

Public-private platform for the pre-validation of endocrine disruptors characterization methods

PEPPER (<https://ed-pepper.eu/en/>) is a non-profit association (under the French 1901 law) created in the context of the French **National Strategy for Endocrine Disruptors**. The initial project was supported by a task force involving Ineris¹, various industries, government departments and NGOs and led to the financial support from the French **“Programme of Investments for the Future”** (PIA) at the end of 2019, supplemented by the funding from PEPPER’s members (private and public organisations).

The objective: to fill the gaps in regulatory science

PEPPER’s ambition is to strengthen a current **weak link** in the **characterization and regulatory systems**, i.e. the **lack of tools available to characterize** endocrine disruptors. Not all the effects and mechanisms at play are indeed currently covered.

PEPPER’s mission is to carry out a « **pre-validation** » of toxicology and ecotoxicology test methods which are deemed necessary to characterize ED properties.

Pre-validation is an “upstream” process which will **accelerate** the validation of these methods by international authorities (**OECD, ECVAM, ISO**) and, ultimately, their **acceptability in regulations** on substances, products, environments or activities.

PEPPER was created based on the following four considerations:

- There are many lists of substances yet to be assessed.
- There is a lack of validated test methods, as highlighted by the European Commission.
- The validation process requires costly testing on methods’ robustness and predictability.
- There isn’t any funding available to support this process, whether at European or national level.

Pre-validation: identifying and testing the methods, and supporting their journey to validation

PEPPER carries out and finances the three following activities:

- Identifying and documenting test methods which are mature, scientifically documented and meeting a need in terms of identification of EDs;
- Organizing tests on these methods, performed by test laboratories, allowing to assess the “transferability” of the method from the development laboratory onwards, the repeatability and reproducibility of results on “positive” and “negative” substances; this is done through ring testing;
- Supporting the developers in forwarding their methods and the required scientific reports to international validation authorities.

PEPPER also runs the operations of the Committees which are part of its governance. We can also, at an extra charge, organise testing around methods which are not yet mature enough to enter pre-validation, in order to accompany their development; we publish scientific monitoring reports on emerging methods; we can assist the developers in their communications with international validation authorities and offer training on pre-validated methods.

Our governance: selecting priorities and maintaining the highest standards

PEPPER’s governance aims at maintaining a balance between all stakeholders involved, beyond their diversity, and at ensuring high scientific standards and the respect of ethical rules of conduct. This is done through three governing bodies:

The Relevance Committee holds a key role, i.e. **prioritising the methods due to enter the pre-validation process**. It is made of stakeholders who have an interest in the identification of EDs: national and international authorities, various industries, health and environmental NGOs, trade unions and scientists/scientific bodies. Composition: <https://ed-pepper.eu/en/opportunity-committee/>

The Scientific Council ensures the right tests are being carried out for pre-validation, the results are of good quality and publishes its **conclusions on the success or failure of a pre-validation process**. It is made of national and international scientists, coming from the public and private sectors, who are appointed *intuitu personae*. Composition: <https://ed-pepper.eu/en/the-scientific-council/>

The Ethics Committee aims at avoiding any bias in the decision making and monitors the process for public declarations of interests. It is worth noting that, by working solely on assessing the methods - and not the substances themselves - PEPPER already avoids many potential conflicts of interests. Composition: <https://ed-pepper.eu/en/ethics-committee/>

PEPPER’s governance and running involves a General Assembly, a Board of Directors and four permanent employees.

Our first achievements

In 2020, an inventory work was conducted to identify methods which are scientifically robust, able to bridge existing gaps in endocrine disruptors characterization and mature enough.

Three of these methods were selected by the Relevance Committee to enter the pre-validation process. The first method resorts to human placental cells and aims at assessing women's exposure during pregnancy. The second method resorts to human adrenal cells to analyse substances' potential effects on hormone synthesis (this method being an extension of an existing OECD guideline). A third method uses human cells (cervical adenocarcinoma) to measure activation of the glucocorticoid receptor. The pre-validation process is underway and involves the CNRSⁱⁱ, ANSESⁱⁱⁱ, EUROFINS, BASF, the Swedish Institute RI.SE, Vrije University in Amsterdam, Inserm, Toxem, Tame Water and Ineris. In 2021 these methods were submitted to the OECD for inclusion in its work plan, and the Relevance committee has selected three new methods for which the building of partnerships is underway.

Members and partners

PEPPER's funding is based on the **mutualisation of resources from a diversity of actors**: public and private organisations, including various government departments and various industries as well as a growing number of international contributors. Direct funding comes from memberships: Founding members (French Ministry of Ecological Transition, Fondation de la Maison de la Chimie, France Chimie et FEBEA^{iv}), Supporting members (French Ministry for Agriculture, French Ministry of Labour, AFISE^v, Bayer and BASF), Ordinary members (ANIA^{vi}, AFSSI^{vii}, Ineris^{viii}, Salveco, Minafin, Altertox and Eurofins), all of which take part to the life of our association. The Swedish Institute RI.SE is also a contributor.

Our membership has grown since PEPPER's creation and must continue to grow as endocrine disruptors, which are in the scope of the "duty of vigilance", are relevant to human health and environmental issues, they mobilise local authorities, directly or indirectly spread over more than 30 European regulations and impact almost every economic activity.

A European outreach

PEPPER is a European organisation: through its governance – involving organisations from several countries – and through its activities (origin of the methods to be validated, tests laboratories, experts involved in our Committees). As an example, the Relevance Committee includes, beyond the French agencies (ANSES, ANSM^{ix}, OFB^x), organisations from other countries (BfR^{xi} and UBA^{xii} in Germany, RI.SE in Sweden, Vrije University of Amsterdam), as well as international authorities (ECHA, OCDE, JRC ECVAM).

First platform of its kind, PEPPER aims at becoming the European organisation which will fast-forward the validation process for test methods in Europe, strengthening the credentials around substances and process classification, at a time when the European Commission aims at establishing by 2022 « hazard classes » for EDs which would apply equally to all existing regulations^{xiii}.

PEPPER's work will contribute to accelerate the pace for consolidating the foundations on which endocrine disruptors are identified, allowing to move forward with a more robust regulatory framework, addressing the human health and biodiversity issues at stake as well as the concerns of consumers and citizens.

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ⁱ The French National Institute for Industrial Environment and Risks

ⁱⁱ The French National Centre for Scientific Research

ⁱⁱⁱ The French Agency for Food, Environmental and Occupational Health & Safety

^{iv} French cosmetics industry association

^v French detergent industry association

^{vi} French food industry association

^{vii} French association for companies operating in life science services

^{viii} French National Institute for Industrial Environment and Risks

^{ix} French Agency for the Safety of Medicine and Health Products

^x French Organisation for Biodiversity

^{xi} German Federal Institute for Risk Assessment

^{xii} German environment agency

^{xiii} Including: phytopharmaceutical products, biocides, toys, cosmetics, food contact materials, REACH, human or veterinary medicines (exposure through the environment), medical devices, water (environment and consumption), electrical and electronic equipment, general product safety and ecolabel...