Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

AgChem Forum:
A Review of Presentations

As a sponsor of this year's CIR 2012 Conference, which included the 12th annual AgChem Forum, SCC was a major participant, both at the exhibition and as presenter. Dr. Brielbeck, Senior Regulatory Manager Agrochemicals and Biopesticides made a presentation regarding the zonal authorization procedure, and Dr. Weissmann, Senior Regulatory Manager Efficacy hosted the pre-conference workshop on the consequences of new efficacy data requirements for dossier generation.

This newsletter provides you with new information and insights made regarding the current status of regulatory frameworks, including the Annex I Renewal Project, candidates for substitution and sustainable use.

For more information, please contact Dr. Bernd Brielbeck (bernd.brielbeck@scc-gmbh.de) or Dr. Albrecht Heidemann (albrecht.heidemann@scc-gmbh.de).

Please note that the following abbreviations appear in the summaries below:

a.s. =	active substance(s)	EFSA =	European Food Safety Authority
ECPA =	European Crop Protection Agency	ECHA =	European Chemicals Agency
MS =	Member State(s)	dRR =	draft Registration Report
zRMS =	zonal Rapporteur Member State(s)	DAR =	Draft Assessment Report
cMS =	concerned Member State(s)	PPP =	plant protection product(s)
NGO =	non-government organization	MR =	mutual recognition
CIRCA =	document management system used by EFSA	EMS =	evaluating MS for MRL setting
RR =	registration report	MRL =	maximum residue level
CA =	competent authority	CLH =	harmonized classification and labelling
ER =	evaluation report	SCFCAH =	Standing Committee on the food chain and animal health

****

Measuring sustainable intensive agriculture

Euros Jones
Chairman, AgChem Forum

In his introductory remarks, the Chairman emphasized that to feed an increasing population, it is mandatory for agriculture to become more efficient; otherwise, the areas used for food production will have to increase. Recent draughts, sending food prices up and sparking food riots, have already shown the vulnerability of the worldwide food supply, which is under additional pressure due to competition with the production for bio-fuels. One target of sustainable intensive agriculture is a yield of 20 t wheat per hectare. To achieve the goals set, an increase in research is needed; however, it has been observed that companies are shifting their research budget towards issues concerning genetic modification (GMO), where Europe is not a key focus!

Linking Environment And Farming (LEAF)

Caroline Drummond
LEAF, UK

LEAF, an acronym for "Linking Environment And Farming", is an organization that promotes environmentally responsible farming, helping farmers produce good food with care and to high environmental standards, identified in-store by the LEAF Marque logo. Through this policy, public understanding of food and farming is promoted in a number of ways, an understanding that has been lost by increased urbanization of the population. At the same time, the growth in population requires a sustainable intensification of agriculture.

To reach sustainability, various factors have to be integrated and measured, such as economic, environmental and social factors, including a happiness measurement (similar to what is well known for Bhutan). LEAF audits to worldwide standards and the LEAF Marque logo shows co-operation along the entire food chain.

AgBalance™ - Decision-making towards more sustainable agriculture

Markus Frank
BASF, Germany

The key drivers for sustainability in agriculture are such basic trends as population growth, changing dietary patterns and the wish for bio-fuel. Resources to address these fundamentals, such as water, soil, arable land and energy are becoming scarce. In addition, there are societal drivers such as the perception of risks and food safety, which are translated into new regulations. Farmers need a sustainable yield increase along with new and creative solutions to manage such scarce resources and to address the regulatory standard as well as the expectations of society. BASF's AgBalance method to measure sustainability in agriculture is a tool that addresses these needs. It is a holistic approach to help make informed decisions on how to manage improvement, covering 200 evaluation factors and 69 indicators in 16 categories. The new concept was developed from the earlier eco-efficiency system by including societal factors to economical and ecological factors. The new

Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

system includes factors from pre-chain through agriculture itself to down-chain, resulting in a full life cycle impact assessment (LCIA).

A case study on winter oil seed rape in northern Germany was presented, where the yield was increased from 2.7 to 4.1 t/ha, showing that intensification of production can lead to improved sustainability.

The assessment of the economic importance of azoles in European agriculture: wheat case study

Luca Camanzi
Universitá di Bologna, Italy

The study presented evaluated the economic importance of azole a.s. in European agriculture. Two scenarios were analyzed: a "reference" scenario based on current trends of the main wheat markets drivers, yield, area, production, trade balance and consumption; and a "no azoles" scenario, assuming no use of azoles at all. For both scenarios, short-term estimates until 2013 and long-term estimates until 2020 were presented. In the case of the long-term scenario with no azoles, a rise in fungicide resistance was also assumed.

Currently, the EU is the largest single wheat producer in the world, with a very high productivity of 5.3 t/ha, as compared to an average yield of 2.9 t/ha worldwide. The EU is also the second largest wheat exporter with 17% of the world trade. Over the last 5 years, EU wheat exports have increased by 60%. Extrapolating the current trends as described above for the reference scenario, the EU would maintain its present position in the world market, i.e. it would be self-sufficient while at the same time being a net exporter of wheat to the world. Assuming a "no azole" scenario would significantly alter the situation due to the importance of azoles for the efficient production of wheat. The estimates show a decrease of hectare yield by 7.0% in the 2013 timeframe and of 12.2% by 2020, as compared to the reference scenario. Thus, self-sufficiency would fall below 100% and Europe would become a net importer instead of a net exporter of wheat.

In the past, technological progress was faster than growth in population and income, leading to a long-term decline in agriculture commodity prices. In recent years, tight market conditions in terms of strong world population, increased demand for feed, and non-food uses (bio-fuels) along with restrained yield improvement that exerts increasing pressure on prices, has been observed.

Progress in the EU peer review of active substances

Ragnor Pedersen
EFSA, Italy

According to EFSA's management plan 2012, EFSA will adopt 77 conclusions in 2012:

- New a.s under Regulation 188/2011: 47
- Green track a.s. stage 4: 24
- Basic substances: 3
- Post approval conclusions: 3

EFSA has to deliver conclusions on 59 green track a.s. by the end of 2012. Currently, the peer review ongoing for 21 a.s. is scheduled to be finalized in 2012. Major progress has been made with the pending new a.s. program. For 61 of the 71 a.s., the peer review was ongoing or finalized by September 2012; however, for almost all a.s., additional information is needed, leading to a stop of the clock. It is therefore expected that the number of conclusions reached by end of 2012 will be less than 47.

There are two major problems affecting peer review planning:

1. unpredictability at several levels (including stops of the clock at RMS levels and during peer review)
2. important yearly fluctuation of workload.

To resolve these problems, the Pesticides Unit has initiated a program to increase staff flexibility.

To integrate Classification and Labelling and the evaluation of a.s. under Regulation (EC) No. 1107/2009, a working document was generated subsequent to a workshop held in Berlin in April 2011. In addition, EFSA and ECHA have initiated pilot projects to test the procedures.

With respect to confidential business information (CBI), EFSA explained that they are obliged to publish the following information / documents:

- summary dossiers
- applications for renewal
- DARs
- EFSA conclusions.

More information can be found on the EFSA website (www.efsa.europa.eu/en/pesticides/pesticidesconsultations.htm).

Currently, there is particular concern regarding bees and pesticides, in particular neo-nicotinoid insecticides. A scientific opinion was published in April 2011. This will be the basis for a guidance document expected to be finalized by the end of 2012. The opinion proposes separate assessment schemes for honeybees and bumblebees/solitary bees, and improves existing testing procedures. EFSA will deliver conclusions on imidacloprid, thiamethoxam and clothianidin, focusing on the uses for seed treatment and granules by the end of 2012 with a conclusion for fipronil anticipated in March 2013.

Interpretations and experiences with 1107: Member State perspective

Sarah Shore
CRD, UK

CRD is operating under several regulatory regimes and therefore has to adhere to different political masters. CRD is involved in the REACH Regulation, the Biocidal Products

Newsletter
Volume 12, No. 3S, November 2012
SPECIAL EDITION

Directive, PPP Directives and Regulations, Detergents Regulations, and the EU Classification, Labelling and Packaging Regulation. CRD's primary aim is "to ensure the safe use of biocides, industrial chemicals, pesticides, detergents to protect the health of people and the environment". Due to economic pressure in the UK, there are fewer resources available to deliver regulatory results. However, there is political resolve to achieve greater efficiency by improving harmonization. In general, the UK coalition government's approach is to de-regulate as much as possible.

To make the evaluation process work, CRD considers the zonal committees and the post-approval issues group as having a central role. Reality has forced established positions to be challenged, such as national data requirements. CRD has already identified specific areas and is putting a program in place to seek a harmonized position in co-operation with the Central Zone Steering Committee.

It was noted that a hazard-based assessment has no tradition in the UK, and that the traditional risk-based assessment is perferred.

Interpretations and experiences with 1107: Industry perspective

Euros Jones
ECPA, Belgium

Regulation (EC) No. 1107/2009 has been in force since 14 June 2011. It was emphasized that legislation since that date has become more complex and resource intensive. The new Regulation does promote harmonization, but some issues, such as data protection and minor uses, remain national issues or have become even more so with the new provisions in the Regulation.

Major challenges currently constitute the transition from Directive 91/414 and the foreseeable substantial workload to be expected by MS acting as zRMS, as the work is focused on only a few MS. The lists of Candidates for Substitution (CfS) and endocrine disruptors will also result in a significant increase in work for the Commission. Furthermore, there is a significant potential interpreting them as black lists of undesirable a.s. To limit the number of a.s. on the list of CfS, only cut-off candidates could be included.

More clarification and harmonization is needed on the interpretation of grace periods (lack of consistency between Articles 20 and 46), on how to define a greenhouse, authorization on seed treatment, and traffic of treated seeds. Finally, industry reporting on scientific peer-reviewed open literature and adverse effects must be assessed.

A very specific issue that needs to be resolved is the refusal of MS to accept mutual recognition for authorizations granted under Directive 91/414. An issue now clarified by the Commission's new Questions & Answers document is the refusal of a national authorization by the zRMS. Any decision, positive or negative, can be considered as the basis for cMS authorizations.

To overcome the uneven distribution of work between the zRMS, work sharing of zone-independent parts of the dRR should be encouraged. To further such co-operation, the applicant should submit dossiers in parallel as much as possible and inform the different zRMS accordingly.

To further simplify the removal or refinement of national requirements, decisions and information from the zonal and inter-zonal meetings should be made known to applicants. For zonal re-registrations, the implications of Article 43 of Regulation (EC) No. 1107/2009 need to be better understood; in particular, the regular product reviews for mixture products must be revised.

Industry experience with AIR 3

Michael J. Carroll
Dow AgroSciences, UK

The Annex I renewal of a.s. is a massive work program for industry and authorities. To deal with the problems envisioned by the tight timelines set in this program, it is recommended to submit as early as possible.

The registration of a PPP in EU is and remains a two-step process:

- Part 1 – approval of the a.s.: harmonizes the process and criteria for considering the safety of a.s. at EU level and establishes a list of endpoints for regulatory evaluation, resulting in a positive list of a.s. considered safe for use in PPP.
- Part 2 – national authorization of the PPP containing that a.s.: uses the harmonized criteria and endpoints at the national level and allows the PPP (with the a.s.) to be sold at MS level. This step is the key to commercial success.

The EU Annex I renewal (AIR) program is set up in individual waves. AIR 1 was run under 91/414 as a pilot program with all seven a.s. up for renewal now re-approved. Nevertheless, substantial confirmatory data are still outstanding for some a.s., which needs to be submitted and evaluated. AIR 1 took over three years to complete.

In AIR 2, 29 (out of a total of 31) substances are currently being defended under the legal framework of Regulation (EC) No. 1107/2009 and Regulation 1141/2010. The renewal is a two-step process consisting of the submission of an updating statement in 2011 and dossier submission in 2012. The timeframe laid out for AIR 2 anticipates three years for completion.

AIR 3 will cover 150 a.s. whose approvals will expire between 1 January 2013 and 31 December 2018. They are separated into three groups. Similar to AIR 2, it will be a two-step process: application, including information on new

Newsletter
Volume 12, No. 3S, November 2012
SPECIAL EDITION

data submission in 2013 through 2015; and subsequent dossier submission in 2014 through 2016.

In the AIR 3 process, pre-submission meeting(s) – as many as might be required and possible – are of utmost importance in order to establish a common understanding between the applicant, the rapporteur and co-rapporteur MS. Important issues to be clarified include:

- new data developed since Annex I inclusion and (new) data requirements to obtain renewal
- reference technical specification
- classification and labelling
- applicable guidelines.

The supplementary dossier to be submitted should address/include:

- copy of the application
- new data, study reports, summaries and risk assessments
- information on one or more representative uses on widely grown crops in each zone
- solo formulation is preferred
- summary on biological efficacy
- summaries and results of scientific peer reviewed open literature
- MRL dossier (if changes are proposed)
- C&L dossier (if changes are proposed)

The total evaluation process is assumed to take 36 months from the date of submission of the supplementary dossier to the RMS and co-RMS.

To assess the full workload of the MS, it is mandatory to include the post AIR 3 ("AIR4") program, as well as the mandatory re-assessments and re-authorizations of the PPP. Assuming an average of four PPP per a.s., the following number of assessments required within the re-authorization program (in addition to the renewal program) would be needed:

Year of AIR	Number of a.s.	Number of PPP (a.s. x 4)	Date for dossier submission (re-authorization)
AIR 1 (2012)	7	28	2013
AIR 2 (2015 – 2019)	29	116	2014 – 2015
AIR 3 (2017 – 2019)	150	600	2017 – 2019
Post AIR 3 (2019 – 2022)	211	844	2019 – 2022

The regulation of co-formulants under Regulation (EC) No. 1107/2009 and REACH

Kerry Gamble
Syngenta, CH

Co-formulants are all ingredients of a PPP, except the active substance. Regulation (EC) No. 1107/2009 stipulates in Article 27 that co-formulants shall not be accepted for inclusion in a PPP if they have harmful effects on human or animal health or groundwater, or if they have an unacceptable effect on the environment. Unacceptable co-formulants will be included into Annex III of Regulation (EC) No. 1107/2009. This annex is still empty and Article 81 allows national provisions until 14 June 2016. Such provisions exist in Germany and Spain, which have lists of banned substances.

The chemicals identified as co-formulants under Regulation (EC) No. 1107/2009 are also subject to evaluation under REACH, whose aim is also to protect human health and the environment from risks arising through the use of chemicals. A draft guidance document for the handling co-formulants under Regulation (EC) No. 1107/2009 is currently being circulated.

ECPA's recommendation is that REACH be the relevant legislation for the regulation of co-formulants in PPPs and that Annex III of Regulation (EC) No. 1107/2009 should to be populated with the outcome of the REACH evaluations, as dual regulation would place an unnecessary administrative and financial burden on authorities and industry.

The procedures established under REACH for down-stream users to amend the extended safety data sheet and assessment schemes are available on the ECPA homepage (http://www.ecpa.eu/information-page/regulatory-affairs/reach).

Comparative assessment from a Member State perspective

Pavel Minár
State Phytosanitary Administration, CZ

(Due to the unexpected absence of the author, the presentation was given by Maarten Trybou (Belgian authorities).

According to Article 80 of Regulation (EC) No. 1107/2009 the Commission has to establish a list of candidates for substitution (CfS). This list must take the legal form of a Regulation to amend the approval regulations already issued for the a.s. renewals. In the future, the original Regulation approving an active substance will, at the same time, specify whether it is a CfS or not. Nothing can be said yet with regard to the contents of the list.

Article 50 of Regulation (EC) No. 1107/2009 obliges the MS to perform comparative assessments and substitution of PPP containing CfSs at certain times/intervals.

Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

An EPPO guideline is available since September 2011 regarding the evaluation of efficacy and resistance management, which, it was emphasized, must be considered to be an integral part of any substitution. Furthermore, a guidance document is under preparation by Sweden addressing the other issues of substitution in the form of a decision tree. EFSA and some MS (at least Belgium) have already commented upon it. Anticipated completion date is December 2012.

The criteria for classifying an a.s. as CfS, as specified in Annex II point 4 of 1107, were laid out:

An active substance will be approved as a candidate for substitution pursuant to Article 24 where any of the following conditions are met:

- its ADI, ARfD or AOEL is significantly lower than those of the majority of the approved active substances within groups of substances/use categories,
- it meets two of the criteria to be considered as a PBT substance,
- there are reasons for concern linked to the nature of the critical effects (such as developmental neurotoxic or immunotoxic effects) which, in combination with the use/exposure patterns, amount to use situations that could still cause concern, e.g. high risk potential to groundwater; even with very restrictive risk management measures (such as extensive personal protective equipment or very large buffer zones),
- it contains a significant proportion of non-active isomers,
- in accordance with the provisions of Regulation (EC) No 1272/2008, it is or is to be classified as carcinogen category 1A or 1B, if the substance has not been excluded in accordance with the criteria laid down in Regulation (EC) No. 1107/2009 Annex II Article 3.6.3;
- in accordance with the provisions of Regulation (EC) No 1272/2008, it is or is to be classified as toxic for reproduction category 1A or 1B if the substance has not been excluded in accordance with the criteria laid down in Regulation (EC) No. 1107/2009 Annex II Article 3.6.4;
- if, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information reviewed by the Authority, it is considered to have endocrine disrupting properties that may cause adverse effects in humans if the substance has not been excluded in accordance with the criteria laid down in Regulation (EC) No. 1107/2009 Annex II Article 3.6.5.

It was indicated that the criteria contained undefined clauses, such as “significantly lower” or “significant proportion”.

Subsequently, the criteria for substitution as given in Article 50 of Regulation (EC) No. 1107/2009 were detailed.

A comparative assessment restricts the use of a plant protection product containing a candidate for substitution to particular crops where the comparative assessment, weighing the risks and benefits as set out in Annex IV, demonstrates that:

(a) for the uses specified in the application, an authorized plant protection product or a non-chemical control or prevention method already exists that is significantly safer for human or animal health or the environment;

(b) the substitution of plant protection products or non-chemical control or prevention methods referred to in point (a) does not present significant economic or practical disadvantages;

(c) the chemical diversity of the a.s., where relevant, or methods and practices of crop management and pest prevention are adequate to minimize the occurrence of resistance in the target organism; and

(d) the consequences on minor use authorizations are taken into account.

The following important points were emphasized by the presenter:

1. if a product was also granted a minor use, the other uses should be protected against substitution, as only the minor use would not allow the producer to support the product in the market.
2. in general, substitution is unlikely to occur because the farmer’s toolbox is already significantly depleted and chemical diversity in crop management is not guaranteed even with all the exiting authorized uses.

Taking practical considerations into account, some proposals were made:

- new authorization should be possible for 5 years without comparative assessment to gain detailed knowledge of the product.
- if an authority refuses or changes an authorization based on substitution, these amendments should enter into force three years after the decision or at the approval expiry date.

Candidates for substitution and comparative assessment: Industry’s perspective

Martyn Griffiths
Bayer SAS, FR

The three-layer process to PPP authorization was presented:

1. a.s. first will be evaluated against hazard cut-off criteria
2. a.s. will be evaluated against risk criteria
3. PPP containing an a.s. which is a CfS will be subject to comparative assessment and their uses may be subject to substitution

Identifying CfS is a complex area. ECPA proposes that the CfS criteria:

Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

- must meet the Regulation (EC) No. 1107/2009 definition
- CfS status must be predictable
- criteria must not catch unnecessarily high numbers of a.s.

As there is currently no authority proposal available, ECPA proposes the following definitions of the uncertain terms used in Regulation (EC) No. 1107/2009:

(a) significantly lower ADI, ARfD or AOEL:

- groups and uses categories = functional groups (insecticides, fungicides etc.)
- majority = all substances approved in functional group, represented by their median value
- significantly lower = < 0.05 x median

(b) it meets two of the criteria to be considered a PBT substance:

- apply scientific rigor in identifying PBT properties (detailed rules needed; to be detailed in separate ECPA position paper)

(c) reasons for concerns linked to critical effects:

- critical effects to be severe in nature and drive risk assessments
- risk to ground water to be demonstrated by monitoring data (not by modeling only!)
- very large buffer zones not necessary when drift reduction technology available

(d) contains a significant proportion of non-active isomers:

- only when purification is possible and pure isomer approved
- significant is >25%
- non-active = biological activity less or equal to 10% of most active isomer on any target

Comparative assessment rules and criteria were integrated into a decision tree. It was indicated that PPPs containing a CfS are eligible for mutual recognition within one political zone, but not across zones.

There was considerable concern on the reception of the list of CfS to be published by the European Commission on 14 December 2013. It is essential for authorities and industry to communicate that this list must not be misused as a "black list" by NGOs and the food chain industry, as all the a.s. on the list have been thoroughly assessed by authorities and were found to be safe and satisfying all the requirements for approval!

It was emphasized that the re-introduction of substituted uses should also be considered when the situation leading to substitution changes. If non-chemical methods are considered an alternative, they too must be evaluated for safety and suitability.

Examining the zonal authorization process – Feedback from the Central Zone

Darren Flynn
CRD, UK

The three zones described in Regulation (EC) No. 1107/2009 were introduced and the concepts of zRMS and MR described. It was emphasized that Regulation (EC) No. 1107/2009 applies directly in the MS. The concept of zonal authorization as laid down in Regulation (EC) No. 1107/2009 is further elaborated in guidance documents, such as SANCO/13169/2010. The tight timeframe of the zonal authorization procedure was explained: a pre-submission meeting six months prior to dossier submission was proposed, with authorization in the zRMS expected 12 months after submission and in the cMS 4 months later. The ability to meet the given deadlines is influenced by the quality of the submission, the capacity of the zRMS, and the extent of commenting during the evaluation period.

It was acknowledged that some MS are now at (or beyond) their limit to act as zRMS. To remedy this situation, MR from another zone was encouraged. Furthermore, "zonal independent" parts of the risk assessments, such as phys.-chem., analytic, toxicology, should be shared for evaluation between zRMS of different zones. Applicants should time their submissions to facilitate such work sharing and should alert the zRMS of each other. At the same time, it was pointed out that Article 75 (3) of Regulation (EC) No. 1107/2009 stipulates "MS shall ensure that the competent authorities (CAs) have a sufficient number of suitable qualified and experienced staff to meet obligations".

A single dRR and a single zRMS for the whole EU is sufficient for inter-zonal applications. Currently the definition of greenhouses (and its differentiation to protected uses) is being taken forward by EFSA. In addition, a guidance document for the risk assessment for seed treatments is under preparation, clarifying how seed treatment might be independent of the zone, but that sowing of the treated seed might differ between zones.

In the commenting phase, the zRMS will upload Part A and B of the dRR on CIRCA and send an email alert to the MS. At the same time, the applicant will be given the possibility to comment. Commenting is not a requirement and it is now a common understanding that not to comment does not constitute an acceptance of the dRR in a future MR. It was proposed and discussed in the Central Zone steering committee that procedures for which no technical assessment was made should not be uploaded for commenting.

The open question on how to proceed in the cMS if the zRMS refuses authorization has been settled in the Commission's new Questions & Answers document and was addressed previously. The existing guidance document will be amended to reflect this new clarification.

Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

The European Commission has confirmed that an MR based on an authorization according to Directive 91/414/EEC and a valid evaluation within Uniform Principles may not be refused.

The 120-day timeframe for MR applies only to identical products and uses. If there are deviations, the normal procedure as described in Article 33 of Regulation (EC) No. 1107/2009 is to be followed.

It was acknowledged that in the Northern and the Southern zones, significant progress has been made in the harmonization of risk assessments and/or management. Work is now also starting in the Central zone and there is a strong political interest for increased harmonization. Concern has been voiced, however, that the harmonization within the zones might (but must not) lead to three sets of requirements, resulting in divergence rather than convergence.

Feedback from the Central Zone

Christian Prohaska
Austrian Agency for Health and Food Safety, AT

The variety of different applications MS currently have to deal with was presented:

- Step 2 (re-registrations according to Directive 91/414/EEC)
- Applications according to Article 33 of Regulation (EC) No. 1107/2009
- Applications according to Article 40 of Regulation (EC) No. 1107/2009 (mutual recognition)
- Mutual recognition based on PPP registered according to Directive 91/414/EEC
- Renewal according to Article 43 of Regulation (EC) No. 1107/2009
- Application according to Article 37.3 of Regulation (EC) No. 1107/2009
- Applications according to Directive 91/414/EEC (submission prior to 14 June 2011)

As of the end of July 2012, the central zone countries (total number: 13!) had to handle 303 applications for first authorization of PPP (not including amendments) and more than 300 applications for re-registration (step 2 according to Directive 91/414/EEC) in addition to amendments and MRs. An unusually large number of applications were submitted just prior to 14 June 2011. The highest number of submitted dossiers or intended submission of dossiers between 2012 and 2014 were for UK with 32.3%, Germany in second place with 26.4% and Austria third with 14.5% of total.

To overcome this heavy workload, it was pointed out that Article 75.3 of Regulation (EC) No. 1107/2009 explicitly obliges MS to support competent authorities with sufficient staff. In addition, it was noted that "new" MS must be integrated into the system by also establishing on the zonal level a mechanism of co-RMS and by encouraging applicants to seek zRMS other than the well-established ones. Austria is currently co-operating with Slovenia, the Czech Republic and, across zones, with France. To further work sharing across zones, the independent parts of the dRR should only be evaluated by one zRMS. To further build trust into such additional work sharing, MS of other zones than the one addressed by a given zRMS should also be included into the commenting procedure.

It was highly emphasized that communication is also key to solving the problem. This includes communication with the applicant including expert-to-expert communication!

To improve the quality of the dRR, it was proposed that each dRR must be a "stand alone document": no cross reference to other RRs or national evaluations should be made. References to the EFSA conclusion/DAR should include a short executive summary and justification where appropriate.

The integration of confirmatory data in the national evaluation was addressed. For new applications, it was recommended that the evaluation of the confirmatory data by the RMS should be awaited. Otherwise, the endpoints agreed in the standing committee at the time of application should be employed.

With respect to setting MRLs, it was highlighted that a MRL must be in place prior to authorization. Therefore, the MRL application should be made in advance of the application for registration. The EMS should be the zRMS in that zone to which the higher MRL may apply.

Classification and labelling must also be done in parallel to evaluation of a registration application. Otherwise, it might be possible that the same product might be classified differently in individual MS. In July 2012, a new EFSA opinion was published on the toxicological relevance of pesticide metabolites for dietary risk assessments. It was clearly stated that more harmonization is needed in this area. Whether classification should be done by self-classification under the responsibility of industry or if classification is the responsibility of the MS competent authority has been addressed in a letter from the Commission to EFSA on 25 April 2012, which clearly puts the responsibility on the MS CA.

Feedback from the Southern Zone

Thierry Mercier
Anses, FR

Before the implementation of Regulation (EC) No. 1107/2009, France collected experience with the zonal procedure through voluntary work sharing. France has acted as zRMS in approximately 90 applications. To cope with the high number of applications, a good predictability of the work load, common procedures and formats for the evaluation, good knowledge of specific requirements (where applicable) as well as adequate capacities in each MS are

Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

needed. Also, the exchange between MS, the zonal Steering Committee and the inter-zonal Steering Committee are very important.

During the pre-meeting, the zRMS and the applicant must discuss the GAP and the data that should be incorporated into the core dossier as opposed to the national addenda, along with other critical issues that are case-to-case decisions. It is also important that the applicant inform the zRMS if the submission is to be postponed. If France will not be able to act as zRMS upon request of an applicant at a certain desired date, France will always be able to propose a submission date two to four months later to fulfill the request if asked early enough.

To facilitate the evaluation, the applicant should indicate important points in the application cover letter. France usually does not grant a full six-month stop-of-the-clock for an initial request. When submitting additional information, or having updated the dRR after a stop of the clock, the changes should be clearly indicated and highlighted by the applicant.

It was again emphasized that the dRR must be a stand-alone document instead of referring to other RRs or national evaluations: the respective part should be copied and pasted into the dRR under evaluation.

Whenever France is involved in an application for authorization, all residue trials (North and South) must be included and assessed in the core dossier.

Addressing issues in the national addenda instead of the core dossier must be justified. For France such specific requirements could be ground water modelling (refined scenarios) or home and garden uses.

The dRR format is currently under revision.

Clarification on the process etc. is available on the ANSES homepage (http://www.anses.fr).

The zonal authorization procedure - A view on data requirements, dossier submission and evaluation. An applicant's perspective.

Bernd Brielbeck
SCC Scientific Consulting Company, DE

The presentation focused on the applicant's perspective of the zonal authorization process. To facilitate that process, the applicant should strive to harmonize the formulations and GAPs as much as possible across the zone.

The respective guidance document (SANCO/13169/2010) emphasizes the role of the zRMS by clearly stating that "…Once the zonal RMS has been appointed, the other MS in the zone shall refrain from proceeding with the assessment of their application, waiting for the assessment from the zonal RMS, in order to avoid duplication of work", and "…Other MS must not re-evaluate the application but shall restrict the assessment to their national requirements…".

Furthermore, the need and importance of an early involvement of the intended zRMS as well as key cMS into the process was emphasized and the different ways MS are handling this request addressed. Also, direct expert-to-expert contacts are handled very differently by different MS.

An area of particular concern is efficacy and further guidance is needed on the adjustment of the three political zones of Regulation (EC) No. 1107/2009 with the underlying four EPPO zones of comparable climates. In addition, particular disharmony currently persists on how and where efficacy data is to be presented with respect to the biological assessment dossier (BAD), core dRR and/or national addenda of the dRR. However, guidance is under development to this respect.

Also highlighted was the rise of new completeness check documents. These documents are considered pertinent to facilitating and accelerating the evaluation by the MS, but a need for harmonization of the different national documents was identified.

In the upcoming revision of the dRR format, whose implementation is foreseen in the second half of 2013, will address the following points (among others):

- Introduction of a new part B Section 0 (for available approvals, a.s. data, etc.)
- All information to be included in the core dossier
- Revision of all sections to avoid duplication of information
- National GAPs to be presented in Part A
- Data protection claims to be addressed in a reference list in Part A (national issue!)

In the evaluation of an application for PPP authorization, the acceptance of new Annex II data varies between different MS. Also, accessibility of authorities and authority experts during evaluation is very different.

Classification and labelling – CLP, harmonized classification and the CLP inventory

Rocky Rowe
ECPA, BE

The CLP implementation schedule was detailed in the presentation. It was emphasized that Article 4 of the CLP Regulation (Regulation (EC) No. 1272/2008) places the responsibility of classification and labelling (C&L) clearly on the manufacturers and/or importers. MS competent authorities (MSCA) argue with a view on Article 31.2 para 2 of Regulation (EC) No. 1107/2009 that this duty is placed on the MSCA authorizing PPP. An opinion expressed by Sweden at a recent SCFCAH meeting supports the ECPA

Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

interpretation above while the EU Commission's legal opinion is different.

In the different procedures for C&L currently in use, it is essential that consistency of C&L for similar or identical products must be assured across the EU.

With the implementation of the CLP Inventory, a major concern for industry was that there was tonnage cut off such that even small (R&D) samples would need notification, resulting in concerns over confidentiality. The EU Commission has meanwhile confirmed that total confidentiality would be maintained.

ECHA, through the Risk Assessment Committee (RAC), exclusively manages the process of harmonized classification and is currently completely uncoordinated with the authorization process of PPP (or biocides). The process focuses solely on hazard assessment and classification criteria. There is no risk assessment. In this process, there is very limited possibility for intervention by industry.

First indication of a RAC process is the notification of intent to submit a CLH dossier by the MSCA. As the possibilities for intervention are limited, companies should take this opportunity to engage in the process. This intention to submit, as with all the other subsequent steps of the process, are announced on the ECHA homepage (http://echa.europa.eu/web/guest/registry-current-classification-and-labelling-intentions). The subsequent steps are:

- MSCA submits its CLH proposal
- Final CLH proposal, after ECHA scrutiny, goes to public consultation
- Draft opinion is prepared and circulated together with public comments (last chance to submit new information!)
- Rapporteur presents proposal to RAC
- RAC meeting(s) (to a very rigid timetable (18 months; even shortening commenting phases to meet it)
- Adoption into legislation.

Currently evaluations under Regulation (EC) No. 1107/2009 and CLP are not linked. They are handled under different data formats, i.e. CADDY and IUCLID, and by different competent authorities. There are intentions to harmonize the approaches. For PPP companies it is therefore very important to also consider CLH in their AIR 3 process.

New toxicology data requirements under SANCO/11802/2010 Rev. 7 for PPP

David Esdaile
CiToxLAB, HU

On 12 July 2012 the Standing Committee voted upon the new data requirements, intended to enter into force on 1 January 2014. In line with the intentions of Regulation (EC) No. 1107/2009 to discourage vertebrate studies, they emphasize the use of *in vitro* and *in silico* methods over *in vivo* tests, at least as initial stages of the assessment.

One new data requirement in the toxicological section is the routine presentation of historical control data for a 5-year period. The details required of these historical data for submission are much more extensive than in any other legislation, including pharmaceutical legislation. Another new requirement is the need for phytotoxicity testing.

Examples of the revised assessments required by the new legislation were given. In the case of eye and skin irritation, the preference of *in vitro* over *in vivo* methods will most probably lead to an over prediction of the effects and thus more severe classifications. Also noted was that the *in vitro* methods required have already been in use under the REACH regime and were developed and validated for chemicals, but not for PPP.

A Dutch viewpoint on data

Lars Hogendoorn
Ctgb, NL

Every applicant has to prove the safety of his PPP. This burden is placed on each individual applicant by the concept of data protection.

Data protection granted for studies is linked to a set of criteria:

- Necessity for authorization/amendment of an authorization
- GLP / GEP compliance
- Data protection was claimed
- "Declaration of honesty" (i.e. no earlier period of data protection was already granted)

Data is protected for:

- 10 or 13 years (low risk PPP) for new approval/authorization
- An additional three months for every minor use
- 30 months for renewal/review of authorization (for many applications Directive 91/414/EEC still applies!).

The Netherlands already had a two-step approach to sharing vertebrate studies prior to Regulation (EC) No. 1107/2009. Without a proper justification, no new vertebrate studies are accepted. The companies involved in data sharing are informed by the Dutch authority and are requested to enter into negotiations on compensation. If the negotiations fail, they can enter voluntarily into mediation by Ctgb, the decisions of the mediation are nevertheless binding.

Another aspect presented are confirmatory data. From a national perspective, they are not to be considered

Newsletter
Volume 12, No. 3S, November 2012
SPECIAL EDITION

"confirmatory" because they are mandatory in the decision-making on the authorization of a PPP.

Finally, the propamocarb verdict by the Dutch CBB (Trade and Industry Appeals Tribunal) on 13 January 2012 was presented, forcing Ctgb to give access to the regulatory data of that a.s. to NGOs. In response to the verdict, Bayer recently opened a reading room with data to three environmental groups.

Experiences with data sharing, data protection and confirmatory data under Regulation (EC) No. 1107/2009

Claudio Mereu
Field Fisher Waterhouse LLP, BE

Article 59 is the legal basis for data protection in Regulation (EC) No. 1107/2009. The data protection period, if applicable, will commence under Regulation (EC) No. 1107/2009 as of the first authorization of a PPP containing the a.s. in each MS. The actual data protection period, although identical in length, can thus be different in each MS. The data protection periods with respect to the different possible cases were detailed.

The legal basis for the data-sharing requirement in Regulation (EC) No. 1107/2009 is laid down in Articles 61 to 62. It was emphasized that these provisions apply to all studies (including non-vertebrate and even non-animal), but are only penalized for vertebrate studies, i.e. use of said data by the authorities, if no agreement is reached by the parties involved (with the data owner having a claim on a fair share of compensation). It was also stressed that the legal texts contain many uncertain terms, such as "every effort", "an attempt" and "sufficient time", "fair share" and "costs".

Currently there is no European system of mandatory data sharing and arbitration, but many MS, such as UK, Italy, Spain, and Greece, adhere to their own procedures. Others have no system implemented.

Under Article 60, the RMS is obliged to prepare a list of studies that were necessary for the first approval (or amendment/renewal) and each MS shall keep the list available for "interested parties". It was noted that it is not clarified as to what constitutes an "interested party" (versus a "prospective applicant") and whether that definition might include NGOs.

Under AIR 2, it is stipulated that applicants shall take all reasonable steps to submit dossiers jointly. If not, applicants must state reasons and provide details of the attempts made to avoid duplicate testing.

AIR 3 allows for a joint application to be submitted by an authorized representative. If dossiers are not submitted jointly, applicants must again state reasons and provide details of the attempts made to avoid duplicate testing.

Also noted in the presentation was that Regulation (EC) No. 1107/2009 refers to studies "involving" animals when speaking of vertebrate studies. Therefore, vertebrate studies do not necessarily involve the sacrifice of animals. In Regulation (EU) No. 544/2011 and Regulation (EU) No. 545/2011, the scope of studies was widened by making reference to Directive 86/609/EEC on the protection of endangered species, which meanwhile has been repealed by Directive 2010/63/EU on the protection of animals used for scientific purposes.

A letter of access (LoA) is defined in Regulation (EC) No. 1107/2009 and linked to the authorization of PPP. Addressed to the MS authorities, it confirms the right to cite and rely upon studies. Any use restriction, such as territorial coverage, identity of licensee, list of studies, conditions and period of validity should be specified in the LoA. It is important to keep in mind that antitrust issues must be considered when issuing or refusing to issue LoAs.

Finally, the much more concise and clear system of data protection and data sharing in the US under FIFRA was presented.

Integrating MRL setting in other EU procedures

Katrin Franke
Federal Institute for Risk Assessment (BfR), DE

An effective integration of the evaluation schemes of the following legislation is strongly recommended:

- Regulation (EC) No. 1107/2009 concerning the placing of plant protection products on the market (dealing in two individual procedures with a.s. and PPP)
- Regulation 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin
- Regulation 1272/2008 on classification, labelling and packaging of substances and mixtures

These are four legally independent procedures, but with overlapping content that needs to be presented in different template formats. Their dependence on each other was demonstrated by indicating that PPP can only be authorized after a.s. approval and an MRL has been set for the a.s. and for each use requested. The a.s., in turn, can only be approved if it does not fall within the cut-off criteria derived from the CLP legislation.

Approval of the a.s., setting the MRL, and C&L of the substance should be done in parallel. Also, the evaluation and the individual pieces of documentation, DAR, dRR, MRL-ER and the CLP dossier should be harmonized, preferably to a modular set-up that would allow compilation of the respective documentation from the available assessments. In the long run, it was proposed that the IUCLID format be used.

Newsletter

Volume 12, No. 3S, November 2012

SPECIAL EDITION

Examining the regulatory procedure of PPP for use in the home and garden

Maarten Trybou
Federal Public Service for Public Health,
Food Chain Security and Environment, BE

A conflict between Regulation (EC) No. 1107/2009, requiring more harmonization between the MS, and Directive 2009/128/EEC, the sustainable use directive (SUD), placing the impetus of heightened protection of the non-professional user on the MS authority, was pointed out. The measures requested by the SUD may include the use of pesticides of low toxicity, ready to use formulations and limits on sizes of containers or packaging. Regulation (EC) No. 1107/2009, on the other hand, stipulates that PPP that comply with the prerequisites as laid down in that legislation must be authorized, i.e. MS are obliged to authorize them. The SUD includes additional cut-off criteria (excluding most toxic PPP) and places additional requirements on formulation types and packaging. As these additional requirements of SUD can only be laid down in national legislation, harmonization cannot be enforced across MS. Although the lecturer did not see a legal conflict in these provisions, the practical conflicts are manifold!

In 2010, Belgium adopted legislation implementing the additional criteria and procedures to distinguish between professional and non-professional uses. Starting August 2012, distinct authorizations for both areas will be granted.

Apart from the big and important issues relating to toxicological and environmental subjects, the following shows some examples of the extra criteria in place in Belgium:

- Packages must be described and a specimen submitted, including a measuring cup (!) and childproof closure
- Measuring cups must have realistic measuring indications and units
- Packaging must be re-sealable
- Label must carry dose rate in appropriate units (mL or g per L) and needed quantity in L per m^2 (for molluscicides: number of granules per m^2), as well as indicating the total possible treatment area of the whole pack.
- Label must not carry misleading or reassuring information or photos.

Only ready-to-use or formulations to be diluted/dissolved in water are to be authorized in Belgium. Powders must be applied in water-soluble bags unless suitable alternatives are available. The application types must be in line with the non-professional user's possibilities. For operator exposure, only specific models and the use of gloves are acceptable. In aquatic exposure, a maximum buffer zone of 10m is acceptable. Combination products can only be authorized when all diseases and pests are simultaneously present. In combinations of fertilizers with herbicides, the dose rate proposed must be demonstrated for both uses.

As these are clearly national provisions for Belgium, they must be compiled in the national addendum of the dRR. In case of MR, specific assessments are made by the Belgian authorities to ensure compliance with these national regulations. In parallel import applications, particular attention has to be placed on the packaging and re-packaging is necessary. It was recognized that the provisions in the SUD create difficulties for zonal evaluation, mutual recognition and parallel import of home and garden products.

SCC Scientific Consulting Company Chemisch-Wissenschaftliche Beratung GmbH
Dr. Friedbert Pistel, President
Am Grenzgraben 11 · D-55545 Bad Kreuznach
Phone +49 (0) 671-29846-0 · Fax +49 (0) 671-29846-100
scc@scc-gmbh.de · www.scc-gmbh.de

Liaison Office Japan
14-24 Tokiwadai,
Kashiwa-shi
Chiba-Ken 277-0087, Japan
Phone/Fax.: +81 (0)4-7162-4262

Mr. Toshiyasu (Ted) Takada, Director
e-mail: toshiyasu.takada@scc-japan.com

Liaison Office Japan
6-2-14 Asagayakita,
Suginami-ku
Tokyo 166-0001, Japan
Phone/Fax.: +81 (0)3-6762-5261

Mr. Kenji Makita, Senior Consultant
e-mail: kenji.makita@scc-japan.com