LRI ECO71 – INTEGRATED ASSESSMENT OF WATER-SOLUBLE POLYMER BIOAVAILABILITY

Background

Polymers are complex materials, composed of typically large molecules across a distribution of molecular weights, and covering a wide spectrum of properties and are essential components of everyday products. Many regulatory frameworks have considered polymers of low hazard since they are often assumed to have poor/negligible systemic bioavailability.

There is an increasing concern related to potential environmental and human exposures to water soluble polymers and whether the assumption of poor/negligible bioavailability is correct. In this context, there is a need to establish methods that can assess polymer bioavailability and better support the future hazard and risk assessment for water soluble polymers.

Bioavailability is a fundamental consideration for both human and environmental hazard and risk assessments, including bioaccumulation potential. Contrary to small molecules, only limited in vitro and in vivo bioavailability data and models exists for water soluble polymers. Bioavailability is defined in toxicology as the relative amount of a material becoming available in the blood stream after exposure via different routes (e.g. oral, dermal, or respiratory). Methods and capabilities to assess bioavailability of polymers will be crucial for exposure-led testing strategies and therewith for a reduction of animal testing. However, when evaluating new methods for bioavailability, regulatory confidence in the data is achieved when comparing the results from new methods to data from established in vivo methods, be that new or existing data, on the same test materials.

Objectives

This project will generate foundational data and learnings on what methods are suitable for assessing systemic bioavailability of water-soluble polymers. The long-term aim is to enable decisions on bioavailability testing for polymers, support human and environmental data hazard and risk assessments (and therefore, hazard data requirements), inform bioaccumulation potential, and aid in grouping assessments of polymers.

The project's objectives are to:

1. Identify existing in vitro and ex vivo approaches that are used to estimate systemic bioavailability of small molecules and evaluate the applicability, feasibility and performance of these assays for selected water soluble polymers.

   Applicants should consider both human and environmental test systems and ensure that appropriate analytical information will be generated to allow for sound interpretation of data. Test system(s) should consider multiple routes of exposure, such as oral (both mammals and fish), inhalation (gill/lung) and/or dermal, and different tissue models. Examples of experimental models that are relevant to this work include, but are not limited to, mammalian cell permeability models (Caco-2), mammalian tissue permeability models (ex vivo intestine, dermatomed skin), fish permeability models (gill or gut barrier models). It is recognized that there is a

greater availability of test systems and legacy data for mammalian species compared to environmental species, and this distinction may be reflected in the components of a project proposal.

2. Utilize and generate information on polymer properties (e.g., structure, phys-chem properties) to evaluate existing assumptions related to polymer bioavailability (e.g., molecular weights cut-offs) and bioaccumulation (e.g., is bioaccumulation unlikely if Dmax >1/7 nm and/or 3>logP>10?).

3. Investigate experimentally water soluble polymers from different classes and varying physicochemical properties. Ideal test materials would already have relevant in vivo ADME data.

Water soluble polymers vary widely by polymer type, molecular weight, functionality, lipophilicity, and other parameters.

If relying on existing *in vivo* AMDE data, the project proposal shall include detailed consideration on the suitability of the data available, the identity of the test material and its availability for the proposed work. Examples of water soluble polymers that may be relevant to this work include, but are not limited to, polyethylene glycols, dextrans, and polysaccharides.

4. Publish research findings and recommendations on how to best conduct bioavailability studies for water soluble polymers.

If suitable (well characterized) test materials with existing in vivo ADME data are unavailable, it will be necessary to generate in vivo anchoring data following the principles of the 3Rs (replacement, reduction, refinement). The newly obtained in vivo ADME data for soluble polymers would be utilized to further assess the performance of in vitro and/or ex vivo bioavailability methods. Prior to submitting a project proposal that includes the generation of in vivo ADME data, a literature review must be conducted to verify the absence of suitable existing in vivo ADME data, thereby justifying the need for the generation of new data. Project proposals intending to refer to existing in vivo ADME data are expected to have assessed suitability and accessibility of the material tested in vivo

of those data before submission of the proposal. Adherence to the principles of Good In Vitro Method Practices (GIVIMP) is strongly encouraged, and test institutes that can demonstrate compliance with GIVIMP may be given preference during proposal evaluation.

Scope

In silico approaches can be integrated into the overall project strategy to complement the experimental data; however, they should not be the primary focus of the project.

Water soluble polymers vary widely by polymer type/chemistry, average molecular weight and dispersity, surface activity, and charge density. Thus, water soluble polymers from a variety of classes need to be investigated experimentally. This research will focus on water soluble polymer classes and not on solid polymeric materials (such as microplastics).

In the context of the current project, "soluble polymer" is defined as a polymer that:

- Dissolution Capability: Can dissolve in a suitable solvent to form a homogeneous solution under specified conditions.
- Physiological Relevance: Remains in solution when introduced into a physiologically relevant test system, maintaining solubility at physiologically relevant temperatures (both mammals and fish) and concentrations.

Out of scope

Insoluble polymers, solid particles (e.g., microplastics) and (N)IAS are out of scope for this project.

In the context of the current project, "insoluble polymer" is defined as a polymer that:

- Dissolution Capability: Cannot dissolve in a suitable solvent to form a homogeneous solution.
- Physiological Relevance: Comes out of solution when introduced into a physiologically relevant test system.

Deliverables

The final report shall contain an executive summary (2 pages max), a main part (max. 50 pages) and a detailed bibliography. It is also expected that the findings will be developed into one to three peer reviewed publications, following poster(s) and presentation(s) at suitable scientific conference(s).

Partnering / Co-funding

Applicants should provide an indication of additional partners and funding opportunities that can be appropriately leveraged as part of their proposal. Partners can include, but are not limited to industry, government/regulatory organizations, research institutes, etc. Statements from potential partners should be included in the proposal package. This project will most likely require participation of partners with experience in advanced polymer analytics.

Fit with LRI objectives / Possible regulatory and policy impact involvements / Dissemination

Applicants should provide information on the fit of their proposal with LRI objectives and an indication on how and where they could play a role in the regulatory and policy areas. Dissemination plans should also be laid down.

DEADLINE FOR SUBMISSIONS: May 31st 2026 at 11:59 PM CET.

Please see www.cefic-lri.org/funding-opportunities/apply-for-a-grant/ for general LRI objectives information, project proposal form and further guidance for grant applications. Please note that, if awarded the project, the institute must be able to accept Belgian Law (or an equivalent European legal framework) in the contract. If there are questions, please email lri@cefic.be.
Timing: Q3 2026 - Q3 2029

LRI funding: €700,000