

Working Hard for the Industry

Since the early 1990s, the evaluation of chemical substances under Directive 91/414/EEC for use in plant protection products has covered a considerable part of SCC's scope of work. Our day-to-day efforts for the benefit of our clients have once again been rewarded by the European authorities! From the scientifically challenging group of organophosphate and carbamate chemicals of list 2, three active substances have now been included to Annex I of Directive 91/414/EEC after the submission of dossiers prepared and successfully defended by SCC on behalf of our clients. This result shows a 100% success rate which SCC, in co-operation with its clients, has achieved on the European level.

With the evaluation of list 2 substances coming to its delayed end, we see the European authorities setting up the next hurdle for the chemical industry. The Commission has published its proposal to amend the review process for stage 3 and 4 substances ("fast track procedure"): actives will be classified into various groups, for example substances of "high concern" or "low concern", or the current procedure will apply. Depending on the classification, substances will be "included" or "non-included" to Annex I. In addition, it has been proposed to significantly reduce (from 12 to 6 months) the time for the EFSA review. It is currently unclear which criteria will be used as a basis to classify substances. We are carefully monitoring the development of the proposal and will keep you updated.

Currently, we are in the process of preparing a number of dossiers on biocidal substances for submission on behalf of our clients by July 2007 to the respective rapporteur member states. In addition to these activities, REACH looms on the horizon, already significantly increasing industry awareness regarding this issue. We have already begun customer support on this issue, and the need for this support is rapidly increasing. Even though capacities are rapidly filling up, we still can accommodate new business before this new piece of legislation regulating chemicals enters into force in June 2007. Please see the Chemicals section for further details.

Although SCC has a very busy work schedule at present and in future, we are and will always be personally available for any of our clients' individual needs. Please contact SCC if you have any further questions.

With best regards,



Dr. Friedbert Pistel
President

In this issue:

Agrochemicals	p. 2
Regulatory Science	p. 3
Chemicals	p. 4
Data Management	p. 5
Biocides	p. 5
Pharmaceuticals	p. 6
Global Affairs	p. 6
Calendar	p. 7

Natural is not necessarily safe!

Although biopesticides are substances which are based on naturally occurring compounds (semiochemicals, plant extracts) or micro-organisms (m-o; fungi, bacteria, virus), they must be reviewed and evaluated under Directive 91/414/EEC (the Directive) before they can be marketed. As these substances/organisms do not fall under the category of "regular chemicals", the data requirements have been adapted to the specific needs of such substances/organisms. In Annexes II B (active data requirements), III B (formulated product requirements), and VI B (uniform principles) to the Directive, data requirements for biopesticides and microbials are listed. Many of them are notified under stage 4 in the review process, which has been revised by documents SANCO/10547/2006 rev. 3 and SANCO/10350/2006 rev 8.

The United Kingdom's (UK) Pesticide Safety Directorate (PSD) has its own Biopesticide Scheme which was presented during a one-day seminar on 28 March 2007. PSD has set up a specific biopesticide unit with three "champions" covering the special requirements of biopesticides in general (e.g. initial contact point) and individual needs of small businesses and growers in the fields of agriculture and horticulture. Fees for the registration of biopesticides are in the range of GBP 13,500 to 22,500.

Prior to submission of an application, PSD offers pre-submission meetings for applicants of biopesticides. The purpose of these meetings is to clear open questions between the applicant and the regulatory authority in advance of dossier submission, especially with regard to data requirements, in order to approve biopesticides as quickly and economically as possible. According to PSD, it is not always necessary to generate new data to address all areas required by the Directive. On the contrary, PSD offers a scope of flexibility to fulfill the data requirements. In many cases public domain data can provide sufficient information, tests can be waived, reasoned cases can be made, or any scientifically sound alternative

source can be taken into account. Co-operation with other applicants can save a lot of money and time, as well.

Before carrying out studies and tests, it is recommended to get in contact with PSD. Using this approach, applicants can avoid the generation of unnecessary data. This approach was strongly recommended because PSD decides on a case-by-case basis which data will be necessary in order to get a biopesticide approved.

From an industry perspective, it was said that obtaining an approval for a biopesticide is very cost and time intensive. The costs for a package of basic core studies fall in the range of EUR 788,000 to 875,000 with residues and environmental fate studies creating at least 50% of the costs. Most of the manufactures are small or medium sized companies (SMEs) with limited financial resources. To reduce costs, it was recommended to use the scope of flexibility for the generation of data to obtain an approval for biopesticides.

Detailed data requirements for biopesticides approval were explained by representatives of the involved branches: efficacy, identity, toxicology, operator exposure, residue and consumer exposure, environmental fate and behavior, ecotoxicology. Further details can be obtained at SCC.

In general, data requirements for biopesticides are less demanding than for conventional chemicals. However, due to the vast biological differences in the three categories of biopesticides (substances and living organisms) and the individual use (different exposure to humans and the environment) of the final product, data requirements can differ significantly, such that it is very difficult to give general guidance for applicants.

SCC offers support for the development of individual application strategies for your biopesticide and its discussion with PSD or any other regulatory authorities in the EU.

For further details please contact Theda Damó at theda.damo@scc-gmbh.de.

MRL regulation 396/2005

On 15 March 2007, EFSA issued an opinion on the possible consumer risks from maximum residue levels (MRLs) in food and feed. Further details can be found on the following website: http://www.efsa.europa.eu/en/science/praper/maximum_residue_levels/mrl_opinion.html. Here you will find the following documents:

- Reasoned opinion
- Appendix 3, Part A: Non inclusions
- Appendix 3, Part B: Pending
- Appendix 3, Part C: Combined risk assessment
- Appendix 4, Part A: Non inclusions
- Appendix 4, Part B: Pending

An overview of what has been done and the outcome of the preliminary dietary risk assessment is summarized in the “reasoned opinion”.

The detailed outcome of the acute and chronic risk assessment is summarized in Appendix 3, Part A for active substances not included on Annex I after review in the 91/414/EEC process (see “Appendix 3, Part A: Non inclusions”). The respective risk assessment for active substances, where the decision regarding Annex I inclusion is outstanding, is provided in Part B of Appendix 3 (see “Appendix 3, Part B: pending”). In Part C of Appendix 3 the outcome of risk assessments is summarized for active substances where related active substances have to be considered.

EFSA conducted a preliminary dietary risk assessment screening using different diets from several EU Member States and the highest national MRLs. In Appendix 3, Parts A-C, the contribution of the TMDI to the ADI is presented, highlighting also the highest contributor. Furthermore, the results are given if the MRL is set on the proposed LOQ. As the LOQ is often set as 0.05 ppm the contribution of the ADI might already be high with these low residue values. The presentation of the acute risk assessment covers two approaches (IESTI1 = variability factor 10, 7 and 5; IESTI2 = variability factor 5 and 3 for lettuce). Furthermore, the threshold MRL was calculated.

In Appendix 4, the MRLs used in the dietary risk assessments are compiled and the

respective dietary risk indicated.

According to this risk assessment, 92 of the 236 active substances evaluated by EFSA were unlikely to present a risk to consumers. For the remaining 144 substances, the first screening could not exclude a potential consumer risk. Thus, more work now has to be carried out on these substances by the Member States and the European Commission with a view to establishing temporary MRLs. The establishment of harmonized MRLs for the active substances is a precondition to make Regulation 396/2005 on maximum residue levels of pesticides fully operational. The temporary MRLs will be established as an interim measure. They will be subject to a detailed scientific assessment leading to the establishment of final MRLs following the comprehensive assessment of the active substances [cited from the respective press release].

The outcome of the first screening shows that further refinements are absolutely necessary, e.g. to check whether the adequate toxicological reference values (ADI, ARfD) have been used. Furthermore, it has to be checked whether the risk assessments could be refined using residue data from supervised residue trials as well as processing data (e.g. for citrus pulp) and by restricting the risk assessment on registered uses. These refinements are very important as the Notifiers will otherwise lose products and uses.

At this stage it seems that the time-frame for the refinement which should be done in a close cooperation between Member States and Notifiers will be very short. Thus, if the European Commission sticks to their schedule, national MRLs will be set on the threshold MRLs or in the worst case on the LOQ.

For the remaining substances which did not result in a dietary risk the MRLs shown in Appendix 4, Parts A-B could be directly used as temporary MRLs for the Appendix 3 of the MRL regulation 396/2005.

For further information, please contact Dr. Monika Hofer (monika.hofer@scc-gmbh.de) or Dr. Monika Eder (monika.eder@scc-gmbh.de).

Registration, Evaluation and Authorization of Chemicals (REACH)

After having been accepted by the European parliament on 13th December 2006 as Regulation No. 1907/2006 of the European parliament, and by the Council on 18 December 2006, REACH will enter into European law on 1 June 2007. The European Chemicals Agency is to be fully operational one year later.

REACH requires the registration of all existing and future new substances, substances in preparations and substances in articles with the European Chemicals Agency. For the first time the burden of proof for guaranteeing chemical safety is transferred from Member States' authorities to producing and importing companies. The regulation further introduces responsibility for downstream users to provide information on uses and associated risk management measures.

Registration is the full responsibility of producers and importers. Registration for non-phase-in substances and substances not registered as new chemicals manufactured in or imported into the EU at quantities ≥ 1 t/anno, starts in June 2008. Substances already notified as "new chemicals" according to Directive 67/548/EEC will be regarded as registered for the purposes of REACH, and the Agency will assign a registration number by December 2008. For phase-in substances, REACH offers transitional provisions.

To benefit from the prolonged transitional provisions for phase-in substances, each potential registrant of such a substance, including without limitation intermediates, should pre-register with the agency. Phase-in substances include those placed on the market and listed in EINECS, no-longer polymers, and those manufactured in the EU (15-year period), but not placed on the market. Pre-registration will start 1 June 2008 and will continue through 1 December 2008, i.e. the pre-registration period is limited to six months.

The transitional periods for registration of pre-registered phase-in substances manufactured in or imported into the EU are:

Substance characteristics / Volumes*	Deadline
- CMR** Category 1 and 2 according to 67/548/EEC - Very toxic to aquatic organisms which may cause long-term adverse effects in the aquatic environment (R50/53) ≥ 100 t/anno - Substances ≥ 1000 t/anno	1 December 2010
- Substances manufactured or imported in quantities ≥ 100 t/anno	1 June 2013
- Substances manufactured or imported in quantities ≥ 1 t/anno	1 June 2018

* average production or import volumes for the three preceding calendar years

** carcinogens, mutagens or toxic for reproduction

After registration, an evaluation process will follow for selected substances (ca. 5% are mentioned frequently) and be carried out by the European Chemicals Agency. Selection will be based on risk, as defined by the substances hazardous properties, exposure and tonnage. Note that tonnage here includes the aggregated tonnage from all registrants. Evaluation will be carried out by Rapporteur Member States and lead to classification and labelling, potential restrictions on use or authorization requirements. In general for chemicals not classified as substances of very high concern (e.g. CMR, etc.), self-classification by industry will apply.

To help fulfill the obligations under REACH, the European Chemicals Bureau, in close collaboration with all stakeholders, is developing methodologies, tools and technical guidance through REACH Implementation Projects (RIPs). The RIPs include 7 main areas (RIP 1 to 7) and a number of sub-categories. Details on each of the projects and the guidance document, if completed, can be found at the ECB website: <http://ecb.jrc.it/REACH/>.

Newsletter

Volume 7, No. 3, April 2007



CHEMICALS

To date 8 projects have been finalized, 9 are currently running, and 1 remains to be started. Note that some RIPs are more of a brainstorming document than a guidance document on technical issues. REACH-IT, a web-based system to allow easier access to all documents available under REACH, including information about the various RIPs (1,2, 3 and 4) and other technical guidance developed for industry and the authorities, will be rolled out on 1 June 2007, the date on which REACH will enter into force.

No data, no market (EC Regulation 1907/2006, Title II, Chapter 1, Article 5)! If your company has not yet started to prepare for REACH, the time has now come. A number of critical steps needs to be taken before pre-registration and registration start next year. Let SCC help you ensure your regulatory compliance and access to the EU market.

For more information, please contact Dr. Werner Köhl werner.koehl@scc-gmbh.de.

DATA MANAGEMENT

SCC to launch new data management system

SCC is currently in the process of finalizing its new Electronic Dossier and Data Management System (EDDMS). EDDMS archives all documents related to the registration of our clients' substances on EU or member state level.

In terms of content, the new and old versions are basically the same. The new system, however, is based on most current technology available.

User friendliness has been significantly improved in such way that the available information is presented much better and therefore is more easily accessed. Without additional effort, all studies submitted to authorities on behalf of our clients can be reprinted. Detailed explanation will follow in a special edition of this newsletter soon.

For further information, please contact dv@scc-gmbh.de.

BIOCIDES

News from the biocidal substance review program

An updated "List of participants" http://ecb.jrc.it/documents/Biocides/GUIDANCE_DOCUMENTS_SECOND_REVIEW_REGULATION/list_of_participants.pdf is now available on the European Chemicals Bureau's (ECB) website. The list provides contact details of participants and producers, formulators or associations who joined or replaced participants according to Article 8 of Commission Regulation (EC) No. 2032/2003. The purpose of the list is to support cooperation among participants who seek to submit a collective complete dossier or to share information to avoid duplication of tests on vertebrates.

On 29 March 2007, "Active substances of the 2nd priority list for which a company has indicated an interest in taking over the role participant" was published by the European Commission – http://ec.europa.eu/environment/biocides/pdf/substances_2ndlist_taken_over.pdf. For seven active substances in PT 18 and for six active substances in PT 19, other companies have indicated interest to take over the role of participant.

Dichlofluanid (PT 8) has been included in Annex I to BPD. The inclusion Directive is not yet publicly available.

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

SCC offers services on environmental risk assessments for pharmaceuticals according to 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 so called EMEA guideline describes the assessment of environmental risks due to the use of medicinal products. Based on the European Directive 2001/83/EC the environmental risks created through the use of medical products must be assessed and possible impacts on the environment should be limited. SCC Newsletter Vol. 7, No.1, January 2007.

Based on its extensive experience with environmental risk assessments (fate, exposure, effects, risks), SCC offers full scientific and regulatory service to fulfill the requirements of the new EMEA guideline, and can provide you with full scientific and regulatory service in this field. SCC can evaluate the available data and, if necessary, can assist by planning and monitoring such studies as:

- studies on the environmental fate and behavior
- studies on effects to aquatic and terrestrial organisms

SCC can prepare expert statements regarding questions on ecotoxicology, environmental fate and behavior.

The performance of environmental risk assessments, comparing potential exposure with potential effects, is an integral part of our services and can be provided as required by the new EMEA guideline including Phase I and Phase II Tier A and B, including PEC modeling and reporting ready for inclusion in Module 1.6 of the dossier.

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

European Commission publishes first summary report on chemicals listed in Annex I to Regulation 304/2003 on Prior Informed Consent

We presented the implementation of the Rotterdam Convention on the Prior Informed Consent (PIC) on the European level in SCC Newsletter Vol. 7, No.1, January 2007. With Regulation 304/2003 (the Regulation), the European authorities put in place the legal framework for PIC. On 23 May 2006, the last update was published: 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 before the export can 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.

With Article 21 of the Regulation, member states (MSs) are obliged to regularly update the European Commission (the Commission) on the status of implementation and "on the operation of the procedures provided". The Commission then will compile a report taking into account all information received from the MSs. The first of such reports was published in September 2006 covering the period of 2003-2005. Information was provided by 22 of the 27 MSs. In summary, a total of around 12.500 tons of pesticides listed in Regulation 304/2003 (for example Aldicarb, Atrazine, Fenthion, Ferbam, Lindane, Permethrin, Methyl parathion, and Cyhalothrine) were exported from EU territory into non-EU countries, the largest share of which was imported by countries from the Asian and Pacific regions.

From a technical point of view, the procedures of the regulation are working well. However, there are still administrative problems which must be solved.

Newsletter

Volume 7, No. 3, April 2007



GLOBAL AFFAIRS

Companies located in EU MSs have attempted to export chemicals listed under Annex I to the Regulation into non-EU countries. In order to achieve explicit consent, industry contacted the authorities in the respective importing countries via their responsible national regulators which are designated to deal with the PIC issues. The approach failed in many cases because authorities in the importing countries simply did not respond, with the consequence that the export could not proceed. To avoid this situation, the Commission proposes amending the current EU regulation: if the exporting country does not receive an answer from the authority in the importing country within two months, export will be allowed on a temporary basis if the substance is approved in the importing country. The respective approval documents will serve as proof for positive consent of the importing country.

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

CALENDAR

Want to meet with SCC staff? Here is a listing of upcoming events that will be attended by SCC.

Focus Degradation Kinetics Workshop Cambridge, UK 2-3 May 2007

Dr. Christine Klein, Regulatory Manager Research & Development, will be attending this informative workshop from 23 May 2007 in England. Topics will include computer modelling and simulation.

Registration of Agrochemicals

Brussels, Belgium 9-11 May 2007

The 14th International Conference on the Registration of Agrochemicals will be held 9-10 May in Brussels. Dr. Monika Hofer and Dr. Albrecht Heidemann will be in attendance from SCC. Topics include the latest updates on European agrochemical policy, progress of the review program, MRLs and a discussion of the changes to data requirements for Annex II and III.

BCPC Conference

Glasgow, UK 15 – 18 October 2007

Once again, SCC will be attending the BCPC Conference and exhibition in Glasgow. We will be at the Pentagon Centre, 36 Washington Street, just across from the Menzies Hotel. Make an appointment to discuss your specific regulatory needs.

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

SCC Scientific Consulting Company Chemisch-Wissenschaftliche Beratung GmbH

Dr. Friedbert Pistel, President

**Mikroforum Ring 1 · D-55234 Wendelsheim · Phone +49 (0) 6734-919-0 · Fax +49 (0) 6734-919-191
scc@scc-gmbh.de · www.scc-gmbh.de**

Previous Newsletters can be found on our website www.scc-gmbh.de, under **Newsletter Archive**. 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.