rates of application in all trials are within the "±25% rule", the scaling is not necessary (Figure 2, case 1).
- If all residue trials are underdosed but within the acceptable deviation of 25%, the proportionality approach may be used to scale the entire residue dataset to the nominal application rate to avoid a systematic bias and in the case where the STMR/HR values derived from this residue dataset lead to a significant dietary exposure (e.g. acute exposure >75% of the ARfD, chronic exposure close to 100% of the ADI with a significant contribution of the commodity of concern) (see Figure 1, case 5). In that specific case the application of the proportionality principle changes the current rule (OECD Test Guideline 509 on crop field trial), i.e. "in case up to 25% increases or decreases of the dose rate of application, the residue levels can be assumed to be comparable provided that all the other parameters of the critical GAP remain unchanged".
- In case of a comprehensive submission to all OECD countries requesting to establish a MRL for a GAP on a specific crop that is uniform in all OECD countries, the number of trials may be reduced, compared to the total number of trials determined by summation of individual country requirements (para 66 of the 2016 OECD guidance document). However, when residue data sets from different geographical regions are combined, at least 50% of the minimum required number of trials should be conducted at or above (within 25%) the cGAP. If more than 50% of the trials were conducted at actual rates below the cGAP (but within 25%), the proportionality approach can be used by scaling of the entire dataset to the nominal dose.
- The trial design for rotational crops metabolism/field trials studies involving application to bare soil and subsequent sowing/planting is similar to a pre-emergence soil treatment in a supervised residue trial on primary crop; the proportionality concept is therefore applicable

allowing scaling (up and down) of residues found in rotational crop plant samples provided that the agreed recommendations to apply this principle are respected. Further details on the use of the proportionality principle for rotational crop studies can be found in the respective OECD guidance document (OECD, 2018).

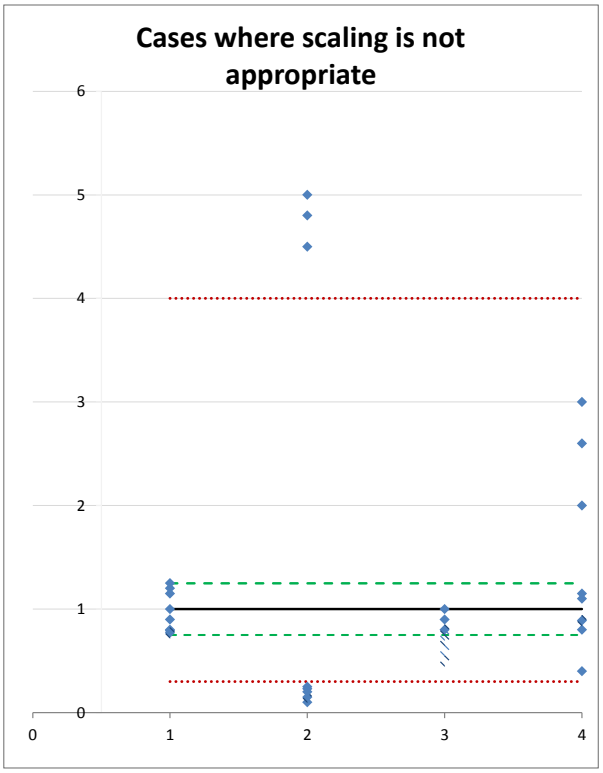
- For post-harvest uses, OECD did not recommend the use of the proportionality approach, because the data were not sufficient to confirm that scaling would lead to reliable results. The experts were of the opinion that the possibility to apply the proportionality principle for post-harvest uses should be further explored to demonstrate that the concept works based on sufficient and robust data related to the different types of post-harvest treatments (dipping, drenching, waxing, etc.).

Figure 1: Cases where scaling is acceptable



y-axis: application rate, compared to target application rate defined in GAP; black line: target application rate (1N); green dashed line: acceptable deviation (±25% of target application rate); red dotted line: acceptable limits for scaling (0.3N to 4N of target application rate); blue diamonds: results >LOQ; white diamonds: results <LOQ)

Figure 2: Cases where scaling is not necessary or appropriate



y-axis: application rate, compared to target application rate defined in GAP; black line: target application rate (1N); green dashed line: acceptable deviation (±25% of target application rate); red dotted line: acceptable limits for scaling (0.3N to 4N of target application rate); blue diamonds: results >LOQ; white diamonds: results <LOQ); Cases 1 and 4: number of trials sufficient to derive MRL proposal; Cases 2 and 3: database insufficient to derive MRL proposal

Different case studies where the proportionality concept was used are presented in Appendix A.

Using the proportionality principle in the framework of regulatory dossiers may lead to additional questions on the most appropriate way to apply the proportionality concept. Thus, additional clarifications may have to be developed on the basis of the experience gained in practice.

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OECD Guidance document on crop field trials – Annex 3 – Background information to chapter 3. Proportionality ((ENV/JM/MONO(2011)50)/REV1/ANN – Annex 3, September 2016)

OECD Guidance document on residues in rotational crops (Series on Pesticides – No.97 – Series on testing & Assessment – No 279) ((ENV/JM/MONO(2018)9) (May 2018))

Abbreviations

a.i.	active ingredient
a.s.	active substance
ADI	acceptable daily intake
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CAC	Codex Alimentarius Commission
CAS	Chemical Abstract Service
CCPR	Codex Committee on Pesticide Residues
CEN	European Committee for Standardization (Comité Européen de Normalisation)
CF	conversion factor for enforcement residue definition to risk assessment residue definition
cGAP	critical GAP
CXL	codex maximum residue limit
DAR	draft assessment report
DAT	days after treatment
DB	dietary burden
DM	dry matter
EC	European Commission
ECD	electron capture detector
EFSA	European Food Safety Authority
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GLP	Good Laboratory Practice
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ILV	independent laboratory validation
JMPR	Joint Meeting of 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)
LOD	limit of detection
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States

MS	mass spectrometry detector
NEU	northern European Union
OECD	Organisation for Economic Co-operation and Development
PAFF	Standing Committee on Plants, Animals, Food and Feed
PBI	plant back interval
PF	processing factor
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
PROFile	(EFSA) Pesticide Residues Overview File
RD	residue definition
RMS	rapporteur Member State
RPF	relative potency factor
STMR	supervised trials median residue

Appendix A – Case studies

Case A: Acaricide – Strawberry

NEU/SEU outdoor GAP on strawberry: 1-2 applications, 0.096-0.144 kg a.s./ha, BBCH 40-87;7 d interval, PHI:1 d

Author, year	MS	Location	Variety	Date and growth stage at last appl.	water (l/ha)	Appl. rate, a.s. (g/ha)	residue (mg/kg)	Scaled residue (mg/kg)	PHI (days)
Northern Europe									
Diehl, 2006	UK	Harvington	Elsanta	28.06.2005 BBCH 85	600	190 190	0.09	0.07	1
	UK	Newent	Florence	29.06.2005 BBCH 81	600	190 190	0.04	0.03	1
Bartolomé, 2012a	FR	Beugny	Darselect	27.07.2011 BBCH 87	1000	180 180	0.13	0.10	1
	UK	Cheltenham	Symphony	07.06.2011 BBCH 89	1000	180 180	0.12	0.10	1
	DE	Goch-Kessel	Lambada	06.06.2011 BBCH 87-89	1000	180 180	0.05	0.04	1
	NL	Wellriooi	Korona	06.06.2011 BBCH 87-89	1000	180 180	0.07	0.056	1
	DE	Kalkar-Wisselward	Elsanta	06.06.2011 BBCH 87-89	1000	180 180	0.09	0.072	1
	NL	Sieben-gewald	Elsanta	06.06.2011 BBCH 87-89	1000	180 180	0.07	0.056	1
Bartolomé, 2012b	DE	Goch	Elsanta	25.07.2011 BBCH 87-89	1000	180 180	0.20	0.16	1
Alé, 2014b	NL	Bergen	Elsanta	10.06.2014 BBCH 87	800	160 160	0.069	0.062	1
	DE	Goch	Elsanta	10.06.2014 BBCH 87	800	160 160	0.104	0.094	1
Southern Europe									
Bousquet, 2003e	ES	Valencia	Pajaro	17.05.2002 BBCH 85	1500	200 200	0.15	Scaling was not applied	1
Bousquet, 2003f	FR	Lannes	Gariguette	16.05.2003 BBCH 89	600	200 200	0.35		3*
	FR	Feugarolles	Agatha	14.05.2003 BBCH 89	600	200 200	0.75		1
Bousquet, 2003g	ES	Cartaya	Camarosa	13.05.2003 BBCH 83	900	200 200	0.18		1
	ES	Almonte	Ventana	13.05.2003 BBCH 83	900	200 200	0.18		1
Sicbaldi, 2003c	IT	Poggio Renatico	Marmolada	19.05.2003 BBCH 86	1000	200 200	0.09		1
	IT	Pevergano	Gorella	03.06.2003 BBCH 86	1000	200 200	1.71		1
Bartolomé, 2012b	FR	Marsillargues	Charlotte	28.10.2011 BBCH 89	1000	180 180	0.08		1
	IT	Postalesio	Fern	10.09.2011 BBCH 85	1000	180 180	0.09		1

Author, year	MS	Location	Variety	Date and growth stage at last appl.	water (l/ha)	Appl. rate, a.s. (g/ha)	residue (mg/kg)	Scaled residue (mg/kg)	PHI (days)
	ES	Quatretonda	Camarosa	21.06.2011 BBCH 89	1000	180 180	0.22		1
Alé, 2014	FR	Bourran	Gariguette	25.06.2014 BBCH 61-87	300	160 160	0.063		2*
	IT	San Antonio	Asia	19.05.2014 BBCH 85-87	500	160 160	0.039		1
	IT	Bosco Mesola	Alba	19.05.2014 BBCH 85-87	500	160 160	0.032		1
	IT	Albosaggia	Asia	25.06.2014 BBCH 85-87	500	160 160	0.261		1
	ES	Xativa	Camarosa	03.06.2014 BBCH 87-89	400	160 160	0.069		1
	ES	Estubeny	Albiol	05.06.2014 BBCH 87-89	400	160 160	0.110		1

*Residue levels are higher at later PHI than 1 day, therefore the later PHI is given in the table above.
The underlined residue values are derived from residue trials conducted with a dose rate of application within the "+/-25% rule" and are used for the calculation of the MRL, HR and STMR values.

RMS assessment:
RMS had the following approach: Residue levels in field grown strawberries in NEU were re-calculated according to proportionality principle to reach sufficient requested number of independent NEU GAP matching trials for a major crop. The scaling was not applied to the SEU residue trials since sufficient SEU GAP compliant residue trials (dose rate of application within the "±25% rule") are available. Only the underlined values have been used to calculate the MRL, STMR and HR and the residue trials conducted at an application rate outside the "±25%" rule were disregarded.

EFSA assessment:
This example is similar to the situation where MRLs are derived from a combined data set of outdoor residue trials performed in the NEU and SEU zones, if the following two conditions are fulfilled: a) the GAP is the same in the NEU and SEU zones and b) the statistical assessment demonstrates that the residues are comparable. If residue trials in one zone require scaling because the application rate deviates by more than 25% from the application rate defined in the cGAP, residue trials in the second zone also have to be scaled if they do not match exactly the cGAP (i.e. if they are all within ±25%). Thus, mixing of a scaled and an un-scaled dataset from NEU and SEU is not acceptable. In that example, the application of the proportionality to the whole SEU residue data set is therefore requested.

Case B: Insecticide – Kale

NEU outdoor GAP on kale: 3 applications, 6 g a.s./ha, BBCH 47-49;14 d interval, PHI:21 d

Trial No/Location/Year	Appl. Rate (g a.s./ha)	L/ha	g a.s./hL	Date of treatment	BBCH	Residues (mg/kg)	PHI (d)	Scaling factor[(1)]	Scaled residues (mg/kg)
S14-01696-01 France (Maine et Loire)	8.01 7.73 7.63	213 206 203	3.76 3.75 3.76	05/09/14 19/09/14 03/10/14	48	0.11 0.06 <0.05 **<0.05** <0.05	0 7 14 21 28	N/A	-

Trial No/Location/Year	Appl. Rate (g a.s./ha)	L/ha	g a.s./hL	Date of treatment	BBCH	Residues (mg/kg)	PHI (d)	Scaling factor [1]	Scaled residues (mg/kg)
S14-01696-03 UK (Lincolnshire)	7.25 7.93 7.63	194 212 203	3.74 3.74 3.76	14/08/14 28/08/14 11/09/14	49	0.05 <0.05 <0.05 **<u><0.05</u>** <0.05	0 7 14 21 28	N/A	-
S14-01696-04 UK (Derbyshire)	7.92 7.42 7.92	210 197 210	3.77 3.77 3.77	03/09/14 17/09/14 01/10/14	48	0.05 **<u><0.05</u>**	15 22	N/A	-
S14-01696-05 UK (Lancashire)	7.91 7.66 8.10	212 205 217	3.73 3.74 3.73	01/09/14 15/09/14 29/09/14	47-49	0.11 0.05 0.05 **<u>0.06</u>** 0.05	0 7 14 21 28	0.74	**<u><0.05</u>**
S14-01696-06 Germany (Baden-Wurttemberg)	8.27 8.27 7.77	220 220 207	3.76 3.76 3.75	10/09/14 24/09/14 08/10/14	48	0.16 0.06	14 21	0.77	**<u><0.05</u>**
S14-01696-07 Germany (Niedersachsen)	8.27 8.08 7.83	220 215 208	3.76 3.76 3.76	25/09/14 08/10/14 22/10/14	48	0.12 0.08	15 22	0.76	**<u>0.061</u>**
S14-01696-08 France (Loiret)	8.01 8.32 7.82	213 222 208	3.76 3.75 3.76	08/07/14 22/07/14 05/08/14	47	0.28 0.05 <0.05 <0.05 <0.05	0 7 14 21 28	N/A	-
S14-01696-11 UK (Lancashire)	8.17 7.86 8.81	217 208 215	3.76 3.78 4.10	27/01/15 10/02/15 25/02/15	47	0.21 0.14	14 21	0.68	**<u>0.095</u>**

[1]: Scaling factors were derived from the last single application rate and not from the seasonal application rate.

<u>EFSA assessment</u>: In that case of multiple applications, the proportionality concept was applied to the last single application rate and not to the maximum seasonal application rate. Indeed, in the case of "Substance C", the decline residue trials showed a significant and rapid degradation of the residues with the PHI and it was concluded that the last treatment contributed the most to the terminal

residue. The scaling was therefore applied to the dose rate corresponding to the last application and not to the seasonal application rate.

A case-by-case approach for scaling either on the dose rate at last application or on the seasonal application rate should be considered taking into account criteria such as the persistence of the active substance, its systemicity (based on metabolism data, decline residue trials), time interval between applications, the contribution of the successive applications to the terminal residues (residue transfer rates). If the last application is shown to contribute the most to the terminal residues, i.e. significant and rapid degradation of the residues along with the PHI after last application (decline residue trials), it is reasonable to assume that the scaling factor can be calculated on the basis of the dose rate at the last application only.

Case C: Fungicide/bactericide - Grapes

SEU GAP on grapes: 1+6 applications ((time interval: 7 days); 0.5+1.25 kg a.s./ha, BBCH 12-89, PHI: 21 days (total applied must not exceed 8 kg a.s./ha/year in any single year)

Location Season	No	kg a.s./ha	kg as/hL	Scaling factor (target: 8 kg a.s./ha/year)	Portion analysed	PHI (days)	Residue (mg/kg)	Result from scaling (mg/kg)
France South 1998	12	2.06	0.69	0.32	fruit	7 14 18	20, 4.3 17, 20 20, 12	- - **6.47, 3.88**
France South 2001	7	1.49-1.54	0.15	0.74	fruit	0- 0+ 7 14 21	11 9.0 27 28 21	- - - - **15.58**
	7	1.97-2.03	0.20	0.56	fruit	0- 0+ 7 14 21	14 15 27 25 21	- - - - **11.82**
Italy 2001	7	1.99-2.09	0.20	0.54	fruit	0- 0+ 7 14 21	21 50 11 24 20	- - - - **10.88**
	7	1.94-2.08	0.20	0.55	fruit	0- 0+ 7 14 21	8.5 47 15 44 11	- - - - **6.04**
France South 1998	12	2.06	0.69	0.32	fruit	21	7.5	**2.43**
	12	1.50	0.50	0.44	fruit	21	12	**5.33**
France South 1998	10	2.06	0.69	0.39	fruit	21	8.8	**3.42**

RMS assessment:

For the representative use on grapes (SEU) the available trials are not compliant with the critical GAP; the RMS proposes to assess the residue trials considering an 'alternative GAP' of 8 kg a.s./ha/year, i.e. the maximum total annual dose rate instead of considering the number of applications and the related single application rates. The proportionality concept was applied to these residue trials with reference to the maximum total annual dose rate (target dose rate of 8 kg a.s./ha/year) independently of the number of applications and the individual dose rate at each application.

EFSA assessment:

In this example, the proportionality approach is not applicable for the following reasons:

- Further information on the growth stage of the crop at last application, the interval between applications and the single application rate (instead of a range) should be provided.
- The application of the proportionality concept is only acceptable if the application rate is the only deviation from the critical GAP and the application of the "±25%" rule to the other parameters (number of applications, PHI) at the same time is not acceptable.