

NEWSLETTER

SCC Newsletter Vol. 17, No. 1, April 2017

EUROPE IN TRANSITION - REGULATORY NEWS

Dear Subscribers,

I would like to start with a few words about the recent European developments, i.e. "Brexit". Finally, nine months after the vote to leave the EU, Brexit has now been formally initiated. The United Kingdom's Prime Minister, Theresa May, has signed the letter triggering the exit procedure of the (in)famous Article 50 of the Lisbon Treaty and had it delivered to European Council President Donald Tusk on 29 March 2017 (the Prime Minister's letter, as well as the relevant strategy papers of the United Kingdom, can be found [here](#)). Thus, the two-year negotiation period has now started and, if this period is not extended, the United Kingdom will leave the EU in March 2019, with all the foreseeable and unforeseeable consequences. *We will follow the process closely and will keep you informed.*

Please find in this issue of the SCC Newsletter a report on the conference "Crops and Chemicals Europe 2017" and further important news about agrochemicals/biostimulants and chemicals/REACH and regulatory science. Regarding biocides, do not miss the chance to take part in a free [workshop](#) on the preparation of dossiers according to BPR, offered by SCC. The workshop will take place in May.

As you know, in the fast-moving world of regulation, SCC is ready to keep its customers on a successful course. Regardless of whether your needs are in scientific and regulatory support (like exposure modelling and risk assessment) for agrochemicals and biopesticides, biocides, chemicals, consumer products, feed and food additives, GLP archiving solutions or Task Force management, SCC can provide you with high-quality services and consulting.

Please have a look at the calendar to find out where you can meet with SCC experts to personally express your needs or find answers to your questions on scientific and regulatory issues.

We appreciate your feedback and comments regarding the SCC Newsletter.

Please drop us an

E-mail at newsletter@scc-gmbh.de.



Dr Friedbert Pistel

Important advice for the last REACH deadline 2018!
Last call to pre-register your low volume chemicals
by 31 May 2017, the latest.

(Please refer to page 15)

IN THIS ISSUE:

Agrochemicals	p. 2
Biocides	p. 14
Chemicals/REACH	p. 15
Regulatory science	p. 16
Calendar	p. 17
Contact details	p. 18

AGROCHEMICALS



Crops and Chemicals Europe, Berlin 8 – 9 February 2017

From 8 to 9 February 2017 there has again been the Crops and Chemicals Europe Conference in Berlin, Germany. The event covered three individual conferences (Agrochemical Formulation, Biostimulant R&D and Regulation of PPP and Plant Health Products). For those who have not been able to participate in the event we are summarising the most important points of the Registration of Agrochemicals and Biostimulants and Plant Growth part of the conference. Please refer also to a [comprehensive overview on low risk substances](#) and [latest developments in efficacy assessment in agriculture](#) presented by SCC's colleagues in Berlin.

After the opening remarks, the first presentation was given by Guy Elitzur, CEO of Stockton STK, who called the cooperation between agrochemicals and Biopesticides a marriage and asked how it was going. He first analysed the megatrends that are currently affecting global agriculture. There is a significant rise in population, which is to reach 9 billion by mid-century, with 66% of that population living in cities. A significant increase of total wealth is expected, as 3 billion people will enter the middle-class by 2050. At the same time, the resources are decreasing; 12 million ha of land are degraded every year and the strain on the water resources is growing significantly. The increasingly wealthy population is developing an environmental, health and fair trade awareness, all of which will influence the future of our agrochemical production system. Also, the regulatory demands are expected to increase significantly. He observed that through the years the regulatory changes had significant impact on IPM practices around the world. For example Regulation 1107/2009, which took force in 2011, required that any crop protection product must demonstrate not only that it is effective, but also not to represent any risk to either human health or the environment. Again this has led and will lead to increasing pressure on conventional crop protection

portfolios, while at the same time allows emerging opportunities for Biopesticides. The speaker assessed the Biopesticides market currently at US\$2.5 to 3.5 billion and expect it to grow 3 to 4 times faster than the broader crop protection market, to be worth approximately US\$4.5 billion in the next seven years.

The trend described above has also been seen by big agrow companies. They are investing into Biopesticide companies, Bayer buying Shemer, Monsanto acquiring Beelogics, Syngenta taking over Pasteuria Biosciences and Du Pont purchasing Taxon. Also the venture capital pouring into alternatives to conventional crop protection has been growing from US\$177 million in 2014 to US\$251 million by mid-2016. Diversity in Biopesticides is also assured in the R&D. While current research in conventional crop protection is dominated by fewer than ten big companies, Biopesticide developers number 170 to 200 companies in the Western world. The advantage of Biopesticides is also emphasised by the costs and timeline to discover and develop such Active Substances. While conventional pesticides take on average almost US\$300 million and significantly more than 10 years to develop, the speaker estimates Biopesticides at US\$10 million and 4 to 6 years development time.

In the US nearly 18 million acres are already being treated with Biopesticides. The US-EPA's Biopesticides division has registered more than 430 biological Active Substances and has awarded more than 70 grants to research Biopesticides for speciality and minor crops. Nevertheless, also integrated control programs must answer to the call for profitability with a farmer.

The speaker also highlighted the use of hybrid products, which are combining the benefits of Biopesticides with the performance of classical crop protection. Synergistic effects improve efficacy, dual modes of action reduce the threat of resistance and prolong the life of an Active Substance. While expanding the spectrum of use, they reduce the chemical load allowing more manageable residues. In addition, reducing the chemical dose, reduces the effects the chemical might have on the environment.

The future of integrated pest management is seen brightly by the speaker, as growers continue to adopt practices to improve the sustainability of agriculture. He expects that by the middle of the century the markets of Biopesticides and conventional pesticides will be similar in size, each worth approximately US\$55 to US\$65 billion. Guy Elitzur concluded that the marriage of Biopesticides and conventional pesticides is healthy and getting stronger with time.

In the subsequent panel discussion it was proposed that Biostimulants should be included in this marriage of Biopesticides and classical pesticides to make it a ménage à trois.

Roger Tripathi of Acadian insisted that a regulatory framework is necessary for Biostimulants, to differentiate them from “snake oil” and for farmers to accept the products. But the stipulations of such a regulatory procedure should preferably be softer than for Plant Protection Products. The main worries brought forward were about the timeframe involved for an evaluation. The message from the panel to legislators: keep it simple - keep the timeframes and: a regulation is needed. Widening the view to also include the farmer, the panel requested that not only the slogan “feed the world” must be kept in mind, but also to assure a sustained growth of the farmer’s income and of agriculture. With respect to chemical Active Substances it was not doubted that they too have a future role to play within integrated pest management! Thomas Mason of Dudutech informed the plenum that recently Bioprotection Global was founded, a group similar to CropLife International, but focusing on biological products and Biopesticides.

Mathew Phillips of Philips MacDougall took the full Agrow Market into view and gave detailed analyses of the world markets of agrochemicals, including trends and causes of these trends. He assessed the total agrochemical market in 2016 to be US\$56 billion (including non-crop uses of agrochemicals). This is a decrease compared to 2015 of 1.7%. The crop protection market (excluding non-crop agrochemicals) decreased over the same period by 2.4%.

In 2016 the Asian market has overtaken the Latin American market to become the largest market in the world. Both are followed by Europe third place and NAFTA fourths, all with market sizes between approx. US\$9 to US\$14 to billion. In final place Africa and the Middle East have a market sizes of US\$2 billion. The speaker is currently undertaking a market review on Biologicals on Biopesticides to be able to describe the value of that industry. In this review Biostimulants will not be included. On the preliminary data available a down turn of 0.5% on Biopesticides was observed, but attributed only to currency effects. The market of Biologicals in 2015 was divided as follows: 7.7% by Macrobls, 30.6% of Microbls, 2.3% of Semio Chemicals, 5% of Natural Products and 54.4% of Fermentation Products.

The speaker then analysed in much detail the key factors for market effects in 2016 and effects coming into focus in 2017. Interestingly, the EU CAP Reform (Common Agricultural Policy) is assessed to result in negative pressure in the EU in both cases. This effect

might mellow out in 2017 as the major negative impact has now passed and the market is adjusted to a lower baseline.

The development of new Active Substances is down from approximately 65 in 1999 to approximately 40 in 2016 (worldwide figures excluding China). Active Substance patents between 2008 and 2015 are attributed in 83.5% to Asia, 11% to Europe, 4.5% to NAFTA and 1% to Latin America. Mathew Phillips observed that there has been an overall growing world plant protection market since 2010 and expects this real growth to continue with 2.7% per year until 2020. The developing markets are the fastest growing markets in this respect.

Eric Liégeois of the European Commission and Claudio Mereu of Fieldfisher addressed the new Fertiliser Regulation in their two presentations. Eric Liégeois emphasised that the new Regulation is a consequence of the circular economy action plan. Its intention is to reduce the administrative burden and to clear legal uncertainty. It is currently, he told us, at the Parliament, for them to amend it in “all their wisdom”. The Council is expected to deal with the Regulation in April/March and the European Parliament could vote in September 2017. Thereafter the trilogue negotiations would be started. Claudio Mereu in his presentation added that its adoption in 2017 would allow its applicability in 2019. Currently, Regulation 2003/2003 only includes inorganic (mineral) Fertilisers as European Fertilisers. In addition there are 28 national Fertiliser Regulations. The speaker acknowledged that due to this diversity, mutual recognition within the European Community is not functioning well. The new Regulation will expand the scope, to also include organic Fertilisers, Soil Improvers, and Plant Biostimulants. With this harmonisation the Commission assumes, a free circulation of CE classified Fertilisers will be possible. Nevertheless, the current situation will be maintained and national Fertiliser Legislation will remain in place. Also, Biostimulants can continued to be authorised under the national Fertiliser Legislations. The Commission has so far received positive feedback from their co-legislators on the above issues. Also the conformity assessment, which can be done by either manufacturers or legal bodies, is seen positively by co-legislators. Eric Liégeois emphasised the double safety net implemented by the new Fertiliser Regulation. First, the components are assessed under REACH and subsequently limit values for known contaminants (CMC) can be set for each CMC. This is currently discussed with Council and Parliament, whose main concern is cadmium contamination.

The scope of the new Regulation is, as described above, extended to include Biostimulants. To differentiate between possible Plant Protection Products and Fertilisers, the mode of action must be assessed. Claudio Mereu in this case referred to US Regulations, which define the difference by making reference to the mode of action as well as the claim and the composition of the product. Secondly, the concentration dependence of the activity as Plant Protection Product can be relevant. Copper would be an example to illustrate the concentration dependency between use as Plant Protection Product and Fertiliser.

The speaker also pointed out that the Regulation will be adapted to the technical process, to become more and more comprehensive. Such adoption could be done by implementing annexes in delegate acts. He reported that the reactions from co-legislators are mixed on this proposal, as it would, through delegate acts, put more power on the Commission. He also reported that Regulation 1107/2009, in his view, would always take the prerogative to dual use products, i.e. they would have to be approved under Regulation 1107/2009. While co-legislators can live with this proposal, multifunction products will be the most critical issue and a controversial discussion with the co-legislators is expected. Particularly, as CE label products would have free movement within the EU, while agro chemicals under Regulation 1107/2009 are bound to national authorisations.

The current proposal in the new Fertiliser Regulation i.e. to put Plant Biostimulants in Product Function Category (PFC) 6 containing Component Material Categories (CMC) 1, 2, 7 and 11 ingredients and the current definition "nutrient use efficacy increase, tolerance to abiotic stress increase and crop quality traits increase" is widely shared and accepted. The heavy metal content of Biostimulants is under discussion, though. Also, the efficacy claim should be clearly stated on the label. On the other hand a shelf-life proposal of at least six months for microbial Biostimulants, as proposed by the Council, is to be removed. For non-microbial Plant Biostimulants, there will be no differentiation between organic and inorganic components, which is a clear simplification compared to the current situation. There are discussions ongoing on the accepted extraction methods in CMC 2 which is to be extended from water only. It is emphasised that no chemical transformation during extraction will be accepted. With CMC 6, Microorganisms, a positive list is compiled and a lot of feedback on that list has been provided. There will be a mechanism to amend the list, with individual quality criteria still to be addressed. Due to the complexity of that issue, a new expert group on microbial Biostimulants

has to be launched and will include participation by EFSA, other experts and industry. Microorganism identification will be at strain level. The prioritisation criterion for such amendments to the list is the market potential for a proposed Microorganism.

Claudio Mereu added, as a point not currently addressed in the Regulation, MRLs for Biostimulants. He sees a clear problem as to their implementation, since there is no system for MRL compliance without an authorisation system, as is the case with Biostimulants in the new Fertiliser Regulation.

Eric Liégeois stated that still no data protection provisions are foreseen in the new Regulation. Data protection can only be awarded under REACH. He acknowledged that it is a very difficult problem, because of the lack of an authorisation system, as was already mentioned by Claudio Mereu. Eric Liégeois confirms that the co-legislators have addressed this issue, but that it does not contain any priority for the Commission at the moment. Claudio Mereu mentioned the example of medical devices CLASS 1, which are also handled under a CE system as a blueprint for further considerations on data protection.

The views of the EU Minor Uses Coordination Facility were presented by Jeroen Meeussen. With a very nice and colourful slide he illustrated, why he would prefer to replace the term "minor uses", which always implies some unimportance, by the American term "speciality crops". He explained that in Regulation 1107/2009 Article 3 (26) the definition of minor uses is either a crop not widely grown in a Member State or a use meeting an exceptional plant protection need. Contrary to their (European) name and their limited cultivated area (3% of the total area) minor uses, are, nevertheless, representing 22% of the value of the entire EU Plant Protection Production.

The task of the coordination facility is to share information and experiences gained at national level, coordinate minor use work between the Member States and stakeholders plus create and maintain a database on minor uses. Finally, stimulation of harmonisation is also encouraged. The coordination facility is currently funded for three years by the Commission (50%) and France, Germany and The Netherlands. In spite of this limited funding the facility is working for all EU Member States. The facility has initiated seven different commodity expert groups (CEG) on different minor use issues. The speaker emphasises that currently the focus of all CEG's is still very much on chemical solutions. The mission of the facility is to encourage collaboration to

improve the availability of chemical and non-chemical tools within an integrated pest management framework.

The facility has initiated a [website](#). A newsletter can be subscribed. Also the EUMUDA webpage will be relaunched in March 2017. Also PPPAMS database is being used and will become mandatory the future. The benefits of the new EUMUDA tool are to provide accurate and consistent information for each project, a better exchange of information, and a harmonised approach. The speaker also indicated that Guidance Documents for applicants (industry as well as growers associations) on registration issues for minor uses are under preparation. Part 1 will deal with the generation of data and part 2 with the application process. The speaker sees as regulatory hurdles for minor uses the renewal programme which influences negatively the availability of a sufficient range of Active Substances, as well as the comparative assessments, which should be closely monitored especially as different Member states are taking different approaches. Member States can contribute effectively to the minor use program by input necessary to fill EUMUDA with life, to participate in joint projects with an EU mind set, to carry out trials and share information with other Member States, to share knowledge about non-chemical solutions, to stimulate harmonisation (which is contrary to the currently observed tendency, which “invents” more and more new Member State requirements). The speaker finally put the endeavours to promote minor uses into a global perspective, mentioning the global minor use summit, which will take place in Canada this year. He also proposed to generate an EU funds to finance minor use projects, a procedure already implemented in the US and Canada and other States in the world.

[Bernd Brielbeck](#) of Scientific Consulting GmbH (SCC GmbH) addressed Low Risk Active Substances. He emphasised that the general political environment for Plant Protection Products is currently difficult in Europe. The recent confusion about the renewal of Glyphosate exemplifies this sufficiently. In contrast, Low Risk Active Substances are seen positively and business opportunities can be expected to thrive in this section of the market in the future. Even the European Parliament has put forward an initiative in 2015 already calling for measures to support such Active Substances.

A broad variety of legislations and initiatives have been adopted. They call for the sustainable use of agro chemicals, the greening of agriculture, and the establishment of ecological focus areas, all of which might eventually benefit Low Risk Active Substance

approvals. Regulation 1291/2013 establishes Horizon 2020; a framework for research and innovation, assigning between 2014 and 2020 80 billion Euro to such work. All details of such legislation can be found on slide 4 of the presentation published on the conference website.

The speaker emphasised that the above initiatives must be seen in the context of limited availability of Low Risk Active Substances in the market, i.e. seven at the time of the conference. The AIR 4 (Annex I renewal) programme is also taking this fact into account, by grouping the Active Substances according to their presumed (low risk) properties!

To allow more Active Substances with adequate properties to fall under the low risk categories, SANTE/11953/2015 and SANTE/12376/2015 are currently establishing revised criteria for such Substances, as well as amending Regulation 1107/2009 to further this goal.

The speaker's brief check of the above intentions against real life realities revealed some sobering facts. The scientific approach is, in various cases, hampered due to the strict and “regulatory” execution of data requirements by the Authorities. Also, practical issues such as the limited number of GLP compliant CROs competent in working with microorganisms, often, but not necessarily always, Low Risk Active Substances, can impede progress. Dossiers based on literature data, encouraged in the case of Low Risk Active Substances, might be complicated by copy right issues. Uncertainty on the implementation of new guidance on endocrine disrupting properties might lead to a loss of natural, presumably Low Risk Active Substances, as Vitamin D3 or caffeine and others.

The conclusion he drew is positive! All issues addressed in the Parliament Initiative are important to further the cause of Low Risk Active Substances and provide the European agriculture with versatile and safe Active Substances again. Little needs to be added – they just have to be done and transferred to the regulatory system!

Daphne De Roode from Charles River elucidated for us Article 43 renewals and the comparative assessment. With Article 43 she drew our attention to the very tight timelines of three months after reapproval of the Active Substance for the applicants to submit their dossiers, six months for the zonal Rapporteur and another three months for the concerned Member States to do their evaluations. Of course, this timeframe can be extended, if category 4 studies are necessary for the reauthorisation of the product. She

called the reauthorisation process challenging for the applicants as well as the competent Authorities. In the second part of her presentation she dealt with another challenge which burdens the Authorities at the same time as the reauthorisations, i.e. comparative assessment. Quoting Article 50 of Regulation 1107/2009, she highlighted, among other points, the fact that the legislation requires the alternative to the product containing the candidate for substitution to have a similar effect on the target organism without significant economic and practical disadvantages. She pointed out that the comparative assessment is done on each individual Plant Protection Product containing a candidate for substitution by each individual Member State. She observed that thus the assessment might be very different depending on the alternatives available in each Member State.

The comparative assessment is a step-wise approach. In Step 1 the candidate for substitution in the Plant Protection Product is identified and consideration of an optional assessment is made. Step 2 will take into account agronomic aspects and chemical and non-chemical alternatives. Step 3 is the first step of an assessment for health and environment focusing on the criteria that were the reason for the classification of the Active Substance as a candidate for substitution. In the final Step 4, a more extended assessment for health and environment will be done.

In her analysis of the national particularities, she contrasted the approaches of The Netherlands and the United Kingdom (UK). She observed that both countries have in common that the applicant is to submit relevant data and that the data is to be submitted along with it dRR. She chose the two respective countries, because The Netherlands is seen as one end of the spectrum where the workload is mainly with the applicant and in the UK, at the other end of the spectrum, the workload is mostly with the Authorities.

In The Netherlands products containing another candidate for substitution are not included in the alternatives, neither are combinations of different products or combinations of non-chemical and chemical methods. Comparative assessment is only conducted for major uses, but minor uses are considered. The Netherlands has stipulated that at least five resistance groups must remain available. Data the applicant has to submit include the identification of alternatives based on a database The Netherlands are compiling. In the agronomic assessment (Step 2), the applicant must refer to published data and must assume that the alternatives efficacy is sufficient, unless the applicant proves it otherwise. In the risk assessment (Step 3 and 4) the applicant may use published evaluations by CTGB. For Step 4, a stop of the clock is possible, if only Step 3 is submitted by the applicant. The risk

assessment on human health will be based on a risk index and existing evaluations will not be updated, although they might have been done according to old Guidance Documents. In the environment a quantitative assessment is not possible and the evaluation starts with the PBT criteria. In residues the assessment will be based on the comparison of percentage of the ARfD or the ADI used.

In the UK there is a slightly different focus on many of the issues raised above. For example, the UK will not consider alternatives which require strict risk reduction measures. And, in the UK only four resistance groups must remain available. Also, in the UK, the applicant has to submit an identification of alternatives based on a UK specific database. UK has a database specifically on non-chemical alternatives. The key properties and risk mitigation measures of the alternative products must be taken from the published labels. The assessments will be conducted by HSE and not by the applicant.

An interesting overview was given on the differences of the comparative assessment with respect to different applications types. The national approaches of Belgium, France, The Netherlands and the UK were compared. In the case of new applications, extension of applications and renewal of applications all four countries will do comparative assessments. In the case of mutual recognition applications, The Netherlands will be the only country which will not do a comparative assessment and for major uses, when minor uses are also included in the authorisation, Belgium will not do comparative assessment.

[Norbert Weißmann](#) of Scientific Consulting GmbH (SCC GmbH) gave a short introduction in the history of regulatory efficacy. Once, guidance on efficacy was provided primarily by EPPO and on national level. As efficacy played no role in the review of Active Substances according to Directive 91/414, there was no legal pressure for harmonization in the entire efficacy. This changed on 14 June 2011 as after this date, following Regulation 1107/2009, all product applications in EU Member States had to be submitted on zonal level. In this context a harmonized dual structure of Biological Assessment Dossier (BAD) and the dRR section 3 (formerly 7) was developed in two EPPO workshops at Berlin and Sofia in 2011 and 2013. The speaker emphasised, that in the course of this development several challenges and regulatory developments in efficacy appeared, such as the need for preparation of comparative assessments, which is obligatory for products containing Active Substances listed as candidate for substitution. A tiered assessment on national level has to be performed, indicating the product's agricultural indispensability,

e.g. because it is needed to sufficiently defend diseases and pests in minor crops.

Furthermore, it became more and more important to provide comprising dose justification information. This is due to the fact that during the course of the renewal of approval of Active Substances a need for reduction of the current dose rate may be evoked by recalculation of risk assessments, e.g. from the ecotoxicology section. Dose justification trials containing a reduced dose rate with lower, but still sufficient, efficacy may preserve the registration holder conducting a new trial program.

The speaker addressed that one of the most important factors regarding efficacy in the framework of product renewals according to Article 43 of Regulation 1107/2009 is an update of the data point resistance risk, based on recent data. Fighting and delaying the process of resistance development is of key importance for the whole plant protection industry, and inclusion of the product in integrated pest management strategies has to be strongly considered.

For future efficacy trials new requirements have to be taken into account. For example the assessment of parameters needed for calculating the leaf-wall-area (LWA) as dose expression for 3D-crops, e.g. the distance between and within the rows, the sprayed height, the canopy density, shape and growing system of high growing crops. This was controversially discussed in the EPPO workshop conducted in Vienna in 2016.

Another example is the new EPPO standard PP1/291 on 'Evaluation of the influence of tank mixture adjuvants on the efficacy of Plant Protection Products', providing advice for better design of trials and a guidance for efficacy testing with mandatory (e.g. twin packs) or voluntary mixtures of product and adjuvant. For the efficacy testing of Biopesticides and Biostimulants specific EPPO standards have to be taken into account, besides the general standards. However, the data requirements (e.g. number of trials, bridging options) for 'Low Risk Active Substances' are reduced, and respective further guidance will be provided in an EPPO standard expected to be published in September 2017.

Raquel Ballersteros, a partner of the law firm Bird & Bird, spoke about some legal issues of the zonal Authorisation under Regulation 1107/2009 Southern Europe. She identified a whole score of different issues and presented many individual law cases of which some are briefly summarised here. With respect to competence issues, she observed insufficient harmonisation in the Guidance Documents. Some concerned Member State are reluctant to accept the zonal Rapporteur's conclusions derived from the use

of the zonal Rapporteur Member States Guidance Documents. Many legal issues arise from the extensive lengths of the procedure and from changes occurred in the meantime. With respect to the use of new scientific evidence, she quoted a Madrid High Court case of 25 September 2013 of Dupont versus the Ministry of Agriculture. New scientific data favourable for the applicant and resulting from the European procedure for the approval of the Active Substance should be considered in the national procedure, it was stipulated. With respect to the use of a new Guidance Documents she quoted Article 36.1 of Regulation 1107/2009 that those Guidance Documents are to be applied, which were available at the time of application. The European Court of Justice has consistently endorsed this principle of legal certainty. Also, late submissions are approached case by case. There is a court decision by the European Court of Justice of 18 July 2007 on Metalaxyl by IQV, where a force majeure reason was acknowledge that prevented the applicant from complying with the time limits (data protection and prohibition of duplication of vertebrate studies). Court cases also result from the access to data of others or from the use of data of others in the authorisation process. Finally, also anti-trust issues are relevant and considered by the courts with respect to access to toxicological vertebrate studies in the case of Fosetyl aluminium in Italy.

"Nothing endures but change", quoted Andreas Wais of Eurofins Heraklitus, to begin his presentation on the potential impact of the Brexit on the EU and global agriculture. In the referendum a majority voted in favour of Brexit, but, in the detailed picture only England and Wales were in favour, while Northern Ireland and Scotland were opposed to the Brexit. Article 50 of the Lisbon establishes a two years periods for negotiations after the notification of the wish to leave. It stipulates, at same time, that the European Council, in agreement with the Member State concerned, can decide to extend this period. If such a notification to leave is received by the European Council in March 2017, as is currently assumed, this would allow, without prolongation, for an exit in March 2019. During this period the UK remains a full member, with all voting rights and all duties, until the actual exit takes place. The exceptions are right to vote as a Member State on the treaty to leave or on the prolongation period of the negotiation period. What are the consequences for the Chemicals Regulation Directorate (CRD)? It is playing a very important role in the EU as an RMS and as a zonal Rapporteur Member State. It is competent and scientifically oriented. Its involvement in the AIR 4 process covers 20% of the Active Substances. Delays and higher workloads of other Member States can be expected.

The speaker made it clear that all decisions made by, or supported by the CRD during the period of the Brexit negotiations will remain in force also after the Brexit. The speaker does not expect any short-term impacts for the next 18 to 24 months. In mid-term, CRD might exit also from the review process, but the procedures are unclear. Applications for EU or products may lead to a situation where applicants may want to search for another Rapporteur Member State or zonal Rapporteur Member State for future projects. In the long-term impact CRD might stay in the EU process, similar to Norway and Switzerland in the Biocides area, but with limited responsibilities. UK might not have voting rights but might be able to influence the decision making through qualified scientific arguments. [The White Paper on the leave, Cm 9417](#) stipulates in chapter 10.14 that the UK wants to continue with EU science research and technical initiatives. Finally, the speaker raised the question what would become of Scotland, raising the possibility that Scotland might leave the UK and could then call upon Article 49 to ascend the European Union or to take over the current role of the UK in the EU. The speaker concluded that the Brexit will certainly impact the European agrochemical system and market with, most probably, more delays and that a careful analysis of single projects is required to come to decisions and strategies case-by-case.

Also Mike Carroll of Arysta LifeSciences started his presentation "Junk science and negative consequences for the regulatory process in agrochemicals" with a quote: "Doubt is not a pleasant condition but certainty is absurd" (Voltaire). A paraphrase the speaker used for the precautionary principle. In his presentation he questioned the basic assumptions we all take for granted in the regulatory process. Regulation, he defined, is the craft of devising temporary remedies for recurring uncertainties - a series of expedients which are finally political judgements that are informed by science but not based on scientific perfection. He also quoted a definition of "safe" by the American Chemical Society. Among other points it states that "safe" is defined by legislators, implemented by regulators and adjudicated by the courts as a level of acceptable risk. These actions are informed by science, but are based on values, politics, economics and other social factors. Such, risk assessment information, it stipulates, should be considered by decision-makers, but cannot, on its own, be used to determine what is "safe".

The speaker identified the necessity to restore confidence in the regulator and the regulatory process for plant protections as paramount. The precautionary principle, according to the speaker, leads into the NGO trap, if taken as the assumption that everything

is unsafe until proven otherwise. In industry this is countered by scientists who believe that scientific studies can answer any question. The speaker concludes that the regulatory result of both together is - chaos.

The speaker observed that academic science is perceived as rational, accurate, true, reproducible, and independent. He stated that this is not true. On the other side industry science is perceived as irrational, inaccurate, false, not reproducible and biased. Again the speaker stated this is not true. With respect to academic science the conclusion is not drawn by industry, but by academic scientists themselves! The speaker then quoted many individually published papers from 1985 to 2016 which come to the conclusion that academic scientific results are not necessarily reproducible, which was shown for the areas of neuroscience, psychology, vitamins, ecology and finally endocrine disruption. In a famous paper John Crabbe, a neuroscientist of the University of Oregon, shows that the duplication, i.e. reproducibility of scientific results is affected by many minor changes which are not clearly stated in the scientific papers themselves. We can learn from these experiments that their results are context dependent and cannot naively be transferred to results in another situation. The second major problem with published scientific results were addressed by John Ioannidis in 2005 under the provocative title "Why most published research findings are false". Ioannidis states that most of the papers published have an experimental design which is faulty and are riddled by statistical problems. Thus the speaker of the presentation concluded that academic science and industry science are two quite different areas of science and mixing the two, especially in the regulatory context, when there is no consensus, is only causing chaos.

He cleared many misconceptions with respect to the place of science in the regulatory process. Approval and authorisation are legal processes which must be based on robust scientific principle, statistically sound experimental design and data analysis. Reproducibility of the test procedure and validation can be achieved by Good Laboratory Practise. Too much junk science is undermining the regulatory process let alone anecdotal statements or mere opinions which lack any data. He compared the regulatory system with an exam and contrasted it to a Ph.D. thesis. In the exam, there is an examination course syllabus specified by a higher authority, which is taught and then a written or practical exam is taken on this syllabus. The examination script is marked and a pass or fail grade is awarded. Unfortunately, the speaker concluded, Regulation 1107/2009 resembles never-ending Ph.D. Thesis and not an examination.

Science is cumulative, but politics must deal with recurring dilemmas via the regulatory process. The best scientifically produced regulatory package of studies can always be overruled by a political decision. He states Glyphosate as an example to this case. The result of the Glyphosate case will show how far we have gone in the system.

A business perspective on the current EU regulatory process was given by Dr. José João Dias Carvalho of Knoell. The speaker identified the needs of businesses as, among others, clear timelines and transparent rules for market access clear and consistent decision-making processes written with requirements and a process (including timelines) to revise them. He observed that Regulation 1107/2009 does not deliver on any these business needs in practise. Especially not on the timelines given! By doing so, the Regulation removes the credibility of the regulatory system. He calls on decision-makers to base their decisions on facts and reliable data generated by regulatory science. Like Mike Carroll before him, he gave a definition of what a regulation should be, in his case taken from a business dictionary. His definition stipulates that regulations "... are enforced usually by a regulatory agency...". He wondered what the regulatory agency for Regulation 1107/2009 would be; putting up the European Commission, the EFSA, the ECHA, and 28 individual Member States, as an answer! This is too complex to be understandable to the general public and to business leaders. Asking about the role of leadership within this agglomerate of different stakeholders, he analysed the role of EFSA, emphasizing that EFSA's independence should not only be towards industry and consultancy, but also towards politics, the general public and NGOs as well. Furthermore, he emphasised the difference between science and regulatory science. Subsequently he quoted, as the previous speaker, definitions of regulatory science. While regulatory science is one step behind science, science has the freedom of no accountability. Regulatory science must answer to questions put to it by regulators and has a much broader influence, because decisions made in this context have a significant impact on productivity, business and market access. Finally, he observed an EU language issue by putting up the difference between food security, which is a condition related to the supply of food and individuals access to it, and food safety. The latter is a scientific discipline dealing with and trying to prevent foodborne illnesses and the area that EFSA is required to assure to the European public.

With respect to the regulatory process, he indicated that none of the AIR 2 renewals of approval were decided on time.

Dr Martine Lans took up again the issue of sustainable plant protection and related experiences and activities in The Netherlands. She observed urgency for industry, growers, and governments to move towards sustainability, shared by all stakeholders. Therefore, The Netherlands, among other EU countries, are putting much effort in programs to speed up the regulatory process, which support such developments. Expert groups on sustainable plant protection have been implemented to identify appropriate actions. In these groups, 19 interested Member States, Commission and EFSA are involved. The recommendations and actions are, amongst others, to increase the availability of Low Risk Products and to accelerate the implementation of IPM in the Member States. One important recommendation is the review of Regulation 1107/2009 to establish a green track for the evaluation of Low Risk Active Substance and the establishment of provisional authorisations. The speaker could not give any timeframe for revising the Regulation 1107/2009.

In The Netherlands steps are already taken in that direction by the Green Deal, where pilot assessments of different Biopesticides are ongoing. Experience shows that pre-submission meetings are important to clarify possibilities, but also difficulties. The Authorities have realised that a specialised "green-TEAM" of assessors is helpful in speeding up the process. She also recommends such a specialisation to all other evaluating Authorities, including EFSA. She also reported on a workshop on the efficacy of Low Risk Plant Protection Products, held together with EPPO. It concluded that efficacy is necessary, but that requirements for efficacy can be lower compared to conventional Plant Protection Products and more variable. Extrapolation possibilities should be further explored and a suggestion was made to consider the EU as one single zone for Low Risk Active Substances. The workshop resulted in a Guidance Document, a draft of which will be published in May 2017 and is expected to be noted by the Standing Committee in November 2017.

According to the speaker, the challenges for the competent Authorities in evaluating products is to focus on the real risk. A tendency towards 100 % certainty blocks innovation. The 120 days evaluation period for Low Risk Products is considered to be the biggest challenge.

The Dutch Authorities are also sharing their knowledge and endeavours on Low Risk Active Substances worldwide and have visited the US EPA Biopesticides and Pollution Prevention Division. They have shared knowledge about Biologicals and have lowered the threshold for contacts on expert level. Zonal applications of products, which had previously already been approved in the US, can be discussed with the Dutch Authorities and a data gap analysis can be done in cooperation with the Authorities.

Currently pilot trials are ongoing on different IPMs in the agri-chains, trying to work out the benefits that are actually in IPM for the farmers.

She concluded that important steps are already taken on European level and that Member States and Commission work on common goals with respect to IPM and low risk. To further the idea of IPM the Authorities and industry would have to find a solution for assessing the total effect of an IPM approach and to implement that in the regulatory framework. In the final slide she came back to and emphasised the importance of the farmers in all these endeavours. The Authorities and industry must find a practical approach to farmers, facilitated by government and industry, to allow IPM to gain momentum.

FERA's impressive database on pesticide usage surveys, stretching back to 1965, was presented by David Garthwaite. The database was initiated to respond to queries from the government, academia, industry and the public. FERA has approximately 100 requests per year for information. The data collected covers all usages, including conventional Pesticides, Biopesticides and living Biocontrol Organisms, published on the FERA homepage. Information on adjuvants is also available, but not yet published.

The initial survey from 1965 was on hops and initiated because of the use of DDT. Arable crops, representing 90% of all usage in the UK, was included in 1974.

The speaker then gave different examples of how to use and interpret the data collected. A significant drop of the use of Cypermethrin in wheat was observed in 1994. The speaker reasoned that the very wet conditions in the fall of 1993 caused a significant infestation with orange weed blossoming. Cypermethrin is not active against this pest, but Chlorpyrifos is and its usage went up significantly. A completely different explanation was derived for the acreage of oilseed rape grown, which decreased significantly from 2012 to 2014. The loss of neonicotinoids made farmers move away from growing oilseed rape, because the speaker claimed, it is impossible to do so without the help of the neonicotinoids. The data on

Biopesticide use on strawberries show a manifold increase in treated area from 2006 to 2010 with the introduction, and significant use, of such special pesticides.

A study done for EFSA 2013 focused on operator exposure. Operators were assessed in Belgium, Greece, Italy, Lithuania, The Netherlands, Poland, Spain and the UK in a number of different crops, and at a large number of different farms. The assessment of professional operators also included home and garden uses in their free time. Across a variety of crops such as barley, rape seed, sugar beet, wheat and non-crop uses was their exposure between 11 and 52 hours per year only. The exposure to individual Active Substances varied between 0.4 and 15.2 hours per year.

The conference gave abroad overview of the current issues discussed in the agro industry.

If you have any specific questions on issues related to this article, do not hesitate to contact us:

albrecht.heidemann@scc-gmbh.de.

Vertebrate studies - data sharing

In accordance with Article 62(1) of the Regulation (EC) 1107/2009, testing on vertebrate animals for the purposes of this Regulation shall be undertaken only where no other methods are available. *In vivo* studies can be either replaced by validated *in vitro* alternatives or calculation methods for mixtures to determine the classification.

Thus, authorities do not accept *in vivo* studies, commissioned after the entry into force date of the regulation (EIF; 14 June 2011) where an accepted alternative is available. The British authority (CRD) outlined in a reminder that in such a case the applicant for an authorisation of a plant protection product, will be informed about the authority action:

New applications (authorisation of a plant protection product - PPP /approval of an active substance - a.s.) will be refused, if the submitted *in vivo* study was performed after the EIF date and an acceptable alternative method is available. A re-submission of the application is only possible by using a calculation method or an acceptable study (e.g. data sharing) instead of the criticised study. The authority will consider in this case, if an investigation in relation to a potential breach of Article 62(1) of the Regulation is to be conducted.

For applications (authorisation of a PPP / approval of an a.s.) which are already submitted, the criticised vertebrate study (performed after the EIF date) will

not be evaluated. The authority will request the applicant to provide an acceptable alternative method (*in vitro* study or classification by calculation). Also here the authority will check the possibility of an investigation about the potential breach of Article 62(1).

For authorisations (PPP)/ approvals (a.s.) which are already granted, the study to be criticised will not be revoked or re-evaluated. CRD will only remind those applicants of their obligations.

Various issues on plant protection

In the Journal 'Stoffrecht' (StoffR, 1, 2017), the lawyer Dr. Peter Quart published an article on the unresolved legal problems in granting plant protection product authorisations in Germany. The article refers to different court decisions on the acceptance of mutual recognition applications in Germany. Additionally, it addresses the significant delays in German evaluations (cMS and MR procedures). An issue also known to the Commission and investigated in an audit which formed part of the DG Health and Food Safety audit programme. The audit took place from 29 February to 4 March 2016 and is detailed in the audit report (DG(SANTE) 2016-8780 - MR). For cMS and MR applications, the only legal requirement is to analyse whether the prerequisites of Article 36.3 are fulfilled, which is totally ignored by the German authority. Instead, the German authority performs full evaluations for all types of applications. The article describes in detail these legal issues currently under discussion in the German regulatory system.

Biostimulants and fertilizers – Problems with the upcoming Regulation

Since the publication of the draft Regulation for fertilizing products (Com (2016) 157 final) within the scope of the circular economy package by the European Parliament (as discussed in our Newsletter by 28th April 2016), extensive discussions are ongoing between experts, regulators and industry about the cruces and problems of the new draft, as well as the required support of scientific research for organic and waste-based fertilizers and "biostimulants". Therefore, in January 2017 EBIC and the EU Danish Permanent Representation hosted an interactive workshop along with industry representatives, key Member States, and other stakeholders, on the potential role of biostimulants within the circular economy.

The draft for CE-marked fertilizers contains a positive list of beneficial microorganisms. However, as agreed by the experts, this positive list poses a major challenge for products containing microorganisms, as it cannot keep up with the pace of innovation in research and development. As characterization of microorganisms on strain level has been claimed mandatory by the new regulation and is used as a widely accepted approach for identification, the list would grow extensively and decelerate the authorization procedure significantly. H.E. Vibeke Pastemak Jørgensen, the Deputy Permanent Representative of Denmark to the EU and host of the workshop, stated that "This fast-paced industry must be supported by a regulatory framework that favours innovation and research & development." Currently, EU sales of biostimulants record an annual growth rate of approximately 12 % and are predicted by analysts to reach € 1 bn by 2019 with a total of 3 % of the annual turnover reinvested into research & development, 60 times higher than for mineral fertilisers. Therefore, the industry demands a regulation to keep up with innovation, providing incentives for continued innovation in biostimulants.

The industries view on the upcoming fertilizer regulation was illustrated by Kristen Sukalac, consultant to the European Biostimulants Industry Council (EBIC) who emphasized the need for a single EU market to foster innovation and unlock the potential of this industry. According to Ms Sukalac, the most striking factor to consider is the need for data protection which has been claimed as amendment by industry directly after proposal of the first draft in 2016. The upcoming regulation has to provide the potential for rewarding research and development, by respecting trade secrets, as well as data protection, to provide conditions for fair competition.

Here, parallel status components (if a component is used in different products with different effects) are a key issue, as they are subject to different regulatory frameworks, depending on the intended use.

Biostimulant producers are facing challenges with products containing these substances, as authorization as plant protection products can block newly discovered uses or retroactively invalidate non-PPP uses of substances. Ms Sukalac highlighted the importance to provide clear definitions to distinguish between product and function and to understand the particularities and needs of a new class of biostimulants such as soil microorganisms.

As a conclusion, EBIC and Member States propose safety criteria (at strain level) supported by harmonized standards which would eliminate the need of a positive list, in line with the New Legislative Frame-

work. They state that “one of the significant advantages of this system is that it neutralizes the issue of data protection, as data is never released.”

Amendments should return to the spirit of the New Legislative Framework to adopt a criteria-based approach supported by harmonized standards. The stakeholders agreed that the market requires a stable and clear regulation, and for this purpose, further consultation is required and collaboration needed to define the most adapted solution.

The European Parliament resolution on low-risk pesticides of biological origin

The European Parliament’s ENVI Committee (Environment, Public Health and Food Safety) voted (59 to 1) in favour of a Resolution on low-risk pesticides of biological origin. Although some changes to the Regulation 1107/2009 related to the low risk criteria is foreseen, the European parliament urged the European Commission to prioritise biological low risk substances.

The European Parliament resolution of 15 February 2017 on low-risk pesticides of biological origin (2016/2903(RSP)):

- “Calls on the Commission and the Member States to accelerate the evaluation, authorisation, registration and monitoring of the use of low-risk plant protection products of biological origin while maintaining risk assessment at a high level;
- Stresses the need to revise Regulation (EC) No 1107/2009 in order to foster the development, authorisation and placing on the EU market of low-risk pesticides of biological origin; is concerned that the current authorisation process for placing plant protection products on the market is sub-optimal for low-risk pesticides of biological origin; points out that the current registration process for low-risk basic substances sometimes, in practice, acts as a kind of patent, making it difficult to use a product based on the same substance which is not registered in another Member State;
- Calls on the Commission to submit, before the end of 2018, a specific legislative proposal amending Regulation (EC) No 1107/2009, outside of the general revision in connection with the REFIT initiative, with a

view to establishing a fast-track evaluation, authorisation and registration process for low-risk pesticides of biological origin;

- Highlights the need for a definition, in Regulation (EC) No 1107/2009, of ‘plant protection product of biological origin’ that covers plant protection products the active substance of which is a microorganism or a molecule existing in nature, either obtained from a natural process or synthesised as identical to the natural molecule, as distinct from plant protection products the active substance of which is a synthetic molecule not existing in nature”

Draft Order for plant protection product use in France

A Draft Order on the placing on the market and use of plant protection products and their adjuvants referred to in Article L. 253-1 of the Rural Code and Maritime Fisheries was published by the French Council of State on the 13th of January 2017, repealing the decree of 12 September 2006.

In particular, it lays down

- the maximum wind speed beyond which these products, if used in spraying or dusting, cannot be applied,
- the pre-harvest intervals (PHI) which is dependent on the classification and labelling according to Reg (EC) 1278/2008 and
- re-entry periods for agricultural workers after application.

Provisions are also set to prevent point source pollution from pesticide effluents and water contamination from drift or from runoff.

The draft order was open for commenting until the 3rd of February 2017. It is not stated when the final will enter into force.

For further information and the draft order, please visit the Ministry of Agriculture website (in French) under:

<http://agriculture.gouv.fr/projet-darrete-relatif-lamise-sur-le-marche-et-lutilisation-des-produits-phytopharmaceutiques-et-de>

Spain –Revised national Regulation on micro-organisms in fertilisers

The Spanish Ministry of Agriculture, Food and Environment has issued a draft legislation amending the rules for new fertilizer products incorporating micro-organisms, thereby amending the basic national fertilizer Regulation 506/2013 (Real Decreto 506/2013). According to the Spanish Ministry of Agriculture, Food and Environment, scientific and technical advances have facilitated the development of new fertiliser products, especially products containing microorganisms that increase the availability of nutrients for plants. In order to enable producers to bring such products on the Spanish market the current legal national framework was revised. Amongst others, the draft regulation introduces the new types of products, updates the labelling requirements, establishes methods of analysis for these new microorganism-containing products and sets out the specific requirements for fertiliser products containing microorganisms, such as information on efficacy and safety requirements for registration.

Ban of plant protection products in Ecological Focus Areas (EFAs)

After reviewing the “greening tool”, Ecological Focus Area (EFA), introduced by Regulation 1307/2013, the European Commission has now issued a draft legislation changing and amending several Articles of the Commission Delegated Regulation 639/2014. EFAs has to be established where the arable land of a holding covers more than 15 hectares from 1 January 2015 onwards whereat an area corresponding to at least 5 % of the arable land of the holding has to be declared as EFA. EFAs are established mainly in order to safeguard and improve biodiversity and to better achieve the objectives of “greening”. EFAs have to be established by farmers e.g. in order to participate in the EU Common Agricultural Policy (CAP) scheme for subsidies. The new draft legislation includes the ban of plant protection products in certain productive EFAs with only a few exceptions: According to the draft legislation for catch crops or green cover, the ban applies from the moment of the harvesting of the main crop until the sowing of the next main crop. For land lying fallow or strips of eligible hectares along forest edges with production, no exceptions are foreseen.



For more information, please contact
 Dr Albrecht Heidemann at
albrecht.heidemann@scc-gmbh.de

The world of SCC at a glance



Access our website at

<http://www.scc-gmbh.de/downloads-scc/brochures>

Invitation to the workshop: Preparation of dossiers acc. to BPR for in-situ peracetic acid products

The workshop aims at regulators searching for practical guidance on dossier preparation. The [workshop](#) is free of charge.

Location: SCC GmbH
Am Grenzgraben 11, 55545 Bad Kreuznach, Germany

Date: 11 and 23 May 2017, 10:00 to ca. 16:00

Registration: darina.nikitina@scc-gmbh.de
Phone: +49 (0) 671 29846-268

Programme:

- Regulatory aspects: authorisation strategies, biocidal product families, technical equivalence, letters of access
- Dossier format and structure
- Working steps: from data-gap analysis to dossier submission - time plan and costs
- Data requirements: storage stability, physical-chemical properties, efficacy and analytical methods
- Exposure and risk assessments
- Preparation of joint dossiers
- Question and answer session

The speakers are experts of SCC GmbH with hands on experience in the preparation of biocidal product dossiers.

SCC GmbH has prepared the active substance dossiers for peracetic acid (including in situ peracetic acid) and accompanied them through the complete assessment process.

Peracetic acid generated from TAED and sodium percarbonate was finally discussed at the December 2016 BPC meeting. The likely date of inclusion in the list of approved active substance is December 2018, date by which dossiers for existing peracetic acid products based on TAED and sodium percarbonate must be submitted.



For more information, please contact
Dr Hans-Josef Leusch at
hans-josef.leusch@scc-gmbh.de

CHEMICALS/REACH



ATTENTION!

Important advice for the last REACH deadline 2018! Last call to pre-register your low volume chemicals

Having the third and last REACH deadline on 31 May 2018 in mind, ECHA calls on every potential registrant of low volume (1-100 tpa) non-CMR, phase-in substances to pre-register these substances with ECHA to benefit from the extended registration deadline.

*Everybody manufacturing or importing such substances for the first time at or above 1 to 100 tpa can still pre-register within six months of starting the activity, at the latest one year before the deadline – by **31 May 2017**.*

Only valid (pre-)registered, low-volume chemicals can be supplied legally on the EU/EEA market until the last registration deadline.

Otherwise – after 31 May 2017 – an inquiry has to be submitted to ECHA and a registration of the substance has to be done before manufacturing/import – comparable to the actual situation for substances ≥ 100 tpa resp. ≥ 1 tpa for substances classified as carcinogenic, mutagenic or toxic to reproduction (CMR).

Consequences from ECHA IT screening program

ECHA prioritized substances by IT screening for further manual check by member states. Registrants were informed by ECHA in January and encouraged to update their dossiers by March 17th. At this date dossiers were forwarded to member states for

further manual check. Member states are currently checking for further actions. Substances are identified by ECHA due to a high hazard (CMR, sensitization, PBT, endocrine disruption) and high exposure based on the use profile and tonnage. Please note that ECHA did not publish the criteria for high hazard in detail (e.g. cut-off values for NOAELs).

So it remains unclear in detail when a substance is judged to pose a high hazard. For evaluation of high exposure ECHA will use worst case tonnages for widespread uses (professionals and consumers) if no detailed information on the tonnage per use and number of sites are given. These values are not mandatory in IUCLID, but SCC recommends considering to give these values in the registration dossiers to avoid being shortlisted by ECHA.

Please note that as soon as a substance is on the ECHA shortlist, the substance remains on that list even though the evaluating member state does not required further actions.

ECHA may initiate further actions to a later time point. In addition ECHA presented a new program to group substances based on their structural similarity. Results of this program may be also used for prioritization of substance for further evaluation by authorities.



For more information, please contact
Dr Werner Köhl at

werner.koehl@scg-gmbh.de

REGULATORY SCIENCE



EFSA Guidance on Dermal Absorption published

As requested by the European Commission¹, the current EFSA Guidance on Dermal Absorption, issued by the PPR Panel in 2012, has been revised by EFSA based on the evaluation² of new human *in vitro* dermal absorption studies submitted by ECPA³ and BfR⁴.

The draft of the revised EFSA Guidance Document on Dermal Absorption⁵ was published for public commenting in late December 2016⁶ and the closing date of the public consultation was 24 February 2017. EFSA currently assesses all comments from interested parties. Assumably the final document is considered to be available at the end of 2017 (intended finalization date: 31/12/2017¹).

The main changes in the new draft document as compared to the EFSA Guidance on Dermal Absorption (2012)⁷ are listed in the following:

- Decreased dermal absorption (DA) default values of 10% (concentrate) and 50% (dilution) for water based/dispersed and solid formulations (previously 25% and 75%) are presented. [p. 20]
- For organic solvent based formulations default values of 25% (concentrate) and 70% (dilution) are listed. [p. 20]

¹ [EFSA-Q-2015-00633 \(Register of questions\)](#)

² EFSA Scientific Report "Assessment of new scientific studies on human *in vitro* dermal absorption" (<http://www.efsa.europa.eu/en/efsajournal/pub/4304>).

³ European Crop Protection Association

⁴ Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)

⁵ EFSA Guidance on Dermal Absorption (Proposal) <https://www.efsa.europa.eu/sites/default/files/consultation/161222.pdf>

⁶ <https://www.efsa.europa.eu/de/consultations/call/161222>

⁷ EFSA Panel on Plant Protection Products and their Residues (PPR); Guidance on Dermal Absorption. EFSA Journal 2012;10(4):2665. [30 pp.] doi:10.2903/j.efsa.2012.2665

- The previous '25% rule' for read-across between similar formulations is changed. The permitted variations now decrease from 100% to 5% depending on the increase of initial concentration range of the constituent. [p.21]

Initial concentration range of the constituent (% w/w)	Permitted (relative) variation (%)
≤ 0.5	± 100
≤ 1.0	± 50
≤ 2.5	± 30
2.5 < c ≤ 10	± 20
10 < c ≤ 25	± 10
25 < c ≤ 100	± 5

c: concentration

- Concerning the active substance (a.s.), formulations are regarded as similar when the a.s. concentration is within permitted variations of that in the reference formulation based on the FAO and WHO specifications for pesticides⁸. The permitted variations decrease from 15 - 25% to 2.5% depending on the increase of initial concentration range of the a.s.. [p.22]

Initial concentration range of the constituent (% w/w)	Permitted (relative) variation (%)
≤ 2.5	± 15 for homogeneous formulations (EC, SC, SL), or ± 25 for heterogeneous formulations (GR, WG)
2.5 < c ≤ 10	± 10
10 < c ≤ 25	± 6
25 < c ≤ 50	± 5
≥ 50	± 2.5

c: concentration

⁸ Manual on development and use of FAO and WHO specifications for pesticides". 1st Edition, 3rd revision, FAO, Rome (2016). http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/JMPS_Manual_2016/3rd_Amendment_JMPS_Manual.pdf

(Continued from previous page)

- The treatment of variability of DA values is modified. If variability is >25% of the study mean, the proposed approach is to use a multiplication factor for the standard deviation (SD) (dependent on the number of replicates) to estimate the multiple of the SD which has to be added to the mean of the DA. [p.14]

Number of replicates (n)	Multiplication factor (k)
≤ 2.5	± 15 for homogeneous formulations (EC, SC, SL), or ± 25 for heterogeneous formulations (GR, WG)
3	2.5
4	1.6
5	1.2
6	1.0
7	0.92
8	0.84

Absorption value = sample mean + (k × SD)

- Regarding the selection of dermal DA for worker/resident exposure, it is proposed that the appropriate dermal absorption value for exposures to dried dispersed residue should be the higher of the values for the concentrate and the in-use dilution. A further revision will follow based on the outcome of on-going research dealing with this issue. [p.19]
- A proposal for reporting DA data for Draft Assessment Reports and Registration Reports is provided (minimum information). [p.24]



For more information, please contact
 Dr. Monika Hofer at
monika.hofer@scc-gmbh.de

CALENDAR



Meet SCC at Chemical Watch Expo 2017 in Berlin, Germany 25 - 26 April 2017

Please [join us](#) at Chemical Watch Expo 2017 in Berlin and visit **our exhibition stand No. 26**.

Dr Anne Bergner, Food Chemist, Manager Regulatory Affairs – Chemicals, and
Dr Ingo Walter, Food Chemist, Senior Manager Regulatory Affairs – Chemicals,

will be happy to welcome you at SCC's stand and discuss your registration needs for Chemicals in the EU or worldwide.

On Day 1, Dr Anne Bergner will hold a workshop "Changes since 2013" in the session "Lessons learned from 2012/13" of the 2nd workshop stream, providing a detailed overview of the recent developments in dossier preparation and chemical safety assessment as well as offering expert advice on high-quality dossier submission.

Meet SCC at Ctgb's workshop on Biocides in Ede, the Netherlands 11 and 18 May 2017

Please [meet](#) our senior Biocides experts at **Ctgb's Workshop on BPR application and re-registration of disinfectants based on the active substances sodium and calcium hypochlorite and chlorine**, taking place in Ede on 11 and 18 May 2017.

Our experts look forward to discussing any regulatory issues you might want to address.

(Continued from previous page)

Meet SCC at the Biocides Symposium 2017 in Barcelona, Spain 09 - 10 May 2017

Please [meet](#)

Dr Martina Galler, Senior Manager Regulatory Affairs Biocides, and

Dr Rebecca Hamm, Assistant Manager Regulatory Affairs Biocides,

at the Biocides Symposium 2017 in Barcelona.

Meet us at Biopesticides Europe Conference in Madrid, Spain 7 - 8 June 2017

Please [join](#)

Dr Annerie Liebenberg,

Assistant Manager Regulatory Affairs, Agrochemicals and Biopesticides – Biostimulants, Fertilizer, IPM,

at the Biopesticides Europe Conference 2017 in Madrid, Spain.

For more details, please visit [the event website](#).

Don't miss a chance to discuss your registration needs for Agrochemicals and Biopesticides with our regulatory Biopesticides specialist.

In order to access links noted in this Newsletter, please copy the address into your browser. We cannot guarantee that links will function and assume herewith no liability. Previous Newsletters can be found on our website <http://www.scc-gmbh.de> under News. You can also subscribe to the Newsletter (free of charge) at this site.

NOTICE: While we have compiled the enclosed information with the utmost care, SCC GmbH is not liable for the consequences of anyone acting or refraining from acting in reliance on any information. Further, SCC has no control over the websites that the reader is linked with using our Homepage/Newsletter. Users linking to other websites do so at their own risk and use these websites according to the appropriate laws governing their usage.

Do you have any comments, questions or suggestions?
Drop us an E-mail at newsletter@scc-gmbh.de.

CONTACT DETAILS

SCC Scientific Consulting Company
Chemisch-Wissenschaftliche Beratung GmbH

Dr Friedbert Pistel, President

Headquarters Bad Kreuznach

Am Grenzgraben 11
D-55545 Bad Kreuznach
Tel. +49 671 29846-0
Fax +49 671 29846-100
info@scc-hq.de
www.scc-gmbh.de



Office Berlin

Dr Achim Schmitz
Branch Manager SCC Office Berlin
Senior Expert Ecotoxicology
Tel.: +49 30 2592-2569
achim.schmitz@scc-gmbh.de

Address
Friedrichstraße 40
D-10969 Berlin

Liaison Office Japan

*Coordinator Agrochemicals & Biopesticides,
Pharma, Pre-Clinical*
Mr Toshiyasu Takada
Director Agrochemicals and Biopesticides
toshiyasu.takada@scc-japan.com

*Coordinator Chemicals/REACH,
Biocides and other services*
Mr Koza Inoue
Director Chemicals/REACH,
Biocides and other services
koza.inoue@scc-japan.com

Chemicals/REACH and OR Services
Mr Kenji Makita
Senior Consultant
kenji.makita@scc-japan.com