German Environment Agency

Umwelt Bundesamt

Workshop „How to achieve an appropriate Environmental Risk Assessment of Veterinary Medicinal Products”

The ERA master file concept

Ines Rönnefahrt

Federal Environment Agency, Germany

Brussels, 07 June 2017

Current situation & UBAs vision

Current situation:

- Knowledge gaps on ‘old’ active substances in legacy products
- Not satisfying situation in the pre-market phase:
  multiplication of data and assessments

UBAs vision:

- Joint development of data, sharing of resources
- Shared use of data

→ ERA masterfile concept (alias ‘monograph system’)

- Information on environmental safety of all relevant products/substances

Example: VMPs containing the same antibiotic substance

Multiple studies are submitted for the same active substance.
Some examples from UBA:

	Substance 1 Number of studies	Substance 2 Number of studies
Fate studies		
Adsorption/desorption test (OECD 106)	6	7
Transformation in soil (OECD 307)	7	6
Effekt studies		
Toxicity to cyanobacteria (OECD 201)	6	7
Acute toxicity to daphnia (OECD 202)	4	7
Actue toxicity to fish (OECD 203)	3	8
Terrestrial plants (OECD 208)	6	14
Earthworm subacute/reproduction (OECD 220/222)	3	8

Examples: VMPs containing the same active substance

Substance 3:
One contract lab has generated a full Phase II experimental data set.
Those studies have been used by several applicants in their applications.

→ **What can we learn from the positive examples on mechanisms of data sharing?**

Substance 4:
The base data set exists with several duplicate studies. However, no applicant has conducted a bioaccumulation test to prove the hypothesis that the substance does not bioaccumulate.

Similar case: several non-labelled degradation tests instead of one labelled

→ **How can resources be better used to generate high quality data needed to draw final conclusions on the environmental safety?**

ERA master files of active pharmaceutical substances

What is it?

Harmonised environmental information of active pharmaceutical substances

- Summary of physico-chemical data and fate and effect data for active pharmaceutical substances (not for products).
- Quality assessed data and agreed end points.
- Data requirements according to EMA/VICH guideline (VICH GL 38)

What is it used for?

- ERA of veterinary medicinal products within the authorisation procedure.
- The generation of ERA master files is not an approval system. Decision on authorisation is taken at product level during the benefit/risk assessment.

ERA master files of active pharmaceutical substances

How to establish it?

Existing active pharmaceutical substances

→ Data available, partially available, not available

→ Consortium of concerned MAHs is needed.

Cooperation between MAHs and authorities (EMA/NCAs) is essential.

Challenges: legislative changes needed

- Procedures including time lines etc.
- Criteria on set up & management of consortia, on data protection (property rights of MAHs, cost sharing etc. are necessary
- Set up of (financial) arrangements for accessing data

Proposal: How to establish an ERA master file for existing pharmaceutical substances in VMPs

COM
Establishment of a list of substances for an ERA master file (based on a priorit. of APIs)

EMA
Initiation of an ERA master file process for an active substance
1. Compilation of a list of products and MAHs
2. Request to the MAHs to provide a draft ERA master file and the respective ERA data/studies

MAHs
1. MAHs form consortium and prepare draft ERA master file
2. MAHs submit draft ERA master file and ERA data/studies to EMA

EMA
Assessment of draft ERA master file by RMS/CMS or by expert group

Proposal: How to establish an ERA master file for existing pharmaceutical substances in VMPs (cont.)

EMA
Assessment of draft ERA master file (by RMS/CMS or expert group)

Draft ERA master file is complete.

Draft ERA master file and its assessment report
Discussion and adoption by CVMP/CHMP

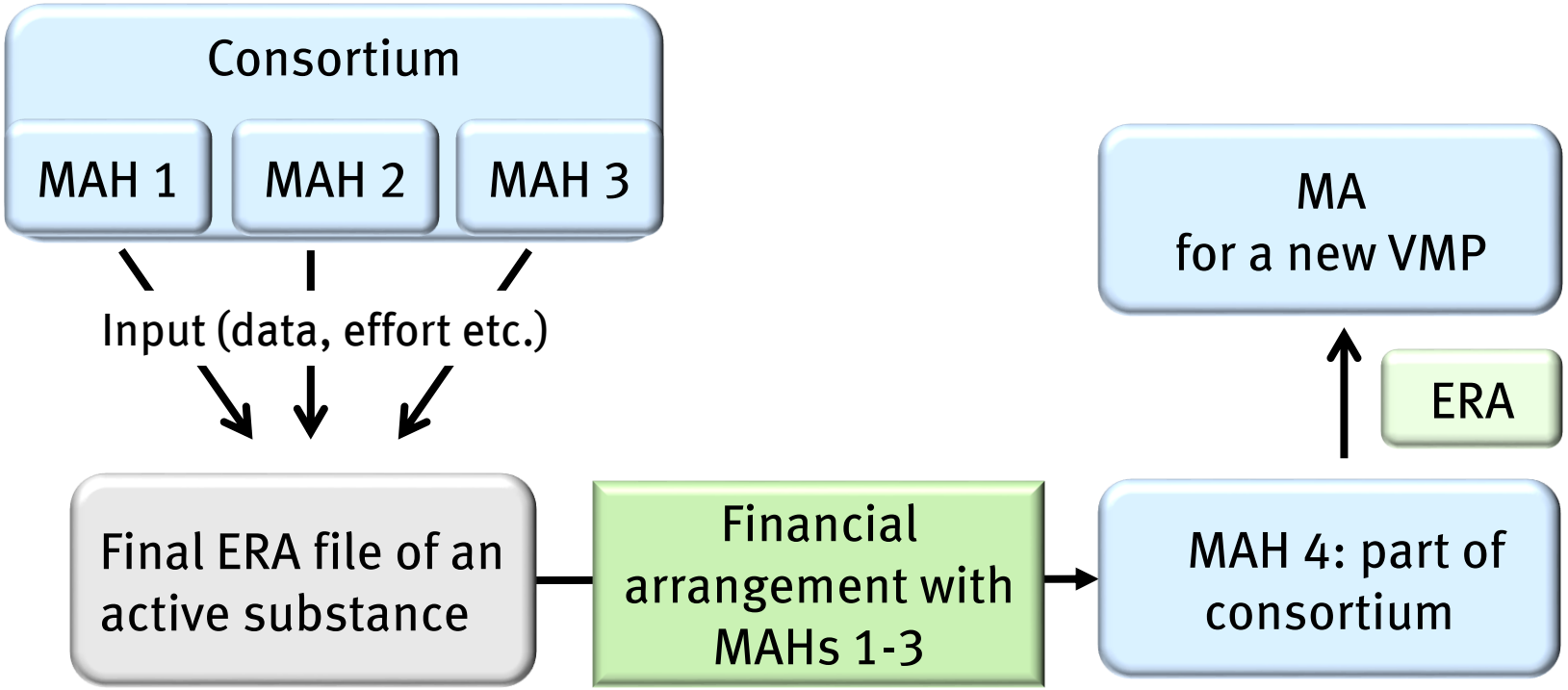
Standing committee of COM
Final adoption of ERA master file.
ERA master file is published in a central EU database (e.g. by EMA).

Draft ERA master file is NOT complete.

Draft ERA master file and its assessment report
Discussion and adoption by CVMP

Submission of requested data and of updated draft ERA master file
→ clock re-start

The link between the substance file and the marketing authorisation procedure of a generic VMP



Information collected in a substance file will be used for applications for marketing authorization for VMPs – access to third parties only by financial arrangements to become part of the consortium.

Proposal: ERA master file for VMPs containing a new active substance

Applicant
Prepares a draft ERA master file for the new active substance and an ERA for the VMP

Draft ERA masterfile is submitted **in parallel** to EMA and undergoes assessment procedure

Application for MA of medicinal product is submitted to EMA or to a national authority according to established procedures

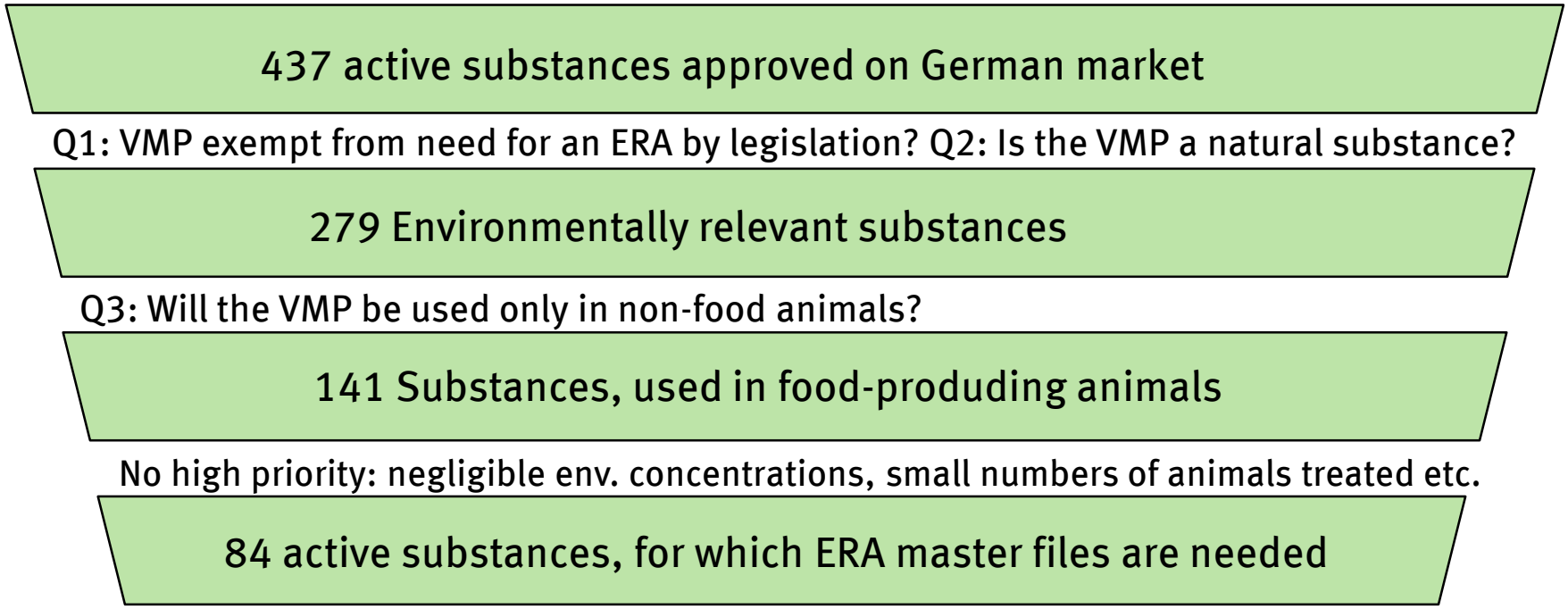
Marketing authorisation of medicinal product

Benefits of ERA master files in the pre-marketing phase

- Provide validated and agreed environmental data of active substances
- Allow harmonised ERAs on similar products and harmonised SPCs
- Improve transparency and reliability
- Shared resources of consortium allow to conduct studies of high quality
- Prevents repetition of experiments
- Saves resources of applicants & authorities needed for application and assessment of a marketing authorization (reduced financial burden)

For how many active substances an ERA master file would be needed?

A proposal how to prioritise active substances based on criteria used in EMA/VICH guideline GL 6.



→ The workload seems to be manageable.

Conclusion

- The ERA master file concept 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.
- ERA files should focus on active substances of high concern.
- Environmental data on active pharmaceutical substances should be publically available. Collection of substance files in a substance-based database. → update and maintenance of the database?
- Should data collated in substance files be adapted to the scientific and technical progress from time to time ? Update with data from pharmaco-vigilance, publications, post market safety studies, etc.?

Thank you for your attention !

Ines Rönnefahrt
ines.roennefahrt@uba.de

www.umweltbundesamt.de/en/topics/chemicals/pharmaceuticals
www.umweltbundesamt.de/themen/chemikalien/arzneimittel