8 December 2022
EMA/CVMP/719874/2022
Committee for Veterinary Medicinal Products (CVMP)

Overview of comments received on the draft report on development of a harmonised approach to exposure assessment methodologies for residues from veterinary medicinal products, feed additives and pesticides residues in food of animal origin (EMA/CVMP/499555/2021)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	German Federal Institute for Risk Assessment (BfR)
2	Residue and Food Safety Unit, Regulatory Product Department, ANSES (FR)
3	Access VetMed
4	European College of Veterinary Pharmacology and Toxicology (ECVPT)
5	EU Association of Specialty Feed Ingredients and their Mixtures (FEFANA asbl)
6	AnimalhealthEurope
7	Federation of Veterinarians of Europe (FVE)
8	Prof. Maria de Lourdes Bastos
9	Dave Parker (Syngenta, Jealott's Hill Research Centre)

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1. General comments – overview

Stakeholder no.	General comment (if any)	Outcome (if applicable)
2	Comment: It seems that this document also considers biocidal product, however, no references to biocidal ECHA ("*Guidance on the Biocidal Products Regulation Volume III Human Health - Assessment & Evaluation (Parts B+C) Version 4.0 December 2017*") and CVMP guidance document ("*Guideline on risk characterisation and assessment of maximum residue limits (MRL) for biocides' (15 January 2015 EMA/CVMP/SWP/90250/2010 Committee for Medicinal Products for Veterinary Use (CVMP)")* are present. To our understanding, it is established that food basket data consumation should be followed for MRL for biocide. However, it has been agreed on at BPC WG HH I/2022 that PRIMo should be used for biocide dietary risk assessment. It would be relevant to explicitly states that the proposed harmonised approach also applies to biocidal products.	Consumer exposure models for biocidal products were not within the mandate of the European Commission and were therefore only mentioned for completeness. However, as the MRL evaluation for substances used for biocidal products used in animal husbandry follows the principles of Regulation (EC) No 470/2009, in this case, the same methodologies as for pharmacological active substances used in VMPs will apply for biocidal substances.
3	Given the length and complexity of the report, an executive summary would be very useful. It would be helpful to include an appendix that shows the breakdown of how TMDI, FACE etc. were calculated	A chapter "Summary and recommendations" is provided in section 7 in which the main statements and conclusions are presented clearly and compactly. An additional executive summary is not considered necessary. A table on calculation of TMDI has now been added in appendix. For the other models, links were already provided in the text.
4	The period of time left at the disposal of stakeholders to comment this protocol was considered to be extremely limited to allow a comprehensive evaluation by a group of more than 50 members.	Noted. Length of the consultation phase has to be in line with the procedures established at the agencies. Based on a stakeholder request, the consultation phase was already extended by two weeks.

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	Our comments will thus be limited to general remarks and do not include detailed analyses: We acknowledge that the draft report reflects a huge amount of work and includes a very comprehensive description of existing methods of investigations in each domain (VPM, feed additives, pesticides) with a clear analysis of the differences for each key parameter. By the way, it constitutes a reliable basis for future attempts towards harmonisation. Chapter 7 confirms the initial impression and shows that extensive work will be necessary to reach a common position valid for veterinary drugs, feed additives and pesticides. We would like to point out that such an harmonisation should start with risk assessment before considering exposure assessment. For example the Pharmacological NOEL is more and more frequently used to determine ADI, hence MRLs, for veterinary substances. This does include e.g., MIC data on human gut flora for antibiotics but also any kind of pharmacological effects depending on the activity profile of the substance. This is often a very difficult point as there are as many pharmacological effects as categories of active substance and there are secondary effects in addition to the main effects that are often difficult to assess quantitatively with enough precision and accuracy to determine a NOEL of even a LOEL. We have not the impression that this is something commonly taken into account for feed additives or pesticides, where ADI appears to be mostly based on toxicology, sometimes with a limited amount of studies (e.g. only	Partially accepted. It is agreed that for a full harmonisation in the different fields, further work will be necessary. However, full harmonisation would include changes in data requirements, which are anchored in the various regulations of the different fields, as can be seen in the current document. The European Commission would need to take a leading role in determining whether such changes should be pursued. Furthermore, it is acknowledged, that risk characterisations play an important role in the risk assessment as it is at least as important as exposure assessment. However, the mandate of the European Commission for the current report was on exposure assessment only and therefore the current report focussed on this issue.

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	90-day study in rat plus a limited number of genotoxicity assays for feed additives containing enzymes). The studies requested for risk assessment are generally speaking described in protocols valid in all OECD countries (OECD guidelines, ICH, VICH etc.). In the same way, manufacturers of Veterinary Medicinal Products, Feed Additives or Pesticides also need global rules to assess residues exposure. Global rules would facilitate the global development and registration of new products and we would encourage the working group to consider a close cooperation with international bodies (OECD, VICH, etc.) to avoid limiting the future rules to the European Union and thereby stimulating research and innovation in a one health context.	A harmonisation of the risk assessment in the different fields would be a more complex work, which will take a lot of time. It is agreed that global rules are to be preferred, and European agencies try to collaborate with international bodies on implementation of such rules. For the current report, experts from JMPR and JECFA were involved. However, as can be seen from the document, it makes it even more complicated, as the database might be different between organisations. But from a scientific point of view, we should use the best data we have (e.g. consumption figures for Europe on an individual base instead of summary statistics).
5	The paper is most welcome and discusses very interesting points and divergences.	
5	It seems fair to propose the EFSA model with its "Comprehensive database". In the EMA/VICH model "Food basket" its simplicity is compensated by very conservative (over-) assumptions of food consumption.	As stated in the report, it is agreed that the "Comprehensive database" used by EFSA (i.e. consumption figures) is the most accurate one for the European population. However, it is important to note that the group did not propose to use one of the "EFSA exposure models" but to develop methodology based on existing data.
5	It would be welcome, for transparency reasons and improving quality of the consumption model in future, that the results from the FACE model are also reported by countries. There are large	FACE already provides exposure results per country and age class.

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	divergences between EU Member States surveys, and it would be necessary to know whether this is really due to different consumption patterns, or rather to the methodology from national surveys (which are usually designed for other purposes). This may add to the degree of conservativeness observed in those models, especially for infants, toddlers and young children. Solutions on how to eliminate those possible biases would be welcome (either by Guidance to Member States on how to conduct survey, or other statistical tools looking at an EU-wide average value).	
5	One of the issues with the FACE tool has been a greater conservatism in children exposure, again maybe also due to some national survey methodology, and it is important that the toxicological profile of the substance is taken into account by risk assessors. Small deviations above the ADI should not be necessarily seen as problematic depending on the toxicology data available, if the average intake over the lifetime is well below the ADI. Although a bit out of scope of the mandate, it is good that the paper discusses those aspects. So far, it seems that this is not applied in practice by EFSA experts. More dialogue between the Agencies in this respect should therefore be encouraged.	Thank you for this comment. It is acknowledged, that risk characterisations play an important role in the risk assessment. They are at least as important as the exposure assessment. However, the mandate of the European Commission for the current report was on exposure assessment and therefore the current report focussed on this issue.
5	It is critical that the Agencies discuss more in depth in which situations it is appropriate to use the mean or the mean +2SD. While it is reasonable to use this approach where the number of animals is limited and the individual variability can be expected to be high (e.g., ruminants, pigs, dogs or where radioactive material is involved), it is a very conservative approach where a large amount	Thank you for this comment. As discussed in the report, currently there are very different legal situations and guidelines applicable in the different fields. This leads to different possibilities in the data evaluation and the implementation of the exposure assessment in the whole risk assessment process.

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	of residue data is available (often the case with eggs, broilers, fish where a clearly identified marker residue is available). Using the +2SD systematically (as currently done by EFSA) leads to a considerable overestimate of the chronic exposure (as seen in the examples, the overestimate would sometimes be a factor 2!). As the paper is aimed at harmonization, it is important that this aspect is discussed more in depth between EFSA and EMA.	However, theses aspects will be discussed by the committees afterwards.
5	Combining residues from multiple sources with the proposal to "*to use the highest mean observed residue from each species/commodity for the chronic exposure*": Although reasonable, this could get complicated because of data availability. Individual studies may be run for food additive use, but it would not be known what the amount of residues from the simultaneous use of the compound e.g., in plant protection would be. The approach to allocate only a ratio of the ADI to derive MRLs for compounds with combined uses might more pragmatic and probably equally safe. The proposal "*to integrate cumulative combined exposure (i.e., multiple sources) to substances belonging to groups with a common mechanism of toxicity*" also raises some concerns with regard to feasibility due to limited data availability. While such a scenario (combined/simultaneous exposure to several compounds with the same mode of tox action) is possible in theory, we wonder whether it really occurs to a relevant degree in real life.	Thank you for this comment. It is agreed, that an approach for combining residues from multiple sources needs more detailed discussion. However, due to the timeline this isn't possible at the moment. Furthermore, this aspect isn't specifically included in the mandate. The group discussed this and decided to move this text to the section "Proposal for harmonisation of some of technical aspects of the exposure approaches" and not to come up with any preferred approach on this for now.
5	The use of monitoring data to potentially refine assessments/limits post approval seems like a good idea at first glance, however, a few caveats apply: Would health authorities accept it and be prepared to	Thank you for this comment. At the moment this point is handled very different in the various regulatory fields, based on differences in the data

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	amend e.g., the MRLs? From an industry perspective, it would also be a very costly data collection effort.	basis resulting from the monitoring programs as well as on differences in legislation is (e.g. re-evaluation versus no re-evaluation of MRLs on a regular basis). Therefore, this point cannot be harmonised at this stage of the procedure, but should be considered for further work.
5	The proposals of using ADME/PK/TK data, consideration of food processing, LLT and probabilistic approaches are welcome.	
6	AnimalhealthEurope welcomes the Working Group's efforts to review the currently used approaches in the Union to exposure methodologies for residues from VMPs, feed additives and pesticides. In principle, the approach to harmonise exposure assessment procedures is appreciated but it also needs to be considered that there are good reasons for using different models to evaluate exposure scenarios (and risk characterisations) for different types of active substances like chemicals, VMPs, feed additives or others *e.g.*, different periods of exposure (8-hour shift 5 days/week vs daily for life time), different routes of exposure, different affected population categories (worker vs general population vs particular susceptible subgroups). A primary intent of the harmonised approach is the use of empirical databases for the evaluation of exposure. Since dietary habits change with time, the new approach would need to be sufficiently robust, as it is now for MRLs, that there will not be a need to periodically update risk assessments for VMPs to reflect changes in consumption data.	Thank you for this comment Please note, that the mandate covers only the dietary exposure of consumers to possible residues in food of animal origin. So, differences between workers and the general population isn't an issue covered here. It is accepted, that this is a new situation in the veterinary field. However, in the field of plant protection products and feed additives this is already handled. If EFSA receive updated consumption data, the purpose is also to update the exposure tools accordingly. For regulatory products, EFSA ensure that the exposure tools are clearly versioned, and that the different versions remain available. The EC

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	The comparison of the different approaches revealed that the current EMA/CVMP approach using the TMDI, and a standard food basket is a very pragmatic method resulting in very conservative exposure estimates for the chronic scenario but ensures a high level of protection for the general population. With respective adaptations it also appears suitable for acute exposure scenarios. Therefore, the establishment of a harmonised approach with a higher level of complexity but little or no benefit regarding the protection of the population should be avoided. Also, the consideration of JECFA/JMPR approaches is appreciated. Applicants pursuing product registrations globally often face questions regarding Global Trade issues in case very different MRLs are set in major import/export markets. During the elaboration of MRLs and the calculation of WPs, applicants face the problem that only chronic scenarios are to be considered for VMPs, while *e.g.*, the consumption of an injection site should be regarded as a rare acute event. In the section "Conclusion and Outlook" the draft report states, "Due to the complexity and multi-layered nature of the various aspects and questions to be addressed, most of the discussions took place ("intentionally") at a relatively high level of abstraction to allow for the identification and comparison of key concepts and key features of the different methodologies, rather than putting too much effort into clarification and agreement at the level of technical detail and terms." At one level this statement is well understood but the industry needs clear guidance how to properly conduct an exposure assessment and subsequent risk assessment. Since this detailed guidance is not provided and many technical details remains unclear	and MSs then need to decide on the implementing measures. Usually no retrospective assessments are performed, it is the date of submission of a dossier/application that usually determines the version of the exposure tool to be used for risk assessment. It is agreed, that especially for the chronic exposure in adults, the TMDI ensures consumer safety and a change in the estimate would not provide a benefit on this aspect. However, with a look at the acute exposure assessment the situations seem to be a bit different and the veterinary field would benefit from a change in the model used. Moreover, the differentiated calculations available from the more elaborated exposure models allow for more flexibility on how to deal with special situations (e.g. injection site residues, certain age groups like toddlers). Furthermore, EMA/CVMP is the only organisation in the international field, still using a food basket approach. Hence, also in the context of global harmonisation, it seems appropriate to make a step forward and use of more elaborated model. As pointed out in the report, the exposure estimate is only one part of the complete risk assessment. Therefore, after agreement on these recommendations by the European Commission, further work may be needed to implement

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	at this stage of the proposal, it is difficult to judge the suitability of the proposed harmonised approach for veterinary medicines. We are concerned that the period for public consultation was far too short for a such a lengthy and detailed document, particularly as it falls through the summer holiday period. This has meant that the document could not be reviewed with the necessary rigour.	these recommendations in the risk assessment procedure and conclusively provide special guidance to the industry. However, this will be a long-term project and will, if changes are made to existing guidelines, include further public consultations, as normally done.
7	FVE welcomes the initiative of the agency to review the possibilities of alignment of approaches with respect to the use of consumption data, the choice of input data for chronic and acute exposure, including field data, and possibilities for a harmonised estimate of a combined intake from multiple sources that will allow for better comparison of results. The data and estimates used should be the reasonably most disaggregated regrading subpopulations and sub-sources (e.g. offal versus meat). However, it remains to be elucidated how the "preferred" and "reasonable" models proposed by the experts will be used in practice, i.e. what are the conditions for using the one or the other. FVE notes that probabilistic models incorporating randomness in their approach should be investigated and supplemented by relevant field data, whenever possible, as part of the standard operating process.	Thank you for the comment. It is agreed, that further discussion on how the proposals would be implemented in the different fields are needed. The group was faced with the situation that legal basis as well as available data are quite different, making it impossible to come up with one strict approach applicable in all fields.
9	Taking into consideration that the guidance document's title is generically applicable across veterinary medicines, pesticides, and biocides, differentiated recommendations where applicable (e.g. in the case of "acute exposure" (lines 1378 – 1399), it could be clarified that the "Preferred proposal" applies to active substances that are veterinary active substances).	Thank you for the comment. Indeed, the mandate from the Commission was to come up with a harmonised approach. Starting the discussion from very different points of view, the group discussed a lot and comes up with proposals which are applicable to all fields. However, as noted in the

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		document, based on the very different regulatory aspects and guidelines, the proposals are at some points vague or give also alternative approaches if scientifically justified. Therefore, the "Preferred proposals" aren't meant only for the veterinary active substances but also for feed additives and pesticides

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
General	6	Comment: Clear guidance on injection site residues is missing from this document. Proposed change: A clear guidance on how to assess the safety of injection site residues is currently missing. Consumption of injection sites is a rare event and hence chronic exposure assessments are not appropriate. However, for substances not being acutely toxic, no acute reference dose can be established. Clear guidance how to handle this (*i.e.,* injection site residues for substances without acute toxicity) is missing.	Not accepted. The current document provides general recommendations for exposure estimates. How these recommendations will be implemented in different regulatory contexts will be decided separately by each relevant committee, panel or organisation. FuFurthermore, this report only includes the exposure assessment, risk assessment isn't within the scope of this document.
82	6	"*input data*" Proposed change: please clarify the input data needed and/or cross-reference to the section/definition where the description is present.	Accepted. Now included **"(occurrence data and consumption data)**"
85-86	8	Comment: "estimate the risk from life-long consumer exposure to residues from animals treated with veterinary medicinal products".	Accepted. Text was amended accordingly.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Proposed change (if any): estimate the risk from life-long consumer exposure to residues **in food commodities** from animals treated with veterinary medicinal products	
125	8	Comment: *"what circumstances".* Proposed change (if any): **Which** circumstances	Accepted. Text was amended accordingly.
135-137	5	Comment: Feed additives are not "pharmacologically active" The definition of MRL is as follows: "maximum concentration of residue resulting from the use of an additive in animal nutrition which may be accepted by the Community as being legally permitted or recognised as acceptable in or on a food". Proposed change (if any): *(…) the Maximum Residue Limit (MRL) is defined as the* ***maximum*** *concentration of a residue from a pharmacologically active substance,* ***or from the use of an additive in animal nutrition****, which may be permitted* ***or recognized as acceptable*** *in a particular foodstuff of animal origin (…)*	Not accepted. It is noted that feed additives can also be pharmacologically active (independent from the regulatory framework) and therefore they are covered by the definition in the report. In fact, in the list of pharmacologically active substance regulation, apart from coccidiostats, there are also substances that are not antibiotic or do not have antibiotic effects, but exert their action on the metabolism (e.g. ammonium chloride) which are also feed additives.

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136-140	6	In the area of pesticide residues (Regulation (EC) No 396/2005), the MRL stands for "Maximum Residue Level" which is defined as the upper legal level of a concentration for a pesticide residue in or on food or feed set in accordance with this Regulation, based on good agricultural practice (GAP) and the lowest consumer exposure necessary to protect vulnerable consumers. Comment: MRL relates to the highest exposure not harmful to the consumer. Proposed change**:** *based on good agricultural practice (GAP) and the ~~lowest~~* ***highest*** *consumer exposure* ***permissible consistent with the protection of*** *~~necessary to protect~~ vulnerable consumers.*	Not accepted. This is the legal definition of the maximum residue level in the field of pesticides, and can therefore not be modified in the report. This definition highlights the different principles applied in the field of pesticides compared to veterinary medicinal products.
137-140	2	Comment: In the frame of the Regulation (EC) 396/2005, no MRLs on feed commodities have been set for the moment. Proposed change (if any): -	Partly accepted. Although it is accepted that MRLs have not yet been set for commodities solely used as feed, Regulation (EC) No 396/2055 may already apply to feed, especially when that commodity can also be used as a food item. Furthermore, the assessment of pesticides in food of animal origin takes into consideration occurrence of residues in all feed items (even when no MRL is set).
143 – 144	5	Comment:	Not accepted. See comment lines 135-137.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Feed additives are not "pharmacologically active" Proposed change (if any): *"(…) considers the metabolism and depletion of* ***the*** ~~***pharmacologically active***~~ *substances in relevant animal species (…)"*	
169	8	Comment: what means nature? Proposed change (if any): Not clear	Accepted. Now replaced "(evaluate the fate of the substance and the nature of its residues)".
173-176	2	Comment: In the frame of the Plant Protection Product Regulation, the approach to propose residue definition is not considering "*that all metabolites have the same pharmacological/toxicological potential as the parent compound*". in the PPP regulation, determining residues to include in the residue definition is based on two main tasks: - to identify residues upper than 10% of Total Radioactive Residues (TRR) in metabolism studies - to have toxicological data for such components. Gathering all these information allow to propose residue definition.	Partly accepted. This report is intended to address the harmonisation of the exposure methods only. Section 3.2 is therefore only intended to explain generic principles on residues of concern (as background information) and is not intended to provide a comparison of the different domains. It is correct however that in the field of pesticides, not all metabolites are considered by default. It is therefore proposed to remove the word "all" in the sentence (line 175).

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		To be noted that a new OECD Guidance Document on the Definition of Residue is on going. Reference to this document could be helpful. Proposed change (if any): -	
184	7	Comment: Though inconsistent with current practices, as the assumption of "all-animals-treated" represents a very pessimistic worst-case scenario, we suggest to add 'equally' for clarity. Proposed change (if any): *"…treated **equally** with or…"*	Accepted. Text was amended accordingly.
187	2	Comment: An overview of residue studies (to derive residue occurrence) used in the different fields and different organisations is detailed. An overview of residue studies to analyse nature of the residues and to propose residue definition could be helpful. For instance, for pesticides, livestock metabolism studies allow to identify nature of residues. OECD guideline 503 explains how to investigate metabolism in livestock. Proposed change (if any): -	Not accepted. This report is intended to address the harmonisation of the exposure methods only, whereas studies on the nature of residues are mainly intended to identify the hazards. This does not fall under the remit of this exercise.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
187	2	Comment: For laying hen metabolism study 9-10 animals per dose group are required according to OECD TG 505 instead of 5 animal per dose group. Proposed change (if any):	Accepted. Table amended accordingly.
187	2	Comment: For honey, a European guideline exists (SANTE/11956/2016 rev. 9). Proposed change (if any): -	Accepted. Table amended accordingly.
187	3	Comment: VICH GL46 and GL48, animal numbers are recommendations as opposed to actual requirements Proposed change (if any): Suggest to detail numbers are recommended, not actually required.	Accepted. New footnote included: "The number of animals mentioned in guidelines are recommendations and no strict requirement."
187	3	Comment: Different font sizes and formatting in table Proposed change (if any): Suggest to standardise across all columns	Accepted. Text was amended accordingly.

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187	6	Comment: Table 1 has no header on subsequent pages, which is difficult to follow. Proposed change: Please repeat table header on each page.	Accepted. Text was amended accordingly.
187	7	Comment: Add Unit on Table 1 on 3rd column – 7th row, i.e. VMPs EMA GL46, GL56, GL57 for 'Milk' Proposed change (if any): Milk → 3 animals/time point	Accepted. Text was amended accordingly.
187	9	Comment: Three EU guidance for pesticide residues in fish have been published (covering fish dietary burdens, metabolism studies, and feeding studies): https://food.ec.europa.eu/plants/pesticides/maximum-residue-levels/guidelines-maximum-residue-levels_en Proposed change (if any): -	Accepted. Table amended accordingly.
201	3	Comment: Footnote is not present in table	Accepted. Table amended accordingly.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
		Proposed change (if any): Suggest to cross-reference	
226	6	Comment: "*ADI being most often based on an acute endpoint*" is there a source for this statement? Proposed change**:** Please add a reference if this statement is valid	Partly accepted. From the nature of a pharmacological effect, it is assumed that the sentence is correct. However, as there isn't a good reference publicly available the sentence is changed to: *"However, the TMDI is assumed to be conservative enough to also cover acute exposure (the term ADI is generally used, although,* ***for the pharmacologically active substances assessed so far by the EMA/CVMP ~19% of ADIs were based on acute endpoints and ~36% on subacute endpoints.****"* For completeness these numbers are already mentioned in section 6.2 of the report.
285 -287	5	Comment: The use of arithmetic mean + 2 standard deviations or the highest value from a single animal is very conservative to assess the risk of chronic exposure. when the dataset available is much larger than 6 animals, which can be the case in e.g., poultry (meat, offal and eggs) or fish. The arithmetic mean more likely represents the chronic exposure, as consumers will never eat every day over a lifetime the products from the animals receiving the highest concentration	Not accepted. Although it is agreed that the use of the mean + 2 standard deviations or the highest value is a conservative approach for chronic exposure assessment, this section only described the models as they are. Discussion on how conservative this approach is, belongs in a different section of the document.

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		of the feed additive and having the highest possible residues. Proposed change (if any): -	
290	8	Comment: "The residue concentration in kidney is applied to the intake of other offal". Proposed change: For the other offal the residue concentration in kidney is applied for calculation.	Accepted. Text was amended accordingly.
294-301	5	Comment: From our experience, two national surveys, namely the NUTRICHILD survey in Bulgaria and the "Food patterns of Spanish schoolchildren and adolescents" survey in Spain systematically come up with very high HRP values, especially due to high egg consumption, in toddlers and children. Whether this really reflects large differences in consumption patterns in those two countries in those age categories, or if this is due to different methodologies in surveys, is unclear. In Spain, the more recent survey (Encuesta de nutrición 2005) seems to give data which are more consistent with the rest of the European Union.	Partly accepted. It is agreed that harmonisation of the methodologies applied in the surveys may result in divergencies, and that harmonisation of the methodologies used is crucial. However, such activities are already ongoing for many years in EFSA. Already for the first establishment of the EFSA Comprehensive Database, survey data provided by Member States were subject to well-defined quality criteria. Furthermore, in 2011 EFSA launched the *EU MENU project*, which provides financial and technical support to EU Member States and pre-accession countries to carry out a dietary survey at national level. As part of this project, EFSA also issued a *guidance document* with clear recommendations for the collection of more harmonised food consumption data among the EU Member States.

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		Proposed change (if any): No change proposed, but cooperation between EFSA/EMA and Member States to design suitable surveys for this purpose would be appropriate.	
323	8	Comment: Which is the meaning of behaviour? Should be clarified Proposed change: Stability/degradation	Accepted. Text amended to "In addition, ~~**quantitative**~~ information on the ~~**on the behaviour during**~~ **impact of** industrial processing".
340-342	9	Comment: Where grains/seeds/pulses are treated post-harvest, they are considered Case 1, with their highest residues used. Proposed change (if any): *"...highest residues (HR) observed in supervised field trial and animal feed studies for unblended commodities (e.g. pieces of fruit or vegetables, meat, eggs)* ***and post-harvest treated grains, pulses, seeds****, or the median residue for blended commodities (e.g.* ***pre-harvest treated*** *cereal grains, pulses,* ~~***oil***~~*seed****s****, milk)."*	Partly accepted. Text amended to "...highest residues (HR) observed in supervised field trial and animal feed studies for unblended commodities (e.g. pieces of fruit or vegetables, meat, eggs, or seeds, grain and pulses treated after harvest) or the median residue for blended commodities (e.g. milk, or seeds, grains and pulses treated before harvest)."
344	9	Comment:	Partly accepted.

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		It could be helpful to be clear that VFs address variability in crop-based commodities. The VFs for livestock commodities, at 1, are default values. Proposed change (if any): *"…describing the heterogenicity of residues in composite samples* ***of crops and processed crop commodities****."*	Text amended to "… a variability factor is considered for some plant commodities to describe the heterogenicity of residues in composite samples."
349-350	8	Comment: *"Since the IESTI model is based on consumption data sub-populations (general population, children, women in childbearing age) are specifically addressed".* Proposed change: Is this sentence complete?	Accepted. Text amended to *"Since the IESTI model is based on consumption data, sub-populations (general population, children, women in childbearing age) i****n accordance with the data available*** *in each survey are specifically addressed"*
351-252	9	Comment: Please consider an alternative hyperlink for the JMPR tools. It could simplify how readers locate them. They can be found in the appendix to the annual on the Submission and Evaluation of Pesticide Residues Data, available here: https://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmpr/jmpr-docs/en/ Proposed change (if any**):** -	Not accepted. The FAO Manual was last updated in 2016, while IEDI/IESTI Models receive more frequent updates. It is highly suggested to refer to the latest version on the cited WHO websites, since these versions will also be considered by the JMPR itself.

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369 – 370	9	Comment: It is suggested to move the following info into the paragraph ending on line 363 since it also applies to earlier versions of PRIMo: "...and a further distinction between different types of mammals (i.e. cattle, goats, sheep and pigs)." Proposed change (if any): See comment.	Not accepted. The previous versions of PRIMo are not discussed. This statement is in relation to FACE only.
392	2	Comment: It could be interesting to have more details about the way residue occurrence data are obtained in the PPP regulation. In the frame of PPP regulation, HRs and MRLs for products of animal origin are derived considering the highest residue levels (mean residue level for milk) observed in the different animal matrices at the different feeding levels and the maximum dietary burden values. Different HR values are proposed, based on three different calculation approaches: - Using the transfer factor (Tf) calculated at the closest feeding level, - By interpolation between the two closest levels (not possible when estimated intake is not within the range of the feeding levels),	Accepted. Note added accordingly below the table.

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		- By linear regression (y = ax +b), considering all feeding levels. The highest value from these three calculation approaches is finally selected as the HR value for the animal matrix considered. Proposed change (if any): -	
392	3	Comment: Would appear that footnote 11 has been incorrectly assigned to "Acute -Not Applicable entry. Proposed change (if any): Suggest amending footnote to 22	Accepted. Text was amended accordingly.
392	6	Comment: Table 3.4.4. no header on subsequent pages, difficult to read Proposed change: Please repeat table header on each page.	Accepted. Text was amended accordingly.
392	6	Comment: Second column of table 3.4.4 has no title Proposed change: Please add the title to column 2	Accepted. Now included: *"**Chronic/acute (if applicable)**"*

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392	9	Comment: It is suggested to simplify this table by focusing it only on livestock residue data info/differences. Proposed change (if any): See comment.	Not accepted. The table intends to give an overview on all parameters, which are important for an exposure assessment.
392	9	Comment: The JMPR acute consumption data for not described. Proposed change (if any): "***Chronic:*** *GEMS Food Cluster diets (trade/production statistics) (g per capita per day).* ***Acute: global food consumption data (individual dietary records) (g/kg bw)***"	Accepted. Text was amended accordingly.
392	9	Comment: The JMPR age classes for surveys providing acute consumption data not described. Proposed change (if any): -	Accepted. Text was amended to "***Chronic****: GEMS Food Cluster diets (trade/production statistics) (g per capita per day).* ***Acute: global food consumption data (individual dietary records) (g/kg bw)*** "
392	9	Comment: Within Europe/EFSA, the chronic input occurrence data derived from crop field trials and feeding studies are medians. Although mean livestock residue are	Not accepted. Considering that the table mainly refers to how values are derived from the livestock samples, the term mean is considered more appropriate in this case.

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		used, after combination with median livestock dietary burdens, the resultant scaled residue data are referred to as medians. Proposed change (if any): "~~***Mean***~~***Median***"	
392	9	Comment: At the JMPR, the chronic input occurrence data derived from crop field trials and feeding studies are medians. Although mean livestock residue are used, after combination with median livestock dietary burdens, the resultant scaled residue data are referred to as medians. Proposed change (if any): "***Median*** ~~***/ mean***~~"	Partly accepted. Detailed explanation would go into too much technical detail. Historically, all input values are still referred to as "STMR" (median) – however, nowadays, some of them are mean values. Proposal: *"Median* ***(occasionally mean)****".*

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
392	9	Comment: For Europe/EFSA's acute input occurrence data, please refer to the comment above on Europe/EFSA's chronic input occurrence data. Proposed change (if any): *"For unblended commodities (i.e. tissues & eggs), highest residue (HR)* ~~***at***~~ ***based on*** *the maximum livestock dietary burden. For blended commodities (i.e. milk),* ~~***mean***~~ ***median*** *residue* ~~***at***~~ ***based on*** *the maximum livestock dietary burden"*	Not accepted. Considering that the table mainly refers to how values are derived from the livestock samples, the term mean is considered more appropriate in this case.
392	9	Comment: For JMPR acute input occurrence data, please refer to the comment above the JMPR's chronic input occurrence data. Proposed change (if any): It is proposed to use the same text as proposed above for EFSA pesticides.	Partly accepted. See proposal above.
392	9	Comment: For the JMPR's chronic exposure output, please refer to the comment above on the JMPR's chronic input occurrence data. Proposed change (if any): *"…using* ~~***mean/***~~*median residue****s****…"*	Accepted. Text was amended accordingly.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
392	9	Comment: For EFSA pesticides and the JMPR, acute exposure outputs are currently the same and appear also to be for PRIMo 4/FACE based on Section 3.4.3.2. If that is correct, their descriptions in the table could be more similar. Proposed change (if any): -	Partly accepted. While PRIMo and FACE use an approach which is very similar to the IESTI equations, they cannot be considered the same as the IESTI equation because PRIMo and FACE consider the large portion and body weight at individual level whereas the IESTI equation relies on a large portion and body weight derived at population level. A footnote will be added to clarify this difference.
392	9	Comment: For estimating exposure from multiple species, the different approaches of EFSA and the JMPR could be noted. The JMPR typically calculate livestock residues for the species used in feeding studies (using that species' dietary burdens) and extrapolate those residues to other mammals/poultry (i.e. all mammalian livers have the same residue value). Whereas EFSA will scale the feeding study's residues using all available OECD dietary burdens (e.g. sheep and goat residues based on a cattle feeding study, and sheep dietary burdens). This can lead to differences in residue estimates that are not explained by the JMPR conducting calculations for three additional OECD regions. Proposed change (if any):	Not accepted. The comment relates to different methodologies to estimate occurrence data in different species, whereas the point was interpreted in terms of representation/differentiation in the dietary exposure models and potential combination of individual food commodities. These are two different aspects and the point mentioned would belong into "Input occurrence data" – but is only one among many deviations and should not be highlighted specifically.

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		-	
392-393	6	Comment: No critical review of table 3.4.4 is possible due to limited time for public consultation.	Noted.
418	3	Comment: It is not entirely clear whether all model data sets are for the same active substance Proposed change (if any): Could this be clarified?	Accepted. A new sentence for clarification is now included: *"For this exercise it was assumed, that they all correspond to the same active substance."*
Tables 5, 6 and 7	3	Comment: No corresponding footnote for **** Proposed change (if any): Please clarify footnote	Partly accepted. The inclusion in the cell "Mean + 2 SD****" was a mistake, therefore **** is deleted in the table instead of adding a further footnote.
448	8	Comment: Not clear the meaning of text enclosed in brackets: Table 6: Summary statistics of residue data for fish (n=10 samples per day)	Accepted. Explanation now inserted below the table, as for table 1-4.

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469-472	6	Comment: The brief description of the GECDE approach does not align with the more detailed explanation in section 3.4.1.2. Using the highest reliable percentile for "highest contributor" is consistent but this section says that the "highest mean" was used for all other food commodities whereas 3.4.1.2 describes the use of the "mean dietary exposure from all the other relevant foods". Proposed change: Please align wording	Accepted. Text amended accordingly
469-472	6	Comment: It is not possible to understand how the data from table 2 were used for the calculation since the wording in this section ("highest reliable percentile", "highest mean") is not reflected in table 2. Consequently, the GECDE calculation and result as presented in table 8 cannot be confirmed. Proposed change: Please align wording in text and table 2	Not accepted. Table 2 represent the residue data. In line 469 it is stated that "Median residue concentrations were used to calculate the GECDE." and the median is included in Table 2. In contrast the "highest reliable percentile" and "highest mean" refer to exposure estimates (please also refer to the comment before.
Tables 8 and 9	3	Comment: The green-red colour scale is easily misinterpreted as acceptable-non acceptable residues	Not accepted. The colour scale is explained under each table. To make this more visible now included "***Colour code:*** *green-red =*

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		Proposed change (if any): Suggest a different colour scale	*lowest-highest values in a row; in bold: highest value in a column"*
482-483	6	Comment: (see also 469-472) Calculations behind the results shown in table 8 cannot be confirmed due to the short consultation phase. Accordingly, it cannot be reviewed whether the identical results of GECDE and IEDI are correct or by mistake.	Accepted. The calculations of GECDE and IEDI were re-checked and are confirmed. The differences in the detailed results are very small, so that rounding to two decimal places gives identical results in this case.
488	8	Comment: The sentence bellow is not absolutely true for adults when compared in Face and PRIMo models: "Concentrations at each time point are at least 2 times above concentrations resulting from all other models/age groups" Proposed change: Concentrations at each time point are **almost always** at least 2 times above concentrations resulting from all other models/age groups Or: **Except for adults in Face and Primo models,** concentrations at each time point are at least 2 times above concentrations resulting from all other models/age groups	Partly accepted. The sentence explained the statement in the previous sentence. However, it is notes that "concentration" should be replaced by "exposure" *"From Table 8 it can be seen that the highest values at all time points result from the TMDI model. **~~Concentrations~~ The exposure** estimate at each time point are at least 2 times above **~~concentrations~~ exposure** resulting from all other models/age groups, showing that TMDI leads to very conservative estimates for edible tissues."*

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492	5	Comment: It would be interesting to report (maybe in an Annex) the results from individual country surveys from the FACE tool. As commented above, it seems that some national surveys give very different HRP, especially for children, and it is unclear if this is really due to different consumption habits within the EU or due to survey methodology or limited data input in those age categories. It would be interesting to compare if the same is found in the PRIMO4 model. Proposed change (if any): Suggest showing an Annex with specific country results for FACE and Primo4 models and discuss/evaluate whether those discrepancies are linked to different survey methodology, and in this case, how this can be fixed in future	Not accepted. FACE is freely accessible on EFSA's website where results per country can be explored. It is true that methodological differences cannot be excluded, but several activities are ongoing at EFSA to harmonise the methodologies for the collection of food consumption data, and data are subject to validation upon reception at EFSA. Hence, differences observed are expected to result mainly from differences in dietary patterns.
504-716	6	Comment: Calculations behind the results shown in the tables cannot be confirmed due to the short consultation phase	Noted
509-512	5	Comment: Same comment as above (line 492 (5) Proposed change (if any): Same comment as above	Not accepted. See line 492(5).

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539	3	Comment: Unclear which columns are being directly compared. Proposed change: Suggest some form of additional formatting/colour coding.	Partly accepted. A colour code seems to be not appropriate in this case. Instead, an explanation is given below the table "Additional calculations were carried out with GECDE demonstrating that, when input values for GECDE are better aligned with the EFSA models (i.e. using milk equivalence instead of cheese and butter or using mean+2SD instead of the median) FACE and PRIMo 4, the obtained results are more comparable.".
563-568	5	Comment: Same comment as above (line 492 (5)). Is it the case in all countries that children consume much more eggs on a bw basis compared to adults, and are there large differences between countries? Proposed change (if any): Same comment as above	Not accepted. See line 492(5).
605	3	Comment: Proposed change: A comparison with the relevant HBGV would be very useful here, if possible	Not accepted. The mandate from the European Commission was to come up with recommendations on harmonised exposure estimates. Therefore, the current comparison is only for the exposure assessment. Comparison with the HBGV is a step of "Risk assessment" and therefore, not included in this mandate.

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608	3	Comment: No * in table 15 Proposed change: Clarify footnote.	Accepted. **"*"** added in Table 15
906-908	5	Comment: For long-established feed additives and during renewal of authorizations, it is possible in principle to provide some market data and refine the residue concentration based on budget method, but this approach does not seem to be endorsed by EFSA. This, in addition to the use of mean + 2SD, probably leads to considerable overestimates. Proposed change (if any): -	Not accepted. As proposed in the text of the report, the possibility to use data on actual occurrence of residues is desirable, however, it is stressed that such data should be obtained through monitoring and surveillance programs. The use of mean + 2*SD in case of feed additives is considered a conservative approach.
984 -	6	*"On the other hand, it was also noted that such exposure calculations based on empirical data and the conclusions derived from them* ***may need to be updated as dietary habits change****."* Comment: Please consider that new product developments including MRL setting and WP determination are done over roughly a decade. Applicants need a long-lasting	Partly accepted. It is accepted, that this is a new situation in the veterinary field. However, in the field of plant protection products and feed additives this is already handled. If EFSA receive updated consumption data, the purpose is also to update the exposure tools accordingly. For regulatory products, EFSA ensure that the exposure tools are clearly versioned, and that the different versions remain available. The EC and MSs then need to decide on the implementing measures. Usually no retrospective assessments are performed, it is the date of

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		model/a reliable food-basket for developing new molecules for food-producing animal species. Also, the impact of a change of the calculation basis (if new empirical data become available) on existing MRLs and WPs needs to be taken into account.	submission of a dossier/application that usually determines the version of the exposure tool to be used for risk assessment. How this will be handled in the veterinary field has to be decided at the time the new model will be implemented.
1016	8	*"…the four standard tissues,…"* Comment: I would put in brackets the tissues	Accepted. Relevant part of the sentence amended accordingly: *"the four standard tissues* ***(muscle, fat, liver, kidney)***"
1047	6	"… *administered as treatment to animals, which can leave residues in food, (VMPs, feed additives) are …*" Comment: A space is missing Proposed change**:** Please add a space	Accepted. Text amended accordingly
1122-1130	8	As for penicillins, I would give another example of compounds that can elicit acute symptoms as beta-agonist compounds. This would give the notion that not only antibiotics can give rise to acute toxicity.	Accepted. Text amended accordingly

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1122-1132	1	Comment: Depending on the toxicological profile of a compound, an acute exposure assessment may be needed. Considering, that EMA/CVMP has only derived ADIs as HBGVs, it might be supportive to harmonisation, if EMA could publish a list of HBGVs for the compounds in EMA's remit, including an indication whether the critical effect was based on acute, sub-acute, sub-chronic or chronic endpoints.	Accepted. A table of ADIs established by CVMP is now provided in the annex.
1211	8	*"…feed additive…"* proposal to change: feed additive**s**	Accepted. Text amended accordingly.
1235	8	Between or **among**?	Noted. Between is the right wording.
1248-1259	7	Comment: FVE agrees that a consistent harmonised policy, procedure and guidance on when and how subpopulations should be considered and included in risk characterization. Proposed change (if any): -	Partly accepted. As already mentioned in comments above, this report focuses on exposure assessment only. Therefore, no recommendations for the whole risk assessment are given.
1288-1293	5	Comment:	Partly accepted. See comment 294-301.

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		In general, it is agreed that the national surveys and individual data are the most reliable and scientifically valid. However, differences in national surveys and their relevance have not been evaluated in this document. We would encourage EMA and EFSA to continue exploring that aspect and formulate recommendations to national authorities on how to generate reliable surveys for this purpose. Proposed change (if any): -	
1294-1298	6	Comment: "reasonable alternatives": the use of reasonable alternatives creates concern as it seems that the database is not harmonised with global data and deviation between the data set can introduce biases. Proposed change**:** The proposed reasonable alternative should be further discussed to possibly reduce biases.	Accepted. The reasonable alternative is now deleted and reference to CIFOCOss is only included in the text.
1309ff, esp. Footnote 46	1	Comment: The document states that for convenience the assumption of normally distributed occurrence data shall be made. It proceeds by recommending confidence intervals based on this normal assumption. An assumption of normally distributed occurrence	Partly accepted. For estimating statistical parameters from a sample one needs sufficient information either in the form of knowing the underlying data distribution or by having a large sample. A conclusion of the central limit theorem is that irrespectively of the underlying data distribution, the arithmetic mean of

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		data is very likely not applicable in many situations, a fact the document itself concedes. For situations like these (unknown underlying distribution of a sample) non-parametric procedures are available for estimating e.g. confidence intervals without making any assumption of the distribution of the whole population. Proposed change (if any): Consideration whether non-parametric estimates of the confidence interval of data should become the default in the recommendation or added as a "reasonable alternative".	independent data asymptotically follows a normal distribution. Therefore, in case there is sufficient data (a common threshold is >30 measurements) the confidence interval for the arithmetic mean can be calculated under the assumption of normality regardless of the data distribution: sample mean ± t × sample sd / square root(sample size). with t the corresponding quantile of the t distribution with (sample size − 1) degrees of freedom. The same formula holds if the sample size is low but the data can be assumed to be normally distributed. In case the sample size is low and there is no plausible assumption on the data distribution the confidence interval might be hard to be estimated reliably: for a parametric approach one has to work with a possibly incorrect distributional assumption, and for a non-parametric approach the data are possibly too sparse. In parts, the text in lines 1301ff is misleading. Therefore, these lines are amended (without significantly changing the content) and include a statement on non-parametric approaches.
1331-1332 and 1364	5	Comment: Clarification on what the experts consider as "reasonably sufficient number of observations" and "limited sample" is welcome. In poultry or fish studies, residue data may be available on more than hundred animals, but the tendency is nevertheless to use arithmetic mean +2SD. As shown in the	Partly accepted. It is very difficult to give a concrete sample size, as this depends on data (e.g. variability, only one study available or also other reliable data) and assumptions (e.g. accepted uncertainty). These data and assumptions are at the moment different in the different fields, as the legal base and guidelines are different.

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		examples, this is a critical factor resulting possibly in a two-fold difference (e.g., between FACE tool and Primo4), so for harmonization purpose, this topic deserves a bit more clarification. Proposed change (if any): Would be helpful to provide further clarification in this respect, ideally with sample size or concrete examples.	Therefore, the group decided to give as preferred approach the proposal to calculate the mean and lower and upper 90% (or 95%) confidence limit of the mean (i.e. describing the uncertainty of the underlying data), to be transparent. With this approach, if more samples are available, the confidence limit would narrow and approach the mean.
1348 ff	7	Comment: There is good reason to assume that data may *not* be Gaussian and therefore, the median is the appropriate measure of choice. Proposed change (if any): -	Not accepted. As outlined in the amended text on chronic exposure the chronic daily exposure is always best described by the arithmetic mean, and this is independent of the underlying distribution of the data, no matter whether this is Gaussian or not.
1366-1368 & 1392-1393	7	Comment: Agree. It is important that all values are assessed over time to confirm accuracy of the model. Proposed change (if any): -	Accepted.
1388	7	Comment: The same consideration of blended commodities can be assumed for mono-ingredient meat products.	Not accepted. The assumption that milk is most often a blended commodity (i.e. milk from different cows is mixed in a tank and

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		Proposed change (if any): -	processed afterwards), is accepted in the field of PPP. But, as already stated in the report this assumption isn't accepted in other fields. However, in case of meat and meat products this assumption isn't acceptable, as meat is not blended in all situations.
1440	8	*"food additive through the labelled route of application"* Comment: not clear for me	Accepted. Amended text in the new section under 7.2.4 (see also next comment).
1435-1466	5	Comment: While the preferred model seems a reasonable approach, in the light of the highly unlikely scenario of exposure from all three uses at the same time, a few situations may occur where an alternative approach may be acceptable: – Not all residue data may be available for the different uses, meaning that the risk assessor may need to restrict to the available studies for selection of the highest exposure scenario; it is not logical that a feed additive applicant must make studies mimicking VMP or pesticide uses. A textual suggestion is added below (line 1452-1453). – Even if residue data for VMP, Pesticides and Feed additives *are* available due to existing	Partly accepted. After further discussion, the whole section is revised and moved to section " 7.2.4. Proposal for harmonisation of some of technical aspects of the exposure approaches"

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		authorizations, there could be situations where multiple uses are highly unlikely, or where the risk manager could decide on certain restriction clauses in the respective authorizations to prevent multiple use. In those cases, it may be relevant to (also) assess consumer safety with the residue data belonging to the application under evaluation, and not necessarily the highest exposure scenario from all uses. The authority mandating the risk assessor may indicate so at the start of the process. Change to: (*Lines 1452-1453*) Identify and use the highest mean observed residue per commodity/species from all **available** uses for the chronic exposure. **In cases where multiple use scenarios can be excluded, the residue data pertaining to the application under evaluation can be used in the assessment, on instigation of the mandating authority.**	
1452-1453	2	Comment: Identifying and using the highest mean observed residue per commodity/species from all uses for the	Accepted.

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		chronic exposure could lead to low consumer estimates. Proposed change (if any): -	
1479	9	Comment: Change proposed based on the EFSA approach for poultry being to use 90:10 for muscle:fat into meat. Proposed change (if any): "(e.g. residues in **mammalian** "meat" being a mixture of 20% fat and 80% muscle vs residues in muscle or fat)."	Accepted. Text amended accordingly.
1480	6	Comment: The preferred model should be based on i) individual-level dietary surveys (preferably using RPC values), ii) provide information on exposure in different subpopulations/age groups (*e.g.*, infants, young children, adults), and iii) allow estimation of exposure levels at different levels of the exposure distribution (e.g., 95th percentile or other values of interest). Proposed change: Organisations (*e.g.*, EFSA) currently using more precise models provide calculation sheets based on the food intake data considered to be relevant. Such	Accepted. This is the goal of this exercise. After agreement on an appropriate consumer exposure model, a webtool similar to PRIMo/FACE could be developed, intended to be used for VMPs, pesticides and feed additives.

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		calculation sheets/programs must be provided for veterinary medicine, too. It has to be ensured that models to be used are harmonised to prevent discussions on the correct model and correct consumption data to be used during MRL or product applications.	
1508	3	Comment: It is worth mentioning that this should also include selection of an appropriate HBGV for short-term exposure scenarios. As stated in Section 6.2, an ARfD will not usually be established if acute toxicity is low. This may result in situations where an acute exposure is compared with an ADI that was derived from (sub)chronic toxicity data which may result in overly conservative outcomes. This is also relevant for scenarios where long-term exposure is inherently unlikely, e.g. consumption of injection site muscle	Partly accepted. This is something that will have to be considered once there is an agreement to implement the new model. As mentioned elsewhere, the risk characterisation and the implementation of both (risk characterisation and exposure assessment) in the whole risk assessment process is out of scope of this mandate and needs further discussion.
1524-1527	5	Comment: A downside of those models is that risk managers may consider any deviation slightly above the ADI during a short period of life as not acceptable, regardless of the toxicological profile of the substance under evaluation, and even if the average intake over a lifetime is far below the ADI. It is critically important	Partly accepted. *As mentioned above, risk assessment and implementation of the recommendations in the different fields are not within the scope of this report. However, this will be done by the committees after agreement on the recommendations in this report.*

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		that risk assessors discuss those situations very precisely as well. Proposed change (if any): -	
1531-1533	9	Comment: The IEDI model, as deployed in the European pesticidal context, explicitly covers a range of subpopulations/life stages. Proposed change (if any): *"The IEDI model is a model for estimating approximate average chronic (lifetime) exposure and refers to* ***~~a general population, but is not suitable to identify specific consumption patterns and, thus not accurate and flexible enough for estimating exposure in certain subpopulations and life stages~~ the range of subpopulations covered by the model.****"*	Not accepted. Even though the IEDI approach may sometimes distinguish certain subpopulations, it is generally referring to average consumption within those (sub)populations. This does not allow to observe within the (sub)population groups.
1534	9	Comment: Since pesticidal TMDIs are based on food survey consumption data, it would be helpful to clarify this section. Proposed change (if any):	Partly accepted. Text amended to the proposed change in the comment to line 1534-1536 *"…The TMDI model* ***as applied in the veterinary field****, is based on a food basket…"*

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		*"The **veterinary** TMDI model is based on a food basket…"*	
1534-1536	9	Comment: The term "TMDI" is used differently in a pesticide context, being based on food consumption surveys rather than a livestock 'market basket'. Proposed change (if any): *"…The TMDI model **as applied in a veterinary context,** is based on a food basket…"*	Partly accepted. Text amended to the proposed change in the comment to line 1534-1536 *"…The TMDI model **as applied in the veterinary field**, is based on a food basket…"*
1609	8	The harmonised methodology for tissues Comment: Not clear for me. Does it refer to samples from animal origin?	Accepted. The sentence is changed to *"The harmonised exposure model (7.2.3) could be extended…"*
1614	6	**"***The exposure estimates currently conducted are based on residue data from pre-authorisation studies conducted under the intended conditions of use. The assumptions underlying the study design are intentionally conservative, and the results may not accurately reflect the "real life" residues in food as they are available on the market. Data from monitoring and surveillance programs (post-market) may be more appropriate here, as they provide information on levels and occurrence frequencies of*	Partly accepted. It is true that monitoring data are usually not available/considered at the time of MRL evaluation. However, in the field of plant protection monitoring data are collected on a yearly basis, and exposure calculations are carried out as part of an annual report. This provides interesting information on the 'real life' exposure compared to the exposure calculated for MRL setting. Additionally, the purpose of this paper was to provide harmonised recommendations for the exposure assessment.

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		residues in food as they are actually ingested by consumers." Comment: This may work for contaminates but is not the appropriate data to set MRLs or withdrawal periods, which is the purpose of this document.	The setting of MRLs and WP goes far beyond this scope and has to be discussed afterwards in each field.
1625	6	"*Where such data are available, it may be appropriate to revisit exposure estimates at appropriate times after approval to refine the original exposure estimate."* Comment: What would be the consequence? Does this mean that withdrawal periods will be adjusted post approval, or would this even result in a refinement of the MRLs established? Who would be responsible in conducting monitoring studies?	Partly accepted. As stated above, this goes far beyond the scope of this report. Furthermore, it should be noted, that this is only an outlook with possible areas for further discussions, if needed. At the moment these points haven't been discussed in detail.
1656 - 1660	7	Comment: FVE agrees that probabilistic models incorporating randomness in their approach should be investigated and supplemented by relevant field data, whenever possible, as part of the standard operating process. Proposed change (if any): -	Partly accepted. As mentioned above, these lines only intend to give an outlook on possible further developments. At the moment no validated methods are available but might be evaluated and included in the future.

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