Newsletter

Volume 8, No. 1, January 2008

MESSAGE FROM THE PRESIDENT

2008 – New Year, New Challenges, New Services

With our first edition of the SCC Newsletter in 2008, I would like to wish all of you and your families happiness, luck and success for the upcoming year. What will 2008 bring for the "regulatory world" and SCC?

A revised guidance document on risk assessments for birds and mammals under Directive 91/414/EEC was published by EFSA. Please read section "Regulatory Science" for further details.

SCC offers its customers a new searchable database on the current status of the 91/414/EEC review of existing and new substances for use in plant protection products. The "Annex I" list shows the most updated overview on the registration status of active ingredients under Directive 91/414/EEC. With our new tool, it is possible to view the entire list of existing and new substances and the related legislation at a glance. The actives can be listed according to their registration status: in, out or pending and/or according to their submission list (existing or new active). A similar database on the status of registrations of biocidal substances under Directive 98/8/EC is under construction. For further details please check www.scc-gmbh.de, Status of Annex I, 91/414/EEC.

To read about specific requirements for the preparation of biological assessment dossiers for the authorizations of plant protection products in UK, please refer to the "Agrochemicals" section.

The European authorities are in the process of revising Directive 98/8/EC regarding the placement of biocidal products on the market. It is foreseen that the revised law will enter into force in 2012 at the earliest. Background information and a detailed analysis can be found in the "Biocides" section.

SCC has again expanded its scientific knowledge into a new regulatory direction: Food & Feed Additives. Although SCC has been partly involved in this field on several occasions, the time has now come to make it one of SCC's regulatory departments. Ruud Huibers will lead the new unit. Read under section "Food & Feed Additives" more details about Ruud's background.

New chemicals have been added to the Prior Informed Consent (PIC) scheme on the European level. Please see section "Global Affairs" for further details.

Also in this issue, you will find information on the registration of pharmaceuticals and SCC's data management system EDDMS.

As in the past, SCC will always be personally available for any of our clients' individual needs. Please contact SCC in Wendelsheim, or at our SCC Liaison Office Japan, if you have any questions.

With best regards for 2008,

Dr. Friedbert Pistel
President

In this issue:

Newsletter

Volume 8, No. 1, January 2008

REGULATORY SCIENCE

Draft of the Revised Guidance Document on Risk Assessment for Birds and Mammals

EFSA's panel on plant protection products and their residues (PPR Panel) has launched an open consultation on the draft of the revised Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC. The intent of this document is to provide guidance to notifiers and Member States on how to conduct a risk assessment for birds and mammals in the context of the review of active substances for inclusion in Annex I of Directive 91/414/EEC. Interested parties are invited to submit written comments by 27 January 2008. The draft guidance document can be found at the EFSA website http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178660551795.htm. Finalization of the new guidance document is slated for April 2008.

The new draft is quite voluminous (120 pages plus 20 appendices). It includes various changes, concretizes several points, and adds several additional approaches compared to the current guidance document. Some of the alterations are discussed in the following. As in the current guidance document (SANCO/4145/2000), a tiered approach is suggested for calculating the toxicity exposure ratio (TER). However, the Tier 1 risk assessment is now divided in two steps: the Tier 1A assessment uses a set of indicator species similar to the current guidance document. The intermediate Tier 1B uses so-called generic focal species (with generic values to derive the exposure estimate). For the acute assessment, in addition to the TER calculation, a second approach is introduced that is based on empirical data and calculates the application rate expressed as number of LD_{50}/m^2. The decision which approach should be used and which trigger values should be applied is left to the risk manager.

In the exposure estimation, new data is introduced to derive the default residue values. Avoidance effects are no longer considered in the exposure estimate but can be considered qualitatively. In the long-term (now reproductive) risk assessment, a phase specific approach is used where the breeding cycle is divided into several stages. For each stage a separate NOEC and a separate exposure estimate are derived and used in the risk assessment. The use of literature data for further refinements of the risk assessments is restricted. For most parameters (PT, PD, residues), data from specifically designed field studies are required. Besides the standard risk assessment, the use of probabilistic methods and the incorporation of metabolism data in the risk assessment are discussed.

In general, it can be concluded that the new guidance document further increases the complexity of the birds and mammals risk assessment, and will most likely lead to the need for the generation of more higher tier field data, and thus will increase the efforts that will need to be done by notifiers.

7th FRESENIUS ECOTOX Conference - Aquatic and Terrestrial Ecotoxicology and Risk Management

On the 6 and 7 December 2007, we attended the Fresenius ecotox conference. Main topics were regulatory aspects (including EU and country specific ecotox requirements), endocrine disruption, birds and mammals (status of the new guidance document, see article above), non-target plants and probabilistic risk assessment. The revision of the Directive 91/414/EEC that most likely will go into effect in 2011 and its consequences for the ecotoxicological risk assessments were discussed. Some studies will no longer be a standard requirement (e.g. 5-day dietary toxicity study birds, 14-day earthworm test), while a set of additional studies will become necessary in most cases (e.g. early life stage fish, chronic study aquatic invertebrates, bee brood test, reproduction study earthworm). A further key point was the interpretation of exposure and effects in the aquatic risk assessment, e.g. the evaluation of mesocosm results. The presented work on endocrine disruption testing showed that for different mode of actions, different endpoints are necessary to be tested.

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

Newsletter

Volume 8, No. 1, January 2008

AGROCHEMICALS

"Accelerated Procedure for Re-submission" published in Official Journal of the European Union

On 18 January 2008 the new Commission Regulation (EC) 33/2008 was published in the Official Journal of the European Union. The so-called "Re-submission Regulation" deals with the evaluation of active ingredients (ais) under Directive 91/414/EEC which resulted in a non-inclusion decision to Annex I. The Standing Committee on the Food Chain and Animal Health (SCFCAH) voted on the draft during their meeting on 7 November 2007. With the publication in the Official Journal of the European Union, the new Regulation will enter into force in all Member States on 25 January 2008.

In principle, the Regulation is applicable to all ais listed under stages 1, 2, 3 and 4. But only for substances listed under stages 2, 3 or 4 can the "Accelerated Procedure" for re-submission be applied. In order to be able to use this procedure, the Draft Assessment Report (DAR) must have been prepared for the specific substances.

Within 6 months from entry into force of Regulation 33/2008, the application must be submitted to Rapporteur Member States (RMS) (list 2) or within 6 months from date of publication of the non-inclusion decision for list 3 and 4 substances. The Draft Review Report with the proposed decision for inclusion/non-inclusion is expected at the earliest 14 months after the application was submitted by the notifier.

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

Product Authorization in UK: Preparation of Biological Assessment Dossiers

During a workshop on 6 December 2007, the British Pesticide Safety Directorate (PSD) representatives explained how a Biological Assessment Dossiers (BAD) must be structured and which data requirements have to be fulfilled.

In principle, PSD accepts BADs which are structured according to OECD Guidelines. In addition, applicants must ensure that the BAD covers all UK-specific requirements: for example, dose justifications, quality transformation processes and taint must be included. Such kind of studies can be conducted under accepted "foreign" guidelines (e.g. BBA, CEB). However, translations of foreign guidelines have to be enclosed. Trials will be taken into account for the evaluation if they fulfill PSD standard requirements which can be found in the related EPPO Guidelines (PP 1/181 (3), PP 1/152 (2), PP 1/135 (2)) and the PSD Guideline 101 prepared according to the EPPO standard. Furthermore, GEP certificates must be provided for all trials.

In the BAD, a minimum number of efficacy trials must be submitted in order to be taken into account by PSD: in principle 10 good trials over 2 years on a major pest (e.g., summer aphids on winter wheat) and 3 trials usually over 1 year on a minor pest (e.g., thrips on winter barely) are necessary to apply for authorization in UK. If the application is made in a controlled environment or if extrapolations are possible, the total number of trials per crop/pest combination can be reduced. The overall results of the trials must be compiled in a summary table which lists the average mean value, the number of trials, and the reference product in a logical manner.

The label must be prepared according to specific PSD requirements. All label claims must be explained in the BAD as well as any unexpected results. Depending on the overall level of pest control, the following label claims are appropriate: "control" (above 80%), "partial, moderate or useful level of control" (60% to 80%) and "reduction or some control" (40% to 60%). The dossier must provide an explanation if the average mean efficacy value is below 80%, for example, if unusual weather conditions occurred, or if the crop was not infected by the pest.

According to PSD, it is not always necessary to generate new data. PSD offers a scope of flexibility to fulfil the data requirements, for example through the use of public domain data or extrapolation of efficacy results between similar crops and pests. In that respect, PSD accepts data that has not been generated in UK. Trials from Germany, North of France and the Scandinavian countries can be taken into account if the applicant can prove or explain that crop and pest as well as the climate and the environmental conditions from the originating country are comparable to UK conditions. Data from all sources must be taken into consideration if claiming for a label.

Newsletter
Volume 8, No. 1, January 2008

AGROCHEMICALS

As resistance problems are increasing, this issue has to be addressed carefully in the BAD (see PSD guideline 606). The applicant must ensure that sufficient data for critical products are made available. Such data sets can be made a condition of approval.

PSD emphasized that they have always supported "using the route of mutual recognition as a way of gaining UK authorizations". The success of using the mutual recognition (MR) route relies on the applicant demonstrating (agricultural plant and health) relevancy to the use of the product's comparability between the MS regions concerned. Data should be generated under as wide a range of conditions as possible. Differences could be overcome by label amendments, if necessary.

For products to be re-registered the previously submitted dossier must be adapted to current regulations. If there are major changes for example in the formulation of the product new efficacy trials must be provided.

If you need help with the preparation of your BAD or you have any questions, please do not hesitate to contact Dr. Norbert Weißmann (norbert.weissmann@scc-gmbh.de) for further information.

BIOCIDES

Revision of the Biocidal Products Directive

According to Article 18 (5) of the Biocidal Products Directive 98/8/EC (the BPD), the Commission is required to draw up a report addressing the implementation of the BPD seven years after its entry into force.

In 2006, the Commission initiated a study to analyze the present regulatory situation. The final report entitled "Impact of the implementation of Directive 98/8/EC concerning the placing on the market of biocidal products" has already been published, and is available on the Internet for download at http://ec.europa.eu/environment/biocides/study.htm). As a result of a stakeholder consultation, the study identified a number of reasons for unwanted impacts of the BPD, such as extensive data requirements for dossier preparation, high and varying fees for approval of active substances and authorization of products, or a lack of legal certainty, to name but a few. In conclusion, the concerns and suggestions of all stakeholders involved show that the BPD in its present form needs to be fundamentally revised.

A further study called "Assessing the Impact of the Revision of Directive 98/8/EC concerning the Placing of Biocidal Products on the Market" was recently launched by the Commission. The overall objective of this project is to identify and evaluate the impacts related to the range of major policy options available for addressing the current problems and shortcomings of the BPD for different stakeholders, in particular the small and medium-sized enterprises. The draft final report of that study is expected to be available by August 2008.

According to oral information, the proposal for a revised BPD could be ready by 2010. Its publication and legal implementation is not expected before 2012-2014.

Apart from major policy issues relating to a fundamental revision of the BPD, there is also a need for ad hoc corrections and clarifications of the biocide regulatory framework.

For instance, the 10-year review program on existing biocidal active substances as laid down in Article 16 of the Biocidal Products Directive 98/8/EC is approaching its official end. However, the deadline of 14 May 2010, by which the review of existing actives should be completed, is highly unlikely to be met, even if the procedures could be significantly accelerated. Therefore, the review program has to be extended and a new deadline must be legally set.

Another example is the clarification of the concept of frame formulations by adjusting the wording of the BPD in this respect. This becomes more important since the first active substances are currently entering Annex I and applications for authorization of existing biocidal products on the national level will have to be submitted.

The Commission has announced that it will come up with a "quick revision" of the BPD, addressing such urgent corrections, at the beginning of 2008.

At the present stage, it can be concluded that – just as in the similar case of the ongoing revision of the Plant Protection Products Directive 91/414/EEC - we will be facing a long revision process of the BPD.

For more information, please contact Dr. Holger Zitt holger.zitt@scc-gmbh.de or Dr. Hans-Josef Leusch hans-josef.leusch@scc-gmbh.

Newsletter
Volume 8, No. 1, January 2008

SCC offers new service as REACH "Only Representative"

The European chemicals market presents many business opportunities for internationally operating companies. With the implementation of REACH regulation (2006/1907/EC) in 2007, manufacturers from outside the EU as well as European importers need to make significant changes to their business.

Manufacturers from outside the EU who wish to export chemical substances on their own, in preparations or in articles, into the EU at volumes of or above 1 ton/annum must comply with the requirements set out in the regulation. If manufacturers from outside the EU plan to register substances under REACH, they must establish a natural or legal person in the EU. REACH offers several alternatives to fulfill this requirement; however, the so called "Only Representative" (OR) option is the most efficient and least costly way.

According to Article 8, a natural or legal person established outside the EU who manufactures a substance on its own, in preparations or in articles, formulates a preparation or produces an article that is imported into the EU may, by mutual agreement, appoint a natural or legal person established in the Community to fulfill, as his Only Representative, the obligations under this Title (Registration).

The OR is the EU focal point for the non-EU manufacturer and downstream users. The OR is responsible for the registration dossier and number. The importer is not obligated to register under REACH, but rather will be considered a downstream user. The OR is integrated into the non-EU manufacturer's supply chain.

The advantages of the OR include:

- Access to the European market without having to establish an EU subsidiary.
- Allows the manufactures from outside the EU to keep full control of their registration(s).
- Assures the confidentiality of trade and business secrets – detailed substances information does not need to be passed on to importers.
- One registration for all importers instead of individual registrations for each importer.
- Anonymous registration through "Third Party" is possible.

The OR needs to provide the following standard services to manufactures from outside the EU:

- Portfolio analysis
  - assessment of REACH requirements
- Pre-registration
  - collection of pre-registration data
  - submission of data to ECHA
- SIEF-representation incl. data provision
  - data provision upon request
- Registration
  - completeness check of technical dossier and CSA/CSR
  - document submission
- Evaluation
  - tracking of information on evaluation
  - supply of additional information
- Communication to the ECHA
  - communication of changes in the registration, including volumes, uses, etc.
- Downstream communication (Article 31, MSDS)
  - communication to downstream users
- Focal point for communication up the supply chain
  - coordination of uses
  - registration dossier updates
- Obligation to keep information (Article 36)
  - period of at least 10 years after he last manufactured, imported, supplied or used the substance, preparation or article

SCC has considerable background in the services needed for Only Representative and can provide you in addition with:

- standard database tools
- data requirement analysis
- pre-registration
- co-ordination of (pre) SIEF requests
- analysis of SIEF data
- consortium representation, management and technical services
- preparation of the technical dossier
- CSA/CSR
- MSDS preparation and updates
- incorporation/exclusion of uses to the risk assessment

Take advantage of SCC's regulatory and scientific experience gathered since 1989 in the areas of chemical, plant protection, biocide and consumer products, as well as SCC's multilingual service and our experience providing regulatory advice to clients throughout the world. For more information on SCC's OR services, contact Dr. Werner Köhl at werner.koehl@scc-gmbh.de.

Newsletter

Volume 8, No. 1, January 2008

DATA MANAGEMENT

SCC further improves its universal regulatory database EDDMS

SCC has further improved its universal regulatory database "**E**lectronic **D**ocument and **D**ossier **M**anagement **S**ystem", EDDMS with the incorporation of an essential update.

It is well-known that our "regulatory world" has become more and more complicated and complex. The preparation of a regulatory dossier has developed into an extremely demanding task in terms of scientific and administrative requirements. Extensive dossiers covering multiple data requirements must be generated by the applicant, requiring reliable documentation and tracking of submissions and corresponding information. With SCC's experience obtained over almost two decades of working for the chemical industry and knowledge acquired from hundreds of dossier preparations and international submissions, SCC has developed its regulatory database system. Our experiences from the past result in a further improved data management system.

Let the advantages of the upgraded EDDMS work for you:

- Universal use, independent of regulatory area
- Instant data access on individual PCs, computer networks, on a local or global scale, depending on your organization
- Complete regulatory information about your substances and products at hand everywhere you need it: in your office or while travelling, including electronic documents, submission details and project documentation
- Flexibility for your specific in-house needs, including integration of already existing databases, guaranteed by SCC specialists

EDDMS can be used for all regulatory submissions: for chemicals (REACH), plant protection products, biocides, pharmaceuticals, consumer products, feed and food additives or any other type of product.

For further details please see SCC's flyer "EDDMS" at www.scc-gmbh.de under section "Brochures" or contact Dr. Friedbert Pistel (friedbert.pistel@scc-gmbh.de).

FOOD & FEED ADDITIVES

Feed Additives new regulatory department of SCC!

SCC has again expanded its scientific knowledge into a new regulatory direction: Feed Additives. Although SCC has been partly involved with feed additives on several occasions, the time has now come to make it one of SCC's five regulatory departments. Here is a short introduction into the world of the Feed Additives.

The World of Feed Additives

Unlike SCC's other fields of work, feed additives have no national authorizations. Since 1970, feed additives have been authorized only at the European level by the European Commission (EC) in cooperation with the Member States (MS). After several crisis situations in animal nutrition between 1998 and 2002 (e.g., dioxins and BSE), and the legal inclusion of animal nutrition into the food safety chain, the initial Council Directive 70/524/EEC was changed into Regulation (EC) 1831/2003. The most important changes were the establishment of a positive list of feed additives (only these listed substances may be used as feed additives), and the fact that the European Food Safety Authority (EFSA) has taken over the Member State role of reporting.

In order to receive authorization as a feed additive, all substances must submit a dossier for registration before 7 November 2010. In the world of feed additives there are two kinds of authorizations: holder specific (the authorized substance is linked to a specified company who has the unique right to sell this product) and non-holder specific (the authorised substance is free to be marketed by any registered company). For the second case (which accounts for over 90% of all feed additives), many consortia have been established in order to make joint submissions of the necessary dossiers. This is where SCC comes into play.

SCC's strategy with Feed Additives

SCC has contracted Ruud Huibers to lead the new regulatory department Feed Additives. For many years, he was the head of the Dutch delegation on animal nutrition in Brussels. He has a strong interdisciplinary background in chemistry and international law, and brings detailed knowledge on

Newsletter
Volume 8, No. 1, January 2008

FOOD & FEED ADDITIVES

all relevant European regulations. Also, Ruud has a wide-reaching network in both the feed additive industry and the international governmental world. SCC has about 50 scientists with a wealth of scientific knowledge and experience covering all registration-relevant areas. These two forces combine to make a very strong team for the preparation of the necessary dossiers for the feed additive industry. SCC can prepare, submit and defend a complete registration dossier. The first step will always be a full data gap analysis by our scientists.

SCC has dealt with over 20 task forces since 1989, and is currently involved in 12. Our experience is your advantage! SCC's philosophy is to replace expensive studies with less expensive expert work whenever scientifically justified! In addition, SCC is independent: it intentionally does not have laboratories of its own (so there is no need to fill them with unnecessary studies) and is therefore free to cooperate with any laboratory which best suits the needs of our clients in case studies are required.

If you have any questions, please do not hesitate to contact Ruud Huibers at ruud.huibers@scc-gmbh.de or at +49 6734 9190. Also you can find more information on our website (www.scc-gmbh.de) under the heading "Feed Additives" and under the link "Brochures".

HUMAN & VETERINARY PHARMACEUTICALS

First experiences of German Umweltbundesamt with the new EMEA Guideline

Since 1 December 2006, the guideline on the environmental risk assessment of medicinal products for human use (EMEA/CHMP/SWP/4447/00) has been in effect. The EMEA guideline describes the assessment of environmental risk due to the use of medicinal products. Based on the European Directive 2001/83/EC, the environmental risks created through the use of medicinal products must be assessed and possible impacts on the environment should be limited. For more details please refer to the SCC Newsletter, Vol. 7, No. 1, January 2007.

During the last conference of the German Language Branch of the Society of Environmental Toxicology and Chemistry (SETAC) on 12 – 14 September 2007, the German Environmental Protection Agency (Umweltbundesamt) gave an overview on the first experiences with the application of the new EMEA guideline: by September 2007, 184 medicinal products (corresponding to 1.5% of all applications) have been evaluated. 37 dossiers from the total of 184 were submitted including a complete data set. In four cases, an environmental risk was identified.

98% of the medicinal products which were evaluated by Umweltbundesamt are not readily biodegradable. It was stated that for substances with endocrine disrupting potential, a fish full lifecycle test will be required. If a water sediment study according to OECD Guideline 308 is requested, the investigation of aerobic conditions is sufficient. A revision of the EMEA Guideline is currently under preparation.

For further details, please contact Dr. Achim Schmitz at achim.schmitz@scc-gmbh.de.

Newsletter

Volume 8, No. 1, January 2008

GLOBAL AFFAIRS

Annex I of the European "PIC Regulation" recently updated

The Rotterdam Convention on the Prior Informed Consent (PIC) is a multilateral agreement which controls and monitors the trade with certain hazardous chemicals on an international basis. It functions under the umbrella of the United Nations (UN). The work of the convention is co-ordinated and facilitated by the Food and Agriculture Organization (FAO) as well as the United Nations Environment Program (UNEP).

The objective of the agreement is to promote shared responsibility in the international trade of chemicals through facilitating information exchange among parties, as the convention text states. The information exchange is guaranteed through the PIC procedure which ensures that no shipment of certain listed chemicals can take place without a positive response of the importing party.

We presented the implementation of the Rotterdam Convention on the Prior Informed Consent (PIC) on the European level in the SCC Newsletter, Vol. 7, No. 1, January 2007. With Regulation 304/2003 (the Regulation), the European authorities put in place the legal frame for PIC. On 23 November 2007, the last update was published with Regulation 1376/ 2007 (EC): new substances were added to Annex I of the Regulation that fall under the scope of the European Union's (EU) legal system in that field. Substances listed under Annex I can only be exported if the importing country gives its permission prior to export: only then can it proceed (principle of explicit consent). For the other administrative tools relating to prior informed consent, please refer to SCC Newsletter Vol. 7, No. 1, January 2007 or check the PIC website: www.pic.int .

For further information, please contact Dr Friedbert Pistel at friedbert.pistel@scc-gmbh.de.

CALENDAR

Food Safety and Dietary Risk Assessment
28 – 29 January 2008
Darmstadt, Germany

Dr. Monika Eder and Dr. Alexander Köhl will be at the conference. For more information, contact the Akademie Fresenius at www.akademie-fresenius.de.

Classification, Labelling and Packaging of Substances and Mixtures
6 –7 February 2008
Brussels, Belgium

Dr. Jutta Görg, Dr. Barbara Wagner-Roth and Mr. Sven Peter will be at this informative conference

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The Biocidal Products Directive
26 – 27 February 2008
Cologne, Germany

Dr. Holger Zitt, Senior Manager Regulatory Affairs Biocides at SCC, will present the topic "Practical experience gathered during the review process". For more information contact the Akademie Fresenius at www.akademie-fresenius.de or Dr. Holger Zitt at holger.zitt@scc-gmbh.de.

To make an appointment to meet with SCC staff during one of these events, please contact Ms. Lisa Hubrich at +49-6734-919115 (tel.) or at lisa.hubrich@scc-gmbh.de.

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