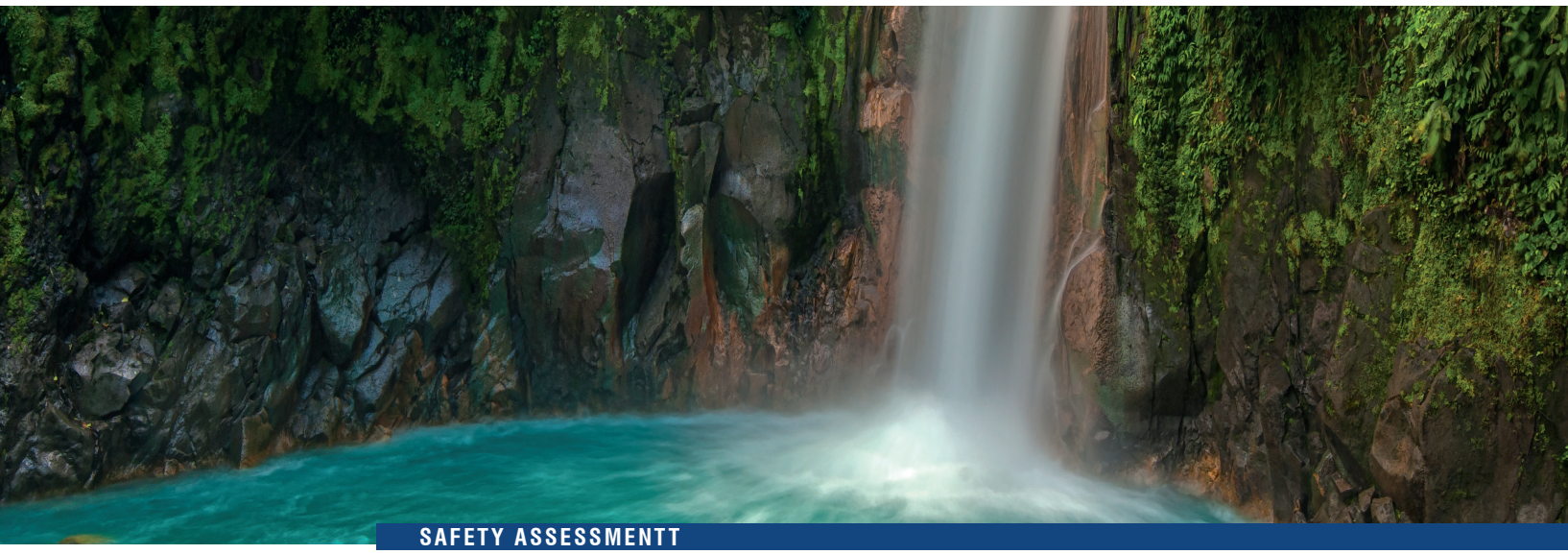
charles river



SAFETY ASSESSMENTT

# Environmental (Risk) Assessment of Human Pharmaceuticals

## Comprehensive service in accordance with global guidances

The environmental risk assessment (ERA) of human pharmaceuticals can be a lengthy and involved process, potentially taking several years depending on the product and target market. Conducting an appropriate and integrated environmental testing program with Charles River eliminates unexpected delays in this stage of the approval process.

The impact of human pharmaceuticals on the environment, by provision of an Environmental Risk Assessment (ERA), is a current regulatory requirement in the EU. Similarly, a US FDA New Drug Application must contain an evaluation of the potential environmental impact of the drug substance, applying to both new and existing products with certain use variations. Legislation is also under discussion in other regions.

Charles River provides a comprehensive service in accordance with the existing guidance documents. We can arrange initial evaluation of potential environmental exposure and risk following review of usage patterns and available environmental effects data and phased refinement of the ERA. We can also liaise with authorities and consultants regarding the detailed design and scientific justification of any nonstandard tests that may be required.

### Environmental Risk Assessment of Pharmaceuticals | Regulatory Support & Testing Services

Global regulatory support

- Preliminary testing (US)/ Phase I assessment (EU)
- Tiers 1-3 (US)
- Phases IIA and IIB (EU)

Physicochemical testing

Environmental fate

Ecotoxicology: terrestrial & aquatic

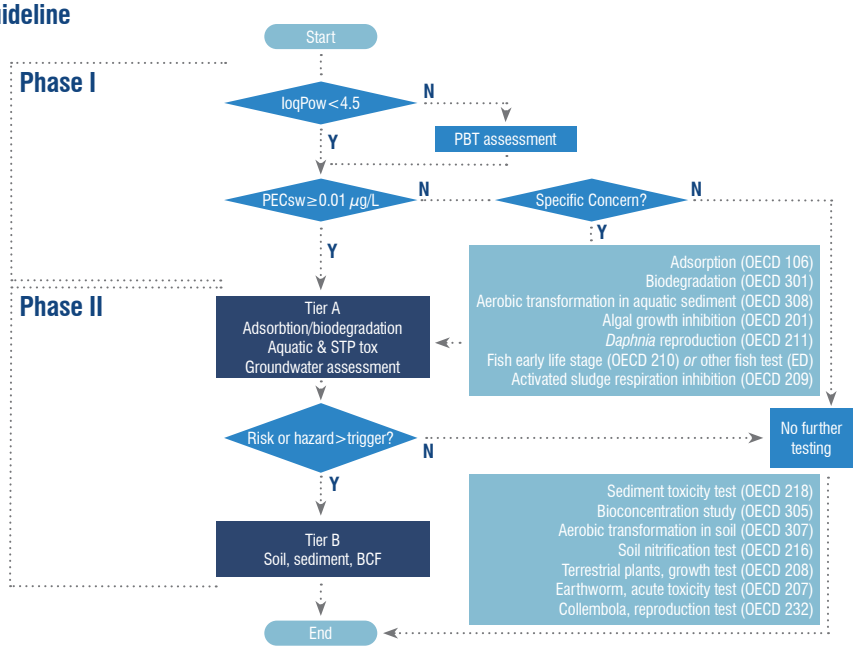
With extensive experience in study design across multiple industrial sectors, our teams have a thorough understanding of these unique regulatory requirements, from study design to the review and interpretation of data. We can assist clients in the pharmaceutical arena with the design of programs and studies tailored to the properties of their medicinal product.

## Environmental Risk Assessment in Europe (EU)

Since 2006, an ERA is required for all new marketing authorization applications (MAA) for medicinal products, including those for generics. The procedure described by the European Medicines Agency (EMA) follows a tiered approach.

An ERA must be documented in an expert report, authored by an individual with demonstrated expertise. Irrespective of the outcome, the result of an ERA will not lead to refusal of marketing authorization, but labeling instructions may be needed. The incompleteness or absence of an ERA will lead to post-marketing commitments with strict deadlines. As the ERA may be a lengthy and involved process, it is recommended that an ERA program is commenced early in the Phase III stage of the drug development process.

### 2006 EU Guideline




## Environmental Risk Assessment in the United States (US)

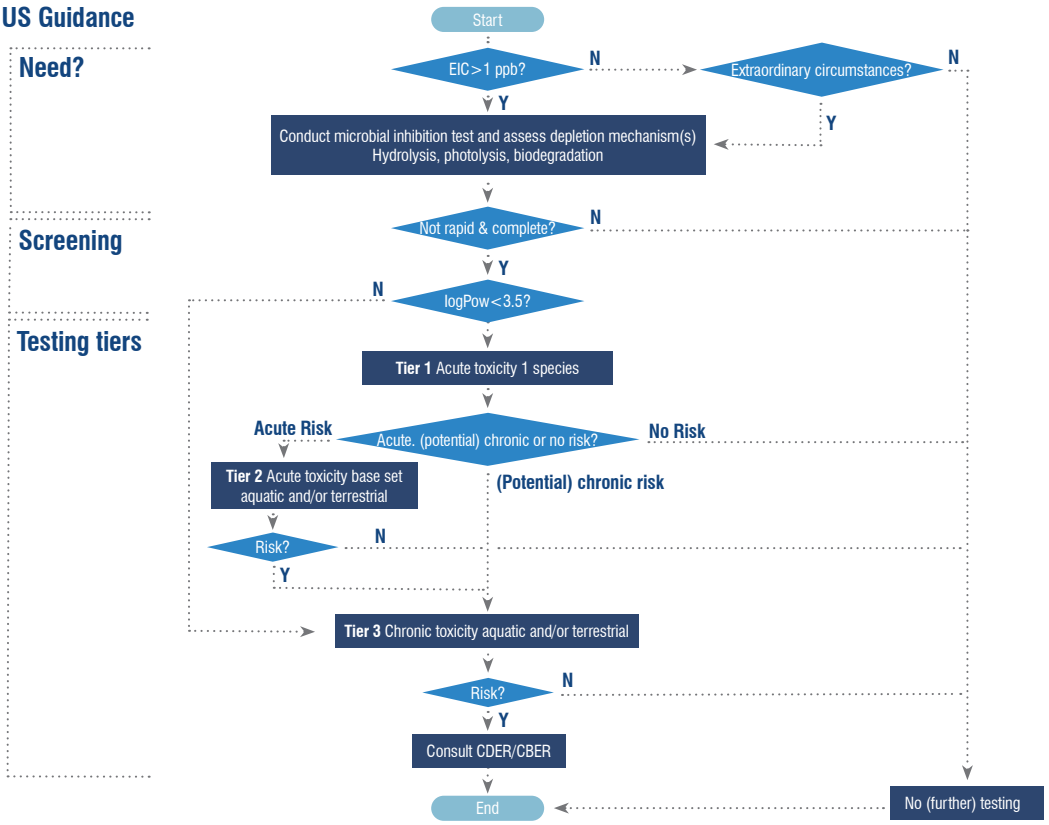
In the US, Environmental Assessments (EAs) must be submitted as part of certain new drug applications (NDAs), abbreviated applications (ANDAs), investigational new drug applications (INDs) and for various other actions, unless the action qualifies for a categorical exclusion (CE) based on an expected environmental concentration of the active moiety below 1 ppb and a claim for no extraordinary circumstances.

After completion of an octanol/water partition coefficient (logPOW) determination and a microbial inhibition test, the EA process also follows a tiered approach, which however does not need to be completed for substances which deplete rapidly from the environment.

Failure to submit either a claim of categorical exclusion or an EA is sufficient grounds for the FDA to refuse to file or approve an application.

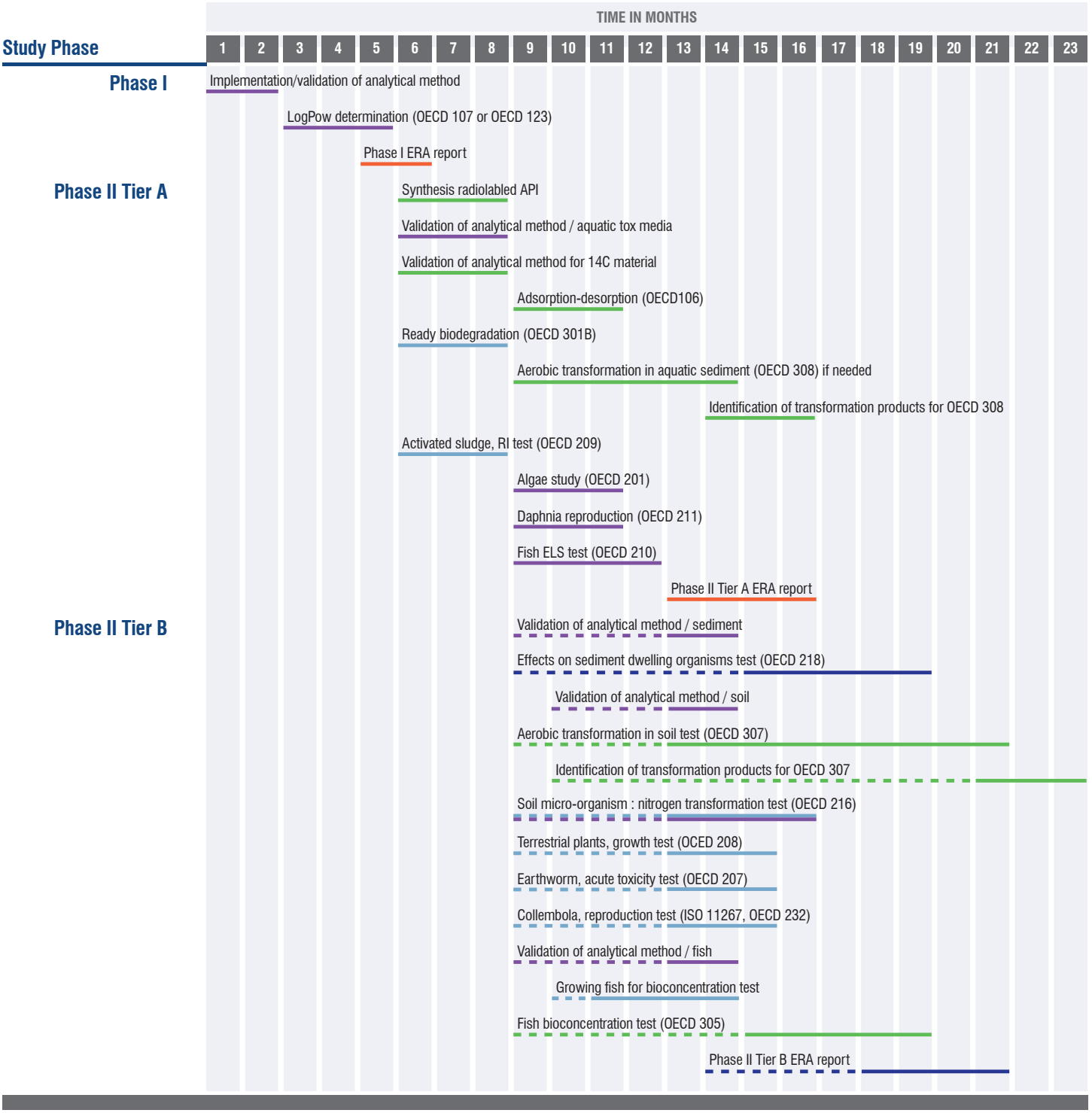
The approach as described by the US FDA is slightly different from the EU approach. In practice, an ERA prepared for Europe is mostly sufficient for the US, while the opposite may not necessarily be the case. However as with the EU, an EA must be documented in an expert report, authored by an individual with demonstrated expertise. Similarly, the EA may be a lengthy and involved process, it is once again recommended that an EA program is commenced early in the Phase III stage of the drug development process.

## 1998 US Guidance




Charles River has extensive experience in environmental risk assessments for human pharmaceuticals. We perform the requested studies and deliver project management, advice during every step of the process, preparation of reports ready for submission to both the EMA and FDA and after care, answering questions from the Agencies. Our track record includes numerous successful ERAs and EAs that were accepted by the EMA and FDA, including many for endocrine-active ingredients.

## Environmental Risk Assessment Timeline

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