DRAFT

Code Number and Title:

LRI-ECO34: Rapid assessment for uptake and biotransformation pathways using multiple lines of *in vitro* evidence.

Background

Recently a CEFIC-LRi and ECHA workshop on recent developments in bioaccumulation research (Helsinki, September, 2014) concluded that the biotransformation rate constant represents the principal source of uncertainty in the bioaccumulation assessment of most chemicals and that *in vitro* to *in vivo* extrapolation to estimate clearance and biotransformation offers a promising path forward. Several research groups, for instance, have expanded their empirical tools beyond simply assessing liver metabolism, and have developed methods to measure fish gut and gill metabolism. These tools can add to a weight of evidence assessment of bioaccumulation and might be used with other indicators of bioaccumulation potential in a tiered approach for deciding the need for *in vivo* bioaccumulation testing. Consequently, it is believed that the development of in vitro screening tools to assess biotransformation, and that extend the applicability domain of tests, can enable improvements in the regulatory assessment of bioaccumulation.

Furthermore, by combining empirical data on the biotransformation of a chemical with internal concentration models, a more robust method for linking toxicokinetics with toxicodynamics is possible, which could be useful in strengthening mechanistic understanding of adverse outcome pathways. It is expected that the development of a suite of *in vitro* tools aimed at quantifying biotransformation pathways could thus support the development of mechanistic tools for estimating internal concentrations that will result in more ecologically relevant chemical risk assessment.

Scope and Objectives

Develop and apply a suite of *in vitro* assays that provide quantification of biotransformation rates through multiple lines of evidence, and which extend the applicability domain of current methods. Combine empirical data regarding the biotransformation of a chemical with internal concentration models that can support the development of more ecologically relevant chemical risk assessment.

Deliverables

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

Cost and Timing
Start in 2015/16, duration 3 years.
Budget in the order of € 500 000.

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.

Fit with LRI objectives/Possible regulatory and policy impact involvements/ Dissemination
Applicants should provide information on how their proposal is aligned with LRI objectives. Furthermore, an indication on how the results could influence regulatory and policy areas should be provided.
Dissemination plans should also be laid down.

DEADLINE FOR SUBMISSIONS: 6 Sept 2015

Please visit www.cefic-lri.org for general information about the LRI funding programme, guidelines for grant applications and links to application documents.