Project title	Assessing and predicting the fate of model pharmaceutical compounds and their transformation products in soils & towards the aquatic systems
Recruiting institution	Aeiforia s.r.l. (Spin-off company of Università Cattolica del Sacro Cuore in Piacenza, Italy)

BACKGROUND

This doctoral position is 1 of 10 doctoral positions offered within the he HORIZON Marie Sklodowska-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

Veterinary pharmaceutical compounds (PhACs) and their transformation products (TPs) enter soil, then water bodies, through various routes imposing pollution, toxicity and selection pressure to the soil microbiota.

The main objective of the project is to develop a ready-to-use version of the TyPol tool for *a priori* estimation of veterinary PhACs TPs fate in soil and potential transfer to aquatic ecosystems, and to develop open access protocols for chemical analyses of selected PhACs & TPs in soils. To do so, this project is divided between experimental work, chemical analyses and statistical analyses.

At AEIFORIA, the hiring institution, field scale dissipation test will be performed for selected PhACs and their TPs, coupled to an in-lab degradation and plant uptake study. Analysis will be performed by LC-HRMS with previously validated methods. In cooperation with Fellow #2, the main TPs of pharmaceuticals in soil samples obtained by a microcosm study conducted at University of Thessaly, Greece, will be analyzed. Data obtained from lab, mesocosm and field scale will then be used during following secondments.

The secondment at INRAE Lyon will be focused on the search and identification methodology for suspected TPs. The method developed for pesticides (Rocco *et al.* 2022), based on LC-HRMS, will be adapted for a selection of PhACs The suspected analysis will be carried out on field samples. Comparisons of results with those obtained at AEIFORIA, using high-res MS/MS untargeted metabolomics coupled to ion mobility, will also be carried out.

The secondment at INRAE Palaiseau will be focused on the use and implementation of the TyPol (Typology of Pollutants) tool, developed to classify organic compounds, and their TPs, according to both their behaviour in the environment and their ecotoxicological effects, and their molecular properties (Servien *et al.*, 2014). It is based on PLS regression and hierarchical clustering. TyPol can also be used to assess the fate and effects of an organic compound from its molecular properties by similarity with compounds having comparable properties, and for which environmental and ecotoxicological parameters are known (e.g., Benoit *et al.*, 2017; Storck *et al.*, 2016; Mamy *et al.*, 2021).

In this PhD thesis, TyPol will be first combined with new analytical methods to identify and prioritize TPs to be investigated in a more comprehensive environmental risk assessment scheme. Then, an improved version of TyPol enabling a robust estimate of the fate of pharmaceutical TPs using the molecular properties of the TPs as main predictors will be developed. Finally, TyPol will be tested and validated by comparing *in silico* clustering results with laboratory measured data on the fate of TPs.

References

- Benoit, P., Mamy, L., Servien, R., Li, Z., Latrille, E., Rossard, V., Bessac, F., Patureau, D., Martin-Laurent, F., 2017. Categorizing chlordecone potential degradation products to explore their environmental fate. Sci. Total Environ. 574, 781–795. https://doi.org/10.1016/j.scitotenv.2016.09.094.
- Mamy L, Bonnot K, Benoit P, Bockstaller C, Latrille E, Rossard V, Servien R, Patureau D, Prevost L, Pierlot F, Bedos C, 2021. Assessment of pesticides volatilization potential based on their molecular properties using the TyPol tool. Journal of Hazardous Materials. 415: 125613. https://doi.org/10.1016/j.jhazmat.2021.125613
- Servien, R., Mamy, L., Li, Z., Rossard, V., Latrille, E., Bessac, F., Patureau, D., Benoit, P., 2014. TyPol - a new methodology for organic compounds clustering based on their molecular characteristics and environmental behavior. Chemosphere 111, 613–622. https://doi.org/10.1016/j.chemosphere.2014.05.020
- Storck, V., Lucini, L., Mamy, L., Ferrari, F., Papadopoulou, E.S., Nikolaki, S., Karas, P.A., Servien, R., Karpouzas, D.G., Trevisan, M., Benoit, P., Martin-Laurent, F., 2016. Identification and characterization of tebuconazole transformation products in soil by combining suspect screening and molecular typology. Environ. Pollut. 208, 537–545. https://doi.org/10.1016/j.envpol.2015.10.027.

- Rocco K., Margoum C.,Richard L., Coquery M., Enhanced database creation with in silico workflows for suspect screening of unknown tebuconazole ransformation products in environmental samples by UHPLC-HRMS, J. Hazard. Mater., 2022, 440, 129706
- Storck V, Nikolaki S, Perruchon C, Chabanis C, Sacchi A, Pertile G, Baguelin C, Ferrari F, *et al.* Lab to field assessment of the ecotoxicological impact of chlorpyrifos, isoproturon, or tebuconazole on the diversity and composition of the soil bacterial community. Front Microbiol (2018) 9.
- Ferrari F., Gallipoli A., Balderacchi M., Ulaszewska M.M., Capri E., Trevisan M. Exposure of the Main Italian River Basin to Pharmaceuticals. J Toxicol. 2011; 2011: 989270. Published online 2011 September 19. doi: 10.1155/2011/989270PMCID: PMC3175726

PRACTICAL INFORMATION

Recruiting institution	Aeiforia s.r.l. (Spin-off company of Università Cattolica del Sacro Cuore in Piacenza, Italy)
Doctoral school	AGRISYSTEM @ Università Cattolica del Sacro Cuore, Italy
Supervisors	Dr. Federico Ferrari (Aeiforia s.r.l, Italy). and Pr. Luigi Lucini (Università Cattolica del Sacro Cuore, Italy), Dr. Christelle Margoum, (INRAE, Lyon, France), Dr. Laure Mamy (INRAE, Palaiseau, France)
Non-academic mentor	Dr. Federico Ferrari (Aeiforia s.r.l.), Italy
Main host laboratory	Aeiforia s.r.l., Piacenza, Italy, Dr. F. Ferrari, to perform experimental work (field scale dissipation tests, in-lab degradation and plant uptake study) and chemical analyses.
Secondments (1 to 6 hosting months)	1) INRAE, Palaiseau, France, to get literature review, training and development of TyPol in silico tool under supervision of Dr. L. Mamy 2) INRAE, Lyon, France, to perform analyses of lab and field samples (from Fellow 2) to obtain measured concentrations of selected PhACs and potential concentrations of their TPs in soils for further comparison with TyPol predictions in soil, under supervision of Dr. Christelle Margoum

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 PhD1

- Good knowledge in analytical chemistry with particular aspect on analytical methods (HPLC) for environmental analysis and residues in soil and water
- Basic knowledge in the use of predictive tools for calculating predicted environmental concentrations of contaminants
- Basic knowledge of mass spectrometry
- Master degree in Environmental Chemistry or Soil sciences or Biochemistry or equivalent

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