



DOCTORAL NETWORK



PhD POSITION N°10

Project title

Assessment and prediction of the toxicity of pharmaceuticals on surface water and sediment model organisms

Recruiting institution

KREATiS, France

BACKGROUND

This doctoral position is 1 of 10 doctoral positions offered within the [HORIZON Marie Skłodowska-Curie Action \(MSCA\) Doctoral Network Pharm-ERA: "Improving monitoring and Environmental Risk Assessment of PHARMaceuticals, antimicrobial resistance and pathogens from terrestrial to aquatic environments"](#).

Global contamination of soil and aquatic ecosystems by pharmaceutical and microbiological pollutants (such as antimicrobial-resistant microorganisms and/or pathogens) raises severe concerns about impacts on ecosystem health and repercussions on humans and animals. Preserving ecosystems from adverse ecotoxicological effects of pharmaceuticals and their transformation products, and limiting the environmental spread of antimicrobial resistance and pathogens is imperative to reach several UN Sustainable Development Goals as well as the European Green Deal, Water Framework Directive and Biodiversity Strategy for 2030. In this context, the main scientific objective of Pharm-ERA is to develop and implement innovative concepts, methods and strategies to improve the monitoring and assessment of the environmental effects and risks of pharmaceuticals, their transformation products, antimicrobial resistances and pathogens from terrestrial to aquatic environments. The ultimate goal is to provide scientific evidence and expertise to contribute to reducing the environmental spread and impact of these chemical and microbiological contaminants and to preserve microbial diversity and functions across the soil-water-sediment continuum.

By joining Pharm-ERA, you will integrate a high-level interdisciplinary and intersectoral research and training network based on 10 doctoral projects covering scientific disciplines including environmental and analytical chemistry, microbial ecology, ecotoxicology, molecular biology (incl. multi-omics approaches) and chemical fate/effect modelling. Pharm-ERA involves 9 Beneficiaries (including 2 non-academics) and 6 Associated Partners (including 5 non-academics), committed to contribute to research, training, dissemination, communication and exploitation of results targeting end-users such as environmental consultancies and agencies.

DESCRIPTION OF THE PhD PROJECT

Pharmaceuticals are widespread in aquatic ecosystems and are known to potentially affect aquatic organisms (Hejna et al., 2022; Cannata et al., 2024), depending on their behaviour in the environment. The hazard assessment of a pharmaceutical in the environment is commonly performed in the laboratory, under controlled conditions and based on biological organism testing amongst others. However, these studies are usually very time-consuming and costly and there is a need for a more efficient and rapid process to evaluate the toxicity and fate of potentially dangerous chemicals. Furthermore, we are now in the era of the 3Rs (reduction, replacement, refinement of vertebrate animal testing) where regulators are increasingly calling for new alternative methodologies (NAMs) to reduce the number of organisms involved in ecotoxicological testing (OECD, 2020). A promising solution is the use of *in silico* methodologies which consist of using existing data like effect concentrations or water solubility values, among others, to predict biological and chemical properties (e.g. toxicity, bioaccumulation, biodegradability).

The aim of this PhD project is to understand the behaviour of a set of pharmaceutical compounds in aquatic ecosystems and their toxicity to aquatic organisms, to ultimately reliably predict their ecotoxicity based on their mechanism of toxic action. Thus, this project lies at the interface of analytical and environmental chemistry, ecotoxicology and regulation and involves both laboratory experiments and model developments. Once the set of pharmaceuticals and potentially related transformation products (TPs) is defined, the first objective of the project is to characterise the fate and behaviour (especially in terms of TPs occurrence) of the selected pharmaceuticals in sediment and surface waters following OECD test guidelines. The detection and identification of potential TPs will be carried out by liquid chromatography coupled with high-resolution mass spectrometry LC-HRMS using an approach implemented at INRAE (Rocco et al. 2022). A second objective is to assess acute and chronic effects of the selected pharmaceuticals including also potentially the TPs to sediment and surface water organisms using single-species bioassays (e.g. *Lumbriculus*, chironomids, algae, ostracods, gammarids, daphnids, fish). *In silico* approaches developed at KREATiS are strongly anchored into the mechanistic understanding of chemical effects on biological organisms (Bauer et al., 2018). Therefore, the third objective is to understand the mechanism of toxic action of the selected chemicals on organisms in different trophic levels using existing data to support the development of predictive ecotoxicological models for pharmaceuticals and develop structural alerts. Finally, the fourth objective of the project is to develop models (e.g. (Quantitative) Structure-Activity Relationship, sophisticated machine learning approach) to predict quantitatively the toxicity of certain pharmaceutical structures, including also the relevant TPs, on water and sediment organisms.

The doctoral candidate will be hired by KREATiS (L'Isle-d'Abeau, France) and will be hosted by the INRAE centre in Villeurbanne (France) 40 km away. Regular visits at KREATiS will be planned. The recruited candidate will also be hosted by the Ecotox Center (Switzerland) and Aquabiotech (Malta) for a maximum period of four months each for the ecotoxicological testing.

References

- Bauer, F.J., Thomas, P.C., Fouchard, S.Y., and Neunlist, S.J.M. (2018). High-accuracy prediction of mechanisms of action using structural alerts. *Computational Toxicology*. 7, 36-45.
- Cannata, C., Backhaus, T., Bramke, I., Caraman, M., Lombardo, A., Whomsley, R., Moermond, C.T.A., Ragas, A.M.J. (2024). Prioritisation of data-poor pharmaceuticals for empirical testing and environmental risk assessment. *Environment International* 183, 108379.
- Hejna, M., Kapuscinska, D., Aksmann, A. (2022). Pharmaceuticals in the aquatic environment : A review on eco-toxicological and the remediation potential of algae. *International Journal of Environmental Research and public health*. 19, 7717.
- OECD (2020), Overview of Concepts and Available Guidance related to Integrated Approaches to Testing and Assessment (IATA), OECD Series on Testing and Assessment, No. 329, Environment, Health and Safety, Environment Directorate, OECD.
- Rocco, K., Margoum, C., Richard, L., Coquery, M. (2022). Enhanced database creation with *in silico* workflows for suspect screening of unknown tebuconazole transformation products in environmental samples by UHPLC-HRMS. *Journal of Hazardous Materials*. Volume 440, 15 October 2022, 129706.

PRACTICAL INFORMATION

Recruiting institution	KREATiS, France
Doctoral school	Evolution Ecosystems Microbiology Modeling (E2M2), University of Lyon, France
Supervisors	Dr. LARRAS Floriane (KREATiS, France), Dr. MARGOUM Christelle (INRAE, France), Dr. PESCE Stéphane (INRAE, France).
Non-academic mentor	Dr. Benoît Ferrari (Centre Ecotox, Switzerland)
Main host laboratory	INRAE, Lyon, France, Dr. Christelle Margoum (Aquatic Environment Chemistry Laboratory, UR RiverLy) and KREATiS (L'Isle-d'Abeau, France), Dr. Floriane Larras to perform analytical developments and measures
Secondments (1 to 6 hosting months)	1) Centre Ecotox, Switzerland, to perform ecotoxicological bioassays on surface water, sediment and potentially soil organisms, under the supervision of Dr. Benoît Ferrari; 2) AQUABIOTECH, Malta, to perform ecotoxicological bioassays on surface water organisms, under the supervision of Dr. Adrian C. Love.

RECRUITMENT CRITERIA

General criteria

- MSCA Mobility Rule: researchers must not have resided or carried out their main activity (work, studies, etc.) in the country of the recruiting beneficiary for more than 12 months in the 36 months immediately before their date of recruitment
- All researchers recruited in a DN must be doctoral candidates (i.e. not already in possession of a doctoral degree at the date of the recruitment)
- Scientific excellence to fit the PhD project
- Fluent (oral and written) English skills as the project operates in English language
- Knowledge of the language of the host country may be considered a merit
- Team-mindedness

Criteria specific for PhD10

- Master degree in aquatic biology or equivalent with a strong interest in analytical and environmental chemistry
- Previous experience in statistics and model development (e.g. linear regression, sophisticated machine learning approaches and database management) and skills in programming languages is a strong plus
- We are looking for a curious and keen to learn candidate. In addition, the doctoral candidate is expected to be dynamic, rigorous, autonomous and willing to have regular interactions with collaborators from different nationalities

- The recruited doctoral candidate must be willing to move for a maximum of 8 months (e.g. two times four months) during the contract as the experimental bioassays will take place in the Ecotox Center (Switzerland) and in Aquabiotech (Malta)

APPLICATION

Documentation to be sent in by the applicants

- Application form completed
- CV + Letter of motivation
- Contact of two reference persons to be contacted by the selection committee (name, relation to the candidate, e-mail address and phone number)
- Complete list of publications and academic works
- Proof of language proficiencies
- Proof of master diploma or 2024 registration to master degree

How to apply?

- Download application form and fill it indicating all the offers you wish to apply for
- Send your application by email to pharm-era@inrae.fr. **The title of your email MUST be : Pharm-ERA PhD x, x, x application** (x, x, x being the number(s) of the PhD position(s) you want to apply for)
- **Be careful to join all documentation required** (see list above)

Deadline for application

April 2024, 14th - 6:00 pm French time

Contact

pharm-era@inrae.fr