PESTICIDES PEER REVIEW EXPERTS' MEETING ON PHYSICAL AND CHEMICAL PROPERTIES AND ANALYTICAL METHODS

PESTICIDES PEER REVIEW 189 DRAFT AGENDA

14 NOVEMBER 2018 H 9:00
16 NOVEMBER 2018 H 13:00

1. Status and discussions on CRD Guidance on physical, chemical and technical properties of PPPs

What is the status of the CRD Guidance on physical and chemical properties? When is the official distribution for comments by SCoPAFF expected?	DE
CRD/EU draft Phys-Chem and Storage Stability GD The Northern Zone (NZ) chemists commented together the storage stability part of the draft GD. The final draft version is going forward to policy colleagues, who will take it to the next available Standing Committee Meeting with the Commission (most likely to be October). 4 areas will be highlighted to the commission where further consideration is required for full harmonisation: • Methods accepted for physical hazards (EC or UN methods) • The requirement for studies to be conducted to GLP • The need for long term storage stability data prior to authorisation in the Northern Zone • The inclusion of a CAS statement for tank mixes. What was the outcome?	FI
Guideline on physical, chemical and technical properties of Plant Protection Products (PPPs) under Regulation (EC) No. 1107/2009 An updated version of the "old" UK guidance document was published on the UK HSE website in 2015. It has since been through two substantial commenting phases with other EU Member States, EFSA, Industry and wider Stakeholders with the aim of producing an EU harmonised guidance document. If the meeting would like we can provide an update on the status of this document and how it is now being taken forward within the European Commission.	UK

2. Physical-chemical properties of a.s. and PPP

If there are two or more applicants with their own complete dossier, which endpoint will be included in the LoEP? In the renewal, there are often different values for each applicant in the LoEP. This is not regarded as reasonable, only one should be an endpoint. Furthermore, if the old value of the DAR is still acceptable, only this value should remain in the LoEP and only the DAR study should be listed in the references relied on.	DE
If there are several studies on the same endpoint from the same task force, should they then all be evaluated?	DK
If new data are provided as supportive even though the old study is still valid, should these new studies still be evaluated? Should they be relied on?	DK
Are all studies, that were evaluated and accepted, relied on? Or is it only those studies whose endpoints ends at the LOEP?	DK
If the studies have been used for step 1 annex II data matching previously but submitted for supportive information, should they still be evaluated and included in the RAR? Should they be relied on?	DK
Pure active substance: When data requirements state 'purified active substance' to be tested, is then one study representing the whole task force acceptable? We tend to think so. However, each Taskforce should fulfil the data requirement. Hence, if there is more than one taskforce, then each should submit a study for each end-point. Unless data protection from last review of the active substance has expired, then these data can be used, if they fulfil data requirement.	DK
Active substance as manufactured: When data requirements state 'active substances as manufactured' to be tested, then it should be demonstrated for each of the technical active substances in each task force? For example when two task-forces of three companies each (total companies of 6 and 6 different technical materials), should then all 6 technical materials be tested to demonstrate appearance, solubility in organic solvents, flammability, self-heating, flash point, explosive properties and oxidizing properties? If not all technical materials should be tested - Should the batch in the studies represent one of the technical materials of the task force or could it just be a completely different batch? If not all technical materials should be tested - If the technical material can be both liquid and solid at room temperature, should both physical states be tested?	DK
According to SANCO/2012/11251, the RAR should contain the original data of the DAR and the supplementary data. The re-assessment of previously accepted studies is not intended unless it is necessary in the light of current scientific and technical knowledge. 1. Except of new data requirements, what are the reasons to re-assess phys.-chem. studies of the DAR? 2. In case that a DAR study is still accepted, the related supplementary data should be marked in the RAR as e.g. "additional information" and only the DAR study will be included in the list of references relied on. Can this be confirmed?	DE
Oxidising properties We experience active substance and PPP applicants to stop after the preliminary test when testing oxidizing properties according to A17 in Regulation 440/2008. According to this test method the preliminary	DK

test can only clarify if the test material has oxidizing properties – not the other way around. If the preliminary test is negative, you have to do the full test. The preliminary test is for security reasons and can only be used to state the positive effect. The negative conclusion has to come from the full test or from a justification based on the chemical structure. See Regulation 440/2008 A.17 section 1.4 'No further testing is required when the preliminary test clearly indicates that the test substance has oxidising properties. When this is not the case the substance should then be subject to the full test.' The statement in section 1.6.2.1 'The substance is to be considered as oxidising if the reaction is vigorous. In any case where the result is open to doubt, it is then necessary to complete the full train test described below.' Refers to the positive reaction in the preliminary test. If you are not sure it was a positive reaction you should continue to the full test. If you are sure it was a positive reaction – you should not do the full test. Do you think there are cases where it is possible to stop after the preliminary test and still conclude the test-material is non-oxidising?	
In case that an endpoint is changed in the renewal, can this be marked in the LoEP? For example by the addition „(new)".	DE
Are studies still accepted, which were initiated before 25 July 1993 but without GLP, when they are scientifically still valid? DE assumes that the guidance on GLP general requirements 7017/VI/95 (June 1996) is still applicable, so that these studies can be used.	DE
GLP status of "interim" shelf-life studies for authorisation of a PPP It is increasingly common for all of the storage stability and shelf-life data generation to be combined within one study i.e. the initial submission of the accelerated data in the form of an interim report, on the basis of which we grant a time limited authorisation; the submission of the final report (2 year ambient shelf-life data) is then set as a data requirement for continued authorisation. The UK GLP authority have recently indicated that any claims of GLP compliance for interim reports may not be justified which has lead us to question whether it is acceptable to make a regulatory decision (to grant authorisation) on the basis of an interim report. We are currently discussing this with the UK GLP Authority but would like to know how other Member States treat interim reports.	UK
What kind of deviations from the methods listed in the Communication is acceptable? (e.g. MT 47.2 used instead of 47.3, or in-house method instead of listed method)	DE
For some technical properties, both, UN-RTDG or EEC methods can be used to address the data requirements. The UN-RTDG method is needed for CLP. Are EEC methods still necessary for these properties? Should these methods be removed in the next revision of the method communication?	DE
Concerning the technical tests (persistent foaming, suspensibility, wettability…), it is not clear if this test should be performed under GLP or not. The regulation (EC) 1107/2009, art 3 point 19 concerning the GLP, refers to the directive 2004/10/CE. FR considers that the directive 2004/10/CE superseded the document 7109/VI/94 Rev 6. According to the directive 2004/10/CE all studies that provide information on properties of the substance and innocuity concerning the health and environment must be conducted under GLP. Therefore, Fr considers that the technical properties should be performed under	FR

GLP. Indeed, for example, an excess of foam can lead to an overflow of the tank and therefore increases the exposure or when the wettability is not good, it can lead to an increase of exposure as the granules can block the equipment.	
Acceptable limits have been set for technical properties such as 60 mL for persistent foaming, 70 for suspensibility …. When the results of the test are outside these limits it is indicated in the draft guidance document for the generation of data on the physical, chemical and technical properties of plant protection products under regulation from UK, that evidence must be submitted showing that there is no unacceptable risk to operators following use of the preparation through the appropriate application equipment. However, currently no field test allowing to demonstrate it is available and no validation criteria are described. How do the member states assess these data?	FR
Reg. 284/2013, Part A Section2, 2.5 Viscosity The Regulation 284 states: For liquid formulations the viscosity shall be determined at two shear rates and at 20°C and 40°C and reported together with the test conditions. In the commission communication method OECD 114 is given to determine Viscosity. OECD 114 describes different methods. Only for rotational viscosimetry shear rates can be given. In our opinion all the other methods can be used for Newtonian liquids as well. What is the view of other experts?	AT
Field test for phys-chem parameters Follow up point 19 (chapter 3 page 46) discussion table PRAS 150. FR indicated that they are working on this issue. Are there any news?	AT

3. Status and discussions on Guidance documents SANCO/3030/99, SANCO/3029/99 and SANCO/825/00

Update SANCO/3030/99 What is the status of the update of guidance document SANCO/3030/99	NL
Guidance SANCO 3030: This guidance is under revision. State of the work. The units for the linearity for the a.s. and impurities in technical material to be discussed. While units for impurities in w/v (e.g. mg/L) and in %w/w are adequate, we think that for active substances units in %w/w has no sense.	ES
Status of the revision of SANCO/825/00 and SANCO/3029/99 after the call to stakeholders to possibly identify points for consideration for revision. Consolidated comments from EFSA, MS, EU ref labs and industry were dispatched at the end of February 2018. What are the following steps and timing foreseen?	BE
Revisions of SANCO/3030/99 and SANCO 825 What is the stage of the process?	FI
Status of guidance documents that are currently under revision 3030/99 3029/99 & 825/00 Significant – non significant change (12638/2011) CRD guidance document (Pyhs-Chem)	AT
Update on guidance documents and their revisions would be important. Guidance document SANTE/11813/2017 rev. 0 on quality control and method validation procedures for pesticide residues and analysis in food and feed should also be taken into account.	LT

4. Analytical methods

Update SANCO/3029/00 Many pre-registration methods are not fully validated to SANCO/3029/00, but may still be considered fit for purpose, e.g. when there is a zero residue situation. What should be the consequences when validation does not fully comply with the requirements? Should the guidance be updated to reflect that full validation may not be necessary in all cases?	NL
Assessment of methods used for the generation of pre-approval data (Reg. (EU) 283/2013) The methods used in a number of studies of tox and the other sections of assessment for data generation are not validated according to the SANCO/3029/99, i.e.: -Limited information is available on precision and accuracy that are derived from procedural recoveries; -Linearity is not fully covered or not addressed; -The methods are not sufficiently specific and confirmatory method are missing; -Insufficient number of recoveries per fortification level available; These issues, however, have been considered by applicants as minor deviations and methods still being fit for purpose. When and why it should be accepted that no new method validation is required? How should the final conclusion on the acceptability of such methods used in different sections of assessment be reached?	LT
Update SANCO/825/00 The guidance document for post-registration monitoring methods is not consistent with the data requirements as laid down in 283 and 284/2013/EU. The ILV for drinking water should be added. In addition, the criteria for requiring a method for blood and tissues should be amended.	NL
With implementation of Regulation (EU) 283/2013, monitoring methods for body fluids and tissues are required for all active substances, i.e. regardless of the classification. Many data gaps originate from this change. Nevertheless not much effort was put so far in deriving appropriate residue definitions for body fluids and tissues. Although it becomes sometimes evident that parent is not a suitable marker compound for monitoring (based on metabolism studies with rodents or livestock), it seems that parent is often set as the residue definition by default. Requiring methods for parent is often not reasonable. From our experience, awareness needs to be raised among toxicologists/residue chemists that a residue definition consisting of suitable marker compounds should be provided to analytical chemists for them to decide if matching methods exist or, if data gaps need to be set. We would like to share our experiences on the issue of monitoring methods and residue definitions for body fluids and tissues with other Member States.	DE
Analyte (residue definition) of the methods for body fluids and tissues (blood)?	LT
For PPP that are capsule suspensions: Do you have any experience/knowledge about the determination of the free fraction? One notifier had a method where the "free" non-encapsulated a.s. fraction was obtained by dispersion of the formulation in water for 30 seconds followed by filtration to remove the encapsulated fraction. The	DK

notifier states that the complete operation should be completed in less than 2 minutes. Another notifier had a method where the "free" non-encapsulated a.s. fraction was obtained by dispersion of the formulation in water for 30 minutes. Should the specified time be justified by e.g. reference to experimental data from the method development? Any requirements in terms of sensitivity, e.g. LOQ <XX of methods for the determination of "free" active substance?	
Applying the guidance document on evaluation of extraction efficiency in residue analytical methods (SANTE/10632/2017 Rev.3 of 22.11.2017). 1.With reference to the document, 5.1 Decision trees for post - registration monitoring methods and pre-registration methods (Figure 1 and 3) indicate that the detailed expert judgement is needed when the compounds of DoR are present in non - extracted radioactive residue. Elaboration of these cases is rather complex issue and the input of experts of residue section assessing metabolism studies would be very important. As long as this is the issue for section 1 and residue section assessing metabolites, sharing experiences on expert judgements would be very important. 2. Bridging between matrices for addressing extraction efficiency. The guidance document (4.2) says that 'the extraction efficiency should be evaluated for all matrix groups or animal commodities for which residue analytical methods are required. ,One example for each matrix group or respective commodity is sufficient. The selection of matrix groups depends on the availability of sample material from metabolism studies or samples with incurred residues Bridging between high water content and slightly acidic matrices is acceptable for slightly acidic matrices but should be justified by applicant. When the bridging would not be acceptable?	LT
Extraction efficiency A new guidance is available for this issue. Extraction efficiency shall be included in the monitoring methods. Who assesses the results of extraction efficiency tests?	AT
SANTE/10632/2017 rev. 3 (22 November 2017) The Technical Guideline on the Evaluation of Extraction Efficiency of Residue Analytical Methods (SANTE/10632/2017) will have to be followed starting from 22.11.2019. It concerns 1) approval of NAS:s as well as renewals 2) authorisations of new ppp:s as well as reauthorisations, and 3) MRL:s. The GD is very complicated and would require some training. Could EFSA arrange this? Does any MS have experience using the GD?	FR
Concerning template for analytical methods We would very much appreciated if the template for analytical methods had a column added to it where references were given to the studies executed on other disciplines, e.g. eco tox and residues – and using an analytical method to generate pre-registration data. This would ease the assessment, and also the communication between the chemist and the assessors working on the other disciplines.	NZ

5. Status of the Guidance of isomers

Guidance of isomers. State of the work on this guidance.	ES
GD on assessment of isomers What is the stage of the process?	FI
Difenoconazole isomers: In EFSA Conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole (2011) it is stated that active substance difenoconazole is a mixture of diastereo isomers, but the possible preferential metabolism/degradation of each enantiomer in animals, plants and the environment was not investigated in the studies submitted in the dossier and was therefore not considered during the peer review. Moreover, the analytical methods used in the studies reported through all sections were not stereo-selective, and all values mentioned as "difenoconazole" have to be considered as "sum of isomers". Recently, one applicant conducted a study for determination of difenoconazole isomers, but with regard to the EFSA peer review of the pesticide risk assessment for the active substance difenoconazole, confirmatory data concerning the impact of isomers of difenoconazole was to be submitted within 2 years from the adoption of specific guidance. No specific guidance has been established according to our knowledge so these methods still aren't a requirement. Will there be any guidance concerning the impact of difenoconazole diastereo isomers?	HR
TTC approach EFSA 2016: we think that the Guidance of equivalence (SANCO/10597/2003 –rev. 10.1) should be actualized taking into account the conclusions of the 2016 EFSA review on TTC approach.	ES
Update on guidance documents and their revisions would be important. Guidance document SANTE/11813/2017 rev. 0 on quality control and method validation procedures for pesticide residues and analysis in food and feed should also be taken into account.	LT

6. Identity, specifications, reference specifications, relevant impurities, batch data

Proposed topic	MS
Impurities	
Relevant impurities: the definition of "relevant impurity" should be clarified. It is necessary to establish criteria to consider when an impurity can be considered relevant. We have only information included in the guidance on equivalence (SANCO/10597/2003 –rev. 10.1). We think that this information is not enough. In addition, the consideration of an impurity as relevant should be done at level of active substance evaluation (for approval), therefore we think that it would be necessary to have an alone document or guidance on this issue. It could be helpful to take into account the ECHA Draft on Definition of relevant impurities (Date of draft: 11 July 2017), where two option are provided: 1. Definition based on hazard properties and 2. Definition based on hazard properties and concentration.	ES
Assessment of relevance of impurities. For the assessment of new unknown impurities of active substances and whether they are (eco)toxicologically relevant, the (Q)SAR modelling using DEREK, VEGA is being performed. It might be implied that the section 1 should assess the relevance of impurities based on the structures and comparability of substances then. Clarification on how much and to which extent the section 1 should be involved in relevance of the impurities assessment	LT

would be appreciated.	
Guidance on equivalence: ecotoxicological assessment of impurities. The proposal of the guidance based on a calculation is simply reduced to a consideration of the concentration and not to the intrinsic hazard of the impurity. To be discussed if this is an adequate approach.	ES
Residual solvents as impurities. Considerations of the ICH guidance as adequate to address this issue.	ES
Process solvents as possible relevant impurities in technical materials. What LOQ would be appropriate for the determination of a process solvent in a technical material? As an example: A second manufacturer is applying for technical equivalence and they use toluene as a solvent in the final manufacturing step. If toluene was not used in the manufacture of the reference source what LOQ should the second manufacturer use in their batch analysis for toluene? Is 1 g/kg sufficient? If they provide screening data to show levels are < 0.5 g/kg should we require further data (full batch data using a validated method)? One approach is to apply a "margin of safety" factor to the C&L trigger level and use this as an indication of a suitable level at which the solvent would not be relevant and ask for data at that level. What approach do other Member States take?	UK
Spectra are required for impurities considered of toxicological, ecotoxicological or environmental significance. The term is confusing as another term is used in the 'Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009' (SANCO/10597/2003 – rev. 10.1, July 2012). Here Significant impurities are all those components present in quantities ≥ 1 g/kg in the active substance as manufactured. Whereas Relevant impurities are those of toxicological, ecotoxicological and/or environmental concern – even if present below 1 g/kg. We would tend to think that the spectra should be provided for those impurities that are considered relevant according to the equivalence GD. How do you interpret this?	DK
Reg. 283/2013, Part A Section1, 1.11 Analytical Profile of Batches It is stated: All of the representative batches shall be within the last five years of manufacture. Where data from the last five years of production are not available, a justification shall be provided. What kind of justification is acceptable? (i.e. QC Data, Lack of production,….)	AT
Confirmation of analyte identification (active substance, relevant and significant impurities) In Reg. 283/2013, Section 1, points 1.10.2 & 1.10.3 regarding significant and relevant impurities, respectively, it is stated that "Information on how the structural identity of the impurities was determined shall be given". In addition, in SANCO/3029/99 rev. 4 (11/07/00), point 3.1.3 "Confirmation of analyte identification" it is reported that confirmatory techniques are required to support identification when the primary method of determination is not GC-MS or another highly specific method as HPLC-UV DAD. - Is HPLC-DAD considered suitable stand alone analytical technique for the identification of the active substances and impurities or should it be used as a second technique to confirm another primary? - Is the chromatographic peak collection followed by DAD or IR considered suitable analytical techniques for the identification of the active substances and impurities or should they be used as a second technique to confirm another primary? - A list/table of the accepted analytical techniques and an appropriate	GR

combination (primary/confirmatory) of them would be useful. - Should the second/confirmatory technique be validated in terms of quantification?	
LOQ for relevant and significant impurities – 5 batch analysis In Reg 283/2013, Section 4, points 4.1.1 regarding additives, significant and relevant impurities it is stated that the experimental determination of LOQ shall not be required. In what means it will be demonstrated that the analytical method is suitable to quantify to the desired level? Is it acceptable to consider LOQ the lowest validated level? Are specific values below the LOQ acceptable to be reported in the 5-batch table? If an impurity is detected but not quantified in some of the batches but quantified in others what should be the value for the not-quantified impurity in the 5-batch table in order to perform the statistical analysis? Is it acceptable that for the calculation of the standard deviations (SD), values below the LOQ to be assumed equal to the LOQ and not detected impurities to be taken into account as zero?	GR
Specifications	
Minimum purity: In case more than one applicant provided a complete dossier and each specification is covered by tox and ecotox, then the minimum purity should be set to the lowest level of the acceptable specifications. In the LoEP should be given only one minimum purity.	DE
Identity/ specification of "naturally occurring substances" Example: Diatomaceaous earth. AT is RMS for the Renewal Currently this is specified as 1000 g/kg diatomaceous earth with a relevant impurity of crystalline SiO2. Therefore all the different metal oxids/salts present in Diatomaceaous earth are active substance. There is however an analytical method to determine the major component SiO2 How to specify such naturally occurring substances? Is an analytical method for the determination of the active substance in the preparation necessary? 1. How to deal with equivalence assessments?	AT
When reference specifications need to be amended and what the consequences are is still often a point of discussion. It would be appreciated to discuss when there is the need to redefine the reference specification and how to exactly address the issues that occur with equivalent sources.	NL
Change of technical specifications during renewal. Considerations of the disagreement between risk assessment and risk management and consequences. How to deal with data gaps regarding representativeness of batches used in tox and ecotox studies and compliance with art. 61 and 62 of Regulation 1107/2009.	ES
Renewal: A clear statement regarding the reference specification is needed, taking all information from identity, tox. and ecotox. into account. If the existing reference specification is covered by tox. and ecotox., this should remain the reference specification. If only the new proposed specification is covered this should become the new reference specification. To be discussed what happens if both specifications (existing reference specification and new proposed) are not covered by tox. and ecotox..	DE
Reference Specification after Renewal of Active substances This was also discussed in PRAS 150, change of specification shall be	AT

included/highlighted in Review Report (COM) / EFSA conclusion. Status on this issue? (point 1 PRAS 150)	
Reference specification : 1. Reference specification to be considered after renewal of an a.s. for equivalence : the situation remains in some cases quite unclear about the reference specification to be considered for equivalence assessments and there is not always a consistent approach within the equivalence reports – some examples: - Propyzamide : From the final review report 2018 and Reg. (EU) 2018/755, the COM seems to have kept the old specification as the reference specification for renewal (min. of 920 g/kg is indicated in both documents) whereas it seems that both RMS and EFSA proposed to update the reference specification for renewal. In DAR, specification seems to be considered covered by (eco)tox batches. However, the review report stated that it cannot be concluded that the (eco)tox. batches were representative of the specification and that the presence and quantification of these impurities in the batches tested in (eco)tox. should be further investigated. Consequently, it is not fully clear which specification should be taken into account to perform equivalence assessments. From the information provided within review report and Reg. (EU) 2018/755, BE would take the initial reference specification as set for 1st approval but this seems to be not in agreement with the conclusions in the RAR and EFSA conclusions… - Florasulam: a lot of equivalence reports since renewal but in some cases the Tier I is done against the old reference specification and in other cases to the new reference specification… 2. Setting a specification: 5-BA and QC data are available. If QC data indicates a lower purity than in the 5-BA but from the QC data it appears that it is not the majority of the batches that will present this lower purity, what is the best approach to set the specification? : lower the min. purity based on the results of the QC data (TC is as really produced) or leave the min. purity higher but with the consequence of a need of declaration from the applicant that batches outside the specification will be discarded (not for EU level) or re-blended to meet the specification (whereas this was not spontaneously proposed by the applicant)… (case of isofetamid) 3. Reference specification: pilot scale data vs. large scale data (i.e. isofetamid): although it is true that 283/2013 mentions that specification should be based on large scale data, a reference specification could be set on pilot scale data if they are the data assessed and considered covered (eco)toxicologically (i.e. most of the (eco)tox. tests performed with batches issued from this pilot scale production). Large scale data are indeed needed and assessed but have not to become systematically the reference specification because large scale.	BE
Co-formulants as active substances Some pesticide formulations contain a co-formulant which has been approved as an active substance. How should they be evaluated according to Reg.1107/2009? Should it be taken into account that the substance has been approved as the active (e.g. basic) substance or is it to be regarded as a co-formulant, e.g MSDS is sufficient? Should we consider the function of the co-formulant?	SK

Is there some difference if the basic substance has a function as preservative in the product (e.g. Sodium benzoate – approved as benzoic acid) or if it is merely the filler (e.g kaolin)	
How to present the ppp composition in the dRR in cases where variants of the active substance are formed during formulation (salts in first place)? Should the excess of the reacting co-formulant be calculated?	DE
How to handle overdosage to compensate degradation of active substance? Is this accepted in other MS? Are there any other cases known than dimethoate?	DE
How to characterise the composition of a ppp in case a pre-solution is used as an alternative co-formulant?	DE

7. Microorganisms

Identity Microbial active substances are often produced in a continuous manufacturing process until the formulation of the microorganism active substance (no technical active substance). The continuous manufacturing process is used as the active substance is not stable and need to be formulated in order to be stored, transported or commercialised / or it is not economically interesting for applicant to stop the manufacturing process at technical active substance step. What do you require to characterise the active substance in this case? FR considers that it is necessary to provide at EU level (in the monograph or in a specification dossier) all information usually required for technical active substance to the formulated active substance here the plant protection product. These requirements should be provided for each new PPP manufactured with a continuous process.	FR
Stability The limit of 10% decreasing of active substance content in PPP is not applicable to the microorganism. The evaluation is based on the minimal certified value, in the appropriate microbial unit (CFU/g or ITU/g in the case of bioassay or OB/g or ……), of the microbial active substance in the formulation before and after storage. During the storage stability study, the content of the microbial active substance has to be higher the minimum certified value before and after storage as indicated in the OECD guidance document on storage stability of microbial pest control products. Therefore, as in the most of cases the microorganism PPPs are not stables 2 years at ambient temperature, FR considers that in the case the stability is proved after Y months (or weeks or years) at Z°C, it would be reported on the label : "Do not store at temperature higher than Z°C" and "Do not store more than Y months"	FR
Analytical method Currently, no guidance document on analytical method for the determination of microorganism is available and no criteria have been clearly established at EU level. The guidance document on analytical method for the determination of chemical active substance is not adapted for the analytical method used for microorganism Indeed, the determination of the microbial active substance can be performed by numeration of petri dishes or in the case of microbial active substances with a biopotency (effect of tone or metabolite) by the determination can be performed by bioassay.	FR

FR considers that positive and negative control and data on the repeatability are sufficient to validate a method. For the repeatability we consider ideally, the following criteria concerning the number of repetition: • For bacteria: 5 batches have to be used, 3 samples have to be taken from each batch and for each sample. 3 Petri dishes have to be sowed. Ideally, the % RSD for each batch should lower or equal to 20 %. • For fungi: 5 batches have to be used, 5 samples have to be taken from each batch and for each sample 3 Petri dishes have to be sowed. Ideally, the % RSD for each batch should lower or equal to 20 %. Do you consider that these criteria are sufficient? Do you consider that additional criteria should be required?	

8. Equivalence, issues for PPP authorisation at MS level

How do we handle equivalence assessments as described below? In cases where COM not has agreed on an increase in purity stated in Vol. 4 specification and EFSA conclusion for the active substance in the renewal, at same time as also impurities have been changed in reference specification (Vol. 4). The question is which reference specification should be used for the impurities in an equivalence assessment, the DAR or the RAR specification? Propyzamide is one example concerning this issue. Also, if we change in the specification regarding the impurities in renewal evaluations, should we then maintain the DAR specification of the active substance to be sure that the Vol. 4. renewal specification will be the valid one?	SE
Changing the reference specification after renewal of the a.s. DE has been considering the process of reassessing equivalent sources in case of changing the reference specification after renewal of the active substance. What was the outcome?	FI
After the renewal of active substance, in the case where the changing of the reference specifications is clearly reported in the RAR or in the Efsa conclusion, how do the member states manage the status of existing equivalence reports? Do you follow the document sent by Germany (Dirk Wolffram) to member states in December 2016? For the assessment of the specifications of active substance at EU level or in equivalency report, the difficulty is to know if the technical active substance contains some relevant impurities. The identity of impurities below 1g/kg are generally unknown. Then you would need to do a theoretical assessment based on the manufacturing process and the starting materials, to consider whether it is possible any hazardous by-products are formed during synthesis of the active. In order to be able to do it, FR considers that the MSDS should be provided to facilitate the identification of potentially relevant impurity present in the starting materials.	FR
New relevant impurities analysis in formulation as an outcome of the EU renewal of AS approval. New relevant impurities of the active substances require the validated methods for their determination in formulations with the sufficiently low LOQ considering their low concentrations (e.g below 0.01 %) in formulation. This is not always feasible to timely address by the applicant. Can the absence of method that does not demonstrate acceptable LOQ be considered a data gap for the product's authorization?	LT

Concerning properties of the variant of the active substance Concerning authorization of PPP - how should we respond when the AS is formulated as e.g. a salt that has not been assessed at EU-level? These compounds could have properties of concern for e.g. mammalian and/or eco-toxicology and CLP. Should data and/or information concerning physchem therefore be requested? This topic is also relevant for PPPs that call for renewal of authorization based on renewed approval of glyphosate. Hence, we would appreciated it if this topic was discussed with glyphosate in mind	NZ

9. Others

Identity of PPP and the decision on acceptability of alternative co-formulants There would be the need of the EU harmonized approach among MSs. It would be good to fully clarify the definitions 'alternative co-formulant' which is also called "option' by applicant and 'equivalent co-formulant'. Should the focus be drawn on the CLP in the risk assessment or identicality as a close similarity (CAS, structure, manufacturer, detailed composition) should be considered? To which extent could the alternative co-formulant contain a rather different substance or mixture that would not trigger CLP and would not change significantly phys-chem properties of formulation (e.g. presence of low content glycerol?) This is important to consider as long as different MS come to different decisions of alternative co-formulants	LT
Limits for co-formulants in the formulation (based on enquiries of applicants). We have been enquired by a non notifying company on possibility to authorize a formulation A which was claimed to be identical to the original product B authorized based on expiry of the data protection for B (Article 34, Reg.1107/2009). In the same time we have been questioned on permissible deviations, i.e. limits to deviate from the co-formulants contents specified. There insignificant deviations from the contents specified meant (e.g. batch to batch variations). Our understanding, however, was that based on criteria of the SANCO/12638/2011, any changes including the smallest ones would be regarded as a formulation change. And the two formulations are not likely to be identical based on their full composition details when manufactured by different sources (not under licence). Other points of view would be appreciated.	LT
Bridging of package materials: Which changes can be tolerated? How is this handled in other MS? Does national guidance exist?	DE
In Croatia, recently there are many cases where applicants require prolongation of shelf-life for more than 2 years (e.g. 3 years). They conduct studies (for the formulation type) according to Technical Monograph n°17, 2nd Edition to demonstrate the stability of the product but not with all the studies necessary for the formulation type (e.g. In WG formulation there is no study for the wet sieve test). Should we consider this as a criteria for a negative evaluation if we have that same study in the 2 years shelf-life study?	HR
Harmonisation on data requirements for different types (mandatory and recommended) of tank mixtures: Could this point be included in the CRD Guidance or in the next revision?	DE
We would like to discuss the necessity to prepare CLH report, respective to use the newest template where CLH is a part of RAR in	CZ

case of AIR IV substances (sheep fat, fish oil, fat distillation residues etc.)	
New dRAR-CLH template The new dRAR-CLH templates should be used for those active substances the applications of which have been delivered after 6.10.2017. For FI, this means that our first case (AIR4) will start next May (FI is the RMS for quizalofop-p-ethyl). Does any MS have experience using the new template and assessing physical hazards? Should the phys chem tests be performed according to the EC or UN test guidelines? In addition, there are three phys chem properties in the new dRAR-CLH template that have not been part of phys chem active substance assessment before and are not included in the 283 Regulation: viscosity, granulometry and relevant degradation products	FI
Discrepancy Reg. 283/2013 with the CLP regulation 1272/2008 Follow up point 12 (chapter 3 page 41) discussion table PRAS 150. As the "new combined Volume 1" of actives also includes the former CLH –report and shall be used by ECHA for classification as well we should urgently discuss how to deal with this issues. There are some points in CLP not required by 283/2013 and some use other tests. There have also been questions from companies/consulters how to deal with the differences.	AT
Classification methods according to Com. Reg. 283/2013 and 284/2013 seem to be equal. Are there any rules when we can ask for EEC A methods and when UN RTDG?	CZ
Variants. There is no formal EU or zonal agreement on how to deal with variants. For example the case of the renewal of the 2,4 D: during the renewal of the 2,4-D, the 2,4-D EHE was not considered and there was a problem with the renewal of the products according to art. 43	ES
SDS should be in accordance to Reg. 2015/830. Should they be actualized every 2 years as it is stated in the Guidance document of Phys/Chem?	ES
Field tests In our last General Phys Chem meeting 2 years ago in Parma, FR announced that it is currently working on this subject, by collecting information from professionals of agricultural equipment /practices. The idea was that further field tests could be used to demonstrate that the preparation can be effectively applied in case the results of laboratory testing do not meet the acceptable criteria and are not fully relevant regarding the intended conditions of use. What is the stage of the process?	FI
Expert meeting phys-chem / Zonal Authorisation Follow up point 3 (page 62) discussion table PRAS 150. Is DE still willing to organize this / IS there a need?	AT
Zonal authorisation meeting In our last General Phys Chem meeting 2 years ago in Parma, DE suggested taking the initiative of organizing a zonal authorisation meeting (e.g. "equivalent" co-formulants, change of formulation). What happened since? As Finland is currently the chair of the Northern Zone (NZ) and as Tukes (Finnish Safety and Chemicals Agency) is the competent authority of the Plant Protection Product Regulation in Finland, Tukes decided to arrange a NZ Physical Chemistry face-to-face meeting in Helsinki 26-27.9.2018. The NZ chemists found it very important that a face-to-face meeting concerning the physical chemical properties, analytical methods and identity of plant protection products and the	FI

respective active substances was held, and consequently, all the northern zone countries wanted to take part even though we had no funding for the meeting. So, we were altogether 9 persons from 7 different countries. Thus, could DE reconsider arranging a zonal authorisation meeting? Most probably it would be very popular	
A general attitude to evaluation of AIR IV substances can be discussed.	CZ
Implementation of "Practical guidance compiling dossiers and assessment reports_final" This document was discussed at the last PSN meeting in June 2018 and commenting was launched. We would like to consider the implementation of this guidance in terms of practicability (especially as regards data gathering methods, overview table).	AT
EFSA Working Document Different documents summarizing PRAPER/PRAS meetings are in existence. There is an EFSA working document (2007), summary documents of the PRAS 120,150,….. AT would like to know if these documents can be combined to have an up to date version of all MS/EFSA expert decisions.	AT
Analytical method requirements for zonal applications Should the ILV for drinking water be addressed for all zonal dossiers which need to be evaluated according to 284/2013/EU?	NL
Change in chemical composition Sometimes a change in composition of the product is evaluated at national level and sometimes it is assessed at zonal. It would be useful to have a harmonised approach on this issue in all zones. Has to the applicant submit the dRR for relevant sections in any case or it depends on the degree of change?	SK
Art 34 of the Regulation 1107/2009 can be applied when the composition of the generic and the reference product is comparable. Our question is what is comparable in MS view from physchem perspective?	CZ
Revision of the equivalence reports after the renewal of active substances. How to deal with this?	ES
How to proceed after comments received to the equivalence reports. There is not harmonization between all MMSS.	ES
Equivalence assessments. Would it be relevant to further amend or peer review the equivalence assessments in case when any new information is coming to MSs? Would the amendment of Article 38 fit into the scope of the Regulation (EU) 1107/2009 revised?	LT
Art. 43 and existing equivalent sources after renewal: What is the experience and approach of the other Member States regarding the re-consideration of the existing sources (previously considered equivalent) after renewal of the active substance? - What is checked? Only min. purity and max. rel. impurity or the overall specification? - Data requested?: new GLP 5-BA/at least QC data/re-analysis of (some) batches from the previous 5-BA study when batches previously assessed are older than 5 years or when re-analysis for a component occurred with a certain delay (exp: more than 2 years). At the TC 150, it was suggested that 5-BA should be requested. Guidance on art. 43 is not fully clear on this point and mentions the following: "The applicant may provide a reasoned argument justifying that its source can still be considered equivalent to the EU reference source." which gives quite a large margin for interpretation on what is expected to be submitted. - Are DE and other MSs using the DE proposal of working document	BE

entitled Working document on the Assessment of Technical Active Substances Sources after the Renewal of Approval (presented in the PAI but apparently not accepted)? - Maybe useful to decide for a naming convention for updated equivalence reports (Active substance equivalence Notifier Source MS YYYY-MM-DD_UPDATE_YYYY-MM-DD?)? A question is also raised on who is finally responsible to update the equivalence report after re-consideration of an existing alternative source. The guidance on art. 43 mentions that in principle it is the RMS of the active substance at EU level who should do it but in practice, it seems that it is rather the zRMS who amends the equivalence report when starting the assessment of a PPP according to art. 43.	
Sources of active substance(s) authorized in PPPs (controls on the market) In BE, only the sources of a.s. and their min. purity as declared and approved in the BE dossier (i.e. based on equivalence reports available on circabc and notification of the authorization holder to BE of his wish to add a new source of an active substance in his BE product(s)) are accepted (art. 44 1107/2009 and 58 of KB BE 28/02/1994). In the LoS, quite often the manufacturer declares the min. purity of the a.s. purchased by company XX but this min. purity is stated/indicated to be the same to the min. purity as set in the Impl. Reg. whereas the real min. purity of that source is higher. So the LoS does not mention the true min. purity of that source as assessed and accepted in the equivalence report. BE is of the opinion that even if the min. purity of the source is well in agreement with the agreed EU level, the declared min. purity of the concerned source of a.s. should be as set in the equivalence report, mention of the min. purity as reported in the Impl. Reg. is not sufficient. What is the approach of the other MSs?	BE
Assessment of Technical Active Substance Sources after the Renewal of Approval (Art 43) In case that the reference specifications of an active substance are changed during the renewal process, what should be the procedure with the sources which were considered equivalent based on comparison with the old reference specification. This is important for the Article 43 process where the sources are used for the renewal of plant protection product. According to Guidance document SANCO/2010/13170 rev. 14 (7 October 2016) it is referred: "Where change of the reference minimum specification occurs, including impurity maximum levels, authorisation renewal dossiers can only rely on those sources already declared equivalent and compliant with the new criteria. The applicant may provide a reasoned argument justifying that its source can still be considered equivalent to the EU reference source. In this case, the RMS should only check the declared minimum purity and the maximum content for relevant impurities" To our understanding the RMS can address this issue with a statement regarding the minimum purities and relevant impurities. Nevertheless, no comment on significant impurities or updated equivalence report is mentioned. Is this acceptable by the other Member States?	GR
Changes in the composition: The assessment of impact on the properties of the formulation cannot be expected without test which is not conducted. How to deal with changes in the co-formulants which belong to the same chemical "family" but are not chemically equivalent	HR

and have different CAS No. but are present in the same proportion in the old/new composition?	
Extrapolation between packaging materials: In the Guidance document for the generation and evaluation of data on the physical, chemical and technical properties of plant protection products under regulation (EC) no. 1107/2009 5. New relevant impurities analysis in formulation as an outcome of the EU renewal of AS approval. New relevant impurities of the active substances require the validated methods for their determination in formulations with the sufficiently low LOQ considering their low concentrations (e.g. below 0.01 %) in formulation. This is not always feasible to timely address by the applicant. Can the absence of method that does not demonstrate acceptable LOQ be considered a data gap for the product's authorization? of the EU parliament and council on placing plant protection products on the market, it is stated: „For aqueous based formulation types e.g. SL, SC, LS, CS or FS, extrapolation between any plastic material types is acceptable. Extrapolation from plastic material to metals is not acceptable. For organic solvent containing formulations e.g. EC, EW, SE or OD, extrapolation from HDPE to HDPE co-extruded with any of the following; EVOH, fluorinated HDPE and polyamide is acceptable. Extrapolation between plastic material types e.g. HDPE to PET is not acceptable." Since HDPE and PET are very different plastic materials, is it really acceptable that in aqueous formulation types extrapolation is acceptable? For example SC formulation can consist of many co-formulants that could impact on packaging material for which there is no shelf-life study conducted. Also, in the Guidance document it is stated: „for where it is proposed that a preparation is to be packaged in a bulk container (a container of size greater than 20 L), it is recognised that it is impractical to conduct EN 44 EN stability tests in the large containers. Therefore results from smaller volume containers (1 L upwards) may be used to extrapolate to the larger containers." Some Member states in the zonal evaluation procedure, don't accept bulk containers (larger than 20 L) if the shelf-life study in conducted in 1 L containers. What can we do in this case? Is 1 L acceptable for extrapolation of bulk containers or not?	HR
CRD Guidance document proposal, Section Exrtapolation of packaging materials Is this approach agreed within the EU experts / EFSA?	AT
During the shelf life stability study, the modification of the packaging should be « measured ». However, there is not clear criteria to consider the packaging as acceptable or not. For example, if after the shelf life the packaging is modified (the form, or the weight, or seepage) what is it considered as an unacceptable modification?	FR
Guidance document Significant – non significant change (12638/2011) This guidance is also used to determine equivalence of generic products. If the formulation type of the generic is different, but the Active/co-formulants are nearly identical, can the product be claimed equal? (i.e. Types: ME/EC or SC/SL)	AT
Tank mixes of pesticides This is the issue for overall risk assessment. Considering the importance of tank mixes the method of analysis could be developed for the determination of both active substances (and relevant impurities) in the mix?	LT
How do member states assess the procedure for cleaning the tank	FR

mixture/machinery provided in the PPP dossier? Does an acceptable residue limit in the tank available?	
Data Protection of studies reported in EFSA Reasoned Opinion: Is there data protection for the studies that are reported in EFSA reason opinions on the modification of the existing MRLs for active substances but that are not presented in the relevant assessment reports for these active substances?	GR