July 2016 - iPiE Newsletter - Num 1

"Intelligent Assessment of Pharmaceuticals in the Environment"

Introductory notes from the coordinator

Dear reader,

You are reading the first edition of the newsletter of the IMI project ***"Intelligence Led Assessment of Pharmaceuticals in the Environment (IPIE)"***. ***IPIE*** is a project under the joint Innovative Medicines Initiative **(IMI),** in which the **European Commission** and the **European Federation of Pharmaceutical Industries and Associations (EFPIA)** co-fund research projects under the public-private partnership concept, in order to promote the development of and patient access to, innovative medicines, particularly in areas where there is an unmet medical or social need.

Reinhard Laenge, Bayer AG, project coordinator

In this context, **IPIE** will help to understand, how we could use approaches in modelling and intelligent testing for the environmental risk predictions of human pharmaceuticals.
Environmental risk assessments are required for all new products coming to the market in the **EU** or in member states since 2006, following agreed, standardized procedures. Commonly, this environmental risk assessment is carried out by the industry at a relatively late state of development. While only a small fraction of compounds assessed in this context so far have a potential for an environmental impact, there is a major societal interest to provide knowledge of the many hundred pharmaceutical compounds, which were placed on the market before 2006 and for which environmental risk information is incomplete or not existing. Additionally, there is a desire to learn about potential environmental impacts of internal early development candidates within industries.
The methodology, which is developed under the **IPIE** project, should provide means for prioritization of the incompletely tested or untested active pharmaceutical ingredients (APIs), which can be used to identify those compounds, which have a significant potential for an environmental impact. On those candidates an environmental testing programme can be carried out efficiently, rather than aspiring to test all hundreds of compounds with the consequence of the use of large number of animals (mainly fish) and laboratory capacity for irrelevant testing of APIs with low environmental significance.
The methodology being developed can also be used internally in the companies to learn at an early stage of development about potential environmental consequences of the API used in therapies. This might in future enable industry to include environmental concerns in the development of new APIs, design appropriate testing strategies for intelligent testing, and to consider mitigation strategies for environmental risks.
Hence, **IPIE** has the goal to help to understand mechanisms, which drive exposure and effects of human pharmaceuticals in the environment, which then can be used to develop appropriate prediction models and screening assays for prioritization and screening

of APIs for environmental risks.
The project started in January 2015 and will run for 4 years. The budget is more than 10 Mill Euros and 25 partners from universities, small and medium sized companies, regulatory agencies and industry are participating.
Together with my colleague Alistair Boxall from the University of York, who is the scientific coordination in this project, I hope that you are reading this newsletter with interest and follow us on our webside http://i-pie.org/.

Project News

- **The third Project Meeting was held in Paris in May 2016, hosted by Sanofi**. The meeting was focusing on certain topic groups: Text Mining, data entry and Quality Assessment of literature data; Data management and software development; Effects and uptake models in invertebrates and primary producers; Exposure modelling and monitoring; Fish plasma model and validation as part of effects modelling.

- **Following the IPIE Project Meeting**, the **SETAC (Society of Environmental Toxicology and Chemistry)** Europe conference in Nantes followed with several contributions from the **IPIE** project. Research presented from work packages 4 and 5, lead by Lina Gunnarsson (Exeter University), highlighted drug target conservation of across taxa using a comparative genomic approach using different ortholog prediction methods. About 85% of human drug targets have orthologs in teleost fish and <1% of active pharmaceutical ingredients (API) lack conserved pharmaceutical drug targets in all fish. Lina also described the relative sensitivity of daphnia and fish to API exposure where drug targets were and were not conserved between these two ecotoxicological models. Gareth le Page (Exeter University) presented an analysis of all publically available ecotoxicity data and clinically relevant data for antibiotics. This meta-analysis of data indicated that cyanobacteria were generally the most sensitive ecotoxicological species and in some cases they were more sensitive than recently published theoretical predicted no effect concentrations for antimicrobial resistance (PNECresistance). Gareth is currently validating a microtitre-based assay for algal and cyanobacteria toxicity screening for a wider range of test species. These microtitre-based assays will allow chemicals and effluents to be screened with greater throughput. Finally, Stewart Owen and Jason Snape (AstraZeneca) presented a poster based on the output of work package 1. This poster described a prioritisation framework, using in silico, in vitro and in vivo assays to predict API uptake, metabolism, elimination and toxicity that could be used to assess the relative risks posed by APIs at local, regional and national levels.

- **Next IPIE Forum meeting** including a session with the **Scientific Advisory Board will be held in Sitges near Barcelona on the 4th to the 6th of October**, followed by a workshop on the 7th October with the **eTOX** Project on common software developments.

Presentations

SETAC Posters

- Le-Page G, Trznadel M, Gunarsson L, Snape J, Tyler CR. Assessing relative sensitivity to antibiotics in freshwater cyanobacteria and microalgae
- Gunnarson L, Kristiansson E, Österlund T, Owen S, Snape J, Tyler CR. Comparative Genomics for Predicting Pharmacological Effects of Pharmaceuticals in Fish: Potential and Limitations
- Snape J, Owen S, Gunnarsson L, Boxall A. Science-based Approaches to Prioritise Environmental Risks Posed by Legacy Human Medicinal Products