EnvironmentalSciences

Environmental Risk Assessment of Human Medicinal Products

COVANCE

Summary of Capabilities & Facts:

- Comprehensive services spanning regulatory consultation, Phase 1 and Phase 2, Tier A & B testing requirements
- Senior Scientific Staff have over 250 cumulative years of experience in a GLP environment
- Experienced in the conduct of over 130 different, GLP-compliant study designs
- Over 35 years in environmental chemistry

Environmental Assessment of the Fate and Effects of Human Medicinal Products

In accordance with Article (8)3 of Directive 2001/83/EC (amended), as of 1 December 2006, an Environmental Risk Assessment (ERA) must now accompany an application for a marketing authorisation for a medicinal product for human use in Europe. Regulatory bodies in the U.S. and other countries have similar requirements for this type of ERA.

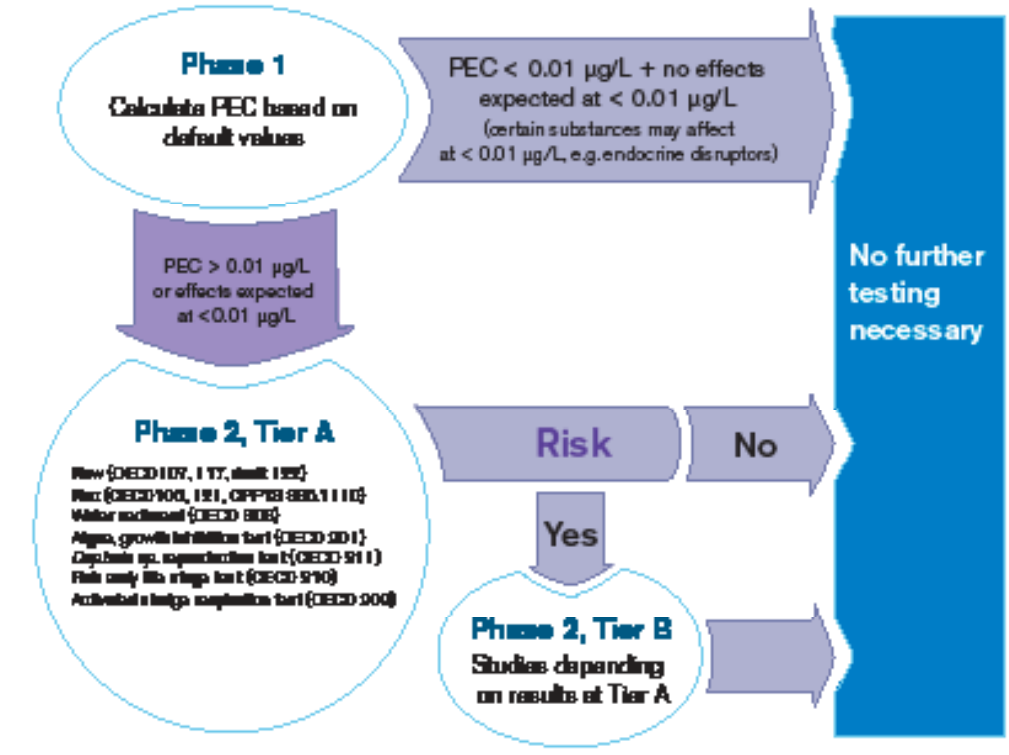
Covance can provide you with comprehensive services for completing an ERA, including consultation and testing for Phase 1 and Phase 2 Tier A and B. Prior to commencement of testing, we can also provide you with a regulatory evaluation of your product, including assessment of:

- Potential risks in the use, storage and disposal of human medicines to the environment
- Environmental impact
- The implications of extended usage that may result in increased environmental exposure

When you place an ERA Study with Covance, you can:

- **Trust in our track record of successful regulatory submissions since the issuance of the European Directive in 2006**
- **Achieve up to a 25% reduction in time to complete an ERA using integrated testing strategies**
- **Submit Risk Assessments with confidence based on our comprehensive knowledge of the global regulatory environment**
- **Streamline communications during your project through a single point of contact**
- **Enjoy flexible service arrangements based on fixed, hourly or FTE contracts**

Risk Assessment Requirements



Phase 1: Estimation of Exposure

Services

- Regulatory Affairs Consultation
- Environmental Risk Assessment
- Screening for Persistence, Bioaccumulation and Toxicity
- Estimations of the Predicted Environmental Concentrations (PEC) in the aquatic environment

Phase 2 Tier A: Environmental Fate and Effects Testing

Pharmaceuticals often exhibit chemical structures that are more complex than those of the organic compounds for which standard environmental tests have been developed. Most pharmaceuticals are charged and hydrophilic, and the sorption of these compounds to particles in STPs and surface waters cannot be predicted from the usual parameters. A well-defined testing strategy will identify the parameters likely to be most significant in predicting the fate of a particular test substance in a specific environmental compartment.

Covance experts offer a comprehensive service for the Tier A assessment, including:

- The conduct and evaluation of experimental studies required when establishing the PEC/PNEC ratio
- PNEC calculation
- Groundwater exposure assessments
- PEC sw and PEC gw estimations

All studies are conducted to the recommended OECD/ISO/OPPTS guidelines, in a GLP-compliant facility by experienced Study Directors/personnel. In addition, Covance offers support with:

- Test design to account for your product's unique chemical properties
- Metabolite profiling
- Test results analysis
- Advice on additional testing requirements and assessment
- Higher tier study designs and interpretation

Physical Chemistry

- Determination of physical chemical properties where required

Biodegradation

- Ready biodegradability test (OECD 301)
- Activated sludge, respiration inhibition test (OECD 209)

Environmental Fate

- Adsorption desorption (OECD 106/OECD 121/OPPTS 835.1110)
- Aerobic and anaerobic transformation in aquatic sediment systems (OECD 308)

Aquatic Ecotoxicity

- Algae, growth inhibition test (OECD 201)
- *Daphnia sp.* reproduction test (OECD 211)
- Fish early life stage toxicity test (OECD 210)

Phase 2 Tier B: Extended Environmental Fate and Effects Testing

Where risk has been identified at Tier A, Covance offers:

- Advice and support in the design of Tier B assessments
- Compartment-specific risk refinements for both metabolites and parent compound
- Regular consultation with the authority to ensure data generated are fit for purpose and meet the specified requirements.

Tier B Testing Requirements

Extended Aquatic Effects Testing

- Sediment-dwelling organisms (establishing PNEC sediment)
- Micro-organisms (PEC/PNEC in STPs)

Terrestrial Environmental Fate and Effects

Investigation into the effects of soil biodegradation, invertebrate toxicity, effects on terrestrial plants and micro-organisms:

- Aerobic and anaerobic transformation in soil (OECD 307)
- Soil micro-organisms: nitrogen transformation test (OECD 216)
- Terrestrial plants, growth test (OECD 208)
- Earthworm, acute toxicity test (OECD 207)
- Collembola, reproduction test (ISO 11267)

Regulatory Services

- Manage the project from enquiry to submission
- Advise on precautionary and/or safety measures in cases where there are potential adverse effects to the environment
- Interpret and evaluate data in collaboration with Scientific Leadership Team
- Compile expert reports for the completion of the Environmental Risk Assessment Report

Related Services

- Physical Chemistry
- Biodegradation
- Environmental Fate
- Ecotoxicology
- Risk Assessment
- Regulatory Affairs

Overview: Environmental Risk Assessments

For many years, drugs and their metabolites have been subject to unrestricted emissions to the environment. Complex mixtures enter the environment via a number of pathways, such as sewage treatment plant (STP) effluents and the land application of sewage sludge. The detection of an increasing number of human medicines at low concentrations in surface waters, coupled with their usual characteristic persistence in the environment, has led to a demand for a better understanding of the fate and potential long-term effects of these materials.

Covance can partner with you by providing a well-defined risk assessment and testing strategy, specific to the unique properties of your product, targeted at the respective environmental compartments of concern.

Our extensive experience in environmental safety testing and risk assessment strategy design, coupled with a sound understanding of regulatory requirements, facilitates the avoidance of potential obstacles and saves you time and money.

Covance is an independent, publicly held company with headquarters in Princeton, New Jersey, USA.
Covance is the marketing name for Covance Inc. and its subsidiaries around the world.

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