A year of challenges and experience with the New ERA guideline

ASPHALION
Knowledge from experience

25 years

A year of challenges and experience with the New ERA guideline

- An environmental risk assessment (ERA) is **required for all new Marketing Authorization Applications (MAAs) for a medicinal product regardless of the submission pathway and legal basis**.
    - Exemptions: Type II variations and extension applications (unless there is an anticipated increase in the environmental exposure); Not required for renewals of MAs.
- The ERA is included as part of the MAA dossier (in Module 1.6).

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

15 February 2024
EMEA/CHMP/SWP/4447/00 Rev. 1
Committee for Medicinal Products for Human Use (CHMP)

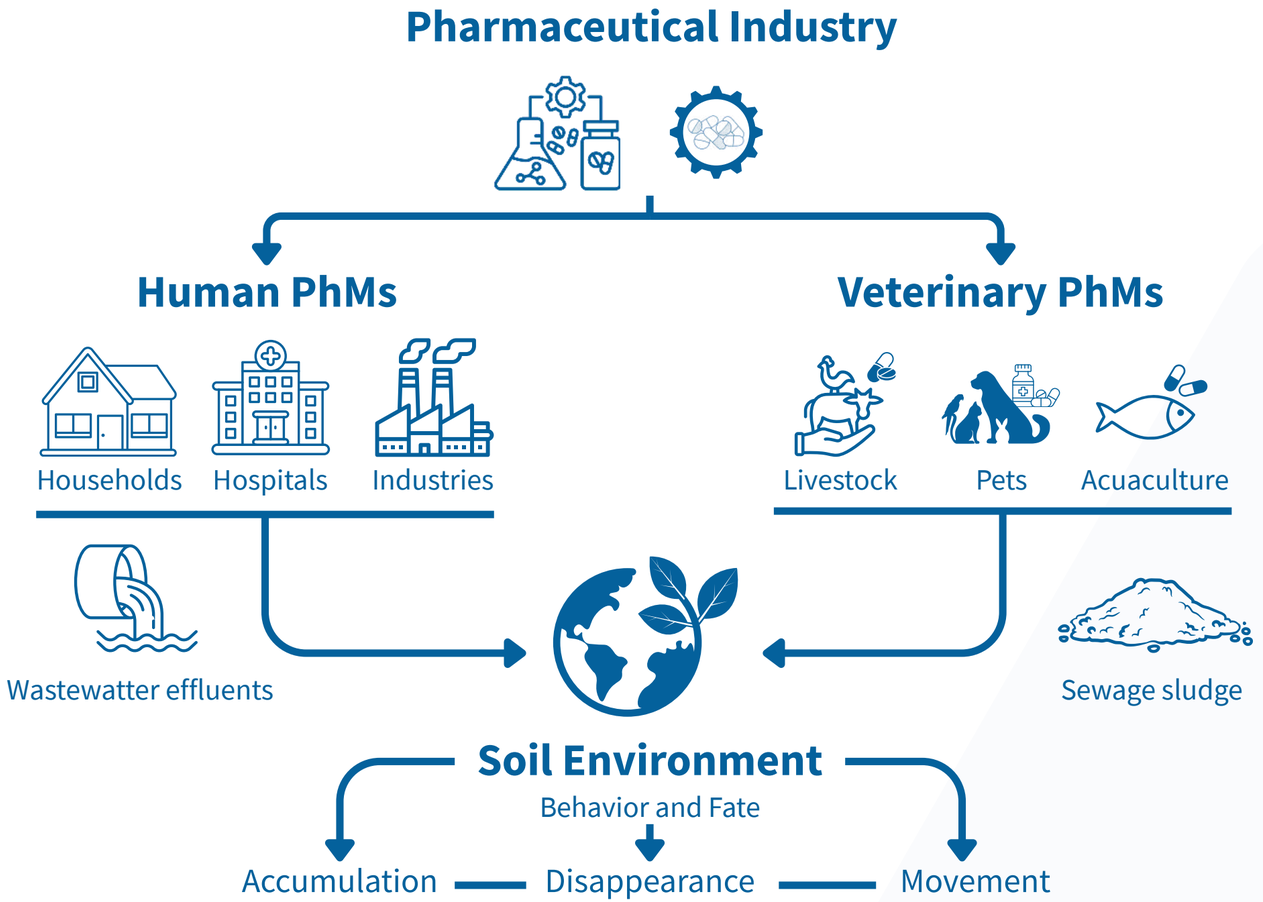
Guideline on the environmental risk assessment of medicinal products for human use

Draft agreed by Safety Working Party	October 2018
Adopted by CHMP for release for consultation	15 November 2018
Start of public consultation	1 December 2018
End of consultation (deadline for comments)	30 June 2019
Revised Draft adopted by Non-clinical Working Party	6 December 2023
Adopted by CHMP	15 February 2024
Date for coming into effect	1 September 2024

This guideline replaces 'Guideline on the environmental risk assessment of medicinal products for human use (EMEA/CHMP/SWP/4447/00 corr 2)'.

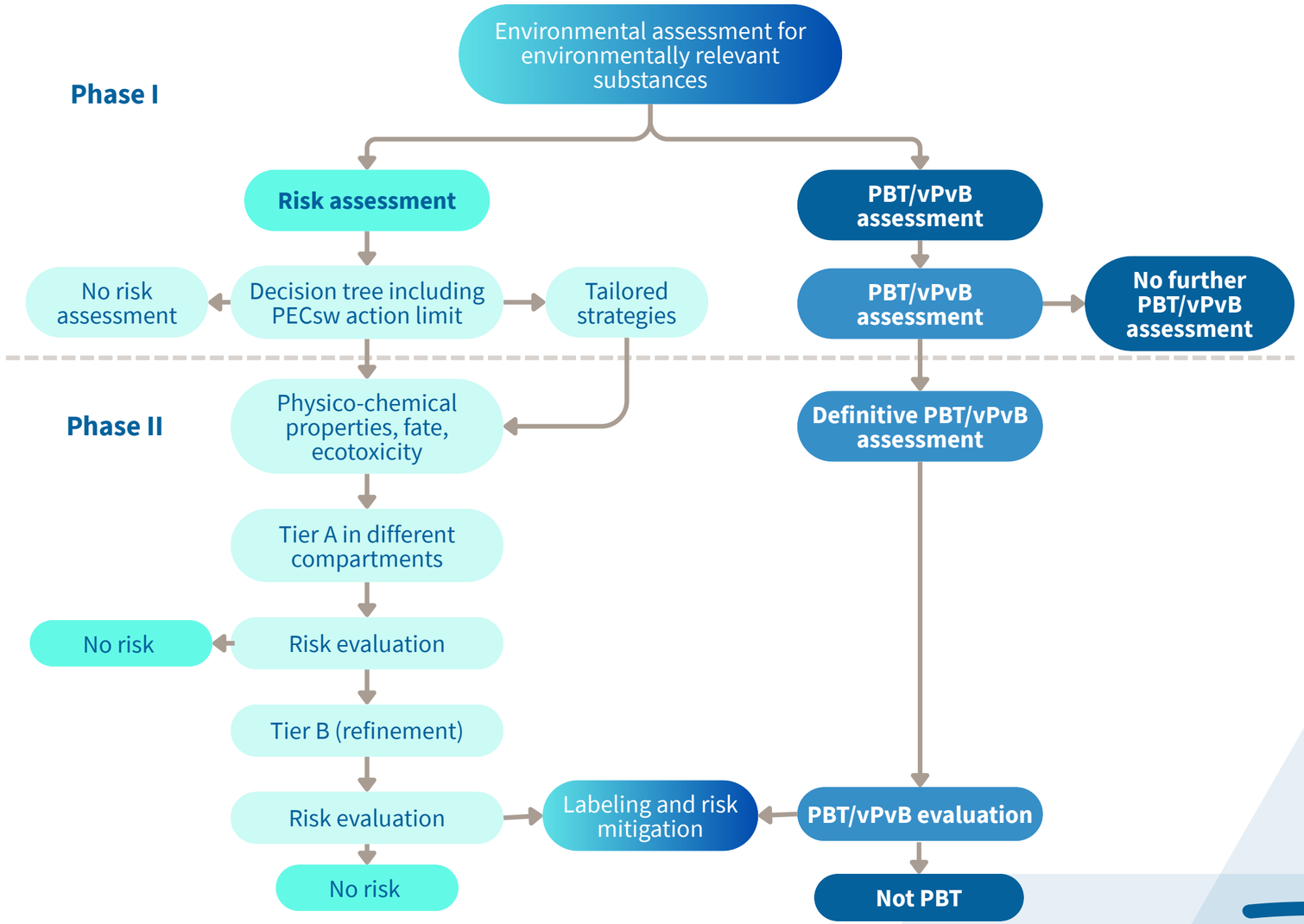
What does ERA evaluate?

An ERA **evaluates the potential risks to the environment** and involves understanding how the medicine interacts with ecosystems including surface water, groundwater, soil, species at risk of secondary poisoning and the risk of microbial processes in sewage treatment plants.



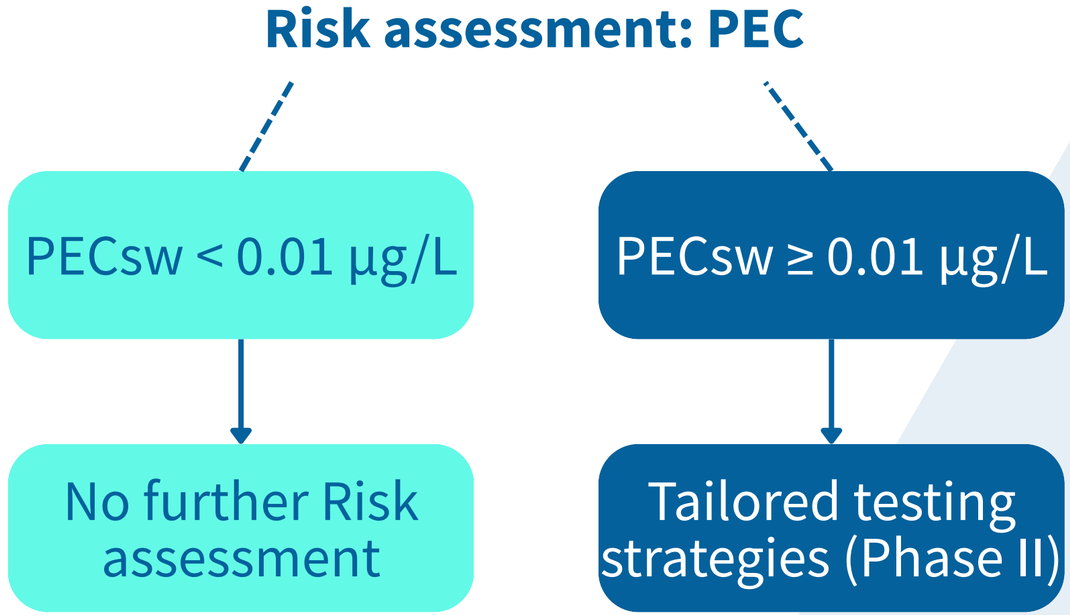
Source: Pérez-Lucas G. and Navarro S. HowPharmaceutical residues occur, behave, and affect the soil environment. *J. Xenobiot.* 2024, 14(4), 1343-1377 https://doi.org/10.3390/jox14040076

Decision tree



Phase I – Initial Risk Assessment

- Phase I **estimates if the medicinal product's use could result in relevant environmental exposure**.
- If the **Predicted Environmental Concentration (PEC)** in surface water (sw) is ≥ 0.01 µg/L, further assessment (Phase II) is required.



Phase II - Risk Assessment

- Phase II **characterizes the effects of the exposure**.
  - Physico-chemical properties, fate and ecotoxicity evaluation and trigger values for groundwater, soil and secondary poisoning assessment:
    - **Tier A:** Surface water, sediment and sewage treatment plant, soil, groundwater, secondary poisoning.

Risk characterization **(final Phase II):**

PEC/PNEC

PEC = Predicted Environmental Concentration (Ph I)
PNEC = Predicted No Effect Concentration – Calculated with NOEC (No observed effect concentration)

If trigger values exceed…

    - **Tier B:** higher-tier studies to evaluate the risk, with refined options.

- If risks are found → **Labelling and Risk mitigation** is required.

PBT/vPvB Assessment

Persistence
(depending on the Level of degradation)

Bioaccumulation
(depending on fish bioconcentration factor)

Toxicity
(depending on preclinical toxicity, aquatic)

- **PBT assessment** is independent of the PEC values and includes two phases:
- A first phase includes the **screening** for potential **Persistence (P)**, **Bioaccumulation (B)**, or **Toxicity (T)** of the substances.

Risk assessment (screening): Log Kow > 4.5

- Triggers additional evaluation in a second phase of **definitive PBT/vPvB assessment**:
  - Concludes if the substances are definitively PBT or **very Persistent (vP)** or **very Bioaccumulative (vB)**.
- If risks are found → **Labelling and Risk mitigation** is required

Screening

Definitive assessment

Impact of new guideline – Known active substances cases

- It is not possible to waive an ERA by justifying a lack of increase in environmental exposure (sales in the last 4 years).
- Data of reference product cannot be used.
  - Do not use innovator data without consent: EPAR, PAR, monographs, Janusinfo.se, Fass.se.
  - Present a bibliographic ERA in the initial dossier (exceptions apply).
- The guideline encourages the applicant to **contact the innovator** to request consent for data use and avoid the repetition of studies **(3Rs)**.
  - Investigate what data can be obtained from the literature.
  - Contact the innovator to request consent.
  - Present the innovator's response to the Agencies showing acceptance (innovator agrees sharing the data) or rejection (innovator does not agree sharing the data).

Contact us!

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