Preliminary background:

Genetically modified (GM) crops have been used globally for around three decades, since the first product was made commercially available in 1994.

Regulatory agencies require rigorous testing for any new GM crop before it can be approved for commercialization to ensure its safety, and to prevent any unintended effects on human, animal, and environmental health. These requirements include: molecular and functional characterization of the genetic modifications introduced into the organism; toxicological studies and allergenicity assessment, to evaluate the potential for GM organisms (GMO) to cause adverse effects on human health, via bioinformatic analysis, in vitro tests such as in vitro digestibility studies, and animal feeding studies with rodents, over an extended period of time; nutritional analysis, to ensure that their nutritional composition is substantially equivalent to non-GMO counterparts; as well as an environmental risk assessment.

In vitro toxicology assays would typically involve exposing cells to extracts or proteins from GMO crops. In some instances, this may represent a challenge, for instance when the GM protein is present in the GM crop in minute concentrations and/or when the protein of interest is difficult to isolate, due to its complex structure, biochemical properties, interactions with other molecules, or expressed in very low level. Proteins that fall within this description are called *intractable proteins* and represent a challenge for safety assessment, both for product developers and safety assessors, under the current regulatory frameworks.

Over the past 30 years, significant advances in analytical methods and scientific understanding of the parameters related to GMO safety have been made. Furthermore, in many areas of the world, governmental policies are being put in place to foster the reduction and replacement of animal use in research and risk assessment (3Rs). Regulatory frameworks may benefit from taking all these new developments into consideration.

This workshop aims to bring together research scientists from academia, industry and government institutions to review current scientific advances and address in particular the challenges related to the safety evaluation of proteins in GM products and novel foods.

The Health and Environmental Sciences Institute (HESI) is a scientific and charitable organization committed to generating science for a safer and more sustainable world. We believe that achieving this goal requires open, active, and ethical collaborations involving scientists with diverse technical and professional expertise. As for all of HESI's scientific programs, this event would abide to HESI's mission to generate science with a public benefit, for improved human and environmental health.

*: *presenting remotely*

HESI Protein Allergens, Toxins & Bioinformatics Committee Workshop:
"Safety assessment of newly expressed proteins in foods: need for evolution?"
October 21-22, 2024 | Porto, Portugal

When: October 21-22, 2024

Where: Campus ICBAS & Faculdade de Farmácia, University of Porto, Rua Jorge Viterbo Ferreira n.º 228, 4050-313 Porto, Portugal.

Format:

- **In person**, with multi-sector participation: regulators from various geographic jurisdictions, academics, industry, with possibility to attend online.
- **Free event** (no registration fees) **and open to all interested stakeholders.**
- **Registration link: click here (deadline to register for in person attendance: October 6, 2024).**

Organized by: HESI Protein Allergens, Toxins & Bioinformatics Committee
Co-host: School of Pharmacy, University of Porto

Contact points: Dr. Lucilia Mouriès, Senior Scientific Program Manager (lmouries@hesiglobal.org) and Dr. Joana Costa, Researcher, U. Porto (Joana Costa jbcosta@ff.up.pt)

Thank you to our co-hosts at University of Porto

and

external sponsors for this event: AEIC; CroplLife Europe; CropLife International.

*: *presenting remotely*

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Final Agenda

DAY-1 (PM only): Session 1
DAY-2 (Full Day): Sessions 2, 3, 4 & 5

All times indicated are local times (Porto, Portugal, GMT +1)

DAY 1 (PM only)

13:30- 13:45 - Workshop Introductory Remarks

Welcome address from co-hosting organizations

13:45 – 17:15
Session 1: Approaches in Protein Safety Assessment: Current Practices and Global Regulatory Perspectives

13:45 – 14:45 *1.a) Technical experts with hands-on experience*

- **Pascale Delzenne (Crop Life Europe):** Protein safety assessment approach for Genetically Modified crops, developers' perspective.
- **Faith Lambert* (HESI PATB committee):** Framework for the *in-silico* evaluation of potential toxicity of NEPs, an ongoing effort from the HESI PATB committee and international ad-hoc expert group.
- **Joana Costa (University of Porto):** Food *in vitro* digestibility assay: overview, current challenges, translatability for allergenicity studies.

14:45-16:00 *1.b) Global Regulatory Perspectives Panel*

- **Antonio Fernandez Dumont (EFSA):** EFSA's experience: current practice, challenges and future opportunities of the safety assessment of newly expressed proteins.
- **Anne Muia (National Biosafety Authority, Kenya):** Safety Assessment of GM Food/Feed in Kenya
- **Jason Dietz (US FDA)*:** Current Approaches in Protein Safety Assessment: Global Regulatory Perspectives-United States.
- **Maria Lucia Zaidan Dagli (University of São Paulo; CTNBio, Brazil)**
- **William Chen (Nanyang Technological University, Singapore):** Next-Generation Risk Assessment Framework for Future Foods: a FRESH Perspective

16:00 – 16:30 - *Coffee break*

16:30 - 17:30 ***Discussion:*** All speakers & Panelists + Moderator

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17:30 – 17:45 **Day-1 closing:** Co-hosts
Preview & Preparation for Day-2

17:45 – Welcome reception *(on-site)*

End of Day-1

Day 2: Full Day (8:30 - 17:00)

8:30- 8:40 – Day-2 Opening Remarks

Co-hosting organizations

8:40 – 10:30
Session 2: Intractable Proteins

8:40 – 9:30 *2.a) Background and Case-Examples*

- **Elizabeth Lipscomb (CropLife International-PSET):** Intractable Proteins – What are they, why are they so challenging, and what are our options?
- Example 1: **Johnathan Napier (UK Rothamsted Research):** Making high value omega-3 fish oils in Camelina - from prototype to product.
- Example 2: **Rong Wang (AEIC, Analytical Excellence through Industry Collaboration):** Examples of Intractable Proteins Expressed in Genetically Modified Crops and Considerations for Their Safety Assessment.

9:30 – 10:30 *2.b) Panel discussion / Round table*
All speakers + Moderator

15 min Coffee break

10:45 – 12:45
Session 3: Readiness for New Alternative Methods (NAMs) in the GM/Novel Foods Safety Space

Lucilia Mouriès (HESI): What are NAMs and why do we need to think about NAMs?

10:50 – 12:00 *3.a) Background and Examples in Development*

- **Yong Yin (CropLife International-PSET):** new approaches for HoSU

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- **Matthew Merrell* (Corteva):** In vitro NAM Development for Protein Safety Assessment.
- **Kazunari Kondo (Showa Women's University; NIHS Japan)**: "allerSTAT": a machine learning method to predict protein allergenicity.
- **Ritu Tomar (Indraprastha Institute of Information Technology (IIIT)):** "CDpred" a web-based tool to predict celiac disease associated epitopes and motifs.

12:00 -12:45 *3.b) Panel discussion / Round table*

All speakers + Moderator

- Implementation of NAMs: Are we there yet?

_____ 12:45 – 13:30 Lunch break _____

13:30 – 14:30

Session 4: "When n ≠1. Assessing Complex mixtures of proteins" (Novel foods, e.g. whole organisms newly introduced in foods)

- New EU funded consortia efforts, developing methods targeted to novel foods/alternative proteins:
  - **Clare Mills (University of Surrey):** "Giant LEAPS", Gap resolutIon in sAfety, NuTritional, alLergenicity and Environmental assessments to promote Alternative Protein utilization and the dietary Shift.
  - **Gabriele Gadermaier (Paris Lodron University Salzburg):** "ALLPreT", Allergenicity Prediction Toolbox for novel foods.
- **Lucie Parenicova (The Protein Brewery)**: *Fermotein* - new, alternative source of proteins.

14:30 – 17:00

Session 5 (Final): Harnessing Our Collective Wisdom

14:30 - 16:45 ***Working session*** *(w/ 15 min coffee break in the middle)*

Integrating learnings of the past 2 days

Forging a path forward?

- Revisiting questions from sessions – do we have clearer answers?
- Learnings so far: what works well; what did not show value in doing? What can be improved?
- What is actionable immediately?
- What needs further progress for prime time and why?
  - What next steps are needed: How/who/when?
- What should safety assessment (SA) look like in the future?

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16:45 – 17:00 **Wrap-up & Closing**

17:00 – End of Workshop

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