EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Environmental risk assessment for generics

CVMP Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/6

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Overview

- Dossier requirements under current legislation
- Dossier requirements under Regulation (EU) 2019/6
- Approach taken by CVMP
- Interpretation of Article 18(7)

Background — Environmental risk assessment for veterinary medicinal products (excl. GMOs)

- Directive 2001/82/EC (Annex I) and Regulation (EU) 2019/6 (Annex II [as amended]):
  - The ERA for VMPs shall be conducted in two phases
  - Phase I (exposure assessment):
    - Always to be performed
    - Applicable guidance: VICH GL6
  - Phase II (fate/effects assessment):
    - To be performed if an environmental risk is identified in phase I
    - Applicable guidance: VICH GL38

Background — Current dossier requirements for initial marketing authorisation applications

- Directive 2001/82/EC:
  - Article 12(3)(j):

"The application for marketing authorisation shall include […] results of:

— pharmaceutical […] tests *[i.e., quality file]*,

— safety tests and residue tests *[i.e., (consumer) safety file]*,

— pre-clinical and clinical trials *[i.e., efficacy file]*;

— tests assessing the potential risks posed by the medicinal product for the environment […] *[i.e., an ERA]*"

Background — Current dossier requirements for generics

- Directive 2001/82/EC:
  - Title III(1.) of Annex I:

    "Applications based on Article 13 (generic veterinary medicinal products) shall contain the data referred to in Parts 1 [summary of the dossier] and 2 [quality file] of Title I of this Annex together with an environmental risk assessment […]."

➢ Although MAAs for generics are exempt from submitting a safety and efficacy file, an ERA must always be provided

➢ Repetitive provision (and assessment) of ERA for the same substances/type of products

Background — The "Veterinary Medicines Regulation"

- Regulation (EU) 2019/6:
  - Acknowledges the general need for ERA in the frame of MAAs (Recital 31):

    "For **all new applications** for a marketing authorisation, **environmental risk assessments should be mandatory** […]"
  - Acknowledges reduced data requirements for generics (Recital 34):

    "**Certain particulars and documents** that are normally to be submitted with an application for a marketing authorisation **should not be required** if a veterinary medicinal product is a **generic medicinal product** of a veterinary medicinal product that is authorised or has been authorised in the Union"

Background — The "Veterinary Medicines Regulation"

- Regulation (EU) 2019/6:
  - Acknowledges that certain MAAs for generics may require an ERA (Recital 35):

    "It is recognised that the potential effect of a product on the environment may depend on the volume used and the resulting amount of the pharmaceutical substance that may reach the environment. Therefore, where there is **evidence** that a constituent of a medicinal product, for which an application for a marketing authorisation for a **generic veterinary medicinal product** has been submitted, is **a hazard for the environment**, it is **appropriate to require data** on the potential effect on the environment in order to protect the environment".

Background — Upcoming dossier requirements for generics

- Regulation (EU) 2019/6:
  - Article 18(1):

    "By way of derogation […], it shall not be required that a [MAA] for a generic veterinary medicinal product contain the documentation on safety and efficacy if all the following conditions are fulfilled:

    (a) […] bioequivalence […]

    (b) […] requirements set out in Annex II

    (c) […] period of protection of the technical documentation […] has elapsed […]"

Background — Dossier requirements set out in Annex II to Regulation (EU) 2019/6

- Commission Delegated Regulation (EU) 2021/805 (i.e., Annex II as amended):
  - Section IV.1.1.:

    "Applications based on Article 18 (generic veterinary medicinal products) shall contain the data referred to in Parts 1 [summary of the dossier] and 2 [quality file] of Section II of this Annex. **If required, pursuant to Article 18(7) an environmental risk assessment shall be included** […]".

➢ Significant change from previous situation: An ERA for MAAs for generics has now only to be provided if required in accordance with Article 18(7)

Background — Article 18(7) of Regulation (EU) 2019/6

7. A competent authority or the Agency, as applicable, may require the applicant to provide safety data concerning the potential risks posed by the generic veterinary medicinal product to the environment where the marketing authorisation for the reference veterinary medicinal product was granted before 1 October 2005.

Background — Article 18(7) of Regulation (EU) 2019/6

7. A competent authority or the Agency, as applicable, may require the applicant to provide safety data concerning the potential risks posed by the generic veterinary medicinal product to the environment where the marketing authorisation for the reference veterinary medicinal product was granted before 1 October 2005.

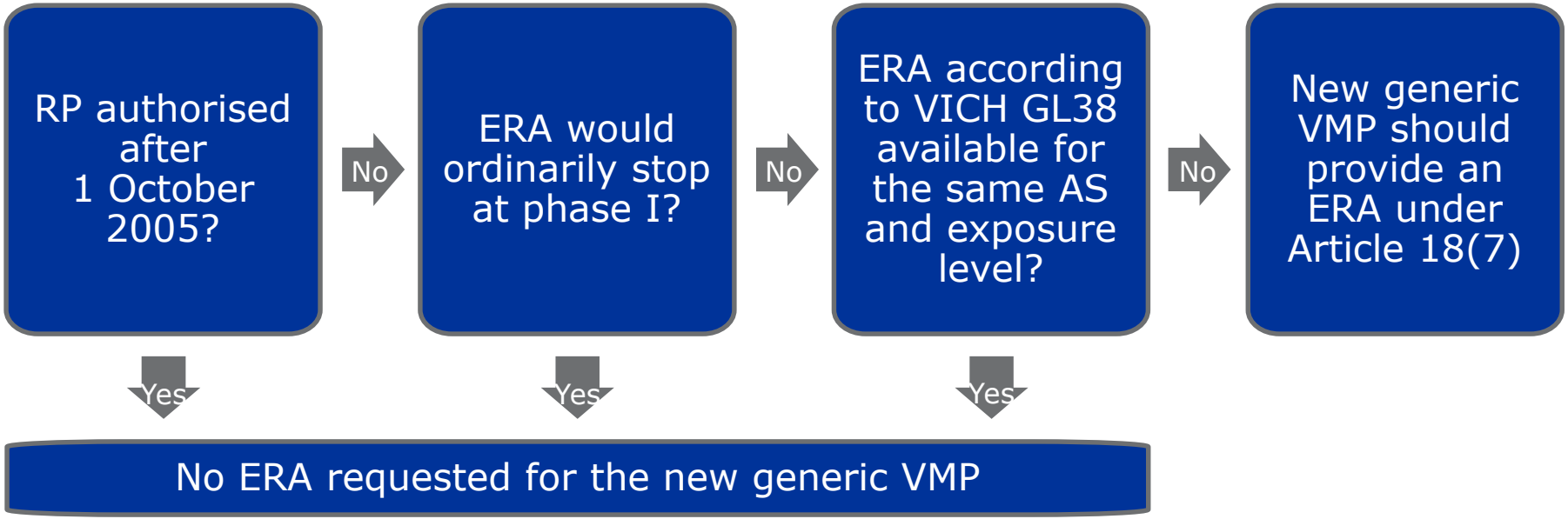
Interpretation of Article 18(7) of Regulation (EU) 2019/6 — Approach taken by CVMP

- Development of a reflection paper by CVMP to ensure a clear and consistent application of Article 18(7) across the EU:
  - Aim: Elaboration of an approach/criteria on when the Agency or a NCA can request the submission of ERA data in the frame of a MAA for a generic VMP
  - Draft reflection paper currently released for public consultation until 17 December 2021
  - Tentative finalisation date: Q1 2022

Interpretation of Article 18(7) of Regulation (EU) 2019/6 — Underlying principles of the reflection paper

- Article 18(7) does not provide for an obligation to request ERA data ("may require")
  - ERA data from generic applicants should only be requested on an **exceptional basis**
- Article 18(7) does only concern generic VMPs whose reference product was authorised **prior to 1 October 2005** (coming into force of VICH GL38)
  - By default, ERA data should not be requested in case a reference product is cited which was authorised **after 1 October 2005**
- General principle: An ERA should only be requested in case no ERA has been performed for the same active substance and exposure level in the EU/EEA in accordance with VICH GL38

Proposed principles for when an ERA should or should not be required in the application for a generic VMP



Environmental warnings in the product information

- Article 18(6) or Regulation (EU) 2019/6:
  - "[…] the SPC of the generic VMP shall be essentially similar to that of the reference medicinal product […]"
- Lack of environmental warnings in the proposed generic PI should not be a reason to request an ERA
- In case environmental information is available in published literature ("current scientific knowledge"), it could be included in generic PI as well as in the PI of the reference product in accordance with Article 130(3)(a) of Regulation (EU) 2019/6
- If an environmental concern is identified, it would also apply to the reference product → Union interest referral

Any questions?

Public consultation: https://www.ema.europa.eu/en/news-events/open-consultations

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