

Development of a New Approach Methodology (NAM) to Assess the Ecotoxicology of Persistent Substances Based on Multigenerational Effects in the Nematode (*C. elegans*)

Keywords

Dynamic Energy Budget (DEB) model, Extremely persistent substances (PFAS), Multigenerational study, *C. elegans*, Environmental risk assessment.

Abstract

Chemicals that resist degradation in the environment, referred to as “persistent”, result in long-term exposure for humans and ecosystems. Persistence leads to the gradual accumulation of these pollutants in the environment, creating an increasing environmental stock that may impact populations over very long timescales (decades to centuries). This persistence criterion is defined in the REACH and CLP regulations through half-life thresholds specified for different environmental compartments (Annex XIII of the REACH regulation).

Assessing the effects—and consequently the risks—of persistent substances at low concentrations and over relevant timescales therefore represents a major challenge. Indeed, regulatory ecotoxicological tests required for effect characterization are often limited to exposure durations covering only a restricted portion of an organism’s life cycle, even for so-called “chronic” tests. While such tests are appropriate for non-persistent substances, they appear disconnected from the temporal scales over which persistent pollutants exert their effects. In this context, multigenerational approaches are essential for determining the long-term effects of persistent pollutants.

The objective of this PhD project is therefore to propose a New Approach Methodology (NAM) based on multigenerational studies, in accordance with the 3Rs principle (Replacement, Reduction, and Refinement). This approach aims to improve environmental risk assessment for persistent substances. Among persistent chemicals, trifluoroacetic acid (TFA) will be investigated as a final degradation product of PFAS.

Nematodes are excellent models for multigenerational studies of persistent pollutants due to their very short life cycle (96 h) and the possibility to measure multiple endpoints at infra-individual, individual, and population levels. In addition, mechanistic and statistical modeling (e.g., DEB TK-TD models) allows the integration of biological and toxicological processes into the analysis of ecotoxicological data and enables the study of interactions between these processes.

The proposed PhD project will therefore aim to (i) characterize toxicity during chronic PFAS exposure through multigenerational experiments using nematodes as a biological model, and (ii) estimate the evolvability and the cost of adaptation of exposed populations in order to propose a relevant toxicological parameter describing these effects. Ultimately, the results of this work will contribute to improving the environmental risk assessment of persistent pollutants.

Proposed PhD timeline

The schedule below plans the application of the NAM approach (experimentation and modelling) to a single compound. Depending on the progress of the work, a second case study may be carried out during the PhD project.

Year 1 (Oct 2026 – Oct 2027)

- Task 0 – Literature review and familiarization with the research topic (3 months).
- Task 1.1 – Characterization of the effects of TFA considering several biological endpoints in the nematode, such as viability, growth and reproduction, sex ratio, and behaviour (dose–response relationship determination) (3 months).
- Task 1.2 – Characterization and modelling of toxicokinetics (TK) in the ancestral population (1.5 months).
- Task 1.3 – Modelling of experimental data using DEB TK–TD modelling in the ancestral population (1.5 months).
- Task 1.4 – Writing and submission of manuscript 1 (3 months).

Year 2 (Oct 2027 – Oct 2028)

- Task 2.1 – Multigenerational experiments to characterize the effects of TFA in the nematode *C. elegans* (9 months): experimental design, implementation of the multigenerational experiment, production and analysis of the collected data, writing and submission of manuscript 2.
- Task 2.2 – Analysis and modelling of multigenerational data using DEB TK–TD modelling (3 months).
- Task 2.3 – Experiments dedicated to the validation of the evolvability metric, including co-supervision (with INRAE) of a Master’s level (M2) student (Jan–Jun 2028, 6 months).

Year 3 (Oct 2028 – Oct 2029)

- Task 3.1a – Continued analysis and modelling of multigenerational data using DEB TK–TD modelling (6 months).
- Task 3.1b – Depending on project progress, the PhD candidate may also contribute to a PERSEE project task aimed at defining new criteria to estimate toxicological impacts on the adaptive capacity of nematodes, and to disseminate these results through a scientific publication.
- Task 3.2 – Multivariate statistical analysis of multigenerational data and writing and submission of manuscript 3 (3 months). In parallel, and with dedicated time throughout the year, the PhD thesis manuscript will be written.

Scientific environment

The PhD project is part of the “PERSEE” project (APR EST ANSES call, 12/2025). The consortium brings together a panel of complementary scientific experts in biomathematics and applied mathematics (INRAE, UMR ECOSYS, and INERIS, UMR-I 02 SEBIO) as well as in nematode physiology and ecotoxicology (INERIS, ICAT).

The PhD will take place at INERIS in Verneuil-en-Halatte, near Chantilly, in the remarkable

setting of the Halatte forest. The site is accessible by public transport from Paris-Nord, offering a good balance between proximity to Paris and a preserved natural environment.

INERIS has been conducting ecotoxicity experiments on nematodes for several years, and previous work has already addressed multigenerational aspects (Goussen et al., 2015a). In addition, bioenergetic models adapted for ecotoxicological data analysis (DEB TK-TD) have already been developed for *C. elegans* at INERIS (Goussen et al., 2015b). The ECOSYS laboratory and INERIS have previously collaborated on several national research projects.

- Doctoral School: ABIES
- Supervisors: Raphaël Royauté (INRAE / UMR ECOSYS), Nicolas Manier (INERIS) and Rémy Beaudouin (INERIS, UMR-I 02 SEBIO).
- Funding for the PhD is provided jointly by the PERSEE project and INERIS (50% each).
- Net salary: \approx €1,850 net per month.
- Desired PhD start date: 5 October 2026

Candidate Profile

We are seeking a highly motivated candidate with one of the following **backgrounds**:

- MSc (or equivalent) or engineering degree in biostatistics, biomathematics, biology, ecotoxicology, or a related field.
- Candidates with a biostatistics / biomathematics background should have solid knowledge of biology, physiology, or ecotoxicology.
- Candidates with a biology or ecotoxicology background should demonstrate a strong interest in both laboratory experimentation and mathematical modelling.

Required skills

- Experience or strong interest in dynamic systems modelling, including solving simple systems of ordinary differential equations (ODEs).
- Programming experience in R, Python, or similar scientific computing environments.
- Interest in ecotoxicological experimentation under controlled laboratory conditions.

Language requirements

- English proficiency (B2–C2); French language skills are a plus.

Personal qualities

- Intellectual curiosity and scientific rigor.
- Strong willingness to learn.
- Ability to work effectively both independently and as part of a team.

Application procedure

To apply, candidates should send the following documents by email to remy.beaudouin@ineris.fr and nicolas.manier@ineris.fr before 11 May 2026:

- A CV and a cover letter,
- At least one letter of recommendation from a program supervisor or a previous academic advisor,
- A transcript of Master's degree grades (or equivalent)