

NEWSLETTER

SCC Newsletter Vol. 18, No. 6, December 2018

LOOKING FORWARD TO 2019 – REGULATORY NEWS

Dear Subscribers,

Welcome to the final edition of the SCC Newsletter in 2018. Our first article is a review of selected presentations on regulatory frameworks that were held at the last CIR Conference in Barcelona. The majority of these focus on the AgChem Forum. The second report focuses on three important efficacy topics: The two long-awaited new general efficacy standards released by EPPO in 2018, which set out the efficacy data requirements for co-formulated mixture products and any changes in formulations; and the recent EPPO workshop, which defined the need for improving the standard PP1/271 (Guidance on comparative assessment). In the first edition of 2019, we will summarise developments in the area of precision farming and outline the effects these are expected to have on regulatory and product development activities.

Concerning chemicals, upcoming changes of ECHA's compliance check process from 2019 onwards and further relevant topics (e.g. Implementing Regulation on registration updates, new SCC Service on eSDS) are presented. This issue of the SCC Newsletter also includes articles that contain further important information about the fields of agrochemicals and regulatory science.

As the UK enters the final stages of Brexit, you may be asking yourself:

Brexit – Quo vadis? Where will the 'journey' finally end?

As political discussions among the many different stakeholders continue, especially in the UK, there are six fundamental scenarios that are still, theoretically, possible:

- Regular Brexit (based on a ratified withdrawal agreement)
- 'No deal' Brexit (without any agreement)
- A UK referendum on the withdrawal agreement
- A second UK referendum on Brexit itself
- UK cancels Brexit decision
- The withdrawal date is postponed (29 March 2019) with mutual agreement

Whichever scenario plays out in 2019, one thing is clearer now more than ever: International companies that operate in EU/UK markets must be extremely well prepared and highly proactive if they want to remain successful and well positioned in their industries.

In the fast-moving world of regulation, SCC is committed to keeping its customers on course for success. We provide high-quality support and consulting services for your scientific and regulatory needs. Our expertise includes exposure

modelling and risk assessment, and extends over a broad range of areas, including agrochemicals and biopesticides, biocides, chemicals, consumer products, feed and food additives, GLP archiving solutions, and task force management.

We would love to hear what you think about the SCC newsletter, so please do not hesitate to share your feedback and comments with us.

Please contact us by email at newsletter@scg-gmbh.de.

Finally, all of us here at SCC would like to wish you a joyful festive period with plenty of opportunity to rest and relax before starting the year ahead.



Dr Friedbert Pistel

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SEASON'S GREETINGS
from everyone at SCC

季节问候 • FELIZ NAVIDAD
JOYEUX NOËL • ΑΓΑΠΗ ΧΡΙΣΤΟΥΓΕΝΝΑ
クリスマスのご挨拶 • BUON NATALE
연말연시인사 • MUTLU NOELLER

Frohe

WEIHNACHTEN

und ein gutes neues Jahr!

AGROCHEMICALS

**CIR Conference Barcelona 5-6 September 2018**

As in the years before, **Bernd Brielbeck** turned the attention of the audience to low risk a.s. In his presentation the speaker did not only present the new criteria but also drew together various aspects such as the need for Guidance documents on microorganisms, which in many cases are considered to be Low Risk Substances as well as the emphasis on integrated pest management. Especially, the latter concept is of increasing importance for European farmers in various ways. It does not stipulate the use of exclusively low risk or biological plant protection products, as is the general perception, but truly integrates all different modes and methods of plant protection. So both Classical Chemicals and Low Risk Active Substances can be combined in this system to the benefit for both the farmer and the consumer. Classical Active Substances which might have some issues with toxicology or the environment can be supplemented by Low Risk Substances, which have no such limitations. In return the possibly lower efficacy, which is acceptable for Low Risk Active Substances, can be augmented by their communication with classical chemicals at the appropriate time. Low Risk Substances, this speaker said, are key to the future developments in the European Union as they will influence all areas of future agronomics, such as precision and digital farming.

The industry speaker **Janet Williams** from the UK emphasised that the UK industry must not be isolated from the access of active substances due to BREXIT. No new national data requirements must be implemented and the evaluations currently ongoing must not be disrupted. Both were confirmed by the Authorities. They also confirmed that there will be no change to procedures as otherwise there would be technical barriers to treat.

They also would like to quicken up the authorisations. She observed that with respect to Pesticide Regulations the EU is currently significantly diverging from the rest of the world by tightening the rules evermore and by misusing of the precautionary principle. The UK is currently publishing technical papers on a possible deal situation after the BREXIT. The speaker emphasised that trade is key to all endeavours and that the MRL system therefore must not be changed in the UK. The CRD confirmed that they intend to complete all there EU work before March 29, 2019, preferably by December 2018. That includes active substance renewals as well as work as a zonal Rapporteur Member State. Since October 2017 industry is already submitting national applications to CRD to stay in the UK market. CRD will continue outstanding concerned Member State or mutual recognition activities after March 28, 2019. Thus, the UK can be seen as a fourth zone with in the EU. The UK will continue to apply all EU rules and accept EU decisions for a transition period until 31 December 2020. In the long term UK intends to return risk assessments, instead of hazard assessments and to endorse their global corporations for example with the United States, Canada, Australia and New Zealand. They will eventually divert from undesirable Guidance Documents of the EU and will accept mutual recognition from across the world. Maybe also a return to a national review process, which would at the same time review active substance and product, could be in envisioned. This would of course help to avoid the confusion of Article 43 the EU is experiencing at the moment. Returning to risk assessments, instead of hazard assessments, would also imply that the candidates for substitution system as well as the cut-off criteria will no longer apply. Another point of interest would be to amend the European ground water limit of 0.1 ppb, which the speaker called unscientific. Instead scientific ground water limits with respect to each active substance, as for example used in the US, should be developed.

Aurelie Dhaussy of ECPA observed that a large number of substances are without decisions right now. Also a large number of active substances have not been defended at all in the AIR process. It is a major concern of ECPA that only a very small number of New Active Substances (NAS) has been sub-

mitted for approval. 59 New Active Substances were submitted since the implementation of Regulation 1107/2009, but only 22 of those have been approved and an MRL for the uses is in place. Of those approved only 13 have a product authorisation. The pipeline is drying-up for Europe. On average 6 to 7 New Active Substances have been submitted for approval per year previously, which has dropped to only 2 per year. ECPA considers the review process unpredictable and, especially in the peer review, which is very late in the process, new requests arise.

ECPA expects a wave of non-approvals by the end of this year. As response to the slow re-approval, the average of emergency authorisation has tripled since the time of Directive 91/414.

The new list of undesirable co-formulation is expected to be adopted early in 2019 (feedback from a meeting yesterday). It is the experience of participants that Member State are already refusing authorisations, because some co-formulants are on the list of 90 undesirable co-formulants. The estimate of ECPA for a proper evaluation of co-formulants is 5 to 10 years, which should be reflected in the legislation. Of particular concern are co-formulants which consist of polymers, as those are not within the REACH assessment and therefore no data available.

The endocrine disrupting properties will apply as of 10th of November 2018 to all Active Substances which have not been approved in a vote by the Standing Committee by that date. The request for additional data can be launched by RMS, EFSA or Commission. ECPA estimates that 10 to 40% of all chemical Active Substances might be affected, while the Commission estimates this to be only 26 chemical Active Substances, which amount to approximately 8%. Commission, EFSA and ECHA are intending a workshop on this issue in the near future.

ECPA observed that the Member States have a significant capacity limit which is worsened by the additional pressure on work intended the expected after BREXIT.

The Article 43 Guidance Document is regularly updated to include recent experience made. ECPA receive Guidance Documents less often and, if at all, late in the process, due to the very high political pressure on the Commission. The major difficulties

for companies are that planning the post Annex I renewal projects coming very difficult as late in the AIR process changes are made. Also, zonal Rapporteur Member States are very late assigned and difficult to contact under these conditions.

The PPPAMS database has high-priority for the Commission. It became very clear that there is absolutely no obligation to fill in the PPPAMS database at the moment and to the knowledge of ECPA it has not yet been used by anyone or mutual recognitions and new products.

The REFIT of Regulation 1107/2009 and 396/2004 is the opening of "The Box of Pandora". ECPA has observed that in any case where such legislation has been reopened and been open for public discussion it has become more hazard oriented. A final report by Commission is expected in mid-2019. Parliament has also issued an own initiative report, to increase the political pressure. The Commission called for a fundamental discussion in Europe on what food production system Europe wants. The Pesticide Committee of the Parliament, which is in place since March 2018, and was implemented because of the Glyphosate case, will focus on emergency authorisation and the independence of studies. The Committee advocates that the industry should not have any choice for the Rapporteur Member State of New Active Substances. This report will be very important for the REFIT procedure, because it is putting out political stakes which cannot go unobserved by the Commission.

The politics which will drive pesticide legislation will be influenced by the upcoming 12 national elections in 2019. For example in the Czech Republic Glyphosate has become a campaign issue. Also there will be an election in May 2019 for the European Parliament.

With respect to the technical Guidance Documents issued by EFSA, ECPA observed a significant increase of complexity. One measure of this complexity is the number of pages of such Guidance Documents and alone the fate area a 900% increase was observed. The birds and mammals is Guidance Document currently under discussion and new groups of animals are to be included. A Guidance document on isomers is currently in consultation and is planned for late 2018. The new Guidance documents are overly conservative which is the position of EFSA. With respect to the residues Guidance Document ECPA has currently a case study on-going to show that it is not feasible

to implement this Guidance Document in its current form.

A very significant proportion of the conference regulatory stream was dedicated to the endocrine disrupting properties and changes in that Legislation. Regulation 2018/605 covers the endocrine disrupting properties in plant protection. The endocrine disrupting properties are based on the WHO definition of endocrine disrupting properties and the OECD framework laid down in OECD Guidance Document 150. The current legislation only covers the EATS modes of action. And it focuses on the endocrine disrupting properties in vertebrates. It provides an assessment strategy in Chapter 3. Appendix B is the template of an excel sheet for reporting the work been done for endocrine disrupting properties. It was observed and expressed by various speakers that filling in this excel sheet is extremely time and effort consuming.

It was observed that a shift of perspective has occurred. During the discussion on endocrine disrupting properties it was assumed that no endocrine disrupting properties are present in an Active Substance and the intention of the assessment was to prove that there were such properties. Now this has completely changed to assume that all Active Substances by default have endocrine disrupting properties and it must be proven by the applicant that no such properties exist.

The ED criteria will apply as of November 2018, although the regulation has not yet been published. The Active Substances currently under evaluation will have to address endocrine disrupting issues if they have not received an approval by the Standing Committee by that date. For that a stop of the clock of up to 30 months is envisioned.

The ECPA has published a position paper on endocrine disrupting properties. The scope of the currently available Guidance Document is to humans, fish and amphibians but not yet birds. In any case the re-assessment of ED properties must re-assess the raw data of the relevant studies since not enough information is available from DAR. It was made clear that all criteria identified in that Guidance Document must apply at the same time, i.e. there must be an adverse effect and the adverse effect must be linked through a mode of action to the Active Substance. This Guidance Document implements new data requirements which will re-

sult in a significant increase in animal testing, because the burden of proof is on the notifier. This is actually contradicting the legal text.

With respect the assessment of undesired co-formulants, which are to be included as on the negative list in Annex III of Regulation and 1107/2009 the speaker indicated that a co-formulants which have a tonnage per year of above 10 and which are hazardous should have an extended SDS. Agrochemical Companies should request such SDSes from their suppliers.

A transitional period for the implementation of this negative list of 3 years would be appropriate and is under discussion. The first list will be made up of such co-formulants which have a classification similar to those for Active Substances in the cut-off criteria, which are SVHC and which are in Annex 40. One question that was raised was: Who would be addressed if not enough data for evaluation is available - the owner of the Agrochemical Product or the producer of the respective co-formulant? And another consequence was that there is clear need for guidance on the criteria that are to be applied in the risk assessments for which are not listed in the Paragraphs 128.

Development of co-formulated mixtures: Release of new General EPPO Standard PP1/306(1)

In their September meeting the EPPO council approved among others two draft PP1 General Standards which are of particular interest for the plant protection industry. The first new Standard PP 1/306 (1) "General Principles for the development of co-formulated mixtures of Plant Protection Products" provides detailed guidance for efficacy justifications when using mixtures, considering their potential advantages and disadvantages. A main focus of this document is the examination of the appropriateness of such mixtures in terms of resistance management, which is getting more and more important for the registration of plant protection products.

Co-formulated mixtures are defined as plant protection products containing more than one active substance. This includes the mixing of different pesticide types, e.g. fungicide plus insecticide, and also considers the mixture of e.g. fungicides with plant growth regulators. Although the new Standard does not specifically address mixtures with safeners or synergists, the general principles may

be of relevance for them as well. The new Standard does not consider, however, the provision of individual active substances in separate containers in a common product package (the so-called 'combi- or twin-packs').

Applicants are required to explain and substantially demonstrate in their submissions the rationale for, and the specific benefits of a proposed mixture product.

The new EPPO Standard describes in detail the potential advantages and disadvantages of mixtures with respect to product efficacy. These considerations are the key for the design of a sustainable product and should be done before starting a development process. They are basic requirements and to be presented as justifications for the selected product in the biological section of the accordant application. In such a process, the comparison of a mixture with the respective solo products should be used as a benchmark. The new standard represents the general principles to be taken into account for mixture justifications as well as the issues relevant for the justification of mixtures as part of resistance management. In case of intended registration of a new mixture across a regulatory zone or even several regulatory zones, the doses applied for in the possibly different climatic conditions should be fully justified, a task which may be more challenging for mixtures than for products containing a single active substance.

Good agricultural practice and the general agricultural policy in the EU, laid down in national action plans (NAPs) both require that the application of pesticides is being constantly scaled down as much as possible. In order to reduce the total amount of pesticides per ha agricultural area, whenever possible single products should be applied in order to avoid unnecessary contamination with pesticides that are not really needed to control the actual pest problem. Unless the mixture is designed exclusively for resistance management, in the absence of a clear benefit in resistance relative to the solo product the mixture may result in an unnecessary use of pesticides. To justify mixtures, the dose and timings for all targets should be considered. Decision to use a mixture product therefore always has to undergo an even more critical review than for single products. As a consequence, particular sound justifications (a number of very useful examples are provided in the new standard) sometimes to be underpinned by experimental data, have to be presented in the registration process.

Of particular importance is the justification of ratio of active substances in the mixture product. The contribution of each active substance to the control of the target pest can be assessed based on the rates of the solo products (in case of no overlap of activity of the single substances) or preliminary tests or a small number of trials (in case of overlap of activity). These (preliminary) trials should include all solo active substances, either as authorised solo products or as test formulations.

An additional reference product should be included if additional claims are made which are not on the label for any solo product. If the active substances target different pests, it is important that the pests regularly co-appear, in particular if application is made over a range of countries or zones.

Much space in the standard is given to the role of mixtures for resistance management, encompassing both positive and negative aspects. If resistance aspects play a role for the justification of a certain mixture, this should be fully supported by argumentation and, if needed experimental data. Justification should in particular be provided for a mixture where resistance is already present in one of the main pests. The components providing resistance management in a mixture should have an activity against the field populations of the pest when used alone and provide a robust contribution to the overall control of the pests considered at risk of developing resistance. The mixture should provide control of the pest when applied at the recommended dose. It is emphasised that mixing of two different MOAs may not always be an acceptable resistance management strategy. Using active substances in mixtures may mean, in practice, reducing the ability to alternate different MOAs in sequence, which is the common strategy to prevent **insecticide** resistance. Detailed further argumentation concerning implications for resistance management is provided for insecticide mixtures in the Appendix 1 to the standard. In the case of **fungicides** (presented in Appendix 2), mixtures have historically been used to control some of the most damaging diseases (e.g. *Phytophthora infestans*).

The main strategy here is to apply a contact multi-site protectant active substance, for example mancozeb, with a systemic partner. Justifications using the argument of coinciding diseases are more difficult to justify as they may be relevant only in special situations. However, in the case of fungicides it is important to check for potential antagonism. In

the past reductions in activity of some systemic active substances against powdery mildews and rusts have been reported when co-applied with some surface-acting contact fungicides. It is also important to consider consequences of mixtures when being used in spray programs.

For example systemic multi-active fungicide seed treatments (e.g. the succinate dehydrogenase inhibitors) with activity against foliar diseases at the doses used in the seed treatment may impose a selection pressure on those diseases for which foliar applications with the same MOA can subsequently be made. Facing a continuous reduction in the number of available active substances, and considering the dynamics of resistance development, the implications for the overall resistance management of the MOA should be considered when developing new mixtures. When doing so, the regional distribution and dynamics of resistant pests has also to be considered as shown with the example of QoI resistance in cereal powdery mildew.

Herbicides (see appendix 3) are traditionally being mixed for various reasons: cover of pre- and early post-emergence, extension of duration of control in general, broadening of weed spectrum and the prevention of resistance, to name a few. In order to prevent resistance development the components should ideally exert a similar duration of control, or at least the one more at risk should have a shorter persistence. Additional reference is made to information provided by Resistance Action Committees, national/regional Resistance Action Groups, the EPPO website and EPPO Standard PP 1/213 "Resistance risk analysis". Appendices 5 and 6 present the main considerations to be made for **PGRs** and **Home garden products**.

Experimental evidence required to support the authorisation of a mixture are the absence of antagonism in the control of the key target species, the demonstration of crop safety and the substantiation of contributions by each active substance. Where the proposed dose of the mixture applies the same amount of active substance as the solo products and the active substances do not have an overlapping activity, a reduced package of effectiveness data may be sufficient, provided no additional claims are made. In such cases existing data may be used to confirm the minimum effective dose against the key pests provided both actives substances are authorized in accordance with the

uniform principles of assessment for the same uses in a relevant Member State. In such cases it may be sufficient to provide a limited data set demonstrating the absence of antagonistic effects against some of the major pests and the absence of a significant increase in phytotoxicity.

Where there are major differences in the composition of formulation between the solo products and the mixture it would be expected that data confirming the activity of the mixture across a range of the key target pests is provided. Data would be required to support any claims for new pests or synergistic effects.

Where the new mixture represents significantly reduced doses of one or more of the actives substances then a full data package would normally be required to demonstrate the effectiveness of the product, and the potential impact on resistance management should be addressed. A bridging approach may be possible where the applied doses of the active substances are comparable to the solo products and no claims for improved control are being made. Reference products should be selected according to EPPO PP 1/214 "Principles of acceptable efficacy". For regulatory purposes it is not necessary to include the corresponding tank mix treatment.

Helpful for applicants is the **checklist** attached to the new Standard specifying the key issues to be considered when supporting the authorisation of a mixture. The most relevant principles encompass i.a. the efficacy of mixtures (e.g. whether there is a clear benefit), the ratio of active substances in mixture products, resistance or relevance of a mixture across the EPPO zone.

In the case of insecticides consideration should be given to the use of the intended mixture in **integrated pest management (IPM) programs**, particularly because of the role that natural predators, parasites and parasitoids play in controlling pest species, including resistant or less susceptible individuals. In some cases, a broad-spectrum mixture may also significantly reduce natural predator populations to a point where they are not able to keep pest species below threshold levels. But equally the application of a mixture, particularly where pest populations are high at the start of the season, may over the long term assist natural predators (following any recovery period). One of the arguments for a mixture may be that over the course of the season the amount of applied insecticides

ticide is lower than when one has to make multiple applications of solo products. If this is the case, then having comparisons of different overall treatment programs over the course of the season can be very helpful in demonstrating this.

The new standard provides very useful information which should be carefully be considered when developing new mixture products. In this context please note that the old standard PP 1/277 *Insecticide co-formulated mixtures* has already been withdrawn and been replaced by the new standard.

Please contact [Dr Norbert Weißmann](#), head of the efficacy group at SCC, if you would like any kind of support related to the development of co-formulated mixtures of plant protection products.

Composition or formulation type changes of PPP: Release of EPPO Standard PP 1/307(1)

For the first time EPPO (European and Mediterranean Plant Protection Organization) has released a detailed guidance about efficacy data requirements and data generation in case of changes of the chemical composition or the formulation type of plant protection products. With Standard PP 1/307 (1) "Efficacy considerations and data generation when making changes to the chemical composition or formulation type of plant protection products" any applicant thinking about a composition change receives an essential tool whether the provision of accordant biological data (efficacy and selectivity) might be required or not and which necessary steps to take into account, if a significant composition change is intended. Also discussed are the requirements for the development of a new product which are to be based on the principle of comparing with, and 'bridging' to, an existing formulation, which for its part should be supported by a full data package.

In the case of generic products the standard mentions that appropriate data access to the reference product is needed. In the case of zonal applications the zRMS will assess the relevance of the data and whether comparability to an authorised product has been demonstrated. However, the individual member states will determine the data protection status and data access to the authorised reference

product and are able to make a detailed comparison of the formulation details.

The definition of chemical composition change follows EU Guidance document SAN-CO/12638/2011 (rev. 2, 2012), whereas any further details about formulation types are given in 'Manual on development and use of FAO and WHO specifications for pesticides' (FAO and WHO, 2016).

The first part of the Standard provides a description of the criteria which are relevant to efficacy of the key components and types of changes which may have an impact on relevant efficacy properties, especially effectiveness and selectivity of a plant protection product.

In the decision process it is essential to have information regarding the nature and magnitude of the proposed change. This encompasses information on the chemical nature of the co-formulant(s) being changed, and explanations of their chemical similarity, if relevant.

For changes which have only a non-significant impact on biological aspects of a plant protection product, no efficacy data are required. Nevertheless, even though no special efficacy data are required, an explanation of the biological non-significance of the composition change should be given as an integral part of a justification to explain why the proposed change is considered as unlikely to have an impact on efficacy.

On the other hand significant changes in chemical composition are those regarded to have some potential impact on the biological activity of a plant protection product, requiring assessment and supporting data.

Changes of active substance content which are within the tolerances in FAO and WHO (2016) and 15% (increase or decrease of original content) require some GEP glasshouse/pot tests to show functional equivalence. In case of active substance changes of >15%, the data set for a new product has to be generated; of course with bridging options to the old data set which can serve as supporting data. In case of changes in solvent, surfactant (different CAS no) and pH adjuster contents of <10% of original content no data are required, in case of changes >10% functional equivalence in effectiveness and selectivity is required in GEP glasshouse/pot tests.

The second part of the new Standard provides substantial information about type and extent of data required for biologically significant formula-

tion changes. The extent of data to be submitted depends on how similar the new formulation is to the existing one of the already approved product. *The extent of the 'bridging' data required depends on the similarity of compositions of old and new formulation, and the number and comparability of intended key pest/crop uses. In case of a high complexity of the intended uses and national label claims; a high diversity of uses a higher number of trials will be required. Furthermore, the extent of existing knowledge on the active substance and any relevant formulations is of importance. The new guidance is very useful as it provides information how to deal with problematic situations, e.g. when the original authorised formulation is no longer commercially available. When conducting glasshouse GEP tests, selectivity testing should be done under worst case situations (most sensitive crops/varieties, n dose plus higher doses), efficacy tests with at least 3 target species at lower doses, 0.8 n proposed, to demonstrate comparable level of activity or to detect possible differentiation. If the new formulation shows to be potentially less effective in small scale GEP pot trials, then GEP field trials are required. The following number of glasshouse/pot trials are required according to the new standard: Herbicides and PGSS: Efficacy: 2 fully supportive pot trials on at least 3 key target species; Selectivity: 3 trials per crop. Other products (e.g. insecticides): Efficacy: 2 fully supportive pot trials on at least 3 key target species; Selectivity: Observations in the efficacy trials should in general be sufficient. If testing in the field is needed, 3–5 efficacy trials per major target are required, in case of several crops the number reduces to 2-4 trials per major target. This number may be further reduced under certain conditions which are explained in the new standard. As a general rule, the trials should be done on major targets and crops under most challenging conditions. Examples are described in the standard. In case of variable results, trials from a second season are required. It is not required to test in all relevant EPPO zones, but it is important to cover worst case conditions. Reference is made to EPPO Standard PP 1/278 Principles of zonal data production and evaluation.*

If crop safety trials are required, e.g. in case of observed effects in efficacy trials or generally for herbicides and PGRs, 3-5 trials are typically required per crop, a number which may be reduced to

2-4 trials per crop in case of a larger crop spectrum as knowledge base increases. Again it is not required to cover all EPPO climatic zones.

If comparability could be not demonstrated in trials based on a trial program as outlined above, further efficacy data may be required. As a worst case, even a full data set according to EPPO Standard PP 1/226 *Number of efficacy trials* might be required, if old and new formulation are shown to be not comparable.

Please contact SCC, Dr Norbert Weißmann, head of the efficacy group at SCC, in case of any questions concerning the data requirements related to composition changes of plant protection products: norbert.weissmann@scc-gmbh.de, +49-671-29846-100.

EPPO workshop on Comparative Assessment of plant protection products – current implementation, challenges, and future improvements

The EPPO Workshop on Comparative Assessment of plant protection products held in Lisbon on 24 and 25 October 2018, dealt with different aspects of comparative assessment requirements and challenges and provided a detailed overview of the current situation with special reference to EPPO standard PP 1/271 (2) *Guidance on comparative assessment*¹. The 72 participants from 19 EPPO countries encompassed 25 specialists from national authorities, representing all regulatory zones, and 44 delegates from industry and consultants.

Concept of Comparative Assessment

In the European Union, Comparative Assessment is required for plant protection products which contain an active substance that has been identified as a candidate for substitution according to Article 24 of regulation EC 1107/2009². With Article 50 the concept of Comparative Assessment was introduced for the first time, stating that EU member states shall assess products which contain one or more candidates for substitution, with the aim to substitute them, whenever possible. Candidates of substitution are e.g. actives which have significantly lower ADI, ARfD or AOEL than comparable substances, exhibit 2 of 3 PBT properties or contain a significant proportion of inactive isomer(s).

Comparative Assessment shall be performed when evaluating an application for authorization or a renewal for a product containing a candidate for substitution weighing up the risks and benefits. When conducting Comparative Assessments member states shall take into consideration non-chemical control or prevention methods, or products containing substance presenting lesser risk. The comparison is performed at national level with regard to efficacy, health and environmental aspects. This means that EU Member states must take into account any economic and practical issues around all chemical and non-chemical alternatives, resistance implications for the target organisms, as well as consequences on minor use authorizations.

Document SANCO/11507/2013³, "Draft Guidance document on Comparative Assessment and Substitution of PPP in accordance with regulation (EC) No 1107/2009" provides useful general guidance on how to determine in a step-wise approach whether there is an option for replacement of a product containing a candidate for substitution. With respect to the evaluation of efficacy, the GD refers to EPPO Standard PP1/271.

Industry experiences with implementation of Comparative Assessment

Industry, represented by Beth Hall (ECPA/Syngenta), appreciates that most member states provide templates which enable a clear presentation of a benefit case within a Comparative Assessment. Applicants have asserted that some member states conduct the Comparative Assessment without requesting applicants' input but allow consultation during the process. There are also examples where member states conduct Comparative Assessments with consideration of efficacy aspects in parallel with the evaluation of toxicology, ecotoxicology and fate issues. On the other hand, there is substantial variability regarding the timing of the Comparative Assessment submission with some member states requesting the accordant documentation to be provided at national submission meanwhile some cMS require the national documents already at time of submission to the zRMS.

Generally, industry appreciates the current step-wise pragmatic approach considering key biological/agronomic factors. Especially challenging is the comparison of products with alternative (chemical and non-chemical) solutions since applicants can only describe the benefits of their own product. It is further difficult to find details on non-chemical

methodologies and there is only little information available about the economic viability of non-chemical alternatives. It further has to be taken into account that some member states do not allow a comparison with products containing other candidates of substitution. Regarding the consideration of minor uses, member states have obviously dealt with this in many different ways. Some countries will not substitute a product if one minor use is on the label. However, if only the minor use(s) will be registered and important major be lost from label, then it is unlikely that industry will further support the minor uses, only.

According to industry experience the conduct of Comparative Assessments on national level means that there is always some variability on process and national priorities to be considered and since the accordant process is repetitive for each submission it is labour intensive and inefficient. It is also indicated as problematic that submissions have to be made for each single product submission and renewal timing.

Concerns highlighted by industry include the following points:

- Some MS allow derogation where a known active substance is used on a new crop for the first time whereas other MS allow derogations only in the case of products containing new AS.
- CA reports are made public in some MS (UK, NL, DK, FI, SE, FR), in the other MS they are treated confidential.
- A particularly high, repetitive workload for all parties involved is caused by multiple CAs in case of renewal of mixture products where the renewal timing of active substances does not allow the combination of renewal submissions. For this group of products a fast track approach was proposed by ECPA.
- Furthermore the difficulty to compare CfS products with chemical and non-chemical alternatives in absence of efficacy data was mentioned and
- explained that some MS do not allow comparison with products containing other CfS substances even though SANCO/11507/2013 requires that "alternative products containing other candidates for substitution should be included in the assessment".

Nevertheless, industry experience to date has been positive in general and it was pointed out that EP-

PO Standard PP1/271(2) is considered as valuable tool.

Member states approach to Comparative Assessment

Prior to the workshop EPPO sent a questionnaire to the EPPO member states concerning the experience made with CA. 16 EU and 3 non-EU member states sent their answers which were presented by Sue Mattock (CRD). Across the EU member states there is a range of different procedures how to deal with Comparative Assessments. Some Member states are following EPPO standard PP1/271(2) as sole guidance and others are using National Guidance based on the EPPO standard. In a third group of member states there is even no experience to date with the CA process and national guidance currently under development.

Main reasons for member states to authorise a plant protection product containing a candidate for substitution are the expected impact on minor uses, resistance issues, the indispensability of the active in organic farming (Regulation (EC) No 834/2007) and the general concern that alternatives are not significantly 'safer' for human/animal health and the environment or that they may have lower levels of efficacy.

Most member states follow a tiered approach, focussing first on the availability of relevant alternatives. This step (along with consideration of minor uses) is a common early point for stopping the CA. Member states consider the steps given in EPPO Standard 1/271 (2), starting with efficacy aspects, but also adapting the sequence of steps pragmatically in order to reach an earlier conclusion. Commonest reasons for stepping out are related to minor uses and resistance issues. Human/Animal health and Environmental risk management define the last step in a Comparative assessment process but with relatively few cases reaching this point.

The most significant knowledge gaps for member states are related to the consideration of non-chemical methods as alternatives, encompassing efficacy aspects, economics, and resistance management. It is furthermore difficult for them to judge the relevance of products for IPM programmes and to conduct the comparison of single actives with co-formulated products and tank mixtures.

Information on efficacy of chemical alternatives are based on e.g. regulatory studies supporting authorisations and authorised label uses together with expert judgements. Information regarding the effi-

cacy of non-chemical alternatives often is primarily based on a study published by UK-DEFRA in 2013⁴. Member states propose a series of measures for improvement of EPPO Standard PP1/271. These relate to a change of the order of the steps in the standard (e.g. earlier assessment of implications on minor uses), addition of steps providing more clarity, consideration of co-formulated mixtures and a widely share of available data resources. In addition examples should be developed which are illustrative for comparable plant protection products. A further simplification and harmonisation may be achievable, if EPPO codes (at present used by 9 out of 16 member states that answered the questionnaire) were used for the definition of uses by all EPPO member states.

Workshop recommendations for an improvement of the Comparative Assessment concept

In the afternoon of day 1 the participants of the workshop split up into three groups rotating around three parallel sessions and discussing in depth 1.) The experiences with using EPPO Standard PP1/271, 2.) Conducting efficacy comparisons with available alternatives (PPP and non-chemical products) and 3) Loss of availability of active substances (including the impact on minor uses, and resistance management).

The results of the sessions were presented and discussed in the plenum on day 2. The workshop concluded that EPPO Standard PP 1/271 "Guidance on comparative assessment" should be revised to provide further guidance and clarity.

The experience of applicants shows, that often assessing comparability regarding the risk of developing resistance and the effects on minor uses are steps which are considered early in the stepwise process for Comparative Assessment. These steps were identified as an efficient filter and a means to reduce or avoid the workload imposed by the other steps and should therefore always be done at an early stage of the assessment. In order to be able to reduce the workload the workshop concluded that the single steps of the CA could be presented in a 'circular' decision making scheme, allowing applicants to start at the point that is relevant to individual country guidance and procedures. It further was noted that the current stepwise process does not give guidance on how to compare a product containing a candidate for substitution when in mixture. Therefore it is essential that an updated Standard should cover both resistance and efficacy considerations when including authorized mixtures into a Comparative Assessment. This

means that further resistance advice should be provided to clarify how to address mixtures where the basis of the mixture is resistance management. Furthermore the provision in article 50(3) of 1107/2009, permitting a 5-year authorisation to “gain experience of a new use”, should be addressed in the new standard and discrepancies between EPPO Standard PP 1/271 and EPPO Standard PP 1/213 *Resistance risk analysis*⁵ be removed. At present these points are interpreted differently between member states.

Further clarification is also needed concerning the assessment of crop safety aspects. These issues could be addressed by comparing general label warnings/restrictions on phytotoxicity. For herbicides, any restrictions relating to e.g. succeeding/following crops are valid comparisons.

It is proposed that all information on how Comparative Assessment is conducted by different member states should be provided on the EPPO website, including links to any available published national guidance documents, Integrated Pest Management (IPM) national guidelines and to the EU Minor Uses database (EUMUDA). In addition, updating and sharing of research information on non-chemical alternatives is considered as an essential tool for the development of time-saving Comparative Assessment approaches.

Summarising it can be stated that despite the situation that there is still no precise guidance available, member states use a practical approach based on SANCO/11507/2013 and EPPO PP1/271 to deal with the sometimes very high number of CAs (e.g. UK 70 on-going/complete and France 46 out of 141 ongoing). A revision of EPPO 1/271 is now expected that will include further steps, practical advice and examples.

Reducing the actual risk to man and environment is an important task of CA. However, one has to recall that all products which are entering comparative assessments had immediately before passed a registration process according to actual requirements and that cutting down the applications to minor uses may kill the viability of products. ECPA expressed the hope that CAs will not lead to a further loss of active substances whose number decreased from >900 in 2000 to 425 in 2008 and 352 in 2008 (thereof 77 CfS and 75 biocontrol).

If you wish competent support concerning Comparative Assessments, please contact [Dr Joachim Kranz](#), Efficacy expert and Senior Manager Regulatory Affairs Agrochemicals and Biopesticides at SCC.

Implementation of new EU fertiliser regulation to be expected in 2022?

On 20 November 2018 European Parliament and the Council agreed on a provisional legislation for fertilisers: The main topics included reasonable limits for cadmium and the access to the market for innovative products that were excluded in the current EU fertiliser Regulation (EC) 2003/2003 such as organic and waste-based fertilisers. The new EU regulation on fertilising products will include all types of fertilisers (mineral, organic, soil improvers, growing matters, biostimulants, etc.) and will replace the current fertiliser regulation 2003/2003.

Cadmium limits

The agreed text introduces a limit value of 60 mg/kg for cadmium content in “CE marked” phosphate fertilisers to reduce health and environmental risks. The limit value will be applicable three years after entry into force of the new regulation. Seven years after entry into force, the European Commission shall review the limit values under the focus of further reduction. Moreover, a voluntary “low cadmium” label is envisaged for EC fertilisers with Cadmium contents below 20 mg/kg. Furthermore, development of decadmiation technologies shall be supported.

Organic and waste-based fertilisers

The new rules shall ease the access to the EU single market for innovative fertilisers made from organic or recycled materials to promote green innovation. The new legislation, provisionally agreed on 20.11.2018, promotes increased use of recycled materials for producing fertilisers according to the circular economy principle and to become more independent from nutrient imports. Currently, only 5% of waste organic material is recycled and used as fertilisers. This value is expected to be increased up to 30% in future. According to Commission up to 2 million tonnes of phosphorus from sewage sludge, biodegradable waste, meat and bone meal or manure could be recovered which is equivalent to one-third of the total yearly EU imports for phosphate.

Finally, the new legislation establishes EU-wide quality, safety and environmental criteria for “EU” fertilisers. If these requirements are fulfilled by the fertilising product, it can be traded freely across the EU single market as CE-marked fertiliser.

Next steps

The new legislation still needs to be confirmed by the EU member states' ambassadors (COREPER) and by Parliament's Internal Market Committee (IMCO). Finally, the draft regulation will be put to vote by the full Parliament and has to be formally approved by the EU council of Ministers. EBIC (European Biostimulant Industry Council), as representative of the biostimulant producers asked the EU institutions to adopt the regulation promptly to allow an implementation of the new regulation by 2022.

Draft Commission Directive amending rules for establishment of Harmonised Risk Indicators on pesticide use on EU level published by Commission

Nearly 10 years ago, in 2009, the valid triple pack legislation on pesticides was published: Regulation 1107/2009 on placing of plant protection products on the market, Regulation 1185/2009 concerning statistics on pesticides and Directive 2009/128 on sustainable use of pesticides. Regulation 1107/2009 introduced the new pesticide categories of low risk and basic substances, Regulation 1185/2009 established the rules for Community statistics on pesticides in the context of the Thematic Strategy on the Sustainable Use of Pesticides and Directive 2009/128 introduced the mandatory rules for Integrated Pest Management, National Action Plans and Harmonised Risk Indicators for pesticide use.

According to Directive 2009/128, the National Action Plans, *inter alia*, are "aimed at setting quantitative objectives, targets, measures, timetables and indicators to reduce risks and impacts of pesticide use on human health and the environment" whereat national indicators, already available in some Member States or to be developed, are to be amended by harmonised risk indicators to be established at Community level.

The new draft Commission Directive amending Directive 2009/128/EC of the European Parliament and of the Council as regards the establishment of harmonised risk indicators (Ares(2018)6076447, Ares(2018)6076447/1) introduces groups, categories and hazard weighting factors for low-risk active substances, non-low risk active substances, candidates for substitution and non-approved ac-

tive substances used according to Article 53 of Regulation 1107/2009 (emergency situations in plant protection) based, amongst others, on the classification under Regulation 1272/2008. Furthermore, it recognises the requirements for "Member States to give wherever possible priority to non-chemical methods of pest management" and thus separates between chemical active substances and micro-organisms. The hazard weighting factors range from 1 for low-risk active substances to 64 for non-approved active substances used according to Article 53 of Regulation 1107/2009.

The Harmonised Risk Indicator 1 considers the quantities of active substances placed on the market in plant protection products under Regulation 1107/2009 and is to be calculated by multiplying the annual quantities of active substances placed on the market for each group by the relevant hazard weighting. The Harmonised Risk Indicator 2 considers the number of authorisations granted under Article 53 of Regulation 1107/2009 and will be calculated by multiplying the number of authorisations granted for such plant protection products by the relevant hazard weighting. For both Harmonised Risk Indicators the baseline will be set at 100, equal to the average result of the calculation for the period 2011-2013. Both Harmonised Risk Indicators will be expressed by reference to the baseline.

According to Commission development of further indicators in the future is envisaged when relevant data becomes available.



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CHEMICALS/REACH



New SCC Service on eSDS: Translations into all European Languages implemented

When a risk assessment according to REACH Article 14 or 37 has been conducted for a registered substance, the corresponding exposure scenarios as well as risk management measures (RMMs) have to be communicated to the downstream users (DU) by providing an extended Safety Data Sheet (eSDS; REACH Art. 31 (7)). This eSDS must be made available in the respective official language of the member state in which the substance is marketed (REACH Art. 31 (5)). Thus, translating eSDS is a crucial step for Registrants in order to fulfil their duties under REACH. In the past no tool was available providing an automatic translation of the Annex to an eSDS containing the exposure scenarios.

With Chesar, one of the most widely used tools for risk assessments, an eSDS can be easily prepared for a substance – however, only in English.

SCC has now implemented a new service that allows translations of eSDS into all European languages with Chesar. The only prerequisites for this service are:

- A risk assessment for the corresponding substance in Chesar is available
- Harmonized phrases according to ECom are applied to describe uses and their RMMs

Of course, both of the above are well-established services of SCC as well. Please get in contact with your SCC partner to learn how easily you may get ready with your eSDS translations.

Improving the workability and quality of extended Safety Data Sheets

In the course of the recent meeting of the competent authorities for REACH and CLP (CARACAL) the member states, the Commission, ECHA and stakeholders discussed how to improve the workability and quality of extended Safety Data Sheets.

The Safety Data Sheet is a mandatory tool for suppliers of hazardous chemicals (substances and mixtures) to provide the users with safety-relevant information. For substances that require a Chemical Safety Report to accompany the registration dossier, the corresponding Exposure Scenarios (ESs) extend the traditional Safety Data Sheet (SDS) to an extended SDS (eSDS), with information on use- or task-specific conditions of safe use.

ECHA has identified a number of root causes that affect the workability and quality of the extended safety data sheet.

- The legal text and ECHA guidance leave it open how exposure scenarios of substances are to be included into the mixture safety data sheet (SDS).
- There is no common understanding whether an SDS for a mixture should have an exposure scenario (ES) Annex like the substance-related SDS, and whether users of mixtures have downstream users' duties under REACH.
- Similarly, the relationship between the ES Annex and Sections 7 and 8 of the SDS is not clearly described in Annex II of REACH, and thus leads to difficulties for recipients of an SDS to identify the information needed for checking their conformity.

The lack of harmonisation/standardisation regarding the data format of the extended SDS prevents the transfer of data in a way that IT systems could directly process the information received. As a consequence, at the moment, all information is to be uploaded manually into tools for processing (when they exist), which consumes a lot of resources and is error prone.

In addition, there is no common assessment standard supporting all the expected processing of safe use information through the supply chain by the various actors. IT providers have developed a varie-

ty of solutions for some of the tasks (mainly based on the clearly enforceable duties). The language of the Annex to the safety data sheet is an illustrative example, easy to check for inspectors but coherent translation is very challenging for IT providers.

The Commission (COM) and ECHA thus called for feedback regarding the experience with current (harmonised) formats and IT tools. Afterwards COM and ECHA will organise a workshop to make proposals for follow on work. The Commission considers including minimum requirements for the exposure scenarios for substances and mixtures in Safety Data Sheets and requesting ECHA to develop a methodology for Safety Data Sheets for mixtures. The results thereof and possible implementation in the legal text may require years. Until then the current status remains.

The Exchange Network on Exposure Scenarios (ENES) has developed harmonised formats and IT tools (e.g. the EuPhraC catalogue for standard phrases). However, uptake and use of the ENES tools remains limited.

Within this context please refer to our news item regarding eSDS translation.

ECHA introduces changes to the compliance check process as of 1 January 2019

In the course of the 27th Meeting of Competent Authorities for REACH and CLP (CARACAL) ECHA published a document (CA/63/2018) concerning the changed dossier evaluation and compliance check on 12 June 2018. The introduced changes will be effective from 1 January 2019.

ECHA has critically reviewed the current process and based on the experience of the past ten years decided to introduce some changes. As a major change ECHA will extend the scope of the compliance check to all relevant dossiers within a joint submission. In particular, this will affect the following most important points:

- In the future, ECHA will firstly check the lead dossier, and, if present, the boundary composition. Subsequently, ECHA will screen the members' dossiers to identify whether the composition is consistent across the joint submission (and consistent with the substance identity profile, SIP)

and whether deviations may impact the hazard assessment.

- Partial or full opt-out dossiers will be assessed at the same time as the data submitted jointly. This will result in a separate decision addressed only to the relevant opt-out registrants.
- CSR related issues will no longer be included in the draft decision unless the CSR is jointly submitted and the request refers to completeness in the sense of e.g. missing exposure assessment or missing exposure scenarios.
- Once a draft decision is issued, registrants will need to comply with the requests in the decision according to the tonnage declared when receiving the draft decision. It will no longer be possible to change the tonnage band or the type of registration (full vs. intermediate) as soon as a draft decision is issued by ECHA. ECHA will no longer consider second attempts made for waiving an endpoint (e.g. a new read-across) via dossier update during an ongoing compliance check procedure.
- As a general rule, ECHA will no longer offer an informal communication to the registrants after the draft decision is issued.
- ECHA will stop publishing a list of substances which are potentially candidates for compliance check.

ECHA strongly highlighted that *"as the phase-in registration period is now over, registrants should shift their attention to the quality of their dossiers and update them without undue delay, as stipulated in Article 22."* Subsequently, ECHA expect that registrants comply with their obligation and ECHA will consistently apply its expectation in the dossier evaluation process.

Thus, ECHA is expecting dossiers to be up-to-date and will not inform registrants or grant a chance for dossier updates prior to regulatory measures.

In light of the planned changes, ECHA strongly encouraged registrants to take a pro-active role, to review the dossiers and update them, if necessary, without waiting for an alert or a draft decision.

SCC has a lot of experience in preparing and updating REACH dossiers according to the current REACH requirements. In case you are planning to update

your REACH dossiers we can provide you with support. Please get into contact with Dr Thomas Roth (thomas.roth@scc-gmbh.de).

Implementing Regulation on registration updates

In the course of the 28th Meeting of Competent Authorities for REACH and CLP (CARACAL) the European Commission published a document (CA/114/2018) regarding the scope of an Implementing Regulation on registration updates.

The Commission is of the opinion that an Implementing Regulation would clarify for all actors under REACH how the duties concerning dossier updates as referred to in Article 22 should be understood in more detail. Especially, how the timing indication “without undue delay” should be understood in the context of the different cases requiring an update, and to provide clarification on the actual trigger for the updates where required.

The Commission proposes the following timeframes for the different scenarios as given in REACH article 22 (see **Table** on the following page)

The planned Implementing Regulation is in connection with the announced change that ECHA will no longer inform registrants or grant a chance for dossier updates prior to regulatory measures, starting 1 January 2019. It is the declared intention of the Commission and ECHA that in case of a compliance check or dossier evaluation the registrant needs to defend the dossier as it is. ECHA stressed that it is the registrant's duty to keep the dossiers up-to-date (e.g. remove or add uses) and not to file updates upon incident. Please also check our news item regarding changed compliance check procedure from January 2019 onwards for more details.

After seeking stakeholder input following the November CARACAL meeting, the Commission plans to bring a proposal for an Implementing Regulation to the REACH Committee in February 2019. After a first discussion of the legal text at this meeting, the Commission plans to bring it back for a vote in April 2019. Thus, it may be possible that the Implementing Regulation will enter into force already in 2019.

SCC has a lot of experience in preparing and updating REACH dossiers according to the current REACH requirements. In case you are planning to update your REACH dossiers we can provide you with support. Please get into contact with Dr Thomas Roth (thomas.roth@scc-gmbh.de).



Table: Proposed timeframes

Changes triggering updates as per Article 22 (1)	Timeframe
<i>(a) any change in his status, such as being a manufacturer, an importer or a producer of articles, or in his identity, such as his name or address;</i>	Within 6 months
<i>(b) any change in the composition of the substance as given in Section 2 of Annex VI;</i>	<p>Within 3 months for substance composition if the new composition is covered by current joint submission;</p> <p>Within 1 year if updated CSR or new Classification & Labelling, triggered by composition change;</p> <p>Within 6 months after the completion of any additional study needed based on composition change but where results do not trigger C&L or CSR changes.</p>
<i>(c) changes in the annual or total quantities manufactured or imported by him or in the quantities of substances present in articles produced or imported by him if these result in a change of tonnage band, including cessation of manufacture or import;</i>	<p>Quantities should be reviewed at least once a year.</p> <p>If quantities changed or manufacture or import ceased, updates shall be done:</p> <ul style="list-style-type: none"> - Within 3 months if the change in tonnage band relates to a decrease in tonnage band or an intermediate use under strictly controlled conditions; <p>If change of quantities trigger higher tonnage band:</p> <ul style="list-style-type: none"> - submission of testing proposal within 6 months for update of tonnage band leading to Annex IX or X requirements; - within 6 months after the completion of any additional study needed at Annex VII or when increasing to Annex VIII, and latest within 2.5 years after the end of the calendar year in which the tonnage threshold was reached or exceeded.
<i>(d) new identified uses and new uses advised against as in Section 3.7 of Annex VI for which the substance is manufactured or imported;</i>	<p>Within 3 months for registrations not requiring a CSR or if current CSR is concluded to cover new use(s);</p> <p>Within 1 year for registrations requiring a CSR where the current CSR does not cover new use(s).</p>
<i>(e) new knowledge of the risks of the substance to human health and/or the environment of which he may reasonably be expected to have become aware which leads to changes in the safety data sheet or the chemical safety report;</i>	Within 1 year
<i>(f) any change in the classification and labelling of the substance;</i>	Within 1 year
<i>(g) any update or amendment of the chemical safety report or Section 5 of Annex VI;</i>	Within 1 year
<i>(h) the registrant identifies the need to perform a test listed in Annex IX or Annex X, in which cases a testing proposal shall be developed;</i>	Within 6 months
<i>(i) any change in the access granted to information in the registration.</i>	Within 6 months

SIEF / SIEF Agreements

The EU Regulation on chemicals “REACH” (Regulation (EC) No 1907/2006) stipulates that Substance Information Exchange Forums (SIEFs) had to be operational until 1 June 2018, the day after the last REACH registration deadline.

Nonetheless, the registrants of a substance are still bound by the obligation to submit the information on their substance jointly and as of 1 January 2019, co-registrants have to coordinate the reply to ECHA, and **speak with one voice during the entire process** if they receive an ECHA decision, due to testing proposal evaluation or incompleteness of their dossiers.

History: The aim of the SIEFs was to help the registrants of the same substance to cooperate with regards to exchange of chemical substance data required for joint registration and so to avoid unnecessary testing, especially on animals and – if possible – to agree on C&L.

But what about the future of the SIEFs and SIEF(-based) Agreements?

In many cases the contractual cooperation basis for co-registrants, the “SIEF Agreement”, was terminated on 1 June 2018. Moreover, SIEF Agreements that are still in place often do not fully comply with the regulation on joint submission and data sharing (Commission Implementing Regulation (EU) 2016/9), which came into force several years after many contracts had been prepared.

However, the legal obligation to cooperate among the co-registrants for the joint registration and for data sharing related tasks persists. This cooperation, e.g. on managing update needs and updates of the registration dossiers (Article 22, REACH), as well as coordinated responses to potential regulatory requests related to dossier and substance evaluation, might become more intensive, depending on the regulatory and scientific issues that might arise and which – **as of 2019** – ECHA will address to **all non-compliant registrants** (no longer mainly to the LR) of a substance.

Furthermore, the dynamic of EU chemicals market, political decisions such as BREXIT, etc. require ongoing data management and lead registrants who should be prepared for cost sharing requests of

new registrants and reimbursements to existing registrants.

Even if the number of co-registrants per substance is lower than the number of SIEF members (some SIEFs now comprise hundreds or even thousands of members), the administrative burden and time for communication should not be underestimated.

Considering all the tasks mentioned above, amendments to existing contracts might be necessary or – as recommended by The Directors’ Contact Group – “SIEF Agreements” should be replaced by new cooperation contracts, addressing the “after-deadline” obligations and ensuring compliance with the available regulations.

ECHA Accounts – new features

ECHA has launched new services for users of ECHA accounts.

When you log into your ECHA account, you now have the possibility to link the substances that are important for you and your company directly to your ECHA account by selecting them from the “Search for chemicals” section. Once you have added the substances to your “My Substances” list, you will receive a weekly notification as soon as one of your substances is included or updated in one or more of the following five regulatory procedures (multiple choice is possible):

- Registration dossier update alert
- Substance Evaluation update alert
- Candidate List alert
- Authorisation process alert
- Restriction process alert

You can also save and reuse your searches without having to fill out the form again. At <https://echa.europa.eu/my-account> there is a short tutorial that is very helpful and will guide you through these new features.

With your ECHA account you can also download the IUCLID software, the Chesar tool, become part of a future poison centres community, and subscribe to the corresponding news for all these applications.

Any ECHA account you have already created to access an ECHA IT tool (i.e. REACH-IT, R4BP 3, ePIC) can be used to log into ECHA’s main webpage. If you have not yet created an ECHA account you must log in first. The latest version of the “ECHA

Account Manual (November 2018) "will guide you step by step and help you to set up.

The pdf is available at

<https://echa.europa.eu/support/dossier-submission-tools/reach-it> under the heading „Signing up“.

Essential aspects of the 2nd REACH review from the point of view of the BMU*

On 6-7 December 2018 the BAuA REACH congress 2018 took place in Dortmund. In the introductory presentation, Dr Axel Vorwerk, ministerial official at the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety in Germany (BMU), outlined the essential aspects of the 2nd REACH review from the point of view of the BMU.

Among other things, he presented the positioning of the Federal Government in the priority area of data quality as follows:

Ensuring dossier conformity is a major concern for the authority.

- The reliability of the data basis is crucial for the benefit of REACH, also for the economy itself.
- Experience has shown that in many cases the registration data submitted are insufficient to varying degrees.
- The BMU's aim is for the registration dossiers for all substances to be reviewed within a manageable period of time, i.e. in the next ten years. This would require a significant multiplication of the number of dossier evaluations per year.
- Furthermore, it must be ensured that the database is not obsolete (e.g. changed use/exposure).

Dr Vorwerk presented the following measures to improve the data quality:

- Significant streamlining of evaluation procedures. Until now, it usually takes several years for missing data to be submitted or for erroneous data to be corrected.
- Substantially increase the administrative resources used, including discussing how registrants should share the costs and what incentives should be put in place to ensure that information is provided in the required quality from the outset.

- The Commission could examine measures to improve own-initiative updating under Art. 22 REACH and could also consider the question of regular updating requests.

The most remarkable statement is that the German authority aims to evaluate all REACH dossiers within the next 10 years. This is of course currently not an agreed position between member states but should raise attention in industry.

The position of Germany again emphasises that REACH is not done after the last registration deadline has passed. You should stay tuned and plan your capacities for dossier updates and substance/dossier evaluation accordingly.

The presentation (only available in German) can be found using the following [link](#).

* Federal Ministry for the Environment, Nature Conservation and Nuclear Safety in Germany (BMU)



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REGULATORY SCIENCE



5th International Fresenius Conference "Worker, Operator, Bystander and Resident Exposure and Risk Assessment" 6 – 7 December 2018

The 5th International Fresenius Conference on Worker, Operator, Bystander and Resident Exposure and Risk Assessment took place in Mainz on 6th and 7th December 2018. Speakers and participants were representatives of national and international authorities, industry representatives as well as academics. New developments in regulatory assessment of plant protection products in the EU and around the globe were presented.

At the moment several projects are ongoing to support the update of the EFSA guidance on non-dietary exposure assessment. One of the projects presented was the BROV (Bystander Resident Orchards Vineyards) project, which focuses on new drift data in orchards and vineyards as well as on worker exposure and dislodgeable foliar residue data in vineyards. A first report is expected to be available in 2019.

A further project, which was initiated by the Seed TROPEX Taskforce, focuses on the update of the operator exposure model for seed treatment. An enlargement of the database as well as a survey of the European seed treatment practices is already ongoing. The project is planned to be finalised in 2020.

The results from those two projects as well as new data concerning the greenhouse agriculture operator exposure model (AOEM) will be utilised to update the EFSA guidance on non-dietary exposure assessment. The revised guidance will include updated default values and risk migration measures and additional scenarios. An update of the OPEX calculator is also envisaged. The open call for data on the guidance document ended on 10th December 2018 and a first meeting of EFSA's working group is planned before end of 2018. The project to update the EFSA guidance will run until 2021.

18th Fresenius Ecotox Conference – "Aquatic and Terrestrial Ecotoxicology and Risk Management" in Germany

The 18th Fresenius Ecotox Conference „Aquatic and Terrestrial Ecotoxicology and Risk Management“ was held on the 29th and 30th November in Mainz. The focus of presentations was on regulatory aspects, the use of models in risk assessments and the use of radiotracking data for risk refinements.

The regulatory aspects discussed were the challenge of implementing protection goals in risk assessment/management and the simplification of the risk assessments of plant protection products in the light of increasingly complex guidance documents. KEMI presented its proposal for simplification (e.g. database tools for faster evaluation, calibration of surface water exposure assessment, facilitating mutual recognitions) which was also discussed from industry's point of view.

With regard to the use of toxicokinetic/toxicodynamic (TKTD) models in the risk assessment, several speakers stated that there are validated models available (e.g. for *Lemna*, and survival of aquatic organisms) which can be used for the risk assessment, not only by applicants but also by authorities.

The use of radio-tracking data for the refinement of the risk assessment for birds and mammals was the main topic on the second day of the conference. The presentations focused on the use and evaluation of PT data (data on the Portion of diet obtained in the Treated area), e.g. by Monte Carlo simulations of the available study results. Views from the risk assessors and risk managers were presented and discussed.

Other talks covered global regulatory developments (presenting regulatory developments in China), endocrine disruption (summarising the ED conference in Cologne in November 2018, *see the following article*), the suitability of watercourse-mesocosms to investigate direct and indirect effects of pesticides on aquatic food webs, and an overview on the ecotoxicological risk assessment for biopesticides.

9th International Fresenius Conference on Endocrine Disruptors

Insight into regulatory implementation of the new criteria for endocrine disrupter (ED) identification under EU Regulations on plant protection and biocidal products was provided at the 9th international Fresenius Conference on Endocrine Disruptors (November 2018, Cologne, Germany). An overview of the corresponding Guidance Document (EFSA/ECHA, 2018) was presented by representatives of EFSA and ECHA, and a view on national level was provided. The resulting challenges were discussed by representatives from industry, academia and NGOs.

The European Commission (EC) opened the conference with a regulatory update on the new ED criteria: The ED criteria are applicable to all ongoing and pending evaluations, *i.e.* for biocides (BC) from 7th of June 2018 and for plant protection products (PPP) from 10th November 2018. All submissions before 0th November 2018 and where the EC has not voted on a draft Regulation concerning the renewal or non-renewal are pending evaluations.

There are three possible scenarios foreseen where additional information can be requested to conclude if ED criteria are met or not (for details, please refer to Regulation (EU) 2018/1659). If additional time is needed to generate data a “stop of the clock” is intended for minimum 3 to maximum 30 months. The length of this period will be decided case-by-case and must be justified by the time needed to generate the data needed.

If ED criteria are met on the basis of the available information, the applicant has three months to apply for negligible exposure and/or Article 4(7) of Regulation 1107/2009. The information to address these derogation conditions can be submitted within the stop of the clock period. After seven years, a review clause is foreseen in order to reflect the experiences gained with the application of the ED criteria. The conclusion of the RMS, EFSA and/or EC as to whether the available information is sufficient to identify ED properties or if additional information is necessary will be done based on the EFSA/ECHA Guidance Document (GD, Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009, EFSA, 2018). The GD was presented in detail by representatives of EFSA and ECHA and should serve as a harmonization tool between RMS, EFSA and EC. It was mentioned that an ED assessment according to the GD is required if the approval decision is after 10th November, even the GD is not legally binding.

To obtain sufficiently investigated ED parameters the GD suggests *i.e.* *in vivo* animal tests (AMA¹, FSTRA²,

LAGDA³, MEOGRT⁴). Conference participants generally agreed that the chronic tests will be the most challenging task. On one hand these tests are animal intensive, which is not consistent with the “3 R” principles of animal testing (reduction, replacement and refinement) and many laboratories lack experience with these tests, as well as capacity. The LAGDA and MEOGRT tests have a long duration and to meet the validity at first run is up to date difficult. Many participants expressed the need for an updated testing strategy (e.g. embryo assays). In addition, effects on adversity could be addressed by population modelling, but this is not currently accepted by the relevant authorities.

The new GD and the associated evaluations can be expected to present a significant workload and a high level of expert knowledge is required to cope with this topic.

¹AMA = Amphibian Metamorphosis Assay, OECD 231; ²FSTRA = Fish Short-term Reproduction Assay, OECD 229; ³LAGDA = Larval Amphibian Growth and Development Assay, OECD 241; ⁴MEOGRT = Medaka Extended One Generation Reproduction Test, OECD 240

Very recent news regarding EFSA Bee Guidance Document

During the meeting of the Standing Committee on Plants, Animals, Food and Feed (SCoPAFF) on 12 - 13 Dec 2018, the taking note on the EFSA Bee Guidance Document (published in 2013) was postponed again.

FOCUS Repair Action Report

End of September, EFSA issued for public commenting a report on the „repair action“ of the FOCUS surface water (SW) models. The “FOCUS repair group” (FRG) acted upon request of the Commission after consultation of the EFSA Pesticide Steering Committee. Many issues of the repair group deal with harmonisation of diverging modelling approaches between the different SW modelling steps and also in comparison to the modelling guidance for the groundwater compartment. Consequently, one main point of the “repair action” is to introduce for the drainage scenarios a 20 years assessment period in MACRO to be in line with the run-off scenarios and the groundwater modelling. In addition, the FOCUS repair group proposes not to use the Pesticide Application Tool (PAT) in the SW model any more, which was introduced by the FOCUS Workgroup to derive a realistic worst-case date for application of the sub-

stance on the base of a user-specified time frame. Unrealistic situations like applications at a date with significant rainfall were avoided with the PAT. Abandoning the PAT approach will make the results somewhat more conservative. However, setting the application date manually instead of using the PAT shall harmonise the approach with the groundwater modelling.

Further points are the handling of the drift percentile in case of multiple applications and the handling of drift rates for early application in vines and early applications for pome/stone fruits. The FRG proposes to use the 90th percentile drift also for multiple applications as a conservative approach instead of the current use of the lower percentiles depending on the number of applications. As a consequence, the separate calculation of “single application” as worst case drift scenario would not be necessary any more when multiple applications are foreseen in the GAP. As proposed by Germany since 2003, the scenario a “early” for vines is excluded as it is based on the tunnel-sprayer technique, which is considered not representative for the EU. In line with proposals from UK, the drift scenario “pome, early” is considered applicable to BBCH 69 and “pomes, late” should be used from BBCH 71 onwards.

Regarding wash-off, it is proposed to use the MACRO assumption that rainfall less than 18 mm does not contribute to wash-off from plants also for PRZM. One point affecting the extend of future surface water simulations is also known from the groundwater guidance: In case of pH dependent sorption and/or degradation, contrasting calculations for low and high pH values using appropriate endpoints for either regime should be conducted for identifying the worst case.

All in all it is expected that the implementation of the proposals will increase the amount of calculations necessary, especially for substances with pH-dependent properties. Some proposals will make the results more conservative. At the end the impact on the exposure assessments depends also on risk managers decisions on the regulatory relevant percentile level of results to be used as a trigger. The Commission is expected to decide upon the triggers based on comparative assessments provided by the FOCUS repair group. There is not schedule indicated in the report regarding the implementation of the recommendations by the FOCUS repair group.

CALENDAR



European Biostimulants Interactive Summit in Madrid, Spain

23 - 24 January 2019

Please meet

Anke König-Wingenfeld, Assistant Manager Regulatory Affairs, Agrochemicals and Biopesticides – Biostimulants, Fertiliser, IPM, at the European Biostimulants Interactive Summit 2019 in Madrid, Spain.

The two-day event will bring together key industry stakeholders from the biostimulants industry to give insights into the current challenges being faced and what opportunities lie ahead. Find out more about the summit on [the event's official website](#).

Anke looks forward to meeting you in Madrid and discussing with you your registration needs for biostimulants and biopesticides as well as any other regulatory or scientific issues you might want to address.



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... coming soon