GERMAN FEDERAL INSTITUTE FOR RISK ASSESSMENT

15 YEARS
Science in the Service of Humanity

BfR
Bundesinstitut für Risikobewertung

How to maintain a robust and objective dialogue between government and stakeholder experts?

- A national authority perspective -

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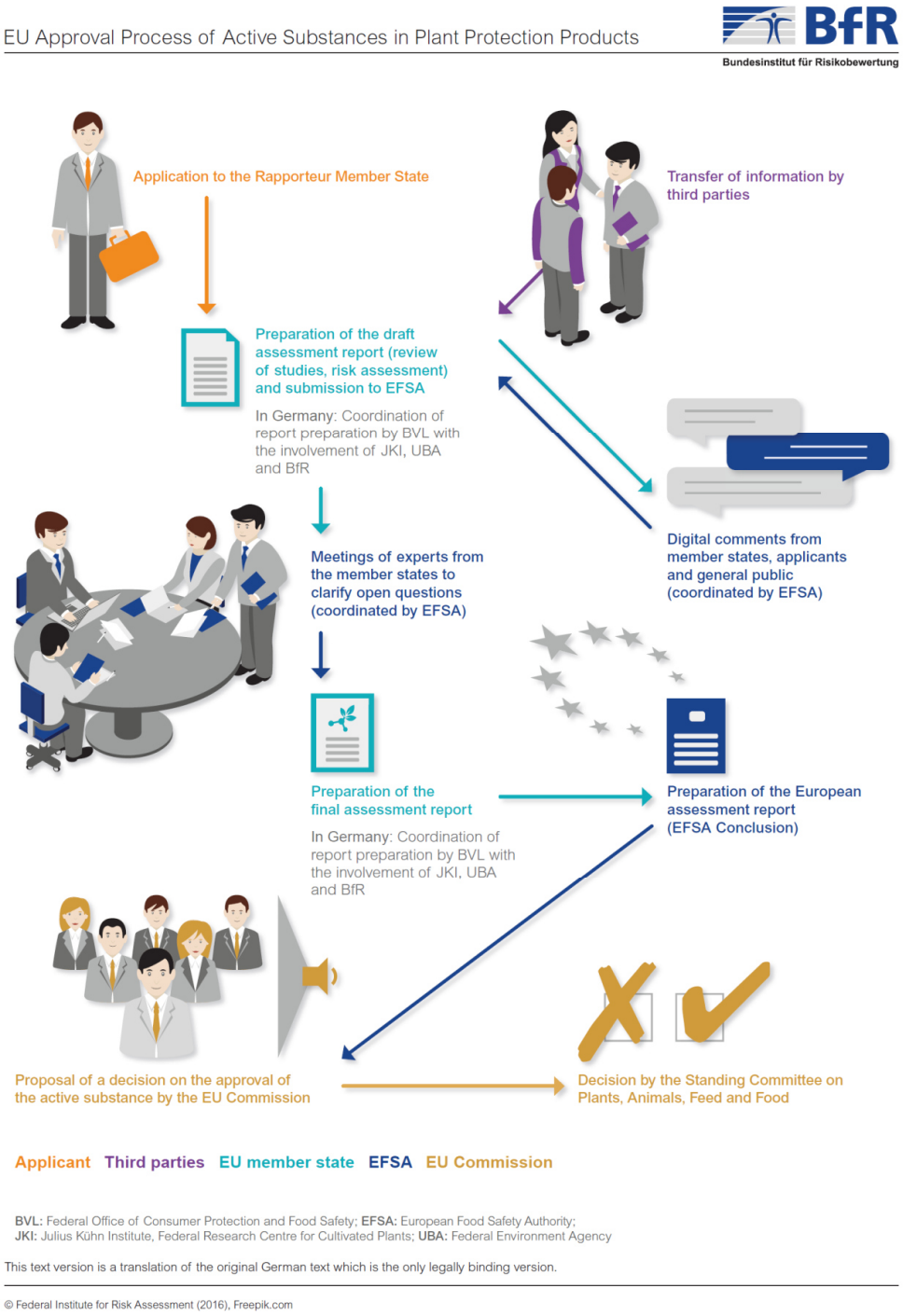
Outline

- EU-Approval Process of Active Substances in Plant Protection Products
- 1st Example: Glyphosate contents in breast milk
- 2nd Example: Follow up of the IARC Monograph on glyphosate
- 3rd Example: Use, reporting and consideration of scientific literature
- Conclusions



- Process according to EU plant protection products regulation (EC) No 1107/2009
- Active substances have to pass an approval process on EU level and have to be re-evaluated every 10 years
- Approval process was improved during the last 15 years
- Applicant need to fulfill all data requirements and has to submit a dossier including original study reports to the Rapporteur Member State (RMS)

EU-Approval Process of Active Substances in Plant Protection Products

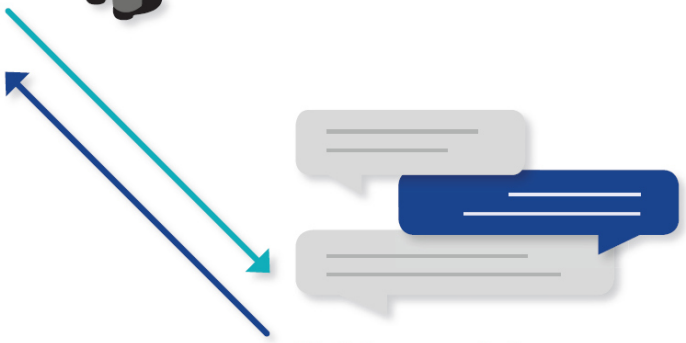
Application to the Rapporteur Member State

Preparation of the draft assessment report (review of studies, risk assessment) and submission to EFSA

In Germany: Coordination of report preparation by BVL with the involvement of JKI, UBA and BfR

Meetings of experts from the member states to clarify open questions (coordinated by EFSA)

Transfer of information by third parties



Digital comments from member states, applicants and general public (coordinated by EFSA)

Applicant Third parties EU member state EFSA EU Commission

EU-Approval Process of Active Substances in Plant Protection Products

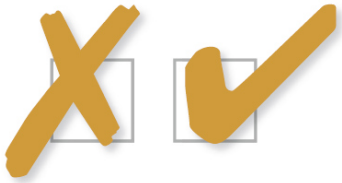
Meetings of experts from the member states to clarify open questions (coordinated by EFSA)

Preparation of the final assessment report

In Germany: Coordination of report preparation by BVL with the involvement of JKI, UBA and BfR

Preparation of the European assessment report (EFSA Conclusion)

Proposal of a decision on the approval of the active substance by the EU Commission



Decision by the Standing Committee on Plants, Animals, Feed and Food

Applicant Third parties EU member state EFSA EU Commission

Recent assessments by the RMS Germany

Pymetrozine

Beflubutamid

Fosthiazate

Ferric phosphate

Dimethenamid-P

Beta-Cyfluthrin

Clothianidin

Glyphosate

Pyraclostrobin

S-Metolachlor

Picolinafen

Bacillus subtilis str. QST 713

Milbemectin

Glufosinate

Isoproturon

Cydia pomonella Granulovirus (CpGV)

Beauveria bassiana strains ATCC 74040 and GHA

Diuron

Glyphosate contents in breast milk

- June 2015: According to media reports, a analysis has been conducted in which only 16 samples of breast milk and only 16 samples of urine were tested for glyphosate residues – the results were labelled as “very concerning”


Source: Fotolia

- The scientific community and the BfR have seen neither the original study nor sufficient methodological information on the analytical methods and sampling procedures used. For this reason, **only a preliminary statement*** can be made with regard to the currently available data.

- BfR expressed **significant scientific doubts regarding the methodology of the applied tests**

* BfR communication No 019/2015 published 26.06.2015

Glyphosate contents in breast milk

- BfR commissioned renowned research laboratories in Europe to develop **two independent analytical methods with high sensitivity in order to test 114 breast milk samples** from Lower Saxony and Bavaria

- February 2016: "The result* shows **how important professionally conducted scientific studies are** to ensure that consumers are not unnecessarily confused in the emotional debate on pesticide residues", says BfR President Professor Dr. Dr. Andreas Hensel§

* no residues of glyphosate detectable in breast milk

§ BfR press release 08/2016 published 11.02.2016

Follow up of the IARC Monograph on glyphosate

- **IARC July 2015**: "*There is strong evidence that exposure to glyphosate or glyphosate-based formulations is **genotoxic** based on studies in humans in vitro and studies in experimental animals.*" and "*Glyphosate is a **carcinogenic** substance Group 2A "Probably carcinogenic to humans*""
  - Epidemiological studies: "*limited evidence for cancer in humans*"
  - Carcinogenicity studies: "*sufficient evidence for cancer in experimental animals*"
- **JMPR May 2016**:
  - "*[…] concluded that glyphosate is unlikely to be genotoxic at anticipated dietary exposure*."
  - "*[…] concluded that glyphosate is not carcinogenic in rats but could not exclude the possibility that it is carcinogenic in mice at very high doses. In view of the absence of carcinogenic potential in rodents at human-relevant doses […], and considering the epidemiological evidence from occupational exposures, **the Meeting concluded that glyphosate is unlikely to pose a carcinogenic risk to humans from exposure through the diet**.*"

Follow up of the IARC Monograph on glyphosate

- **EFSA Conclusion** based on an addendum in **September 2015**:
  - *"Glyphosate did not present genotoxic potential […]"*
  - *"[…] glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential according to Regulation (EC) No 1272/2008."*

- **ECHA March 2017:**
  - "*Taking all data into account, and based on the overall negative responses in the existing gene mutation and oral mutagenicity tests, RAC concluded that there is not sufficient evidence to warrant classification of glyphosate for germ cell mutagenicity.*"
  - "*RAC did not find sufficient evidence to support a genotoxic mechanism of action for glyphosate and concluded that based on the epidemiological data as well as on data from long-term studies in rats and mice, taking a weight of evidence approach,* ***no hazard classification for carcinogenicity is justified for glyphosate according to the CLP criteria***.

Follow up of the IARC Monograph on glyphosate

- Divergent evaluations of the same substance! – And now…?
- **IARC Preamble:**
  - "*A cancer 'hazard' is an agent that is capable of causing cancer under some circumstances, while a cancer 'risk' is an estimate of the carcinogenic effects expected from exposure to a cancer hazard.* ***The Monographs are an exercise in evaluating cancer hazards****, despite the historical presence of the word 'risks' in the title. The distinction between hazard and risk is important, and the Monographs identify cancer hazards even when risks are very low at current exposure levels, because new uses of unforeseen exposures could engender risks that are significantly higher.*"
- **IARC November 2017:**
  - "***In the interest of transparency****, the IARC Monographs are based on independent scientific review of published research and not on the basis of unpublished of "secret data" unavailable publicly**.

Use, reporting and consideration of scientific literature

- Public opinion:
  - Human health risk assessment relies only on studies from the industry
  - Search for peer reviewed scientific literature is not adequately performed
  - Peer reviewed scientific literature is not sufficiently described
  - Peer reviewed scientific literature is not considered in the final risk assessment

- Contrary to this opinion hundreds of studies performed by manufacturers of glyphosate and a large amount of references from open literature were evaluated for the human health risk assessment and reported in the RAR!

Relevance and Reliability of experimental data

- Experimental data for use in regulatory processes have to be:
  - **relevant** for the addressed problem and
  - **reliable** in order to draw robust conclusions from it

- Data sources may vary considerably:
  - Guideline-compliant studies
    submission required by law; most often unpublished
  - Non-Guideline studies
    e.g. from literature searches; often published scientific research papers

- Most important: **Transparency of the evaluation!**
  Recently published paper from the pesticide unit of BfR*

*Kaltenhäuser, Kneuer, Marx-Stoelting, Niemann, Schubert, Stein, Solecki; Relevance and reliability of experimental data in human health risk assessment of pesticides; Reg. Tox. Pharm 88 (2017) 227-237.

How to evaluate **relevance**?

- Guideline-compliant studies:
  - Each data point according to current data requirements (Regulations (EU) No 283/2013 and 284/2013) is matched by harmonised test guidelines that are suitable for addressing this point
  - ➢ Adherence to Guidelines is evaluated

- Non-Guideline Studies
  - Transparent criteria for relevance in guidance documents, etc.
  - Basically, all data containing information on the substance/product and concerning the problem that is addressed are relevant
  - ➢ Usefulness for regulatory purposes depends also on the reliability of the data!

How to evaluate **reliability**?

- Guideline-compliant studies:
  - Test Guidelines contain “checklists” with necessary information
  - GLP certification of Laboratory
  - Raw data has to be submitted, so that the drawn conclusions can be reproduced.

- Non-Guideline Studies
  - Scientific approaches may vary tremendously
  - No uniform evaluation possible; Transparent criteria are needed!
  - Helpful:
    - ✓ Detailed reporting
    - ✓ Adherence to standards like GSP
    - ✓ Access to additional information

Conclusion

- Intensify the use of already available resources for participation in the scientific evaluation process
- Explore further ways for interaction with all stakeholders to enhance the scientific trialogue (e.g. establishment of a permanent platform/forum should be considered)
- Further improve transparency in the assessment of plant protection products (e.g. improve presentation of study reports, consider the establishment of a publicly available database presenting already existing study reports as well as information on ongoing/planned studies)
- Further improve/develop possibilities to make peer reviewed scientific literature more useful for human health risk assessment
- Pushing the scientific trialogue between **A**uthorities, **A**cademia and **A**pplicants (3 A´s)

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Thank you for your attention

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