Environmental Risk Assessment of Human Medicinal Products

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.

Smithers Viscient 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.

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.

Smithers Viscient can provide you with comprehensive services for completing an ERA, including consultation and testing for Phase I and Phase II 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
Environmental Risk Assessment of Human Medicinal Products

When you place an ERA Study with Smithers Viscient, 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

Smithers Viscient 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, Smithers Viscient offers support with:

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

Phase I: 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 II 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.

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)
- Aerobic and anaerobic transformation in aquatic sediment systems (OECD 308)
Aquatic Ecotoxicology

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

Phase II Tier B: Extended Environmental Fate and Effects Testing

Where risk has been identified at Tier A, Smithers Viscent 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
- Compile expert reports for the completion of the Environmental Risk Assessment Report

Related Services

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

Summary of Capabilities and Facts:

- Comprehensive services spanning regulatory consultation, Phase I and Phase II, Tier A & B testing requirements
- Experienced in the conduct of GLP compliant study designs
Environmental Risk Assessment of Human Medicinal Products

Phase I
Calculate PEC based on default values

- PEC > 0.01 µg/L + no effects expected at <0.01 µg/L (certain substances may affect at <0.01 µg/L, e.g. endocrine disrupters)
- PEC < 0.01 µg/L + no effects expected at <0.01 µg/L

Phase II, Tier A
- Kow (OECD 107, 117, 122, 123)
- Koc (OECD 106)
- Water sediment (OECD 308)
- Algae, growth inhibition test (OECD 201)
- Daphnia sp. reproduction test (OECD 211)
- Fish early life stage test (OECD 210)
- Activated sludge respiration test (OECD 209)

Risk
- Yes
- No

Phase II, Tier B
Studies depending on results at Tier A

No further testing necessary