EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update from the CVMP Environmental Risk Assessment Working Party

Assessment of VMPs containing persistent, bioaccumulative and toxic substances (PBTs)

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Outline

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1. What are persistent, bioaccumulative and toxic substances

- Persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) substances, are substances of very high concern because of their persistence, their ability to accumulate in living organisms and their toxicity.
- Due to their intrinsic properties these substances can pose serious concerns for the environment.
  - High resistance to biotic and abiotic degradation → long retention times in various compartments
  - High mobility in the environment → widespread distribution
  - High order of bioaccumulation
  - High toxicity

2. Assessment of PBT substances in the EU

- Several EU legislations require the identification of PBT substances (PPP, Biocides, REACH and medicinal products for veterinary and human use regulation)
- **REACH** (Regulation (EC) No 1907/2006) on **R**egistration, **E**valuation, **A**uthorisation and restriction of **Ch**emicals (REACH)), Annex XIII, lays down the criteria for the identification of PBT/vPvB substances and are used as a point of reference for the assessment of the PBT/vPvB of a substance/product within different legislative frameworks in the EU (e.g, for pesticides or biocides)
- However, differences still exist on how P-, B- and T-properties are established which can lead to divergent PBT-assessments for the same substance

3. PBT substances and assessment of veterinary medicinal products – Development of the guideline (1/2)

- CVMP guideline on «Environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38» requires a PBT/vPvB screening to be performed
- Further guidance was considered necessary on how to assess PBTs in veterinary medicinal products (CVMP Concept Paper released in September 2010)
- The CVMP adopted in July 2012 the draft guideline on the assessment of PBT/vPvB substances in veterinary medicinal products
- The first public consultation of the draft guidelines was completed in February 2013

3. PBT substances and assessment of veterinary medicinal products – Development of the guideline (2/2)

- Extensive comments received during the first public consultation
- Draft guideline revised considering comments received and with a new part providing general principles on how VMPs containing a PBT should be further assessed
- Revised draft guideline release for second public consultation in October 2014
- The second consultation ended in January 2015 and the ERAWP is currently considering the comments received
- Expected publication of final guideline Q2/Q3 2015

4. Guideline on the assessment PBT/vPvB substances in veterinary medicinal products – Main principles (1/3)

- **Part 1**: Identification of PBTs in VMPs:
  - according to REACH Annex XIII
  - considering available data for VMP applications.

- **Part 2**: General principles on how VMPs containing a PBT (or vPvB) should be further assessed within the context of a marketing authorisation application.

4. PBT/vPvB Guideline (Part 1) - Main principles (2/3)

Part 1. Identification of PBT/vPvB properties

- Hazard identification according to REACH Annex XIII and its guideline documents
- Objective: to determine whether the substance fulfils the criteria for persistence, bioaccumulation and toxicity
- Conducted as part of the Phase II assessment
- Based on all relevant data available

4. PBT/VPvB Guideline (Part 2) – Main principles (3/3)

Part 2. Assessment of VMP products containing a PBT substance

- **Emission assessment**: clarify the potential for an environmental impact.
- **Risk management**: control and limit the environmental emission as much as possible for PBT substances (e.g., limiting certain uses of the product, using different application methods, setting appropriate RMM, hazard communication to end used).
- **Risk mitigation measures**: product must be evaluated according to its intended use, and all options for reduction of environmental release of the PBT substance must be used.
- **Risk communication in SPC and labelling**: PBT information to be reflected in the package leaflet so the end user can respect the risk mitigation measures adequately.
- **Benefit risk considerations**: must take into account all available data from quality, safety and efficacy to ensure that the expected benefits outweigh the potential risks of the product.

5. Conclusions

- CVMP PBT guideline provides for a hazard assessment and includes general principles on how VMPs containing a PBT (or vPvB) should be further assessed within the context of a marketing authorisation application (publication by Q3 2015 of final guideline)
- If the product contains a PBT substance:
  - Further aspects can be considered with regard to the MA such as the use and possibility of effective RMM
  - An authorisation should only be granted if it is shown that the risks can be adequately controlled, or if the therapeutic benefits outweight the risks to human and animal health and the environment arising from the use of the substance, and if there are no suitable alternative substances or technologies
- Assessment of risk to the environment is still necessary even if quantitative assessment/risk ratio PEC/PNEC as per VICH GLs is not applicable

6. Next steps

- Need to gain experience in applying the PBT guideline in respect to assessment of risk to environment and benefit:risk considerations
- Need to develop an approach on how to assess PBT substances within the context of a marketing authorisation application
  - Avoid a case-by-case decision on any new application.
- CVMP, ERAWP and Member States are committed to have a common approach on the assessment of PBTs and ensure consistency between the different routes of authorisations (centralised, decentralised, mutual recognition, national)