July 2024

NEWS Pepper

The newsletter of ***Pepper***, the public-private platform for the validation of endocrine disruptors characterisation methods

Pepper seeks partner labs to validate two new endocrine disruptors characterisation methods

Building on its ongoing mission, Pepper is calling for partner laboratories to join the validation effort. Through this collaboration, 23 partner laboratories already participate in assessing the transferability of the methods and in blind ring testing, paving the way for more effective identification of endocrine disruptors.

The first method, Retinoid and PPARδ-dependent neurite outgrowth assay, developed by Uppsala University (Sweden), tackles the growing concern of developmental neurotoxicity, a field witnessing rising diagnoses of learning and neurodevelopmental disorders in relation with endocrine disruption.

The second method, Transthyretin (TTR) binding assay with FITC-labelled thyroxin (T4), developed by Vrije Universiteit Amsterdam (Netherlands), focuses on thyroid function disruption, linked to various health issues. It measures the ability of a substance to displace the thyroid hormone from its transporter.

> The first call ended on 15 June (read more on our website or LinkedIN) and the call for the second method was launched on 26 June.

Latest key scientific events in early 2024

EURION pioneers the horizon of ED characterization through collaborative research

EURION is a cluster group of eight research projects (ERGO, SCREENED, GOLIATH, ATHENA, EDCMET, OBERON, FREIA, ENDpoiNTs) funded by the European Commission focusing on developing new testing and screening methods to identify endocrine disrupting chemicals (EDCs). The EURION Cluster Final Event was held in Brussels, Belgium on 13-14 June 2024 and will "pass the baton" to ENKORE, the new cluster group funded under the call Horizon focusing on the health impacts of EDCs.

Pepper was closely related to EURION. It was involved in its follow up and participated in the conclusions of 2 projects: ENDpoiNTs (11-12 June; Amsterdam) and EDCMET (Stakeholder forum; 24 April; online).

In summary, 5 methods (2 methods for thyroid from ATHENA, 2 methods on neurodevelopment from ENDpoiNTs and 1 method on hepatic lipidic physiology from EDCMET) developed within the cluster are undergoing validation at Pepper.

In the conclusions of EURION, the importance of validation to move the results towards regulatory applications, and the role of Pepper were put forward.

SETAC

The **Society of Environmental Toxicology and Chemistry** (SETAC) is a scientific society gathering 1.500 researchers from government, universities, and industry who collaborate to advance our understanding of how chemicals impact the environment. Andrea Rivero Arze from Pepper presented her work at the annual meeting last May. Her presentation highlighted ED assessment for avian species and gave an update on the ongoing validation process for the test method "Avian *in ovo* assay for sex steroid hormone disrupting properties".

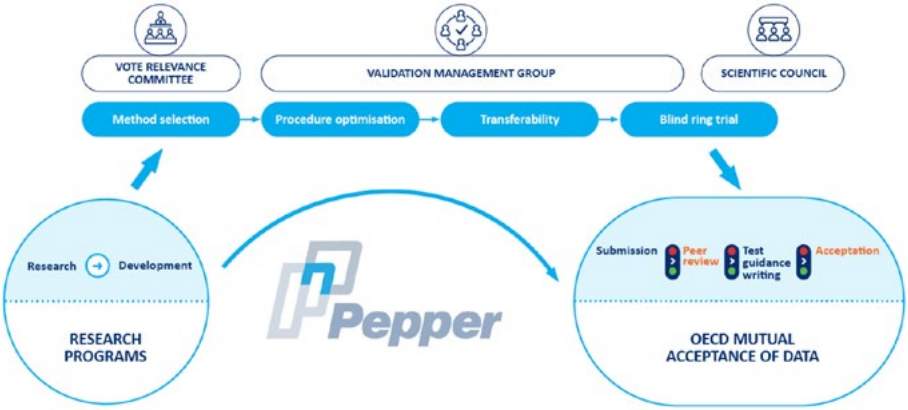
>> Read the abstract here : link

Celebrating the 30th anniversary of ESTIV

Pepper's team actively participated in ESTIV 2024, held in Prague from 3-6 June. In 2024, the International Congress of European Society of Toxicology *In Vitro* celebrated 30 years devoted to *in vitro* toxicology for development of NAMs (*New Approach Methodologies*) in drug discovery and safety assessment.

This event showcased two sessions on validation and a panel discussion on the future of validation. Philippe Hubert, Pepper's director, delivered a presentation on *"Validating NAMs: Experience Gained on the Pepper Platform"* and Andrea Rivero Arze focused on a specific method with a poster entitled: *"Time Frame Comparison in Steroidogenesis Assay"*.

>> Read Andrea's abstract here.
>> Read Philippe's abstract here (p.17).



New incentives in regulation

European action on PFAS

While PFAS crystallizes the main attention of ED, the European Union is actively addressing the environmental and human health concerns posed by PFAS and launched a project for restrictions.
Pepper's activity is crucial in this transition, as it validates new methods for chemical safety evaluation. US and other European countries prepare this transition, France for example launched recently an interdepartmental plan on PFAS.

EU Commission Roadmap for phasing out animal testing in chemical safety assessment

A European Citizens' Initiative (ECI) called "Save Cruelty-Free Cosmetics" is pushing for a complete ban on animal testing for cosmetics ingredient. This initiative triggered a response from the European Commission (EC) not only adressing cosmetics. In its communication it defined three objectives : Protect and strengthen the cosmetics animal testing ban ; Modernise science in the EU and Transform EU chemicals legislation.
EC has initiated a series of activities to design a roadmap to stop using animals for testing chemicals ; a goal for which validation is crucial. Thanks to the acquired expertise on ED, Pepper acts as a key player and participated in the EC initial workshop in December 2023.

>> Presentations available **here**

CLP regulation

European Union's CLP Regulation (EC) No 1272/2008 for the classification, labelling, and packaging of substances and mixtures applies to all chemicals sold in the EU. The EU regulation is being implemented with new categories including endocrine disruptors and persistent/ mobile/toxic substances. The implementation of the CLP impacts the overall commercial and industrial activities demanding a proper identification of endocrine disrupting properties.
>> Read more **here**.

The European Union will also advocate for a subsequent evolution in the Globally Harmonized System for classification and labelling of chemicals of the United Nations Organisation.

(R)evolution of validation worldwide

The enhancement of validation processes is garnering widespread attention due to the importance of ED and to the global impetus for developing the use of Non- Animal Methods.

The OECD Project Group

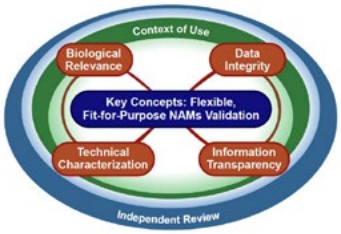
This validation procedure is described in an OECD Guidance Document (GD34), and there is a global momentum towards its revision. An OECD Project Group is at the forefront of this revision, aiming to address the urgent need for improved validation methods on the identification of EDs and implementation of NAMs. Pepper participated in this project and was part of the 22-23 April meeting. As support, a collaborative project was set up, involving the Joint Research Center (JRC) and its entity the European Centre for the Validation of Alternative Methods (ECVAM), the Netherlands and the US. These combined efforts represent a significant step forward in developing and validating robust methods, ultimately leading to faster detection of harmful chemicals and better protection of public health and the environment.

ICCVAM

The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) is a permanent committee composed of representatives from U.S. federal regulatory and research agencies. Last March, it released a document on *"Validation, Qualification, and Regulatory Acceptance of New Approach Methodologies".*

Developed with the input from stakeholders, including Pepper's comments, the guidance emphasizes the importance on integrating results from multiple *in vitro* and *in chemico* assays and *in silico* approaches. The ICCVAM document opened a discussion on the relevance of *"fit for purpose validation"*.

Key concepts to consider during development and implementation of flexible, fit-for-purpose NAMs validation strategies. Adapted from Van der Zalm et al. (2022)



2023 OECD Stakeholders Workshop on Operational and Financial Aspects of Validation

This first workshop stressed the practical aspects of validation beyond procedural aspects and so was a key landmark on the road of the ongoing validation process update. It is also a useful resource for method developers considering embarking on the validation of a method.
The take home messages of the workshop are:

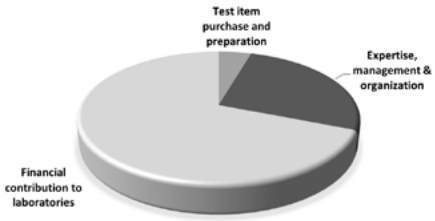
- Need to professionalize the validation process,
- Existence of a consensus on the cost-sharing between developers, authorities and industries for funding the validation process.

Presentations of stakeholders, including Pepper, are available online.
In his presentation, Philippe Hubert shared lessons learned at Pepper, highlighting where there are opportunities to reduce the time and cost of a test method validation process.

>> Watch Peppers' contribution here.

Publication

"The benefits of validation of methods for toxicity testing outweigh its costs"



Representation of the distribution of validation costs, as experienced by Pepper.

With colleagues from OECD, Vrije Universiteit Amsterdam, JRC and Anses, Pepper participated in a publication describing ways to advance the process of validation.

As the validation is still largely underfunded and unattractive to the scientific community, this publication proposes steps to streamline the process. Validation is also a profitable investment as its costs are also relatively minor when compared to the cost of "no validation". OECD estimated the savings that come from the Mutual Acceptance of Data to be at the level of 309 million EUR each year (Saving costs in chemical management).

>> Click here to read the full publication.

TEAM NEWS

New Leadership

Philippe Prudhon, representing the Fondation de la Maison de la Chimie, was elected Chairman of our Board and is our new President. He brings a wealth of experience, and we look forward to his continued guidance as we accelerate the validation of methods for the characterisation of endocrine disrupters.

Welcome Aboard

Torben Österlund has joined Pepper as new Chief Scientific Officer (CSO). Torben brings a wealth of knowledge and experience in the field of toxicology and will be instrumental in guiding Pepper's scientific strategies and innovations.

Farewell

After 4 years, **Elise Grignard** concluded her time at Pepper in May. Elise has played a crucial role in Pepper's creation and development.