Network on Pesticide Steering
Minutes of the 20th meeting

Held on 14-15 June 2016, Parma

(Agreed on 17 August 2016)[1]

Participants

- **Network Representatives of Member States (including EFTA Countries):**

Country	Name[2]
Austria	Albert BERGMANN
Belgium	Herman FONTIER
Czech Republic	Jana JEZKOVA
Denmark	Vibeke MØLLER
Finland	Kaija KALLIO-MANNILA
France	Thierry MERCIER
Germany	Herbert KÖPP
Greece	Dimitra GKILPATHI
Hungary	Tamás GRIFF
Ireland	Aidan MOODY
Latvia	Līga BRENCE
Lithuania	Kristina VALIONIENE
Netherlands	Hanneke WESTLAND
Poland	Paweł STRUCIŃSKI
Portugal	Bento DE CARVALHO
Slovakia	Bronislava SKARBOVA
Slovenia	Milena KOPRIVNIKAR BOBEK
Spain	Maria Carmen LOPEZ GOTI
United Kingdom	Susy BRESCIA

[1] The publication of the minutes shall be made without delay in compliance with the Founding Regulation and no later than 15 working days following the day of their agreement.
[2] Indicate first full name and them surname (John Smith) all throughout the document

- **European Commission DG SANTE:**

(via tele-web conference, participated in agenda point 3, under the plenary discussion)

Wolfgang REINERT

Sofie HOFKENS

Mark WILLIAMS

- **EFSA:**

Pesticides Unit (José V. TARAZONA, Head of Unit, Chair)

Applications Desk Unit (Karine LHEUREUX, Head of Unit)

Pesticides Unit (Bénédicte VAGENENDE, Coordination Team)

Pesticides Unit (Maria ARENA, Ecotoxicology Team)-participated in agenda point 4

Pesticides Unit (Danièle COURT MARQUES, Mammalian Toxicology Team)

Pesticides Unit (Frederique ISTACE, Mammalian Toxicology Team)-participated in agenda point 5

Pesticides Unit (Claudia HEPPNER, MRLs Team)

Pesticides Unit (Anja FRIEL, Residues Team) - participated in agenda point 8

Pesticides Unit (Christopher LYTHGO, Fate and Behaviour Team)

Pesticides Unit (Jürgen STURMA, Coordination Team)-participated in agenda points 9,10,11

Pesticides Unit (Dimitra KARDASSI, Coordination Team)

1. Welcome and apologies for absence

The Chair welcomed the participants.

Apologies were received from Sweden (SE).

The Chair presented the scope and objective of this meeting. A significant part of the June meeting (one full day) is dedicated to an open discussion on how to improve the peer review process, and in particular, the involvement and cooperation of EFSA and Member State experts. EFSA proposed to hold this discussion as a workshop type approach, with three groups discussing in parallel specific elements, followed by a plenary discussion and a drafting session on action points for the identified improvements. The workshop on how to improve the peer review process came as a follow up of the discussions at the expert meetings and the Standing Committee on Plants, Animals, Food and Feed (PAFF), questioning the overall quality of the peer review process (quality of the experts/quality of DAR/RAR) and the concerns claiming that Member States' (MS) view is not adequately presented within the EFSA conclusion.

2. Adoption of agenda

The agenda was adopted without changes.

It was proposed to discuss the points raised by France (FR) under Any Other Business (AOB).

3. Workshop on improvements in the peer review process

The workshop focused on three main blocks with the following points for discussion.

Block A: Process, improvements, clarification of roles and expectations

1. Selection of experts for the peer review meetings
2. Role of Rapporteur Member State (RMS) expert also after the meeting, updating the draft assessment reports (DAR/RAR) following the peer review process proposal including section 1 of volume 3.
3. Role of EFSA and non-RMS experts and internal coordination in the MS
4. Training needs in the MSs, additional support by EFSA to the RMS, EFSA support to the RMS in meetings with applicants if requested by RMS

Block B: Recurrent issues on regulatory and risk management issues influencing the risk assessment

5. Risk assessment/risk management interaction
6. Addressing previous risk managers decisions during the risk assessment
7. New data requirements and scientific progress
8. Assessment of micro-organisms

Block C: Transparency and involvement of the MS experts after the meeting

9. Reporting expert meeting discussions, naming MS, minority views
10. Interaction with other sections
11. Involvement of MS expert for issues arising after the meeting
12. Consultation of the final draft Conclusion

The break out discussions in the three working groups were followed by a plenary discussion and a drafting session on action points for the identified improvements. Generally the open discussion on the possible improvements of the peer review process was very much appreciated by the members of the Network.
The draft summary of the outcome of the break out discussions is presented in the Appendix. PSN Members are invited to comment on the draft outcome of the break out discussion that is integrated in the Appendix.
As a next step, EFSA will propose a preliminary action plan as a follow-up of the proposed recommendations and a second commenting round will be organised, also involving PPR Panel Members. A draft implementation plan will then be presented by EFSA to the PAFF Standing Committee.

4. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA PPR Panel, 2013): State of play

EFSA presented the state of the art regarding the guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA Journal 2013; 11(7):3290). The guidance has been noted in July 2014 and implemented since January 2015. The experience with the use of the guidance document has allowed MS and EFSA identifying issues which need further clarifications, e.g.: the application of the PECsw;twa in the risk assessment or the use of geometric mean as Tier II for chronic toxicity endpoints. The majority of those items were discussed at the general ecotoxicology Peer Review experts' meeting 133 and are listed in the related technical report[3] (EFSA, 2015). A corrigendum or a revision of the EFSA aquatic guidance document was recommended in the technical report for making corrections and improve clarity. The Panel on Plant Protection Products and their Residues (PPR Panel) was consulted in December 2015 in order to decide the type of corrigendum to be issued, according to Standard Operating Procedures (SOPs). It was then decided that the corrigendum will be developed in consultation with the Pesticides Steering Network (PSN). EFSA informed that a call for nomination of experts will follow soon. The corrigendum is foreseen to be published by the end of this year, pending on the availability of internal resources. Besides the MS experts, two additional experts from the PPR Panel involved in the development of the guidance will be engaged in the process. It was stressed that this is perfectly in line with the overall aim of having more interaction between Panel experts and MS experts involved in the peer review process. The corrigendum will be formally endorsed by the Panel. Germany (DE) already proposed to participate in the working group.

5. Outcome of the pesticides peer review meeting on general recurring issues in mammalian toxicology

EFSA presented an overview of the outcome of the pesticides peer review meeting on general recurring issues in mammalian toxicology which took place in January 2016. A draft EFSA technical report was produced with the scope to reflect the meeting discussions and conclusions. A written procedure on the draft technical report was performed. The main issues identified were related to the quality and level of details of the renewal assessment reports (RAR) and the adherence to the new data requirements. General issues regarding the proposals for classification and labelling, the assessment of the potential for endocrine disruption, the assessment of metabolites and impurities and the assessment of the literature search were also discussed. EFSA commented that in some points the conclusion was agreed based only on the majority of the experts.

EFSA reminded that according to the Commission Implementing Regulation (EU) No 844/2012 (AIR III), the supplementary dossier should contain information demonstrating that the approval criteria of Regulation (EC) No 1107/2009 are fulfilled, but also data and risk assessments which were not part of the approval dossier and which are necessary to reflect changes in legal requirements and in scientific and technical knowledge which have occurred since the approval. The experts agreed that sufficient details should be provided regarding the old studies in order to judge if their assessment is still aligned with the current scientific and technical knowledge. Some experts pointed out that the MS should

[3] EFSA (European Food Safety Authority), 2015. Technical report on the outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology. EFSA supporting publication 2015: EN-924. 62 pp.

encourage applicants to provide robust OECD summary reports. A distinction should be made in the RAR between what the applicant drafted and what is the RMS's assessment. Also changes to the old conclusions should be clearly indicated in the RAR. Regarding the new data requirements under the Regulations (EU) No. 283/2013 and 284/2013, the following were discussed: good laboratory practice (GLP), analytical methods, toxicokinetic parameters, *in vitro* metabolism and phototoxicity / photomutagenicity. The GLP status was required for studies performed from July 1993. Studies conducted before this date may be integrated into the assessment, when accepted by the competent authorities as scientifically valid, thereby removing the need for repeating animal tests. The experts were in favour of studies with GLP status but there are cases in which non-GLP studies are appropriate (e.g. mechanistic data) and acceptable (pending availability of raw data and well-documented study report).

Regarding the analytical methods to be used in the toxicity studies these should be specific for the entity to be measured and adequately validated. The limit of quantification (LOQ) shall be adequate for the measurement of the range of concentration anticipated to occur in the generation of the toxicokinetic data and validation of the analytical methods should be provided for all studies including the old studies (original peer review) and the new studies (for the renewal). For old studies to which the current guidance for the validation of the analytical methods could not be applied, it was clarified that it should be assessed whether the method is fit-for-purpose and supports the toxicological studies (in Vol.3, chapter B.5). It was clarified that in the section "physicochemical properties and analytical methods", it can be concluded that the method is not validated according to current guidance but is nevertheless fit-for-purpose and in support of the toxicological studies.

Sources of uncertainties for old studies should be identified during the re-evaluation of old studies (i.e. actual amount of test substance administered, identity of the test substance, possible isomers, impurities, etc.). Considering the new data requirements, validated analytical methods should be provided for all substances and not only for those classified and labelled for acute toxicity cat 1, 2, 3, STOT-SE/RE cat 1 or CMR cat 1A and 1B.

Regarding toxicokinetic parameters, information on blood and tissues concentrations for the active substance and relevant metabolites, shall be generated in short and long term studies on relevant species (additional parameters). For additional toxicokinetic parameters missing data should be required on a case-by-case basis. A further guidance should be developed to address interspecies and intra-species differences for these endpoints. Comparative *in vitro* metabolism studies shall be performed in order to determine the relevance of the toxicological animal data and to guide in the interpretation of the findings and in further definition of the testing strategy. Data requirements for these data are supported, noting that protocols are already available in the public domain (i.e. pharmaceuticals). The experts supported the need for practical guidance on *in vitro* metabolism that should provide clear indications on how to perform and how to interpret *in vitro* metabolism studies.

Phototoxicity study shall be required where the active substance absorbs electromagnetic radiation in the range of 290 to 700 nm. Need for photomutagenicity testing may be indicated by the chemical structure of a molecule. The experts agreed that further guidance on follow up of positive results *in vitro* is needed. It was acknowledged that there are difficulties in

testing below 320 nm and further guidance is necessary how to test with UV wavelength between 290 and 313 nm.

Regarding the classification proposals, for substances with harmonized Classification and Labelling (C&L) as carcinogen and/or toxic for reproduction category 1A or 1B, applicant should indicate already if they apply for negligible exposure or/and essential use (article 4(7)) and provide the appropriate data. RMS should assess the evidence for negligible exposure or/and essential use if the applicant applied for it.

A detailed comparison with CLP criteria at least for the Carcinogenic, Mutagenic or Toxic for Reproduction (CMR) hazard classes should be performed in the RAR/DAR.

Concerning endocrine disrupting properties, no specific data requirements are mentioned in the Regulation (EU) No. 283/2013. However, if there is evidence that the active substance may have endocrine disrupting properties, additional information or specific studies shall be required to elucidate the mode/mechanism of action and provide sufficient evidence for relevant adverse effects. The interim criteria may lead to false positive or false negative results. In parallel, a scientific assessment should be provided, in line with the opinion of the Scientific Committee on the hazard assessment of endocrine disruptors (2013). One expert identified that the development of Adverse Outcome Pathways (AOP) knowledge could be a way to better identify endocrine-mediated mechanisms relevant to humans.

Regarding the genotoxicity testing and the *in vivo* follow-up for *in vitro* gene mutation, it was noted that according to the Regulation 283/2013 if either of the *in vitro* gene mutation tests is positive, an *in vivo* test to investigate the induction of gene mutation shall be conducted, such as the Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (TGR). Historically the *in vivo* Unscheduled DNA synthesis (UDS) test was the common *in vivo* follow-up of positive results in either of the *in vitro* gene mutation tests; however, it was recognised of low sensitivity. The majority of experts agreed that the applicant shall provide a Comet or a TGR test as *in vivo* follow-up for *in vitro* gene mutation. Regarding aneugenicity, if the *in vitro* micronucleus test for numerical chromosome aberrations on mammalian cells is positive or the *in vitro* mammalian chromosome test is positive for numerical chromosome changes, an *in vivo* micronucleus test shall be conducted. In case of positive result in the *in vivo* micronucleus assay, appropriate staining procedure shall be used to identify an aneugenic and/or clastogenic response. The experts agreed that the nature of the positive response in the *in vitro* and/or *in vivo* micronucleus test shall be investigated and that if the test battery did not address properly aneugenicity, an *in vitro* micronucleus test should be required.

On tissue exposure there shall be convincing evidence (i.e. cell toxicity or toxicokinetic data) that the relevant tissue will be reached by the chosen exposure route and application method. Agreement was reached that evidence of tissue exposure shall be demonstrated in particular for metabolites where the data are not normally submitted. Discussion on whether the intraperitoneal (i.p.) route might be used (where no evidence of tissue exposure at the limit dose by oral route) took place but no agreement on this was reached in the expert meeting.

Regarding the assessment of metabolites and impurities and for the assessment of the toxicological profile of metabolites found as residues (plant and livestock), no guidance document is currently available and a case-by-case approach is

used. The EFSA PPR opinion on Evaluation of the Toxicological Relevance of Pesticide Metabolites (EFSA Journal 2012; 10(7):2799) is not aimed to be used as guidance. The development of the PPR Guidance on the establishment of the residue definition is under finalisation. It was noted that it will be difficult to match the guidance on groundwater metabolites with the new guidance on residue definition, since different tools are used in each of them.
For the assessment of the compliance of the test material used for the toxicity studies in comparison with the technical specifications and the equivalence of different technical materials, the European Commission Guidance on equivalence of technical material (2012) is used. In the expert meeting it was highlighted that the analysis of batches would be necessary at least in CMR studies and critical studies (used to derive reference values) and should support the proposed specifications. The relevance of impurities should be also considered for monitoring purposes with regard to their intrinsic toxicological properties and preferably assessed with alternative tools to animal models (e.g. (Q) SAR).

EFSA informed that the technical report on the outcome of the meeting on the general recurring issues in mammalian toxicology will be published in July 2016. EFSA clarified that the purpose of the report is to have a common agreement and harmonised interpretation amongst experts on the approach followed regarding the scientific interpretation of the relevant guidance documents when preparing the dossiers and the renewal assessment reports. EFSA noted that even if not legally binding the document provides recommendations that can be applied during the EFSA peer review of the active substances and are expected to provide additional clarifications to applicants and RMS. Recommendations regarding further guidance can be also considered by European Commission (EC). However, it was noted that it is the EC decision to mandate EFSA to prepare specific guidance. The need for updating the Commission Communication in the framework of the implementation of Commission Regulation (EU) No 283/2013 (2013/C 95/01) was highlighted by MS, especially in the area of endocrine disrupting properties where EC submitted new scientific criteria. Regarding the outcome of the scientific assessments for endocrine disrupting properties it was proposed to follow the Scientific Committee opinion on the hazard assessment of endocrine disruptors (2013) where the OECD conceptual framework for the test methods is proposed. According to the stepwise approach of the OECD conceptual framework no new studies are requested at all levels. A case-by-case approach was proposed for the time being.
The United Kingdom (UK) commented that there was no consensus on some issues and the agreed position was taken only based on majority view. A relevant comment was made during the commenting period. It was noted that new data requirements should not generate new animal testing and a case-by-case judgement might be needed in many cases. However, UK acknowledged that the meeting was very useful and a similar meeting was proposed also for the residues section. EFSA mentioned that the guidance on residue definition will be adopted by the Panel in the following plenary and this will trigger additional exchange of communication with EC/MS. A dedicated PSN meeting was also organised in June 2014 on MRL procedures.
One MS mentioned that the technical report might need to be revised taking into consideration the new endocrine scientific criteria. The need for updating the list of genotoxicity tests in the Commission Communication in the framework of the

implementation of Commission Regulation (EU) No 283/2013 was also mentioned.
Spain (ES) and UK commented that the compliance of the batches used in the toxicity tests with the technical specification cannot be demonstrated in many cases where no detailed information can be retrieved from batches used in the old studies (in the case of the active substances renewals). This would challenge the animal testing that use "old" batches. UK also supported a more pragmatic approach considering the toxicological relevance of the impurities as covered when the batches used in toxicity studies are concluded representative of the technical specification. EFSA explained that this is a case-by-case consideration. If the analysis of the old batches used in the toxicity studies is not available, a robust case should be presented to exclude the toxicological relevance of impurities, demonstrating that even without this information the technical specification can be supported from the toxicological point of view. It was highlighted that the applicant should present sufficient information on whether the old specification might be still valid and cover the impurities at appropriate levels. Impurities that have different profiles than the parent compound, might be of no concern at the level proposed in the specification but should still be considered as relevant impurities (they might alter the toxicological profile of the active substance if their levels are increased for example due to changes or variability in storage).

Action point

- EFSA to publish the technical report on the outcome of the pesticides peer review meeting on general recurring issues in mammalian toxicology considering the comments received.

6. Feedback from Pesticide Steering Network meeting on methodology for assessing Article 4(7) applications

The Chair gave a short feedback from the Pesticide Steering Network meeting on the methodology for assessing Article 4(7) applications. EFSA was mandated to provide scientific assistance as regards data on evidence that application of the herbicide flumioxazin is necessary to control a serious danger to plant health which cannot be contained by other available means, including non-chemical methods within the context of Article 4(7) of Regulation (EC) No 1107/2009. EFSA set up a working group (WG) on flumioxazin consisting of Plant Health experts to prepare a methodology for this assessment. A dedicated PSN meeting took place on 10 March 2016 where the methodologies proposed by EFSA and MS were discussed (minutes of the meeting are available on: http://www.efsa.europa.eu/sites/default/files/event/160310a-m.pdf). The PSN meeting concluded that EFSA shall develop a protocol comprising a methodology to be agreed by all MS for the evaluation of data on the necessity of the application of herbicide active substances to control a serious danger to plant health which cannot be contained by other available means (including non-chemical methods) and a harmonised template outlining what kind of information, data and evidence need to be provided by applicants and MS during such an assessment. The agreed protocol will be used by all MS when assessing applications for herbicide active substances within the context of Article 4(7) of

Regulation (EC) No 1107/2009. EFSA will issue a scientific report on the evaluation of each herbicide for which a derogation under Article 4(7) of Regulation (EC) No 1107/2009 is requested. EFSA prepared the draft protocol on the methodology to be applied which was circulated in May 2016 to MS for commenting.

EFSA noted that the need for developing similar protocols for other modes of action (i.e. fungicide) will be triggered on a case-by-case basis and encourage applicants/RMS to identify at early stage active substances that fulfil the non-approval criteria and are possible candidates for Article 4(7) applications (i.e. active substances that have harmonised classification in accordance with Regulation (EC) No 1272/2008, and which trigger the non-approval criteria). UK mentioned the case of epoxiconazole (fungicide under the AIR IV renewal program) which has harmonised classification as toxic for reproduction 1B (Repr. 1B) triggering the cut-off criteria. UK informed that as RMS for epoxiconazole they already contacted the applicant to consider the need for Article 4(7) application.
EFSA plans to complete separate protocols for insecticides and fungicides. However, this would be triggered by specific applications and it will not be finalised in one goal. Following comments from MS it was elucidated that a more generic document that would encompass the different protocols might be elaborated in the future, consisting of the common principles relevant to all types of plant protection products (PPP).

Action point

- EFSA to publish the protocol for the evaluation of data concerning the necessity of the application of herbicide active substances to control a serious danger to plant health considering the comments received.

7. Feedback from the ECPA workshop on higher tier studies

EFSA informed that the summary of the ECPA workshop on higher tier environmental risk assessment is already available. The ECPA workshop was organised following the applicants' concern that 'higher tier studies for the environment are not sufficiently covered by the RMS in the DAR and in the EFSA conclusion'. The aim of the workshop was to allow industry to present their concerns using examples. EFSA mentioned that several case studies presented in the workshop were not focusing on the use of higher tier studies but on general issues and in a many cases the discussion revealed that the applicants cannot justify that the use of higher tier studies can address all the concerns raised under the intermediate or lower tier. Generally the workshop was beneficial. DE commented on the unfortunate situation that the participants did not have the opportunity to give feedback/comments on the minutes prepared by ECPA.

The Network agreed and confirmed that the position paper (minutes) of the ECPA workshop on higher tier studies does not represent any kind of consensus or agreement with MS/EFSA during the workshop.

8. PSN consultation-PPR Guidance Residue definition for risk assessment

EFSA updated on the PSN consultation on the draft Guidance on the Residue definition for risk assessment. 38 comments were received during the consultation period. Comments regarding comprehension/clarity issues were considered by default and 16 comments agreed on for detailed discussion. A PSN teleconference (TC) took place on 25 May 2016 with a limited number of experts to discuss the comments. Overall the feedback was that the consultation was useful and provided clarification on the guidance. Some experts supported the need for a proportionate approach to ensuring consistent assessment and to cover the main contribution of the risk in the residue definition for risk assessment. Wherever possible this should be done without an increased need for animal testing. Regarding the main comments and recommendations on the assessment approach the threshold of toxicological concern (TTC) and the complexity of the proposed approach were mentioned. There was a general expression of agreement to apply non-testing approaches, (Q) SAR, read-across and especially TTC. However, it was commented that cumulative TTC is too complex and hampered by lack of adequate exposure data. An early TTC exit option was proposed to simplify assessments and eliminate huge number of metabolites.
Regarding potency / toxicity considerations & vertebrate studies, it was recommended that a lower percentile of distribution should be proposed to define potent compounds, or even to drop the special approach elaborated for the potent substances. It was noted that the approach developed for the potent compounds might be far too complicated.
A concern was expressed regarding the possible high number of vertebrate studies; it was proposed that the acceptance of alternative testing should be better highlighted in the text. It was also noted that with the systematic application of the grouping, read across, TTC, the number of studies required would be reduced. Extrapolation of data for high number of similar compounds would be possible. Regarding the toxicological burden to be covered by the risk assessment residue definition, there were expressions of agreement on $\geq$ 75% coverage proposal compared to some more flexibility requested (70% was also proposed).

The minutes (with PSN comments & recommendations) were sent to the Panel WG and considered during the meeting held from 6 to 8 June 2016. The updated guidance document is scheduled for adoption by the PPR Panel on 22 June 2016. After being published the guidance will be submitted to PAFF for Note Taking. EFSA plans to issue a technical report in September, containing all comments & responses related to the public consultation and PSN consultation. EFSA will also organise a Technical meeting with stakeholders on 26 and 27 September 2016 in Parma to present the guidance document.

Action point

- EFSA to prepare the technical report containing all comments & responses related to the public and PSN consultation by September 2016.
- EFSA to organise a Technical meeting with stakeholders to present the guidance document.

9. Joint DAR/CLH template - comments received during consultation, progress report and next steps

EFSA gave a short update on the Joint Template for the DAR/CLH Report development.

EFSA informed that the first TC of the expert group took place in July 2015 with the aim to integrate the CLH content in the DAR Template. Commenting on the new template was conducted from 22 January to 12 February 2016. ECHA launched a commenting period with its stakeholders as well, CARACAL (i.e. MSCAs involved in REACH and CLP) and RAC simultaneously. All the comments will be collated in a commenting table and will be addressed or further discussed. Next meeting (TC) of the working group on the alignment of DAR/CLH template is foreseen in August/September 2016. It was mentioned that ECPA declared interest on the new template, however it was clarified that the template is addressed to MS authorities for submitting assessment reports/CLH reports and not to applicants. No specific timeline for the implementation of the new template was indicated.

10. DAR template for micro-organisms

EFSA gave a short update. The DAR template for micro-organisms is under development as part of the EC WG on biopesticides. A first draft of the new template was developed by NL, UK. It was decided that the template would be split in a part for the micro-organism active substance and for the formulation (as it is the case for the DAR/RAR of chemical active substances). Comments on the template were collected and discussed with the members of the WG. EC will develop the next version of the template, which will be presented in the next PAFF to MS. Comments will be also requested from MS. DE commented that most of the RMS for the AIR IV micro-organisms are part of this WG and that RMS should benefit from the new template soon, already for the first AIR IV substances (microorganisms; dossiers due by 31 Oct. 2016), even if the date of legal implementation of the template would be the usual six months after taking note in the PAFF Committee.

11. EFSA MATRIX and OECD GHSTS

EFSA gave an update of the MATRIX Project in EFSA. EFSA is exploring for quite some time the feasibility to develop an electronic platform for the management of all the applications/dossiers for regulated products received by EFSA in the context of the various sectorial legislations. The MATRIX project aims to provide applicants with a more efficient solution for regulated products applications by improving the process, particularly the management of the application lifecycle and electronic dossiers, enhancing the submission of applications in electronic formats, the management of applications' administrative workflows and the communication between EFSA and applicants (Matrix-IP Phase I) as well as the support to risk assessors and integration with the Scientific Data Warehouse of EFSA (Matrix-IP Phase II).

According to the Summary of Phase I: Matrix is a project to provide structuring of dossiers in all food sector areas, including the identification and harmonisation

of structured sections of the dossiers. The project will implement a full electronic submission of dossiers including a tool for applicants for editing dossiers, automated administrative workflows and improved communication and feedback from applicants/EC/MS. The project will also analyse and prepare for possible automation of publication of non-confidential parts of the dossier for applicable sector areas.

It was noted that although the dossiers are very well structured in the pesticides area, this project will cover also other areas of regulated products where the dossiers are not fully structured.

Regarding the involvement of PRAS unit, the following actions are foreseen in the different Work Packages.

- Structuring of the dossiers in all food sector areas, definition and implementation of administrative workflows (The PRAS unit will be in the pilot),
- Requirements and implementation of file transfers (The PRAS unit will be in the pilot.)
- Definition of the communication to applicants (communication functionalities) (The PRAS unit will be in the pilot)

EFSA launched a discussion group on E-Submission aiming in the engagement with stakeholders in the areas of Regulated Products. The discussion group will be set up to discuss with and consult external stakeholders on the technical aspects of the MATRIX Project with objectives to foster the engagement and enhance the quality, clarity and usability of the electronic platform to be developed. The discussion group is coordinated by the APDESK unit. Nominations have been received from three Member States but a maximum of five representatives from the MS should be achieved. EFSA informed that the nomination phase was extended to 24 June 2016. MS were encouraged to nominate experts in the discussion group (via the EFSA Advisory Forum).

EFSA gave a short feedback on the OECD Globally Harmonised Submission and Transport Standard (GHSTS) Project (more information can be found on https://www.oecd.org/chemicalsafety/submission-transport-standard/). GHSTS is an XML-based Interchange Format for Pesticides Registration Applications which aims to replace the currently used electronic submission format for pesticides CADDY-xml standard v3.0. The OECD Expert Group on the Electronic Exchange of Pesticide Data (EGEEPD) was mandated to investigate the possibility of harmonisation of the information technology used in the pesticide regulatory process. The GHSTS is a standard describing a set of technical specifications used to assemble electronic files for a pesticide package in a predefined manner for electronic submission.

The following were reported:

- The GHSTS system is consisting of the Builder and Viewer tools. The Viewer is a software that allows the standalone display of a submission package in a web browser. The Viewer can display a subset of information available in the submission package; e.g. select to see only changes done in the last update (delta file) e.g. following clock stop. Export files following filtering e.g. export the additional information submission or

summary dossiers for publication. Extract metadata into other formats e.g. list of studies extracted in excel file is also possible.

- Dossier compilation is based on a Table of Contents (ToC) schema. These standard ToCs are supplied as XML files that follow a ToC schema definition.
- The new xml format of the pesticides dossiers (GHSTS) and especially the Viewer is of high interest for EFSA.
- The GHSTS is based on human readable data and attachments e.g. OHTs (OECD Harmonised Templates for Reporting Chemical Test Summaries). OHT is machine readable information, easily to be incorporated in the databases.
- Document and Dossier lifecycle is one of the key areas of the GHSTS. Benefit is the easily visible amendments of the dossier.
- PID (persistent identifier) is an internal company identifier. A product is identified with a unique identifier that will be created by the submitting company and will follow the substance in the GHSTS.
- Reference list with hyperlinks is provided in the GHSTS.

Some companies are already prepared to submit dossiers in the new format (one dossier at least is available). In light of the MATRIX project, EFSA will volunteer for a "test-run" to examine the usability of the new features in the GHSTS. The system integration in EFSA's IT environment is also to be explored. Missing participation of EU MS representatives for the GHSTS expert group was noted, however, nomination is still possible for interested MS. Questions on technical features were raised by MS. PT questioned whether a file similar to index file of CADDY-xml will be available. UK stressed the possible interference of the GHSTS with the national IT security systems; also the size and the time spent for opening studies were questioned. (*Post meeting note*: IT experts in EGEEPD confirmed that GHSTS is much quicker. EFSA will test with one dossier). EFSA clarified that EGEEPD does not solve national issues, but EFSA will check the information in the "test run". EFSA mentioned the possibility that all dossiers might be centralised in EFSA (only one reference point for the dossier), however; this discussion is quite pre-mature and the technical possibilities are still to be explored. This idea was born under the MATRIX project and seems to be also supported by applicants. DE reminded that there is no EU decision for official adoption of the system. Need of political decision/support from EC for promoting/implementing GHSTS was noted.
DE expressed concern on the lack of supplementary information being implemented in the CADDY dossier following additional information request (time pressure, currently pdf files are submitted) and questioned whether GHSTS could integrate this information. (*Post meeting note*: IT developers clarified that this is not an IT issue as updating of an existing dossier is quick (20 min approximately); so technically the solution is quick but might be in practice more resource issue (scientific experts are different persons than IT persons in company)).
EGEEPD can assist authorities by providing basic architectural integration patterns. Canada is currently developing a free dossier builder (for those that don't have own builder e.g. small companies) and it will be ready by April 2018.

PT asked if there is a possibility to separate physically the confidential information as laid down in the legislation (not the case for CADDY-xml). PT also referred to problems with navigators' compatibility in CADDY-xml. (*Post meeting note*: In the EGEEPD meeting it was clarified by IT developers that the GHSTS is working on its own browser and not on common browsers like Internet Explorer or Chrome. Current problems with CADDY xml not running properly on some internet browsers should be solved for GHSTS. EFSA will receive GHSTS dossier to perform real testing).
PT mentioned that the CADDY dossiers are used also for PPP zonal authorisations and therefore a much bigger storage capacity should be developed in case of one reference point. EFSA clarified that all technical features are still under discussion. UK mentioned that similar system has been developed in ECHA for biocides (R4BP). (*Post meeting note*: ECHA clarified that R4BP2 is a workflow system but does not carry dossier as biocides dossier is submitted through IUCLID). PT commented that the new system should not create unnecessary burden to small applicants relevant not only for active substances but also for PPP applications in zonal system. PT welcomed the workflows integration for both systems.

The Chair highlighted the different procedures laid down in different legislative areas (electronic submission of the dossier to EFSA, in some areas applicants submit dossier directly to EC or MS, only in one case, dossier is directly submitted to EFSA). In the pesticides area where the dossier is submitted first to RMS, and when considered admissible to all MS, EFSA and EC, a decision at EU level should be taken for creating a central EU system. For the time being EFSA is working on the MATRIX project which could in the future accommodate all workflows, including information and communication channels. The benefits were highlighted. The system must be compatible, robust and should cover all the areas of regulated products. The size of the server and the access rights for all stakeholders is still to be further explored.

Action points:

- EFSA to raise the MS comments during the next OECD EGEEPD meeting held in Paris in 27-28 June 2016.
- *Post meeting note*: Replies to the MS comments following the OECD EGEEPD meeting are incorporated in the text.
- MS to provide asap comments/feedback to EFSA on the proposal of hosting all a.s. and PPP dossiers on one central platform.

12. GAP tables in the frame of active substance application for approval

The item was proposed by AT. AT noted that indications in the GAP table should be given in relation to the type of glasshouse use. The type of use might have impact on the ecotoxicology and fate assessment. A better explanation of the type of use in the GAP table provided by applicants (document D1 of dossier) was proposed. The EFSA Guidance on protected crops (EFSA Journal 2014;12(3):3615) should be followed.

EFSA clarified that the issue was discussed in the pesticides peer review meeting on general recurring issues in ecotoxicology. In the minutes (publicly available at

http://www.efsa.europa.eu/en/supporting/pub/924e) it states that if it is not clearly indicated in the GAP table, then it will be assumed that the representative use can be made under all types of structures.

The definitions for types of protected crops are provided in EFSA (2014). It was agreed that the applicants should indicate in the GAP table the type of glasshouse use they apply for. It is recommended to indicate the type of glasshouse use by using the specific codes in the Remarks field of the GAP table.

13. Applications Desk feedback

APDESK gave a feedback on procedural issues. The following elements were mentioned as result of the centralisation of the reception of applications.

Admissibility (for renewal): Reminder for RMS to send the admissibility for Applications and Dossiers.

Justification Form (JF) related to sanitisation of Applications and Dossiers (requirement of the legislation). Delay in the provision of JF countersigned by RMS, after admissibility, was reported. EFSA proposed that if the JF is not sent after 30 days, and for transparency, a document will be uploaded in the Register of Questions stating that the publication of application is not available pending the sanitisation agreement by RMS. This is relevant for the public access to the sanitised version of the application.

UK finds the sanitisation exercise of the DAR/RAR cumbersome and proposed that sanitisation should be carried out only by EFSA. EFSA clarified that is the RMS responsibility to assess the confidentiality requests according to the legislation. It was acknowledged that this split process is not efficient especially in cases of public access to documents requests, where third parties are seeking documents (i.e. sanitised summary dossiers) that are not submitted timely due to the sanitisation exercise not being finalised. Even if EFSA is not involved in the sanitisation process EFSA should respond to public access requests though. EFSA will explore options to facilitate the practicalities but still the responsibility lies with RMS.

APDESK referred to the file naming of the DAR/RAR files. It was noted that RMS should follow accurately the agreed naming convention, i.e. *Bromoxynil_RAR-01_Volume_3CP_B-1_2016-05-27.*
APDESK proposed to hold *ad-hoc* teleconferences between MS and APDESK to clarify and review any potential procedural issues on the submission of DAR/RAR. This would avoid several exchanges of e-mails that are sometimes following the submission of a DAR/RAR and for which some documents are missing. Ad-hoc teleconferences should be requested using the functional mailbox APDESK.applications@efsa.europa.eu
APDESK presented the GLP initiative recently developed in REPRO department. The SOP_022_S "Selection of studies performed in compliance with Good Laboratory Practice for audit purposes" is in place since 14th March 2016. The initiative covers:
Part I: EFSA Yearly GLP Studies Audit Programme to all dossiers from all REPRO units
Part II: EFSA Ad-hoc GLP studies audit in case of doubt

The EFSA GLP Studies Audit Programme for 2016 (draft) will be ready end of June 2016. 15 studies have been selected from all REPRO units : pesticides area (7), food ingredients and packaging (FCM) (1) and feed additives (5). Furthermore, a surveillance study audit will be requested.
In total, seven MS are involved in the specific working group of EC on GLP audits consisting of the relevant GLP Monitoring Authorities. A specific platform in the DMS/APDESK section is used for this purpose. The selection of the studies for audit purpose is based on three criteria; the study is part of the applications for regulated products for which EFSA has published an opinion/conclusion in the past year; the study report includes a statement that the study was conducted in compliance to the GLP principles; and the study has been performed in a test facility for which the relevant GLP Monitoring Authority has scheduled an inspection. The audits outcome will be sent to the unit for follow up actions. REPRO units can request *ad-hoc* GLP studies audit in case of doubts; only studies that are part of an on-going risk assessment or assessment still to be started can be selected.
France (FR) welcomed the GLP initiative. MS will be informed by EFSA on the outcome of the audit.

DE raised the issue of dossiers being distributed to MS (other than the RMS) at a very late stage, i.e., only when the RMS submits the RAR for peer review. Applicants in these cases claimed that this was done in agreement with the RMS and/or EFSA. DE asked EFSA and all RMSs to not agree to such proposals. This practice allows applicants to distribute the dossier only once, ('updated' version including any additional information requested by the RMS during the RAR preparation phase). Legally, the dossier as it was accepted by the RMS as complete should have been circulated immediately after the completeness decision of the RMS. Only any 'updates' during the RAR preparation should be distributed later. DE noted that this 'developing' practice causes severe problems with their participation in the peer review. DE complained that since the dossiers are distributed via secure portals to their evaluators, when the dossier is submitted only after RAR completion, the time is usually too short to get the dossier distributed before the RAR is circulated for peer review. The evaluators then have to review the RAR without having access to the underlying dossiers. This is unacceptable and also creates unnecessary comments which might have been avoided if the evaluator could have accessed the study in question. In this case the legislation is ignored. DE referred to the examples of iprodione and fludioxinil. EFSA took note of these cases and will come back in due course.

Action point:

- EFSA to provide feedback on the point raised by DE on the late distribution of dossiers.
- *Post meeting note:* APDESK already provided response to DE.

14. AOB

Two points raised by FR were discussed. Points raised by UK addressed to EC were not discussed since EC participated only the first day.
FR questioned if a mandate was received by EFSA on the development of new greenhouse operator exposure model as announced by DG SANTE. EFSA informed that no new mandate was received. However, EFSA announced that

there is a formal issue with the calculator for operator exposure model (Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products, EFSA Journal 2014;12(10):3874). EFSA is looking for the best way to solve the issue; a dedicated working group will be convened with experts involved in the development of EFSA guidance and experts from MS/Panel.
As a second point from FR, Chair gave a short update on the development of the EFSA database that aims to cover the full list of end points of all EFSA pesticide outputs on active substances (conclusions and reasoned opinions). The procurement is still ongoing. EFSA informed that the MRLs reasoned opinion (RO) template was also streamlined in line with the conclusion outputs. The database will also include information on regulatory decisions. The aim is to be publicly available and to include all end points agreed at EU level (not studies submitted for zonal authorisations and not peer-reviewed at EU level). Following BE comment, EFSA clarified that all the endpoints would be integrated in the database, even if those are part of confirmatory data assessment as long as are peer-review at EU level. Advanced search function tool is developed. The export to other formats (e.g. excel) will be also possible. The final delivery is foreseen by end of November 2017.

Next PSN meeting is planned to be held in February 2017. A TC might be organised in between to discuss the follow up of the outcome of the break out session (if internal resources allow to further develop the action plan (cfr item 3 above)). MS are invited to provide proposals and recommendations for the follow up actions. An implementation plan will be then proposed by EFSA and adopted in February 2017 meeting.

NOTE: Documents and presentations distributed during the meeting are considered documents under discussion and thus cannot be disclosed to third parties except MSs and the EC.

APPENDIX
DRAFT SUMMARY OF THE OUTCOME OF THE BREAK OUT DISCUSSIONS

It is noted that this is the draft summary as presented in the meeting on 14/06/2016. It does not reflect all details of the discussion in, or agreed positions of, the plenary.

Group A

Early interaction of other MS experts/EFSA during dossier preparation and risk assessment phase:

- FAQ: publication of previously given answers by EFSA to other MS technical questions on DMS; open to public (confidentiality issue)? When they become obsolete because GD is outdated? Date of publication should be given.
- Ad-hoc TC between EFSA/RMS/co-RMS/(COM) to discuss critical technical issues during risk assessment phase (so during drafting of DAR/RAR or even at pre-submission phase)
- Pre-submission discussion with APPL: involving co-RMS (useful but extra workload). No need for EFSA involvement; issues will be discussed with EFSA before or after APPL/(co)RMS pre-submission meeting
- When new data requirements and new guidance document are applicable: foresee discussion in standard Peer Review expert meeting on general topics

Bilateral TC EFSA/RMS:

- APPL to be invited on case by case/always (equal treatment?) to part of the discussion; APPL could be able to close some issues/open points at early stage or identify critical issues at an early stage
- Co-RMS is invited and RMS/co-RMS decide on participation or not; especially in case of major disagreement, useful to participate
- COM on ad-hoc basis for very specific issues, not for discussing general recurrent issues
- ECHA participation in case of classification issue at request of RMS. In case of parallel assessments, ECHA always invited.
- Ad-hoc involvement of experts in bilateral TC; encourage discussions between experts of EFSA and RMS before TC takes place

Better involvement of MS experts during peer review:

- Yearly plan of substances under peer review and MS identify the substances on which they will comment, based on particular interest/risk based arguments (might be also on specific section of DAR/RAR)
- Way of commenting to be changed: what is expected from the comment, how will it contribute to risk assessment?
- Experts to prepare and actively participate in expert discussions for specific active substances, to be allocated to specific experts at moment of sending of meeting invitations to the experts

Group B:

- When science is not clear (contradictory evidence) or data are missing, so uncertainty in an overall dataset is higher than 'normal', options (with associated uncertainty) might be presented by the risk assessors to the risk managers and not just one endpoint. This discussion to present options should always be an expert meeting discussion when scientific consensus for one reference value could not be reached. I.e. when standard uncertainty factor would not be applied (eg. tox endpoints >100 needed) but experts could not reach consensus on the additional factor. As a consequence, the list of endpoints might include more than 1 option. Risk Managers would have to state which one they chose and why when deciding on approval.
- Conclusions should address uncertainty. Thus agreed noted guidance moving forward has to address uncertainty. Protection goals should be explicitly stated for all areas of risk assessment. High level protection goals must have agreement by risk managers.
- Action to produce a document that describes the roles experts peer reviewing by commenting and attending expert meetings are expected to fulfil. Both the role of presenting the consensus view of their organisation and their role in providing a personal expert view are important contributions. Being prepared during meetings to update the view coming from their organisation when new evidence and discussion is presented by other experts is important. Best practice was considered to be s that those that comment and attend expert meetings would also comment on the EFSA draft conclusion and written procedure for additional information whenever possible.
- For microorganism evaluations it is important to ensure that experts with experience and expertise in this area be involved in their peer review. It is also important that experts have the technical competence for proportionate peer review taking into account the biology of the organisms. This means training of Member States who do not have such expertise in microorganism evaluations is essential to build and maintain a broad capacity base for microorganism risk assessment.
- For microorganisms produce a document that identifies data requirements and uniform principles considered to have lower impact or importance for decision making. Outcome of OECD Stockholm workshop and later workshops to be consulted when developing the document. Risk management input needed / is essential for this. For the long-term, legislation to be updated.
- For botanical / plant extracts, application / implementation of the existing guidance to be followed to identify and produce a record of best practice approaches with utility for addressing uniform principles decision making requirements.
- Early at presubmission it is essential that applicants select representative uses that include a balance between challenging and less challenging uses so that the assessment at EU level has maximum utility later on in zonal and national assessments.
- Action needed to update the commission communications supporting the data requirements. Identify when just study guidelines are needed or when guidance is needed in addition to the study guideline.

- Commission to reflect on changes in legislation or if possible by just updating procedures so the provision of new data and RMS assessment of this after the peer review on the original dossier was completed would be possible. This was particularly in the context of new substances.

Group C

Requirements regarding review of old studies

Update the AIR guidance document

- Stand-alone summary dossier from the applicant and stand-alone RAR
- Highlight any change from previous evaluation, including in the LoEP
- Update summary to current levels of details considering OECD templates and IUCLID RSS (robust study summary) which are equivalent
- Statement on the GD used and which version

Participation of external experts/panel members

Increased value may go in both senses:

- further strength of the scientific expertise in the peer review
- when developing GD, increase awareness in the WG or panel members of the peer review needs and practices

RMS and Co-RMS to identify key sections of specific a.s. with potential critical issues that would benefit from specific expertise and communicate to EFSA.

EFSA to involve an expert or ask the panel to nominate an expert, if involvement of the panel is required.

The selected expert should follow the dossier from the beginning – commenting on the RAR - to the end– commenting on EFSA conclusion.

EFSA reporting of diverging opinions in the EFSA conclusions

- If a new issue is raised after the experts meeting, EFSA to communicate it to the experts involved in the experts meeting or all MSs? Preferably organising a TC.

- Report minority / RMS views for critical issues including the reasoning of each opinion in the text.
    - Should this be also reported in the LoEP, issues not finalised, critical area of concerns?