NEWSLETTER

SCC Newsletter Vol. 19, No. 2, May 2019

REGULATORY NEWS

Dear Subscribers,

Welcome to the latest issue of the SCC Newsletter.

We are delighted to announce that we recently launched a new regulatory group in our Chemicals division. The new group allows us to expand our range of services aimed at providing registration support for the medical devices industry. The new group is headed by **Dr Alexander Theis**, a polymer chemist with many years of hands-on experience in the medical devices industry.

Moreover, as new SCC spin-off '**SCC LEGAL Law Firm**' was founded. On regulatory issues SCC LEGAL cooperates closely with SCC to help navigate our clients through all stages of the regulatory process. A close partnership within walking distance has proved to be a valuable asset in consulting our clients, since it translates into a gain of regulatory expertise and efficiency.

In this issue, we focus on REACH obligations for non-approved plant protection products (PPPs) that require emergency authorization; you can find out more about this on the next page.

With regard to PPPs, this issue also features a number of reports dealing with Article 43 and the registration of adjuvants in the EU.

Further topics include REACH data compliance, international registrations, and the impact of nanoforms on medical device manufacturers.

With respect to endocrine disruptors, we report on the updates to Appendix E of the ECHA/EFSA guidance ('ED-Table'). This newsletter also features a short report on the 5th International Fresenius Conference "*Worker, Operator, Bystander and Resident Exposure and Risk Assessment*" (6 – 7 December 2018).

The UK's Brexit journey continues. The EU and UK have agreed on a further delay to Brexit until 31 October, 2019. The UK can leave earlier, however, if a withdrawal agreement is ratified by MPs. The UK will now have to take part in the upcoming European elections on 23 May, 2019. If it refuses to do so, it will have to leave the EU on 1 June without a deal. Regardless of how the situation develops in 2019, one thing is clear: 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. Check out our Brexit website for further information.

In the fast-moving world of regulation, SCC is committed to keeping its customers on course for success. We provide high-quality consulting services for your scientific and regulatory needs. Our expertise extends to exposure modelling and risk assessment, covering a broad range of areas, such as agrochemicals and biopesticides, biocides, chemicals, cosmetics, consumer products, feed and food additives, food contact materials, medical devices, GLP archiving solutions, and task force management.
For your information, the statement of GLP compliance was recently reissued (see note on p.7).

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. Simply send us an email at newsletter@scc-gmbh.de.

Dr Friedbert Pistel

IN THIS ISSUE:

REACH obligations for non-approved plant protection products with authorisation due to an emergency situation

Chemicals in the European Union are regulated by several different regulations. Active substances in plant protection and biocidal products are exempted from the REACH obligation (REACH article 15) as specific regulations for these groups of chemicals are in place. It is important to know that these exemptions require that the active substance is listed in the respective Annex 1 of these regulations, in other words that it is approved for the use in plant protection products or biocidal products. In case these conditions are not met the respective substance is subject to REACH.

However, there is a specific scenario for plant protection products which is not clear from the legal text itself and also not covered in the ECHA guidelines.

The Regulation (EC) No 1107/2009 (article 53) states that in special circumstances a Member State may authorise the placing on the market of plant protection products, which have no authorisation in accordance with Article 28, where such a measure appears necessary because of a danger to plant health which cannot be contained by any other reasonable means ('emergency situation').

Based on the legal text of article 53, one could assume that in case of an authorisation of a plant protection product in an emergency situation the REACH obligations are repealed in order to respond to this emergency situation.

However, REACH article 15(1) links the exemption from the REACH registration to the listing in Annex 1. Thus, in case the active substance is not approved for use as plant protection product, the exemption from REACH obligation does not apply. Thus, if an active substance for plant protection emergency use is manufactured or imported in quantities above 1 tonnes per year a REACH registration prior to the emergency use is required.

In case you have any question regarding this specific issue please get into contact with Thomas Roth or Monika Hofer.

For more information, please contact
Dr Thomas Roth at
thomas.roth@scc-gmbh.de

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

AGROCHEMICALS

Re-authorizations according to Article 43 of Regulation (EU) 1107/2009 – efficacy aspects

According to Article 43 of Regulation 1107/2009, authorizations of plant protection products shall be re-authorized. After renewal of the approval of an active substance, the EU member states have to review all authorizations for plant protection products containing the accordant active substance.
Concerning efficacy data requirements the relevant general EU guidance document on Art. 43 procedures, **SANCO 2010/13170**, provides only short remarks indicating that in cases where a GAP change is necessary efficacy data addressing the revised GAP have to be assessed. If no GAP change is implicated, only information about resistance should be assessed in the efficacy section for re-authorization applications. The option to include new uses (*e.g.* as use extension) as part of the application for re-authorization is not foreseen. This general approach is consensus in EU all member states.
However, when planning concrete Art. 43 submissions, is important to look into detail and follow-up the slight differentiations which have developed between registration zones and individual member states.
The member states of the **Southern Zone** have specified the efficacy requirements for renewals according to Article 43 in their common ***Working Document on the Work-sharing of the Southern Zone Member States under Regulation EC 1107/2009 Revision 7.0 Dec 2017***. If the re-authorisation needs no change of GAP compared to the already registered uses which were done under Uniform Principles, no efficacy evaluation will be conducted by the zRMS, hence a complete efficacy data package is not required. In such cases, only the assessment related to the resistance risk has to be updated in the dRR, based on the current resistance situation of an active substance. For the rest of the efficacy section reference to the originally submitted dRR is sufficient. A BAD is not necessary.
New efficacy data are generally not necessary if the dose is just changed within the authorised range, if the number of applications within a zone is reduced or the application period changes within the period already authorized in the zone. Under these circumstances, applicants shall provide a dRR with a complete efficacy section highlighting only the new information e.g. resistance update or – if relevant - data supporting the GAP change.
Where a GAP change is necessary due to the change of endpoints in the course of the active substance renewal, efficacy data addressing the revised GAP have to be provided by the applicant but just encompassing a reduced dataset for representative uses.
The **Northern Zone** on a regular basis updates "**Guidance Document on the Work-sharing in the Northern Zone in the Authorization of Plant Protection Products Version 7.0 May 2018**" which also compiles the efficacy requirements for renewals according to Art. 43.
Only already authorized uses and GAP adaptations resulting from new endpoints in the evaluation of the active substance will be accepted in the course of applications according to Art. 43. These forced GAP changes are only accepted if they fall within the risk envelope assessed in the renewal process, if the accordant changes are covered by efficacy data previously evaluated and if the changes can be defined as minor changes.
Applicants applying for renewals in the Northern Zone are strongly encouraged to submit in addition to the dRR, Section B3 also a full BAD.
A common guidance document for the member states of the **Central Zone** is currently not available but individual member states have provided relevant information discussing their efficacy requirements.
In general the above mentioned rules of **SANCO 2010/13170** apply. Unlike the Northern zone, there is no need to submit a BAD in the countries of the Central Zone. If an authorisation granted under Regulation 1107/2009, based on a dRR, Section B3, exists already, then only the resistance assessment has to be updated. For the rest of the efficacy section reference to the originally submitted dRR is sufficient. Nevertheless, some member states still require a "complete dRR" including an efficacy

Section B3 addressing all annex points with information as part of an application according to Art. 43. If the existing authorisation is still based on old law (Directive 91/414), meaning that no dRR is available, efficacy results on which the old authorization was based have to be shown in a dRR, Section B3.
Please also note that if an original product application had been made before 2016, efficacy assessment was dealt with in Section B7 of the dRR which now has to be moved into Section B3 in the course of an application according to Art. 43, even if there has been no change of the GAP.

Please contact SCC, Dr Norbert Weißmann, head of the efficacy group at SCC, in case of any questions concerning the efficacy requirements as part of renewal processes according to Article 43 of Regulation (EU) 1107/2009:
Norbert.Weissmann@SCC-Gmbh.de, +49-671-29846-100.

Registration of adjuvants in EU – 10 years after publication of Regulation 1107/2009

Adjuvants are used to increase the efficacy of plant protection products and thus, at least theoretically, fall under the scope of the EU plant protection Regulation 1107/2009 - published in October 2009 and entered into force in June 2011.

Given the needs of EUs agriculture in regards to reduction of dose rates for many active substances and plant protection products, copper reduction programs, human, animal and environmental safety and resistance issues or the impact of global change, innovative adjuvants are a valuable tool in the farmer's toolbox. Therefore, according to Article 58(2) of Regulation 1107/2009 on placing on the market and use of adjuvants, an additional regulation should be adopted laying down "detailed rules for the authorisation of adjuvants, including data requirements, notification, evaluation, assessment and decision making procedures" but - 10 years after publication, 8 years after entry into force of Regulation 1107/2009 - such a regulation on adjuvants is still missing.

Thus, practically, registration of adjuvants is still the objective of national plant protection laws of the EU Member States. In consequence, registration procedures for adjuvants differ hugely between countries, quite comparable to the current procedure for organic fertilisers or biostimulants. The differences between registration procedures established in the Member States concern the data requirements as well as the administrative procedures.

In regards to data requirements Germany for example belongs to the countries which have no or very low data requirements (including efficacy-related topics) besides a detailed analysis of the composition of the product as well as of the composition of possible co-formulants used in the adjuvant. The procedure established for adjuvant registration in France on the other hand is quite similar to the authorisation procedure for plant protection products according to Regulation 1107/2009 including submission of a draft registration report and, if applicable, studies for all relevant sections such as physical chemical parameters and analytics, toxicology, ecotoxicology and efficacy as well as information on environmental fate and residues if implied by the specific product characteristics. Especially efficacy requirements vary depending on the Mode of Action of the adjuvant, *i.e.* if the product modifies the physical properties of the product only or if the product modifies the effect of the spray mix on the target. As for the efficacy of plant protection products, respective EPPO guidelines as well as national guidelines are in place in certain Member States (see the article "*Registration of adjuvants in EU – efficacy requirements laid down by EPPO and defined in national guidelines"* by Dr Joachim Kranz and Dr Lars Huber in the present newsletter).

Administrative procedures for adjuvants also vary between Member States. This applies not only for direct application for authorisation but also for procedures such as mutual recognition or the authorisation of generic products. In Germany for example, mutual recognition is not possible, whereat France accepts both procedures in addition to the direct application for authorisation. Thus, in France adjuvants are already handled more or less in compliance to Regulation 1107/2009 in regards to data requirements as well as administrative procedures whereat in countries such as Germany the registration procedure is purely a national one. Some countries such as Spain for example have a mixture of both procedures.

In regards to administrative issues, adjuvants are handled on a national basis in Spain as no mutual recognition is accepted and existing authorisations are re-evaluated on a national basis thus preventing generic product registrations. On the other hand, data requirements for registration of adjuvants in Spain are comparable to France, the respective national guidance referring also to the relevant EPPO guidelines for product efficacy issues.
Pending the establishment of harmonised EU rules for adjuvant authorisations, an appropriate registration strategy for national applications for authorisation, incorporating generic product registrations and/or mutual recognitions, is necessary.

Lars Huber (Senior Manager and Head of Biorationals, Fertilisers, IPM) and *Joachim Kranz* (Senior Manager), Regulatory Affairs Agrochemicals and Biorationals

Registration of adjuvants in EU – efficacy requirements laid down by EPPO and defined in national guidelines

Basically adjuvants are classified as substances or preparations which consist of co-formulants, or preparations containing one or more co-formulants, in the form in which they are supplied to the user and placed on the market to be mixed with a plant protection product in order to enhance effectiveness or other pesticidal properties of this product. Considering the issue of increased efficacy, adjuvants fall more or less also under the scope of the EU plant protection Regulation 1107/2009, as described in the article "*Registration of adjuvants in EU – 10 years after publication of Regulation 1107/2009*" by Dr Lars Huber in the present newsletter.
The main focus for an efficacy evaluation of an adjuvant as part of the registration process is laid on the evidence that the accordant use in a mixture with a plant protection product presents an overall benefit over the use of the same plant protection product used alone. This evaluation has to be conducted according to EPPO Standard PP 1/291 (1) *Evaluation of the influence of tank mix adjuvants on the efficacy of plant protection products* but also considering EPPO general and specific Standards which provide the necessary more detailed instructions on trials for specific crop–pest combinations.

The mixture of the adjuvant and plant protection product should normally be applied at the dosage specified for the intended use. Additionally, any efficacy or selectivity trial intended to show the benefits of an adjuvant with regard to the enhancement of efficacy properties of plant protection products should contain a treatment in which the plant protection product is applied alone. For reasons of comparison at least some of the trials of an accordant trial program shall in addition include treatments in which the adjuvant under investigation is applied alone to determine the lack of intrinsic pesticidal activity. Additionally, further treatments could be the mixture of the chosen plant protection product with another registered adjuvant or the application of an independent reference plant protection product with a high efficacy against targets that are specifically difficult to control but for which a specific label claim of the adjuvant under investigation is made.

Doses lower or higher than the intended dose rate may be tested to determine the margin of effectiveness and to show the crop safety with this last kind of treatments being of special relevance for herbicides and plant growth regulators.

The requirements as laid down in EPPO Standard 1/291 (1) for efficacy evaluation of adjuvants are generally binding for all member states of EPPO which includes besides others also all EU member states. Nevertheless, some member states (to name here especially France and Italy) have some national requirements for efficacy evaluation of adjuvants reflecting the fact that registration of adjuvants is still the objective of national plant protection laws of the single EU Member States. In consequence, registration procedures and therefore also efficacy requirements for adjuvants might differ between countries.

Since the procedure established for adjuvant registration in France is similar to the authorisation procedure for plant protection products including the submission of suitable and requested efficacy studies the accordant efficacy requirements as laid down in CEB Guideline are more detailed in comparison to those given in EPPO Standard 1/291 (1).

The general principles for efficacy testing of adjuvants in France are presented in CEB Guideline MG 08 (CEB, Méthode N° MG 08, *Principes généraux d'expérimentation des adjuvants*). The purpose of this document is to specify the experimental conditions for trials with adjuvants applied in mixtures with plant protection products. The trials can be conducted on a crop or group of crops and for one or more uses and shall consider efficacy and selectivity aspects in the field to show the practical value of a mixture. In addition, preliminary and complementary studies of the physico-chemical compatibilities between the plant protection products and the adjuvants must be carried out. Besides the general consideration of requirements related to the conduct of efficacy field trials, it should be demonstrated by the applicant that the addition of an adjuvant to an authorized plant protection products improves the effectiveness or the conditions of its use (physical properties) of the mixture, without modifying the sensitivity of the crop. The aspect of comparison is thus constituted by the plant protection product applied alone to justify the addition of the adjuvant or an already authorized adjuvant.

The general requirements as laid down in CEB Guideline MG 08 are comparable to those described in EPPO Standard 1/291 (1). In addition France has provided more detailed recommendations for trials conducted with an adjuvant in order to specify its field of use (Document Technique N° 22 Recommandations concernant l'experimentation d'un adjuvant en vue de preciser son domaine d'utilation) which have to be considered and should be used in conjunction with the general basic methods as determined in CEB Guideline MG 08.

The document DT N° 22 proposes models (crops, pests) and classes of active substances to be tested for efficacy and selectivity (phytotoxicity) in order to determine areas of use by adding an adjuvant. Depending on the claimed functions of an adjuvant, specific adapted test models have to be chosen which are representative for the areas of use claimed by adding an adjuvant to a plant protection product.

Generally, the efficacy and selectivity of the adjuvant mixture preparation must be demonstrated according to its type of function (e.g. the improvement of penetration, retention and spreading), considering that the effectiveness of an adjuvant depends on the properties of the active substance. Based on properties like the degree of solubility of an active substance in water, herbicides for example are divided into four classes. This means for each of these classes, if the efficacy of the adjuvant has been demonstrated with a single active substance, the results are considered as transferable to all active substances within this class of herbicides. Document DT N° 22 provides the classes of actives for the main groups (herbicides, insecticides and fungicides) considering relevant properties to be enhanced by adding adjuvants. The accordant classification in turn represents the basis for extrapolation options in order to optimize an efficacy trial program for the registration of adjuvants as mixing partners improving the efficacy of a plant protection product.

Being a second example, Italy has laid down the data requirements for the registration of an adjuvant in a specific guideline (*Linea guida per l'autorizzazione all'immissione in commercio e all'impiego dei coadiuvanti di prodotti fitosanitari, LG-Coadiuvanti* Ver. febb.2016). Some of these aspects are comparable to those defined also by France.

For the purpose of assessing the risks and benefits associated with the use of the adjuvant mixture with a specific plant protection product, tests and studies must be performed with the mixture in question; the assessment requirements and principles provided by Regulations (EC) 1107/2013 and relevant implementing regulations and by Regulation (EC) 396/2005 and subsequent amending regulations have to be considered. In case of efficacy aspects these requirements encompass e.g. also a detailed assessment of the effects on the quality and yield of treated plants and plant products, the assessment of phytotoxicological impacts on target plants (including various "cultivars" in case of ornamentals) and the assessment of unwanted side effects.

Much more extensive are the efficacy data requirements in case these data shall generally support the use of the adjuvant as mix partner with a range of different plant protection products. If an applicant seeks to get a registration for the use of an adjuvant e.g. with many types of insecticides the data of at least eight accordant efficacy trials are required. For each possible mixture, half of the

trials have to be performed with the mixture and one test with the plant protection product alone. As an alternative to the test performed with the plant protection product, the applicant can present a LoA (Letter of Authorization) issued by the holder of the plant protection product in question. In case the mixture options encompass more chemical classes e.g. of insecticides (like pyrethroids, neonicotinoids, carbamates and organophosphates) at least two trials per chemical class are required to be conducted covering representative cultures.

Efficacy data requirements for registration of adjuvants *e.g.* in Spain is comparable to those published by France, with the respective national guidance referring also to the relevant EPPO guidelines for product efficacy issues.

Joachim Kranz (Senior Manager), Regulatory Affairs Agrochemicals and Biorationals and *Lars Huber* (Senior Manager and Head of Biorationals, Fertilisers, IPM)

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

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GOOD LABORATORY PRACTICE STATEMENT OF GLP COMPLIANCE according to § 19b Abs. 1 Chemikaliengesetz

SCC GmbH is very proud to announce its statement of GLP compliance was reissued!

As an independent test site in the national GLP Compliance Programme, we are inspected on a regular 3 year basis. Our contract archive was inspected on 24.10.2018 and the statement of GLP compliance according to the German Chemikaliengesetz, EU Directive 2004/9/EC and OECD Principles of GLP was certified on 18.02.2019 by the Landesamt für Umwelt, Mainz, Germany.

For the GLP certificate, please refer to:
https://www.scc-gmbh.de/business-units/archiving/glp

CHEMICALS/REACH

ECHA's Executive Director demands: "REACH data compliance needs to improve"

In the recent months SCC has regularly reported about the increasing pressure from REACH authorities regarding the compliance of the REACH dossiers (for detailed information, please see also the article: "Constantly keeping your dossiers up-to-date"). In this context, ECHA gives advice to registrants on how to improve compliance as part of their annual evaluation report.

In the course of the evaluation, ECHA checked the compliance of 286 registrations in 2018. ECHA focused on so-called super endpoints, *i.e.* key information related to carcinogenic, mutagenic, or reprotoxic (CMR) or persistent, bioaccumulative, or toxic properties (PBT) of a substance. Altogether, the Agency adopted 274 final decisions, in which 888 different information requests were asked for.

ECHA noted that in the majority of registration dossiers that were evaluated, important safety information is missing. After ECHA's request, most registrants updated their dossiers with compliant information.

On 28 February 2019, Bjorn Hansen, ECHA's Executive Director stated: "Efforts from all actors are needed to ensure that the safety data companies provide complies with the law. As an Agency, we will further improve the efficiency of our work on compliance checks, and both ourselves and Member States must do more to accelerate the evaluation process. But companies also need to treat their registrations as business cards. Compliant registration dossiers are their key investment to a predictable and sustainable future."

Based on the evaluation outcomes and observations, ECHA has published recommendations on how registrants can improve their dossiers. https://echa.europa.eu/de/recommendations-to-registrants

As the pressure from authorities is continuously increasing, proactive action is indicated. One needs to keep in mind ECHA's changed rules of procedure. As soon as ECHA initiates a compliance check, dossier updates will not be taken into account any longer and dossiers need to be defended as they are.

SCC can assist you in checking the data quality of your dossiers, support you to improve the dossier quality, and help to set up an update program. In case you have any question regarding this specific issue, please get into contact with Dr Thomas Roth.

Constantly keeping your REACH dossiers up-to-date: this is NOT a 'nice-to-have legal option'

With the completion of the third and last REACH registration deadline in May 2018, ECHA and several other REACH stakeholders have quickly moved their focus to dossier quality, demanding clear dossier quality improvement from industry. While the regulation obliges all registrants to regularly update their dossiers with relevant new information, fact is that 64% of the dossiers have never been updated since initial submission, which dates back to 2008 for substances with >=1000 tpa! To address the concern and to pre-empt a potential binding regulation on dossier update requirements, Cefic urges its members to develop a plan for systematic dossier reviews and updates, considering this as a key issue for industry.

Several important events all together point to the same conclusion that industry needs to take regular dossier updating much more seriously than until now.

- ECHA implemented several changes to the dossier evaluation and compliance check process, effective since 1 January 2019. From now on, members' dossiers are no longer excluded from checks for composition consistency across the joint submission. Partial or full opt-out dossiers will be assessed in parallel with the data submitted jointly. Once a draft decision is issued, it will no longer be possible to change e.g. the tonnage band, the type of registration (full vs. intermediate), or the uses. **ECHA is clearly expecting dossiers to be up-to-date and it will not inform registrants or grant a chance for dossier updates prior to regulatory measures.**
- More of the same: the European Commission published a document regarding the scope of an Implementing Regulation on registration updates, proposing fixed timeframes for the relevant change triggers. After collection of stakeholder input, it plans to present a proposal to the REACH Committee and voting may take place as early as in April 2019. Just as an example: the draft document recommends an at least yearly review of quantities. **If approved, such an Implementing Regulation would impose strict binding requirements for dossier reviews and updates.**
- The BfR (German federal institute for risk assessment) published a widely noticed report on their assessment of dossier quality in which they stated that rather high percentages of the 500+ assessed dossiers were deemed "not compliant". While the applied methodology was very specific and differed from the official Compliance Check process as REACH Art. 41, the publication triggered enormous attention in the press and media.
  It was used by the German Government as a reason to demand significantly higher percentages of dossiers to undergo the Evaluation process than the formally required 5% of all dossiers.
  Government officials outlined their position to have all (100%) of the dossiers being evaluated in the next 10 years.

- On 21 December 2018, Cefic reached out to its members highlighting the urgent need for industry to respond to the pressure for higher dossier quality. As part of its immediate actions, Cefic representatives met with ECHA leadership in an informal meeting at the end of January 2019 to understand their views on the improvement priorities. Cefic also issued a checklist by which companies are guided in their internal assessment of dossier quality. This is definitely a proactive step in order to avoid far-reaching new regulatory obligations. **Join the initiative and ensure your dossiers are up to the expected level of quality and compliance!**
- On 9 January 2019, ECHA informed the public about upcoming EU/EEA inspections for compliance with REACH registration obligations. The initiative in which both inspectors and customs authorities will be involved is part of an EU-wide Forum* enforcement project (called REF-7). The project aims to verify REACH compliance for the obligations of manufacturers and importers. The checks will cover substances in all tonnage bands. **The inspections will also include a check of parts of the registration dossier** and of other duties related to registration, e.g., **whether the registrant is compliant with the duty to update a registration dossier.**

  *The Forum for Exchange of Information on Enforcement (Forum) is a network of authorities responsible for the enforcement of the REACH and other chemicals related regulations in the EU and the EEA countries.

In the light of these circumstances, SCC strongly recommends a dossier update program to its clients in order for them to stay ahead of the foreseeable changes in the regulatory environment. We already set up such systematic projects for a number of mostly bigger internationally acting companies.

What is your plan for keeping your REACH dossiers up-to-date? Please come and talk to us if you want to enhance your ability to stay agile and to ensure compliance for your chemicals in Europe!

For more information, please contact SCC at info@scc-hq.de – thank you.

International registrations

On focus: K-REACH

On 1 January 2019 the amendments to K-REACH by its second novel came into force. If South Korea is high on your list of attractive target markets, please note that the amendments require importers and local manufacturers to pre-register existing substances supplied to the Korean market by no later than 30 June 2019 in order to benefit from a grace period for continued importation or manufacturing prior to the actual registration. The grace periods per tonnage band for pre-registered substances are as follows:

- By 31 Dec 2021: ≥ 1000 tpa and CMRs ≥ 1 tpa
- By 31 Dec 2024: 100 - 1000 tpa
- By 31 Dec 2027: 10 - 100 tpa
- By 31 Dec 2030: 1 - 10 tpa

Like in the EU, joint registration is required. However, differently to EU-REACH, even small amounts < 0.1 tpa of new substances must be notified prior to import ("low volume notification"). The grace period of PEC substances has expired and they must be fully registered prior to manufacturing or import.

With certain exceptions, the Korean chemicals legislation has a lot in common with the European REACH, which enables know-how transfer and avoidance of numerous pitfalls. With our hands-on expertise in REACH and in cooperation with our experienced and trusted partner in South Korea, SCC looks forward to taking care of pre-registration for your substance portfolio in

the next months as the first step, and compilation and submission of the registration dossier as second step.

Please contact us today to discuss the envisaged pre-registration, since the countdown is on: the pre-registration deadline expires **on 30 June 2019**.

KKDIK pre-registration in Turkey is running: Do not miss your opportunity!

The KKDIK-Regulation (Turkey REACH) came into effect in December 2017. All substances manufactured or imported into Turkey with a volume ≥ 1 tpa must be pre-registered by the end of 2020 and registered under KKDIK by 31 December 2023.

Do not wait too long with planning your product portfolio for Turkey: Pre-register your substances now to confirm your KKDIK compliance to your Turkish customers as well as your further intention to register. Turkish authorities urge companies to pre-register early, since this would provide clarity during potential inspections and guarantee a speedy and smooth registration process later on.

With our profound experience in REACH and in cooperation with our competent partner in Turkey, we are best equipped to pre-register your substances with the Turkish authorities and take care of the subsequent registration process.

Contact us to learn how SCC can help you with regard to KKDIK.

For more information, please contact
Dr Thomas Roth at
thomas.roth@scc-gmbh.de

Segment CHEMICALS/REACH

MEDICAL DEVICES

SCC launches a new regulatory group – Medical Devices

We are happy to announce that we have recently launched a new regulatory group within our Chemicals division to expand the range of our services to registration support for the medical devices industry.
The new group is headed by **Dr Alexander Theis**, a polymer chemist with a hands-on long-standing experience in the medical device industry.

Our services for medical devices currently include:

- Offering support in product development and in-market compliance
- Individual gap-analysis in context of new MDR (EU) 2017/745 requirements
- R&D support
- Providing guidance with regard to biological evaluation of medical devices in line with ISO 10993
- Literature search and supply service
- Clinical evaluation following Article 61 and Annex XIV MDR (EU) 2017/745 and MEDDEV 2.7/1 revision 4
- Qualification and validation of production and quality control equipment and methods
- International approval of your medical devices

For more information, please contact
Dr Alexander Theis at
alexander.theis@scc-gmbh.de

Tel: +49 671 29846-0
Fax: +49 671 29846-100

Are You Ready for the new European Medical Device Regulation?

For medical device manufacturers, the next 13 months will be quite labour intensive from the regulatory standpoint in Europe. Beside the uncertainty due to the Brexit, the transition period for the current European Medical Device Directive 93/42/EWG expires in May 2020 and aside from a few exemptions all changes introduced by the new Medical Device Regulation (EU) 2017/745 need to be implemented until this date.

The major changes are:

- More precise specifications for planning of clinical evaluations;
- Stricter requirements for quality of clinical data, consideration of equivalence, and waiving clinical investigations;
- Detailed regulation for the approval of clinical investigations;
- Tightening of regulations governing vigilance and post market surveillance;

- New classification rules for material-based medical devices, additional rules for products with nanomaterials and software;
- Installation of a scrutiny procedure for specific class IIb and III devices;
- New rules for the reprocessing of single-use devices;
- Introduction of the Unique Device Identification (UDI) system;
- Extension of the European database for medical devices (EUDAMED);
- Nomination of a "qualified person";
- Requirement for manufacturers to provide sufficient financial coverage in respect of their potential liability.

While several aspects have not yet been established, e.g. the accreditation of most of the notified bodies for the MDR (EU) 2017/745, the EUDAMED database extension, and the finalisation of the announced common specifications, manufacturers should implement the new regulation in their QM system as soon as possible in order to avoid the need for doing all the work within a few months next year. Many new procedures are becoming clear right now, so *e.g.* the new manufacturer incident report form (MIR) which was published in January this year.

In particular, medical devices which will need to be classified in higher risk classes, *e.g.* many devices that are composed of substances or include nanoparticles may require time intensive additional biocompatibility and/or Post Market Clinical Follow-up (PMCF) studies, depending on the data which is currently available.

Further, clinical evaluations will need to be precisely planned and renewed for all medical device classes.

To support customers specifically in the medical device business, SCC has established a new international service for regulatory and scientific needs. More information about our new services for medical devices can be found under: https://www.scc-gmbh.de/business-units/medical-devices.

Impact of REACH amendment (EU) 2018/1881 to address nanoforms for medical device manufacturers

With the new MDR (EU) 2017/745, a part of medical device industry is challenged by introduction of new classification rules, in particular for products with nanoparticles and material based medical devices. For products, which contain nanomaterial, the new classification rule 19 is challenging for 3 reasons:

1. The definition of nanoparticles is based on the EU Commission recommendation of 18 October 2011 using the number size distribution, which may lead to the result, that powders with a broad polydispersity in grain size may be considered as nanoform, even when the absolute weight portion of nanoparticles is very small.
2. For most raw materials, no specific data for nanoform structures is available in the safety data sheet.
3. The resulting medical device classification is based on the potential for internal exposure, whereby a high or medium potential is classified as class III, a low potential is classified as class IIb and a negligible potential as class IIa. However the MDR (EU) 2017/745 does not give any specification, when a potential for internal exposure has to be considered as high, medium, low or negligible.

While the third point has been addressed at least in parts by the SCENIHR in the Opinion on the "Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices" in January 2015, it may still be difficult for some medical device manufacturers to address, whether fine powders used *e.g.* in composite materials need to be considered as nanomaterial or not and how to obtain reliable data for the specific nanoform.

For the new REACH amendment (EU) 2018/1881, which was published on 3 December 2018, the same nanoparticle definition based on the recommendation of 18 October 2011 is used and manufacturers and importers are asked to assess and, where relevant, generate the necessary information and documentation in the chemical safety report that the risks, arising from the identified uses of the substance with nanoforms they manufacture or import, are adequately controlled.

For medical device manufacturers purchasing fine powders for use in their products, the new REACH amendment may help to evaluate the existence of specific nanoforms and potential risks generated by them. For consideration of the specific application - which may also modify the nanoform of the substance - downstream users should check, if their information to the manufacturer or importer is up to date, to ensure that the intended use is adequately covered by the registration dossier, or alternatively cover the specific use in their own chemical safety report.

For more information, please contact
Dr Alexander Theis at
alexander.theis@scc-gmbh.de

Segment MEDICAL DEVICES

LEGAL SERVICES

New SCC spin-off: SCC LEGAL Law Firm

Dr. Burkhard Funk
lawyer and head of SCC LEGAL

Dr. Funk has studied law at the universities of Lausanne, Geneva and Heidelberg. Afterwards he studied at the university of Nürnberg and obtained his doctorate degree in economics. He completed his legal clerkship at the Higher Regional Court of Frankfurt am Main. Dr. Funk has worked as a lawyer since 2007 focusing on various fields of corporate and chemical law.

The complexity of regulatory requirements has increased dramatically over the last years. Scientific and legal issues more and more interlock, which calls for an extensive exchange between science and law. SCC LEGAL Law Firm has been founded to meet the upcoming challenges in the field of regulatory compliance within the EU. It emerged as an independent spin-off of SCC.

On regulatory issues SCC LEGAL cooperates closely with SCC Scientific Consulting Company to help navigate our clients through all stages of the regulatory process. A close partnership within walking distance has proved to be a valuable asset in consulting our clients, since it translates into a gain of regulatory expertise and efficiency.

We offer legal services in the following fields of expertise:

- **Data Sharing Services**
  - Letters of access (EU and non-EU)
  - Data evaluation
  - Data compensation audit
  - Arbitrations (for mandatory and voluntary data sharing)
  - Conception of settlement agreements

- **Consortium / Task Force management**
  - Consortium contracts
  - Representation of client companies within consortia or SIEFs (e.g. meetings of steering committee)
  - Escrow account services
  - Membership management
  - Voting procedures

- **Agrochemicals**
  - Regulation 1107/2009
  - Representation to authorities (EU and national)
  - Legal actions against inactivity of the competent authorities

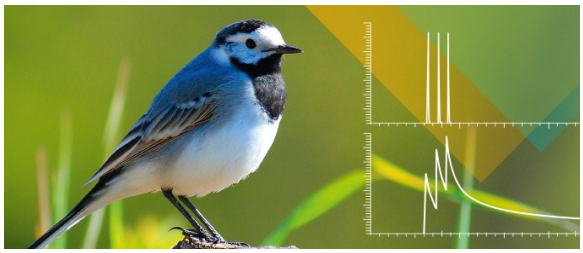
- **Biocides**
  - BPR Regulation (EU) No. 528/2012
  - Representation to authorities (e.g. ECHA)
  - Data sharing / Letter of Access

- **Chemicals**
  - REACH Regulation (EC) No. 1907/2006
  - CoRAP (Community Rolling Action Plan)
  - Compliance audit
  - Representation to Authorities (e.g. ECHA, Board of Appeal)

- **Contract Law**
  - Conception and review of contracts and general terms and conditions
  - Competition law
  - Dispute resolution and arbitration

For further information on our legal services, please do not hesitate to contact Dr. Burkhard Funk at:
b.funk@scc-legal.com
Tel.: +49-671-29846150

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 dislodgable 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.

Update on Appendix E to the ECHA/EFSA Guidance on endocrine disrupting properties: Data gathering with the Appendix E excel file

On 20-Feb-2019 a **new version of the Appendix E Excel template** for reporting the available information relevant for ED assessment according to the Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009 and a new Guidance on how to use the ED Excel template have been published. The purpose was to resolve some technical problems of the previously updated Appendix E template of 20-Dec-2018. The actual version can be downloaded from the EFSA webpage https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311 under 'Supplements' and be verified checking the file name, where the date 2019-02-15 is reported.
This new version of the Appendix E incorporates several changes especially with regard to the amended and increased pick-lists of the study type and the effect target. As a result, parameters are depicted in association with the respective endpoints and less parameters are presented under the "not in list" category. In addition, for each study generations and/or life stages are depicted separately in one row each.
In comparison to the original Appendix E, new features have been added such as the possibility to create sub-matrices and lines of evidence tables.
Relevant points also reflected in the instruction sheet (https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311) are highlighted below:

- 4 tables compare the pick-lists between the Dec-2018 and the Feb-2019 version of the excel file to facilitate the data transfer
- Information concerning the lines of evidence tables:
  - The columns with 'effect description' and 'effect determination' shall contain quantitative information such as percentage or number of animals af-

fected, dose-response dependencies and statistical analysis. This data will be included in the lines of evidence tables to be assessed concerning potential EATS-mediated adversity and/or endocrine activity
- Column K of the lines of evidence table ('Observed effect (positive and negative)') shall be filled manually with the effect description/effect determination
- If new lines of evidence tables need to be created, a new data summary must be created first
- Two separate lines of evidence tables should be created: One for the T-modality and one for EAS-modalities. Besides the endpoint/modality-specific selection, target organ toxicity and systemic toxicity must always be selected to evaluate potential secondary target organ toxicity or systemic toxicity

Further updates are expected in the future potentially comprising additional implemented features including further methods such as *in silico* methods to be captured in the pick-list. In the actual version methods which cannot be implemented into Appendix E shall be added manually to the lines of evidence table and highlighted. Furthermore, additional filling of column K of the lines of evidence table with the information from the effect description or effect determination of the data sheet could be implemented in the future.
SCC is your well experienced partner when it comes to establishing whether the ED criteria are fulfilled. We will support you in gathering, evaluating and considering all relevant information for a scientifically sound ED assessment in line with current requirements.

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

CALENDAR

MedtecLIVE in Nuremberg, Germany
21-23 May 2019

SCC is exhibiting at MedtecLIVE in Nuremberg on 21 – 23 May 2019. Running parallel to MedTech Summit, one of the most important events of the health sector in Europe, MedtecLIVE exhibition will offer an insight into future developments in the medical technology industry.
Join SCC at **Booth 222 /Hall 10.0**.

Dr Alexander Theis, Senior Manager Regulatory Affairs – Medical Devices, will be happy to welcome you at SCC booth and discuss your needs with regard to conformity assessments of medical devices as well as any regulatory or scientific question you would like to address.
Please use this chance to claim your free ticket and join SCC at MedtecLIVE in Nuremberg.

Claim your free ticket and request a meeting with our regulatory expert at MedtecLIVE 2019.

The ECPA Regulatory Conference in Ghent, Belgium
22-23 May 2019

SCC is joining the ECPA Regulatory Conference, which runs this year alongside the IUPAC International Congress, both taking place in Ghent in May.
Please visit our **Booth 27** at the ECPA 2019 and meet our senior regulatory experts:

Dr Karin Lauber, Senior Regulatory Specialist – Agrochemicals and Biorationals – Regulatory Affairs
Dr Norbert Weißmann, Senior Manager Regulatory Affairs – Agrochemicals and Biorationals – Efficacy.

Don't hesitate to approach our experts regarding any challenges you might be facing with the registration of agrochemicals and biorationals or any regulatory or scientific question you are interested in.

Request a meeting with SCC experts at the ECPA Regulatory Conference 2019.

Biocides Symposium 2019 in Rome, Italy
23-24 May 2019

SCC is joining the 10th Biocides Symposium, taking place in Rome, Italy, on 23-24 May.
The upcoming symposium will focus on the authorisation of products within the Biocidal Product Regulation. For more information, please visit the event's official website.

Please meet our regulatory specialists for biocides in Rome:
Dr Annamaria Vickus and **Dr Julia Kolling** look forward to talking to you about your regulatory needs for biocides registration.

Biopesticides Europe 2019 in London, UK
29-30 May 2019

Please meet

Dr Carla Lorenz, Assistant Manager Regulatory Affairs – Biorationals, Fertiliser, IPM,
at the 4th Biopesticides Europe conference, taking place in London, UK, on 29-30 May 2019. For more information on the conference, please visit the official event website.

Don't miss this chance to discuss your registration needs for biopesticides with our regulatory specialist in London.

Chemspec Europe 2019 in Basel, Switzerland
26-27 June 2019

SCC is exhibiting at the 34th International Exhibition for Fine and Speciality Chemicals, taking place at Messe Basel, Switzerland, on 26-27 June 2019.
Chemspec Europe is a powerful and well-known industry platform spurring professional discussions on recent market trends, technical innovations, business opportunities and regulatory issues in the rapidly changing chemicals' market.

Meet our senior regulatory experts at **Booth RS/F170** and talk to them about any regulatory or scientific challenge you would like to address.
Claim your free voucher for Chemspec Europe 2019 and request a meeting with our senior experts on site.

SCC will also contribute to Chemspec's conference programme. **Dr Mathias Rietzel-Roehrdanz**, Senior Manager Regulatory Affairs, Chemicals – International Registration, will provide an *update on chemicals regulations in South Korea, Turkey and other international markets*.
So, don't miss out on Mathias' talk to hear recent international developments and future trends of chemicals regulatory compliance. For more information on the conference' and workshops' programmes, please view the event's website.

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

SCC Scientific Consulting Company Japan K.K.

Atsushi Ohtaka
Representative Director
Phone: +81 3 6629-3166
Fax: +81 3 6629-3167
atsushi.ohtaka@scc-japan.com

Address
8F Tri-Seven Roppongi,
7-7-7 Roppongi, Minato-ku
Tokyo, 106-0032 Japan

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Drop us an E-mail at newsletter@scc-gmbh.de.