

Für Mensch & Umwelt

Umwelt 
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Monograph system of active pharmaceutical substances: necessity, challenges and perspectives

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Experiences with the current legislation

For many VMPs in use no or not sufficient data on fate and effects are available.

Existing (,legacy‘) products: VMPs were approved before the requirement for an ERA was introduced into the legislation

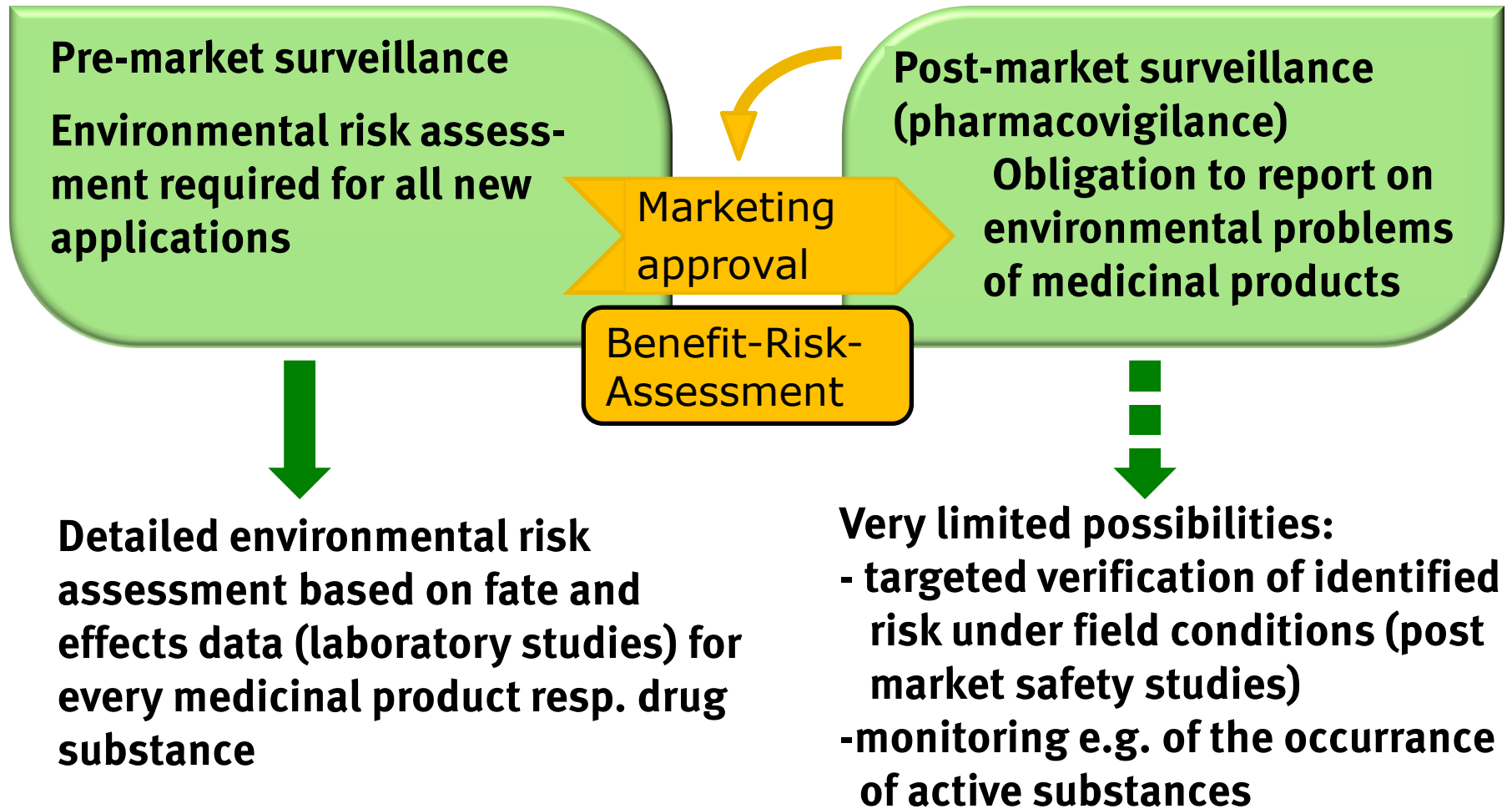
→ A review programm of these ,legacy‘ products (substances) was/is not envisaged.

Studies are of insufficient quality (incomplete dossiers):

→ Sometimes even for new approved VMPs no full data sets required for an ERA are available.

Environmental risk assessment in the authorization procedure

- complex authorization procedure, life-long surveillance
- approval is always related to a single medicinal product



Experiences with the current legislation : Pre-market surveillance

Different applicants apply for a MA of a medicinal product intended for the same indication and containing the same active ingredient.

Applicant A
(Product A)

Marketing
Application

ERA 1

Applicant B
(Product B)

Marketing
Application

ERA 2

Applicant C
(Product C)

Marketing
Application

ERA 3

- Duplication of data / ERAs
- some studies are of insufficient quality
- results of fate and effect studies may vary
- contradictory assessments
- different risk mitigation measures (worst case)
- non harmonized SPCs

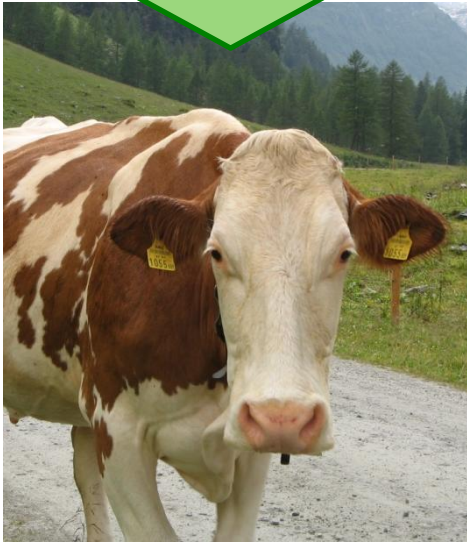
Not acceptable.

Neither from a scientific nor from a economic point of view.

Experiences with the current legislation: Post market surveillance

Obligation to report on environmental problems of every single veterinary medicinal product in the Eco-Pharmacovigilance.

Medication



Spreading of manure

- **How to observe potential environmental effects ?**
- **Evidence of the causal relationship ?**

photos: Ines Rönnefahrt

Summary: Experiences with the current situation

pre-market surveillance:

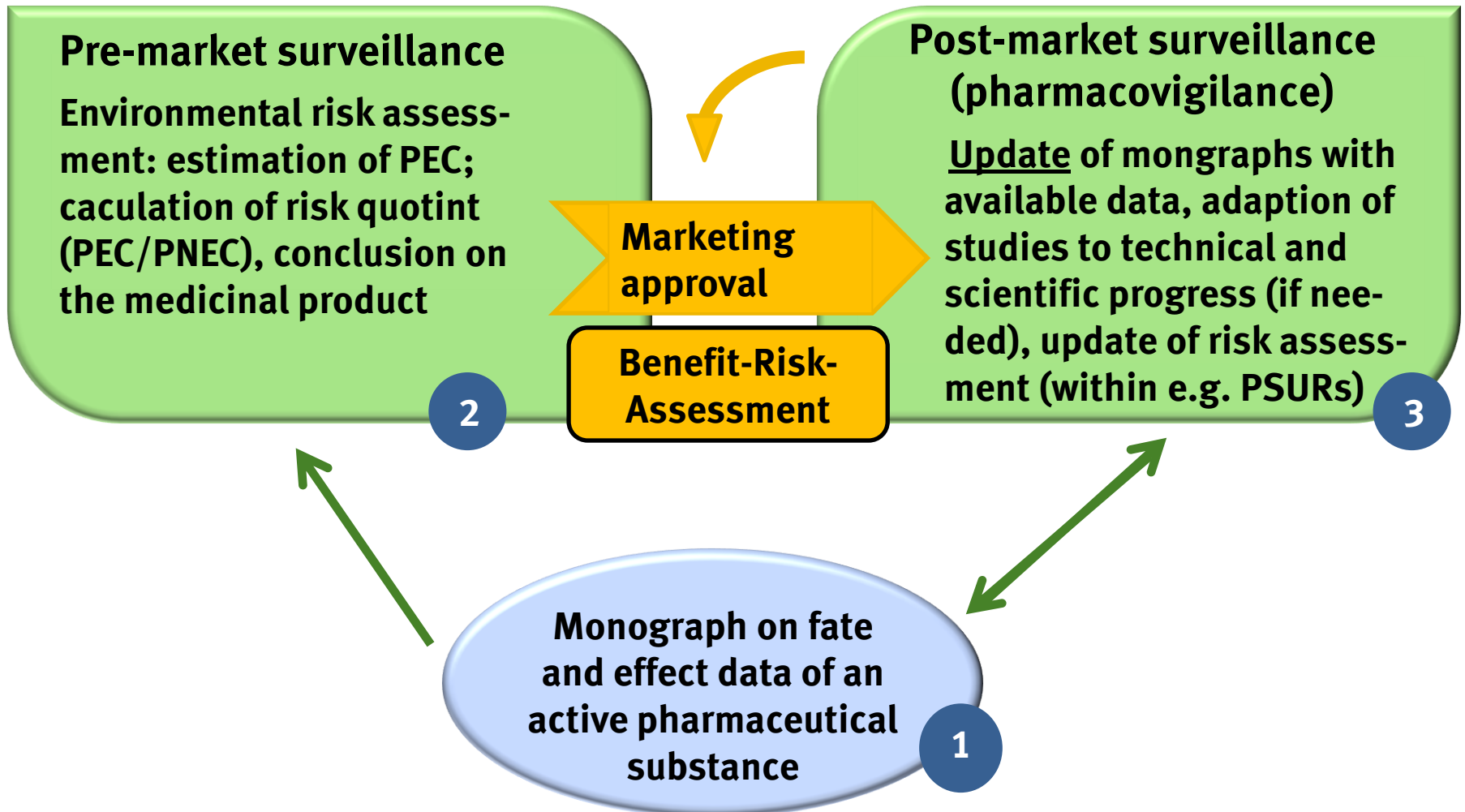
There is a need for harmonization of ERAs and SPCs.

post-market surveillance:

The existing pharmacovigilance system does not ensure that necessary data of environmental adverse effects are provided.

The aim of a monograph system is to collate existing fate and effects data on active pharmaceutical substances, to generate missing studies and data of high quality, to evaluate studies and to agree on the endpoints to be used for ERAs of medicinal products.

Marketing authorization of medicinal product applying a monograph



Benefits of a monograph system: pre market surveillance

Benefits of the establishment of monographs in the pre-marketing phase:

- provide validated and agreed environmental data and assessments
- allows harmonized ERAs on similar products and harmonized SPCs
- improve transparency and reliance
- shared resources of consortium allow to conduct studies of high quality
- prevents repetition of experiments (animal welfare, saving of testing material, etc.)
- saves resources of applicants & authorities needed for application and assessment of a marketing authorization (reduced financial burden)

Benefits of a monograph system: post market surveillance

Benefits of an update of monographs in the post-marketing phase

- **update of monographs with data from pharmacovigilance, publications, post market safety studies, etc.**
- **regular update of fate and effect studies collated in monographs to adapt them to the scientific and technical progress, if needed.**
- **update of the monographs on active pharmaceutical substances allows for up-to-date risk assessments and risk-benefit-analyses of the medicinal products, if needed.**
- **The interval for an update could be 10 years.**

Monograph system on active pharmaceutical substances

Content of a Monograph

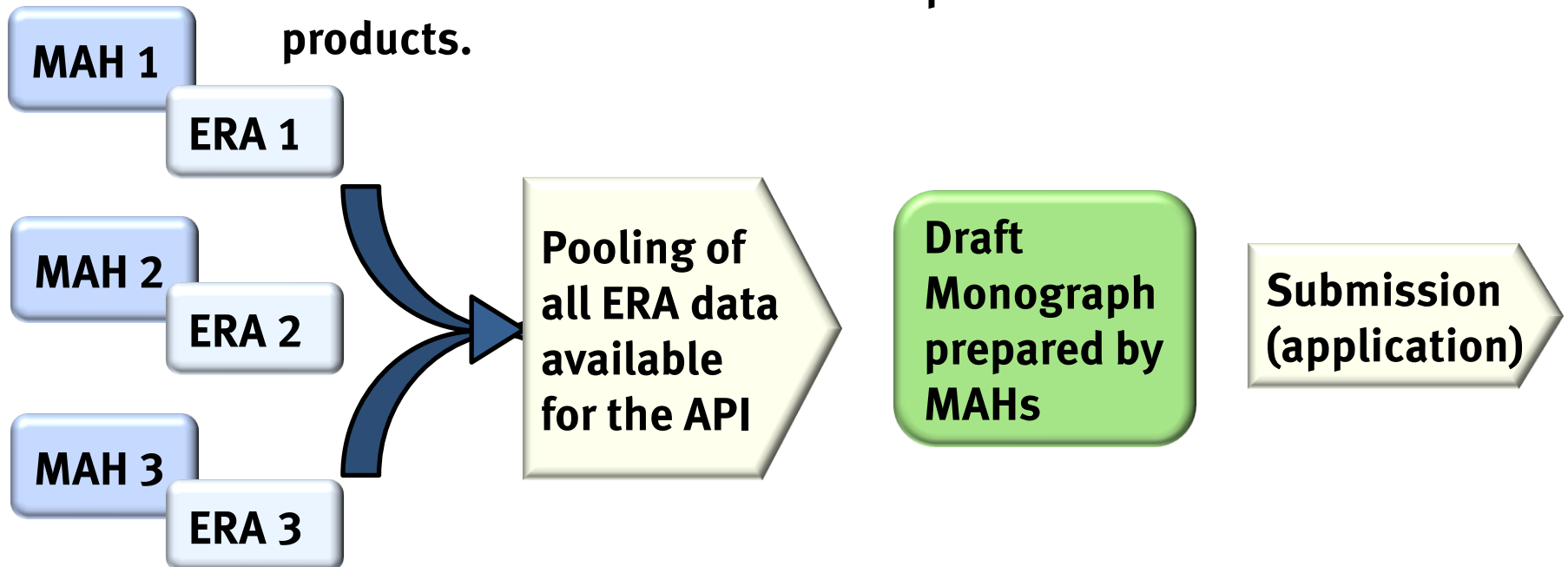
- all data needed for an environmental assessment of an active pharmaceutical substance
- data requirements according to EMA/VICH guidelines (VICH GL 38): physical-chemical data, fate & effects data
- assessment of the monograph dossier leads to validated endpoints of studies as well as short summaries of the respective study reports.
- no risk assessment (calculation of risk quotients; PEC/PNEC).



Identification of validated data to be used for an ERA. Data allow identification of potential environmental hazards.

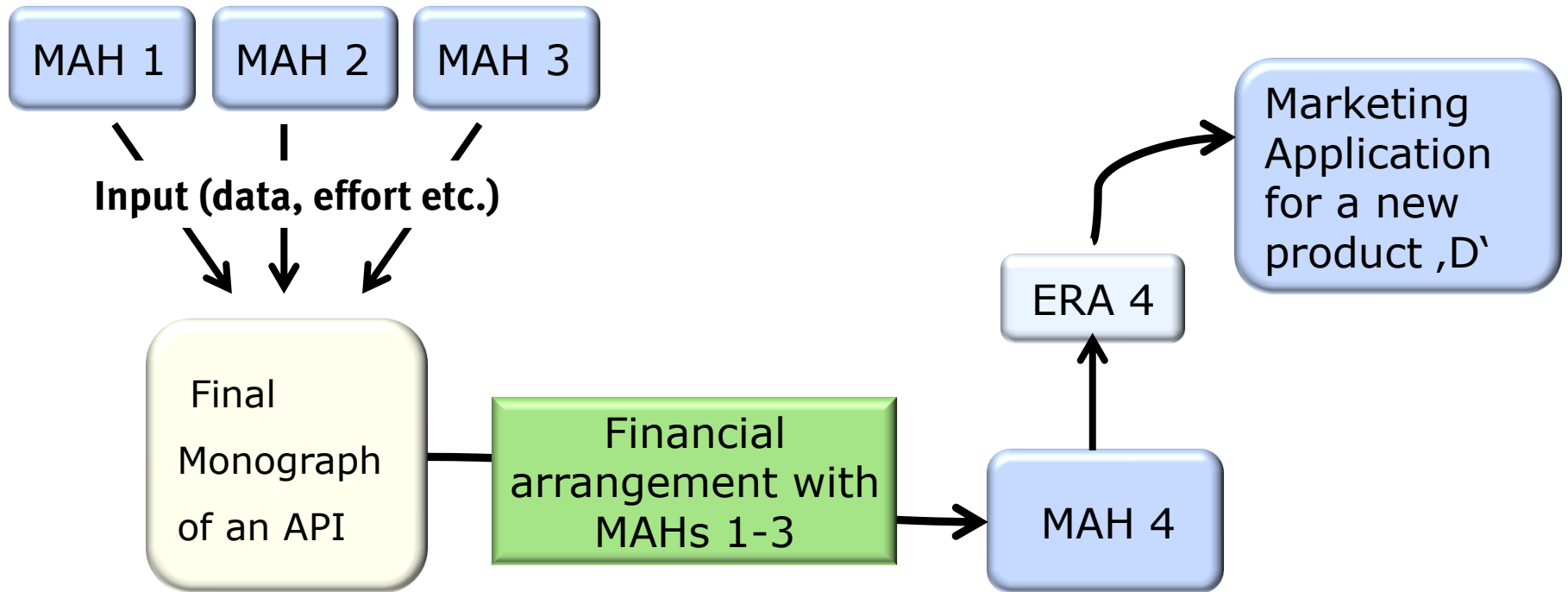
Establishment of a Monograph: Pre-approval phase

Monographs could be established in a similar way as e.g. the decentralized authorization procedure of medicinal products.



Further assessment of the draft monographs in a system of Rapporteur Member States (RMS) and Concerned member states (CMS).

The link between the monograph and the MAA for a medicinal product



Information collated in a Monograph will be used for applications for marketing authorization for VMPs – access to third parties only by financial arrangements (e.g. ,letter of access‘).

Challenges

The monograph system will only be implemented with precise legislative specification!

- **Clear rules on set up & management of consortia, on data protection, cost sharing etc. are necessary**
 - **examples of successful collaborations from REACH, biocides etc. exist**
- **Collection of monograph dossiers as well as study summaries, assessments and validated endpoints in a substance-based database**
 - **update and maintenance of the database?**
 - **different levels of accessibility to protect property rights?**

(e.g. UBA report ,2013, in German only: Based on a review of the existing regulations on REACH, pesticides, biocides, MRLs etc. a proposal on how to implement a monograph system into the pharmaceutical legislation was established.)

Public availability of environmental data on pharmaceuticals

Data on environmental fate and ecotoxicological effects are the essential base for any kind of identification and management of risks and should be adequately available.

Current situation:

- Lack of public information
- Outcome of ERA of a medicinal product are published in EPARs and in PuARs (partly)
- Environmental information is hard to be found due to product based databases

Benefit of Monographs:

Monographs on APIs provide opportunity for publication of data in a harmonized format. Database on active substances (not on products).

Property

and exploitation rights on the respective studies must remain unaffected.

Conclusion

- **ERA data should be available for new and existing („legacy“) substances!**
- **Harmonization of assessments and of SPCs are important.**
- **By means of monographs competent authorities could comply with the requirements of the environmental information act.**
- **Property rights on the respective studies have to be respected.**
- **The monograph system will only be implemented with precise legislative specification!**
- **Clear rules on set up & management of consortia, on data protection, cost sharing, data management etc. are necessary. Experiences from other legislations (REACH, biocides etc.) are available.**
- **Monographs should focus on substances of high concern. Prioritization schemes are available to identify substances for which monographs should be established.**

Conclusion

- Only a pre-market monograph system on fate and effects data of active pharmaceutical substances in conjunction with an effective monitoring within the post-market surveillance will be able to ensure the environmental safety of veterinary medicinal products in use.
- Data collated in monographs should regularly be adapted to the scientific and technical progress (update e.g. within the pharmacovigilance system).
- This ensures up-to-date risk assessment within PSURs of veterinary medicinal products.
- Monographs on active pharmaceutical substances are the key measure to ensure the environmental safety of VMPs in use.

Vielen Dank für Ihre Aufmerksamkeit

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