Annual Biocontrol Industry Meeting Lucerne

EFSA and List-4 Review

by Ulf Heilig – IBMA Global

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EFSA (European Food Safety Authority) [AESA]

- **Creation in 2002**
  Involved in PP **active substance assessment** for all procedure in which the completeness decisions was taken **from 1st July 2002** onwards.

- **Location**
  Via Carlo Magno 1A,
  I-43126 **Parma**,
  Italy

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EFSA – Who is who?

- Science Directorate of Regulated Products includes:
  ⇨ **Pesticides Unit** (formerly PRAPeR)
  Head: *Herman Fontier*

  Can organise Pesticide Peer Review Meetings with MS experts and WGs

- EFSA Scientific Committee and 8 Scientific Panels which include:
  ⇨ **PPR Panel** [Panel on PPPs and their Residues]

- Coordination with Member States:
  ⇨ **PSC** [Pesticide Steering Committee]

EFSA – Mission and tasks related to Pesticides

Scientific Evaluation of Regulated of Products

- ➜ **Scientific advice on the risk assessment** [RA] of pesticides, incl. development of RA methodologies
- ➜ **Peer review** of safety of all active subst. used in PPPs in the EU
- ➜ RA in the framework of **MRL setting**
- ➜ Preparation of the **Annual Report on Pesticides Residues** based monitoring by Member States incl. assessment of the actual consumer exposure to pesticide residues

Who can ask EFSA to take action?

COMmission – Member States – Members of European Parliament [MEPs] – Own-initiative

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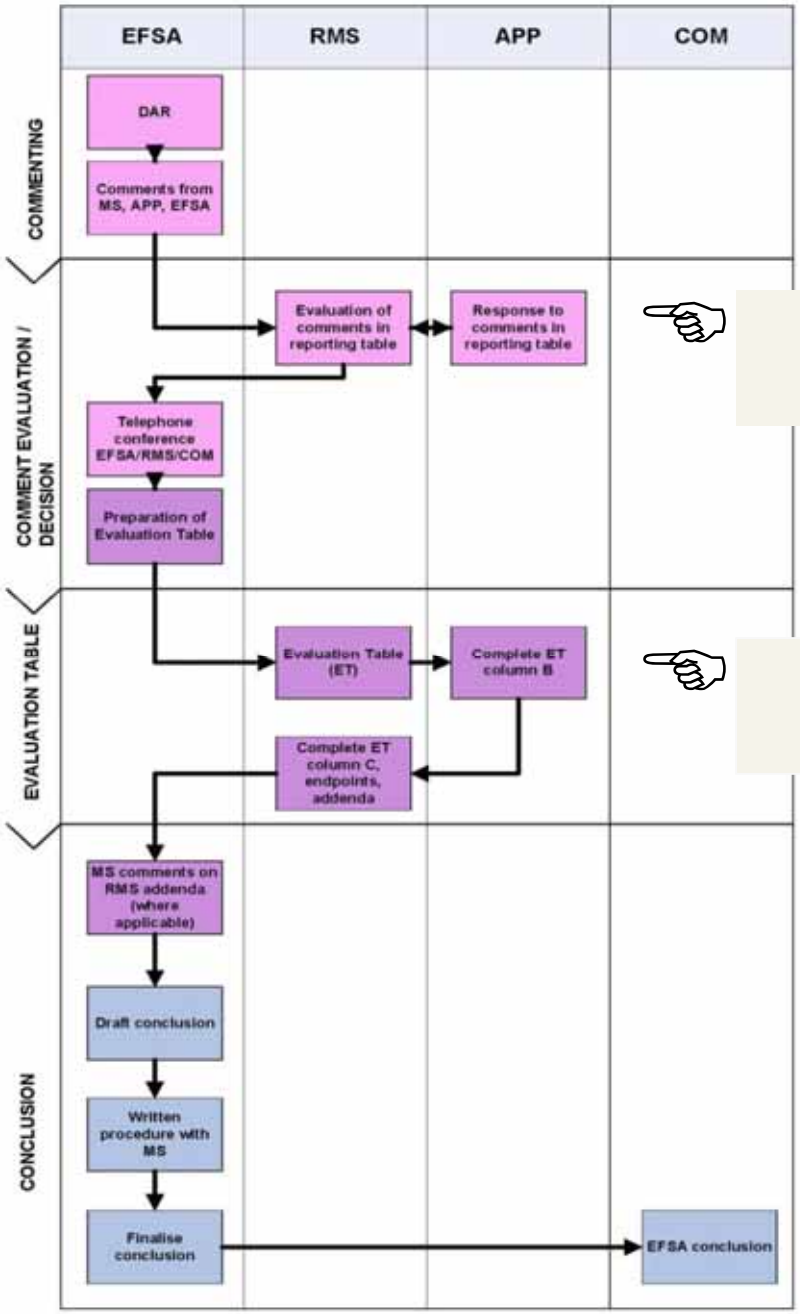
EFSA

List-4 review and conclusion procedure



Applicant input into **reporting** table

Applicant input into **evaluation** table

EFSA

List-4 review and conclusion procedure

with **expert** consultation

Current status of EFSA list-4 review

Microorganisms: 17 were green-track included

- *Bacillus thuringiensis subsp. aizawai*
- *B. t. subsp. israelensis*
- *B. t. subsp. kurstaki*
- *B. t. subsp. tenebrionis*
- *Beauveria bassiana*
- *Cydia pomonella* Granulose Virus (CpGV)
- *Lecanicillium muscarium* [*Verticillium lecanii*]
- *Metarhizium anisoplae*
- *Phlebiopsis gigantea*
- *Pythium oligandrum*
- *Streptomyces* K61 [*St. griseoviridis*]
- *Trichoderma aspellerum* [*T. harzianum*]
- *T. atroviride* [*T. harzianum*]
- *T. gamsii* [*T. viride]*
- *T. harzianum Rifai*
- *T. polysporum*
- *Verticillium albo-atrum* [*V. dahliae*]

Current status of EFSA list-4 review

Microorganisms: 4 conclusions, 13 in progress

- ☞ *Bacillus thuringiensis subsp. aizawai*
- ☞ *B. t. subsp. israelensis*
- 👍 *B. t. subsp. kurstaki*
- ☞ *B. t. subsp. tenebrionis*
- ☞ *Beauveria bassiana*
- 👍 *Cydia pomonella* Granulose Virus *(CpGV)*
- 👍 *Lecanicillium muscarium* [*Verticillium lecanii*]
- 👍 *Metarhizium anisoplae*
- ☞ *Phlebiopsis gigantea*
- ☞ *Pythium oligandrum*
- ☞ *Streptomyces* K61 [*St. griseoviridis*]
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- ☞ *T. atroviride* [*T. harzianum*]
- ☞ *T. gamsii* [*T. viride]*
- ☞ *T. harzianum Rifai*
- ☞ *T. polysporum*
- ☞ *Verticillium albo-atrum* [*V. dahliae*]

Source: Efsa Register of Questions, 12/10/2012

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Current status of EFSA list-4 review

Botanicals (plant extracts): 11 were green-track included

- Extract from tea tree (RE)
- Garlic extract (RE)
- Gibberellic acid (PG)
- Gibberellins (PG)
- Pepper (RE)
- Citronella oil (HB)
- Clove oil (RE)
- Rape seed oil (IN, AC)
- Spearmint oil (PG)
- Sea-algae extract (PG)

- synthesised: Ethylene (PG)

[+ pyrethrins (IN)]

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Current status of EFSA list-4 review

Botanicals (plant extracts): 10 conclusions, 1 in progress

- Extract from tea tree (RE)
- Garlic extract (RE)
- Gibberellic acid (PG)
- Gibberellins (PG)
- Pepper (RE)
- Citronella oil (HB)
- Clove oil (RE)
- Rape seed oil (IN, AC)
- Spearmint oil (PG)
- Sea-algae extract (PG)
- synthesised: Ethylene (PG)

[+ pyrethrins (IN)]

Source: Efsa Register of Questions, 12/10/2012

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Current status of EFSA list-4 review

SCLPs and other Semiochemicals were green-track included

- **SCLP**: group as a whole;
  22 individual compounds;
  "blends" and "blend mixtures"
- Two **non-SCLP** pheromones:
  (Z)-13-Hexadecen-11yn-1-yl acetate
  (Z,Z,Z,Z)-7,13,16,19-Docosatetraen-1-yl isobutyrate
- Three non-pheromone semiochemicals:
  Ammonium acetate;
  Hydrolysed proteins;
  Trimethylamine hydrochloride.

Current status of EFSA list-4 review

SCLPs and other Semiochemicals were green-track included

- ☞ SCLP (group and related inclusions):
  - ♦ Review was scheduled among last ones ⇨ in progress
  - ♦ TF (+ members) responded to Reporting Table in Jan and to draft Evaluation Table in Aug 2012.
  - ♦ Will there be an expert consultation?
- ☞ Two non-SCLP pheromones:

  (Z)-13-Hexadecen-11yn-1-yl acetate
  (Z,Z,Z,Z)-7,13,16,19-Docosatetraen-1-yl isobutyrate

- 👍 Three non-pheromone semiochemicals:

  Ammonium acetate;

  Putrescine (1,4-diaminobutane);

  Trimethylamine hydrochloride.

Source: Efsa Register of Questions, 12/10/2012

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EFSA review programme in general

Access to up-to-date information …

"Register of Questions" on status, dates and reference of publications in EFSA Journal

http://registerofquestions.efsa.europa.eu/roqFrontend/questionsListLoader?panel=ALL

- Choose **Unit Filter** → "*Pesticides*"
- And **Food Sector Area** → "*Pesticides Peer Review included active substances (green track)*"
- Use **Status Filter** → …

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EFSA general approach to review

- EFSA conclusion gives opinion but no decision yet
- EFSA highlights data gaps
- In a **workshop** organised jointly by ECPA and IBMA with EFSA on 26/04/2012:

EFSA evaluators identified among others the following issues (list can be completed)

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EFSA approach to Microbial BCAs

Tox assessment – key issues

- Which **specificity for** analytical method specific to strain?
  ➜ down to which level?
- Which **contamination** limits **by** potential pathogens?
  ⇨ Risk manager to agree!
- Is extrapolation **between strains** possible for mammalian tox?
- Which models to use **for exposure assessment**?
- Are there **toxins or** (secondary) metabolites of unknown tox
  ➜ **applied** with PPP to crop or plant?
  ➜ **formed** on / in crop or plant or in the envi?

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EFSA approach to Microbial BCAs

Ecotox and E-fate assessment - key issues

- "Experimental data are normally required" unless assessment with data already available …
- Often no **data**, **insufficient** summaries or no use of primary source!!!
- Is **extrapolation** **between strains** possible for envi assessment?
- Which **study design** for NTO testing?
- Risk assessment for wild animals or for sewage plants required?

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EFSA approach to Microbial BCAs

Typical questions raised ⇨ Possible data gaps

- **Background levels** of MO in representative soils?
- **Persistence** of MO in representative soils?
- **Survivability** in sediment & water?
- Production of relevant **toxins/secondary metabolites** by MBCA?
- **Mobility** in different envi compartments of MO or metabolites?
- ... evolution of levels over time?

EFSA approach to Botanicals (plant extracts)

Global remarks

- Great **heterogeneity of quality** dossiers and data
- Often non-GLP studies, **non-validated methodology** or insufficient details
- Often literature but no primary source

- **No guidance document available** ⇨ need for guidance

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EFSA approach to Botanicals (plant extracts)

Typical questions raised ⇨ Possible data gaps

- If the a. s. is a **mixture**: How to characterise it?
  Which components are representative and shall be followed in fate and residue studies?
- If only acute tox studies: **How to** conduct quantitative risk assessment and **calculate reference values** (ADI, ARfD, AOEL)*?
- For tox and ecotox: Are there known **toxic breakdown compounds**?
- For envi: What are the **background levels** (quantification?) and is there complete mineralisation?
- In risk assessment: How to move from "natural" exposure levels to PPP-use exposure levels?

* ADI = Acceptable Daily Intake,
ARfD = Acute Reference Dose,
AOEL = Acceptable Operator Exposure Level

EFSA approach to Semiochemicals

SCLP key issues

- "Critical areas of concern" are not expected.

Remaining issues

- Who is going to assess the large number of **specifications**?
- How to address **blend** and blend mixture specification?
- The threshold **value of 375 g a. s./ha/y** for mating disruption use has been questioned. EFSA wants primary source for reference …
- Some MSs have made comments on non-dispenser applications of pheromones.

Related issue

- Will MRLs be required to cover non-dispenser applications?

EFSA conclusions

General remarks

- Be aware that a positive conclusion of the DAR by the RMS does **not necessarily** mean that in the peer review EFSA (and other MS) will consider the submitted data to be complete or **satisfactory**.

- Applicant / notifier comments in EFSA review: to be made on comments in “reporting table” and on “evaluation table” received during process,

  EFSA does not use comments after conclusion
  ⇨ last opportunity when invited by COM

EFSA conclusions

Data gaps

Not all appear to be critical

- **Critical areas of concern**: they must be addressed by notifier. Occur in particular if Efsa cannot calculate risk according to an established model.

  Example: **Endpoints** to calculate ADI, ARfD and AOEL **are key**

- **Less critical data gaps**: unlikely to put at risk the inclusion, data can be submitted either at MS level or in renewal procedure

  Example: Depending on application technique and exposure, data gaps for phys-chem or long term storage for MBCAs **can be less critical.**

EFSA conclusions

Recommendations for applicant approach

- Unfortunately, **no facts can be taken as known** by EFSA evaluators without being addressed.
- **Everything** has to be expanded, demonstrated, documented, argued and justified!
- Do **not ignore "critical areas of concern"**: provide answers, data or justifications of non submission of data.
- Stick to scientific / technical arguments
- EFSA risk assessment does **not consider economic aspects**
  e.g. high costs of studies

After the EFSA conclusion

Decision on approval or non approval (confirmation of inclusion)

- DG SANCO (= “Risk Manager”) invites applicant in letter to take position on EFSA conclusion: => Comments and justifications are accepted but normally no new studies
- **COM proposal** must be justified on basis of facts, data or arguments
- **Decision**: voted by Standing Committee (SCoFCAH) on proposal by DG SANCO / COM
- **Observation**: So far no known case of exclusion of a List-4 active substance which previously benefitted from green-track inclusion
- **But**: Confirmation of inclusion or approval decision might be linked to **use restriction** or demand for **confirmatory data**.

EFSA and IBMA

Occasions for exchange on key issues

- EFSA **P**esticide **S**teering **G**roup Industry hearings on 1st Dec 2010 and on 25th April 2012
- ECPA-IBMA Workshop with EFSA on 26th April 2012

Issues raised by IBMA delegates in PSC hearings include

➜ Need for Guidance Documents: adopt OECD documents and develop new GDs for biocontrol substances

➜ Delayed EFSA-review and missing agreed endpoints cause problem for Step-2 dossier

➜ Develop Lessons-learned Document

➜ Hold regular PSC industry hearings

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EFSA and IBMA

Perspective

- IBMA got impression that EFSA management is globally aware of the shortcomings which occurred in the review programme
- **New PPR Panel** which had inaugural meeting in July 2012 includes experts with experience in microbiology and biocontrol
- In latest PSC Industry hearing in April, following an IBMA proposal, EFSA made the promise to initiate work on a **Lessons-learned** document in early 2013
- Regular (annual) PSC meetings

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EFSA and IBMA

Objective for IBMA

Improve the understanding of the specificity of different BioControl Agents and the context of their practical use

The way to this ... IBMA global shall

- ⇨ pursue and increase contacts with EFSA (at high ethical standard)
- ⇨ send delegates to EFSA hearings and events whenever possible (on general as well as biocontrol issues)
- ⇨ comment on EFSA documents
- ⇨ highlight key issues for biocontrol substances
- ⇨ suggest working issues (e.g. Guidance Documents)
- ⇨ listen to the needs and identify possible shortcomings
- ⇨ exchange / submit relevant scientific background

and IBMA shall be invited to contribute to Lessons-learned Document!

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Merci !