EPAA collaboration in the development of the EU Roadmap

Dr Gavin Maxwell, EPAA Industry Co-chair / Unilever

FELASA, Athens, 1st-5th June 2025

European Partnership for Alternative Approaches to Animal Testing (EPAA)

The European Partnership for Alternative Approaches to Animal Testing

Collaboration between European Commission and Industry stakeholders from 8 sectors (est. 2005)

Vision: The replacement, reduction and refinement (3Rs) of animal use for meeting regulatory requirements through better & more predictive science (e.g. New Approach Methodologies (NAMs)).

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39 Companies (including 1 SME)

symrise, Johnson & Johnson, novonesis, L'ORÉAL, DSM, Dow, LVMH, essity, Boehringer Ingelheim, ESTĒE LAUDER, CLARIANT, Merck, dsm-firmenich, Shiseido, Gowan, Evonik, ADAMA, Beiersdorf, CHANEL, Unilever, Colgate-Palmolive, Henkel, Bayer, Corteva agriscience, P&G, Reckitt Benckiser, novo nordisk, Novartis, sanofi, GSK, Zoetis, BASF, Solvay, Syensqo, Revlon, syngenta, MANE, Kanebo, stratiCell

5 DG's of the EC

European Commission

- DG GROW
- DG ENV
- DG SANTE
- DG JRC
- DG RTD

Including Partner Agencies

ECHA European Chemicals Agency, efsa, European Medicines Agency – Science Medicines Health

9 Sectoral Associations

A·I·S·E since 1952, animalhealth europe, cefic, Cosmetics Europe the personal care association, CropLife Europe, efpia European Federation of Pharmaceutical Industries and Associations, FOODDRINK EUROPE, ifra International Fragrance Association, sme United

Mirror Group *(Advisory body)*

Emily McIvor (Chair), Tuula Heinonen, Christiane Hohensee, Helena Kandarova, Sirpa Pietikaïnen (MEP), Vera Rogiers, Emma Grange, Julia Baines, Winfried Neuhaus, Monique Janssens

Transitioning Europe to Animal-free, Sustainable Innovation

EU Parliament resolution

On 15th Sept 2021 the EU Parliament resolution adopted to '**Accelerate a Transition to Innovation without the use of Animals in Research, Regulatory Testing and Education**' calling for an **action plan with**:

- **ambitious objectives**
- **reduction targets**
- **replacement timelines**


European Parliament
2019-2024

TEXTS ADOPTED

P9_TA(2021)0387

Plans and actions to accelerate a transition to innovation without the use of animals in research, regulatory testing and education

European Parliament resolution of 16 September 2021 on plans and actions to accelerate the transition to innovation without the use of animals in research, regulatory testing and education (2021/2784(RSP))

European Parliament

EU Commission response

EU Commission response to EP resolution stated that:

- '**ultimate goal of full replacement is enshrined in EU legislation**'
- 'transition to innovation without the use of animals is **best supported by focusing on & intensifying current efforts**'
- transition accelerated via **EU Replacement Roadmap**


Follow-up to the European Parliament non-legislative resolution on plans and actions to accelerate a transition to innovation without the use of animals in research, regulatory testing and education

1. Resolution tabled pursuant to Rules 132(2) and (4) of the European Parliament's Rules of procedure
2. Reference number: 2021/2784 (RSP) / RC9-0425/2021 / P9_TA-PROV(2021)0387
3. Date of adoption of the resolution: 16 September 2021
4. Competent Parliamentary Committee: N.A.
5. Brief analysis/assessment of the resolution and requests made in it:

The resolution recalls the objectives of the Directive on the protection of animals used for scientific purposes (2010/63/EU) and notably the replacement of procedures on live animals as soon as it is scientifically possible. It asks that these objectives be observed in all sector-specific pieces of legislation that require testing (recitals A and B). It stresses the

European Commission

EPAA is helping accelerate the transition through:

1. **Bridging the research to regulatory use gap** by identifying NAM-based frameworks that address regulatory needs
2. **Building confidence in non-animal approaches** by facilitating scientific dialogue between industry safety assessors & regulators
3. **Enabling transition to new global regulatory paradigm** through the EU roadmap to phase out animal testing for chemical safety assessment

In 2025, EPAA focussed our activities to provide input to ‘Roadmap towards phasing out animal testing for chemical safety assessment’

1. **Bridging the research to regulatory use gap**
2. **Building confidence in non-animal approaches**
3. **Enabling transition to new global regulatory paradigm**

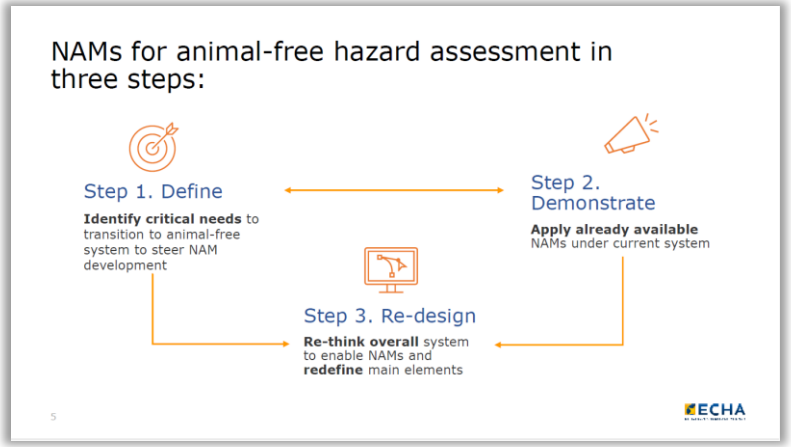
European Commission Roadmap input

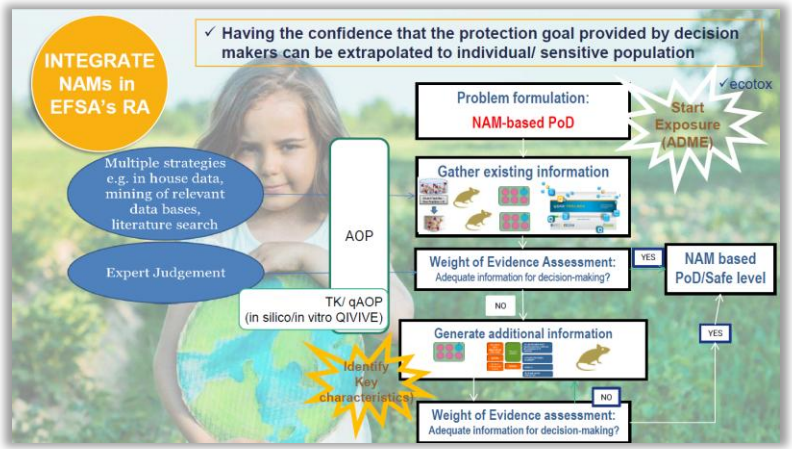
NAMs for the assessment of endocrine disruption partners forum	**Systemic toxicity NAM user forum**	**Animal-Free Chemical Safety Assessment Conference**
2nd species in sub-chronic toxicity project	**Skin Sensitisation user forum**	**NAM designathon challenge – systemic toxicity classification**
Carcinogenicity project	**Acute toxicity project**	**Environmental safety assessment project**
	Harmonisation of 3Rs in Biologicals	

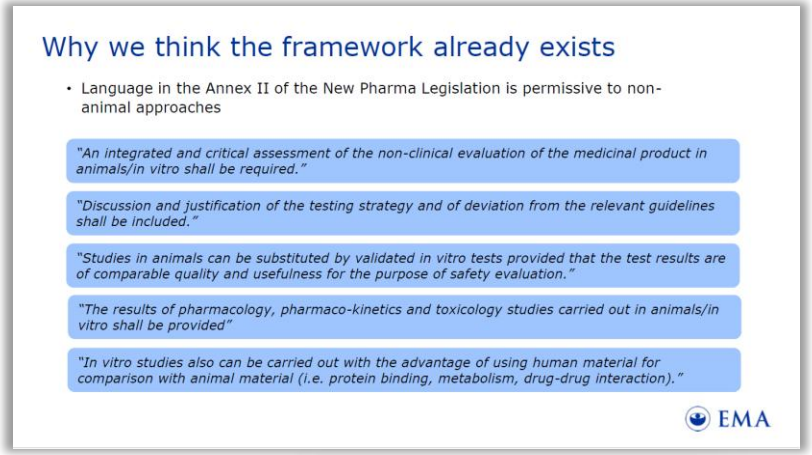
Goals:

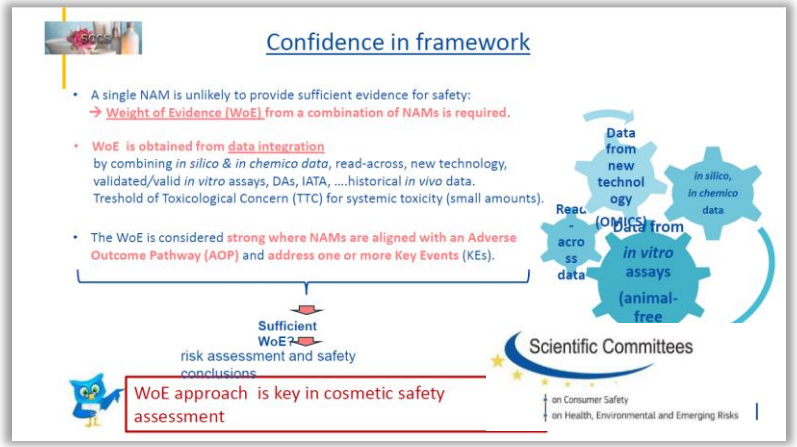
- To **perform a strategic, cross-sector review** of NAM-based frameworks for Chemical Safety Assessment in the European Regulatory Context
- To share learnings & **identify**:
  - Opportunities for **scientific dialogue**
  - **Scientific gaps** and **research challenges**
- To **recommend short, medium & long-term actions** for:
  - Commission Roadmap to Phase Out Animal Testing for Chemical Safety Assessment
  - EU Test Method & Validation Strategy

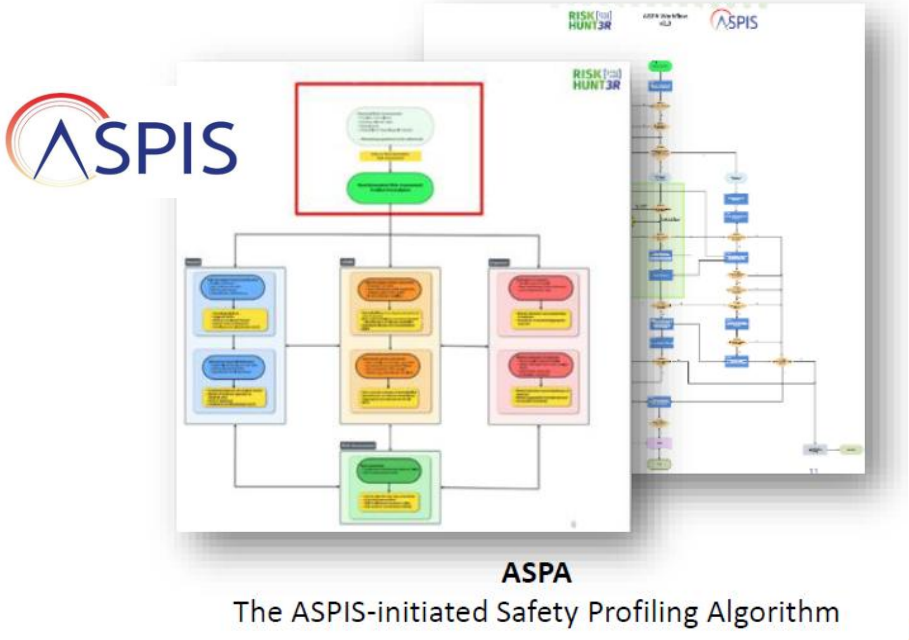
Animal-Free Chemical Safety Assessment concepts











‘Safe spaces’ for industry-regulator dialogue

Regulatory Clarity on Acceptance Criteria

Establish **transparent qualification frameworks** (e.g., EMA’s Qualification of Novel Methodologies).

Early Regulator Engagement Without Risk

Non-binding pilot studies to refine methodologies.

Confidentiality & Data Protection Mechanisms

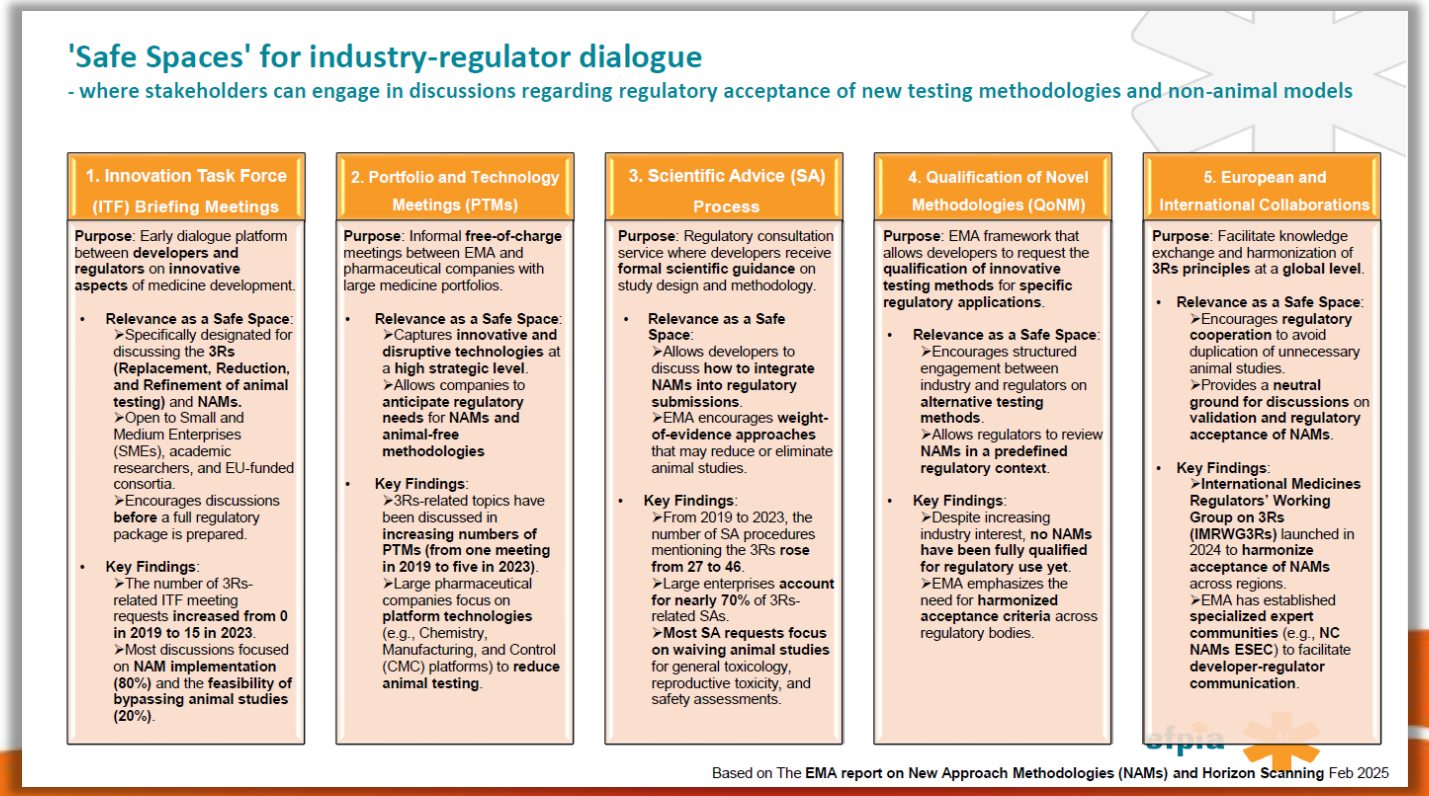
Industry needs **assurances that data won’t trigger new regulatory burdens**.

Harmonized Regulatory Validation Pathways

Alignment across **EU, US, and OECD guidelines** to streamline global adoption.

Establishing regulatory sandboxes

Introduce controlled environments to allow companies to test innovative solutions under a **flexible regulatory framework** using real-world evidence.



Days 2-3: Breakout Groups & Feedback:

1. Human Health Paradigm Shift
2. Environmental Safety Paradigm Shift
3. Measuring Change so we can Manage it
4. Integration of Human Health & Environmental Safety
5. Use of NAMs for the assessment of Endocrine Disruption
6. Implementing a new paradigm for Carcinogenicity Assessment
7. ISTNET Developmental & Reproductive Toxicology (DART) Testing Roadmap
8. Recommendations for phasing out second species sub-chronic toxicity testing
9. Towards Animal-Free Acute Toxicity Assessment

	Short-term actions NAMs that can be immediately adopted into regulatory practice	**Medium-term actions** NAMs requiring validation or regulatory adaptation	**Long-term actions** Strategic efforts to redefine safety assessment paradigms for NAMs
Human Health Safety Assessment Paradigm Shift	• Expand use of **existing replacement methods** (QSARs, read-across, exposure-based waiving) • Initiate **pilot projects** for regulatory applications of systemic toxicity toolboxes & SMART in vivo studies. • Establish **reference dataset for benchmarking** NAM-based safety assessments.	• Implement **cross-sector regulatory use** of NAM-based systemic toxicity toolboxes. • Develop **higher-tier testing strategies** for complex endpoints such as DART & ED effects • Use bottom-up & top-down evaluation approaches to **assess effectiveness** of NAM approaches.	• Fully **integrate NAM-based assessments** into regulatory frameworks. • Establish **robust higher-tier testing approaches** to replace remaining *in vivo* studies. • Ensure **cross-sector harmonisation** of risk assessment methodologies.
Environmental Safety Assessment Paradigm Shift	• Establish a **cross-sector network** to continue discussions and refine the new paradigm. • Conduct **case studies** using existing data to assess gaps in current frameworks. • Identify **key partners & funding** sources	• Define the **ultimate goal** of environmental safety assessments within the context of chemical use • Conduct **gap analyses** to map existing frameworks, exposure pathways, and mixture effects. • Develop a **centralised data platform** to consolidate hazard and monitoring data. • Advance **in silico models** • Refine **testing thresholds** • Connect **mechanistic data** with **population-level effects**. • Adjust **regulatory processes** to facilitate the faster adoption of NAMs.	• **Fully transition** to an animal-free environmental safety paradigm. • Explore the concept of **environmental digital twins** to provide real-time predictive capabilities. • Implement **probabilistic & landscape assessments** to better handle uncertainty. • Establish **toxicokinetic models tailored for invertebrates**, ensuring a broader range of species are covered in risk assessments.

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Integration of Human Health and Environmental Safety Assessment	• Remove **disciplinary silos** • Identify **stakeholder networks** • Establish **common terminology** • Introduce **integrated toxicology training** programmes • Assess readiness of regulatory systems to accept **mechanic data** and identify key changes to support this transition	• Generate evidence to **build confidence in mechanistic approaches** (e.g. case studies) • Identify **common toxicokinetic & toxicodynamic data streams** conserved across species • Develop **HH-Env testing strategies** • **Prioritise mechanisms & species** that require protection • **Advance PBK models** for vertebrates and invertebrates • **Target research** to address knowledge gaps & build mechanistic understanding	• Implement **data-sharing platforms** to integrate (eco)toxicology datasets • Develop **tiered, integrated regulatory frameworks** that acknowledge the mechanistic commonalities between human and environmental health • Embrace the '**One Safety**' concept • Promote a **unified risk assessment approach** that addresses the combined impacts of chemicals on humans, wildlife, and ecosystems
Use of NAMs for the Assessment of Endocrine Disruption	• Develop **tiered NAM strategies** for **oestrogen & androgen modalities** • Define **testing limits** & establish **benchmark chemical lists** • Create **NAM-use case studies** & **multi-stakeholder forum** for scientific dialogue (e.g. pesticides, biocides)	• Develop **tiered NAM strategies** for **thyroid and non-EATS modalities** • Evaluate **tiered NAM strategies** using benchmark chemicals (addressing MoA & adversity) • Address **metabolic competence** of in vitro systems to build confidence • Identify **hub-KE NAMs** that measure conserved key events to enable consolidation of test batteries • **Target research** to close methodological gaps	• **Review performance & efficiency** of tiered NAM strategies • **Integrate hub-KE NAMs** into standardised human health and environmental safety assessment frameworks

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	Short-term actions (0-5yrs) NAMs that can be immediately adopted into regulatory practice	Medium-term actions (5-10yrs) NAMs requiring validation or regulatory adaptation	Long-term actions (10+ yrs) Strategic efforts to redefine safety assessment paradigms for NAMs
PARADIGM SHIFT **Implementation of a New Paradigm for Carcinogenicity Assessment**	• Scope **cross-sector Weight of Evidence (WoE) approach** • Define & validate set of **NAMs designed to screen** for chemically-induced perturbation of biological pathways related to cancer • Develop &/or refine **NAMs targeting later key events** in carcinogenesis • Use a WoE approach to **integrate NAM data with sub-chronic repeated-dose toxicity (RDT) study data** • Use sector **case studies** to assess **applicability** • Remove **mouse cancer bioassay** as a standard regulatory requirement	• Add **NAM-based WoE approach** to regulatory frameworks & update **regulatory guidance** docs to support widespread adoption • Concurrently, **refine (internal) TTC approach** to build confidence • Adapt **regulatory processes** to permit assessments based explicitly on mechanistic understanding • Update **classification & labelling criteria** to explicitly incorporate NAM-based approaches	• Fully implement NAM-based WoE approach, **eliminate the regulatory reliance on animal-derived data** altogether • Conduct **extensive validation case studies** on a large scale will be conducted across diverse regulatory contexts • **Comprehensive training** programmes in non-animal approaches for carcinogenicity assessment
ROADMAP ACTIONS	• **Obtain regulatory buy-in** from EU Commission & other authorities. • **Develop communication roadmap** targeting different stakeholders • **Identify and secure funding** for NAM validation, case studies, and industry readiness. • **Establish safe spaces for pre-submission consultations**, where industry and regulators can discuss NAM data before formal submission	• **Adapt regulatory frameworks** to allow NAM-based carcinogenicity assessments • **Revise CLP/GHS criteria** to align with NAMs • **Secure funding** for the development of missing NAMs and for translational activities	• **Fully implement the NAM-based WoE approach** across all regulatory sectors. • Implementation of the **revised CLP/GHS criteria** • Implement **education and training programmes** for industry, regulators, and scientists on new assessment methodologies

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ISTNET Developmental and Reproductive Toxicology (DART) Testing Roadmap	• Publish the **ISTNET-DART roadmap** • Define **funding strategy** for research, validation, & regulatory acceptance of NAM-based DART methods • Establish a **benchmark chemical list** for validating NAMs • **Validation studies for existing NAMs** to use with guideline DART studies • **Case studies** to demonstrate practical regulatory applicability	• **NAM development & qualification** to refine DART applicability domains • Further development of **AOPs** & DART **case studies**	• **Complete replacement of traditional DART assessments** with fully mammalian-free methodologies
Roadmap towards phasing out the non-rodent species for (sub-) chronic toxicity testing	• Develop a framework & criteria to **prospectively determine when the dog study can be waived** drawing on EFSA & US EPA agrochemical projects • Consider **integration of non-animal approaches**, e.g. uncertainty factors	• Further **refine of study design** using NAMs & virtual control groups • Use **historical data** to replace or reduce the number of concomitant control animals • Develop **standard in vitro assays** to support comparative toxicokinetic and/or toxicodynamic studies	• Develop **computational models** to ultimately phase out animal studies
Towards animal-free acute toxicity assessment	• Amend regulatory frameworks to establish **computational models** as defaults for acute oral toxicity • **Assess performance** of computational tools like CATMoS • **Compile & analyse reference datasets** for acute dermal and inhalation toxicities	• Use **ADME studies & PBK modelling** to define scenarios where acute systemic toxicity studies could be waived (e.g. chemicals lacking systemic bioavailability)	• Leverage advances in non-animal human safety assessments to **further refine acute toxicity testing**

Next Steps

- 60 page, AF-CSA Conference Report will be used as the basis for a scientific manuscript for publication
- 5th June 2025, EPAA Steering Committee meeting
  - AF-CSA Conference report used as basis for draft EPAA 2026-2030 Action Plan
- 9th Sept 2025, EPAA EU Parliament Lunch Debate (tbc)
  - MEP feedback on draft EPAA 2026-2030 Action Programme
- 5th-6th Nov 2025, EPAA 20th Anniversary event & Annual Conference
  - Review of EPAA's progress over the last 20 years and stakeholder feedback on how EPAA can best support regulatory use of 3Rs going forward.

Thank you to Animal-Free Chemical Safety Assessment Conference Organizing Team for all their help:

Amaia Irizar, Amelie Ott, Andreas Schepky, Barbara Schmitt, Bob van der Water, Bruno Campos, Christian Desaintes, Denis Mottet, Effrosyni Katsanou, Ellen Fritsch, Elisabet Berggren, Frederic Pipp; Gavin Maxwell, Georg Streck, Irene Manou, Katia Lacasse, Katrin Schutte, Iris Muller, Jelle Vriend, John Colborne, José Tarazona, Julia Baines, Marco Corvaro, Marco Fabbri, Mathieu Vinken, Matthias Herzler, Mirjam Luijten, Nathalie Printemps, Orla Moriarty, Pascale Oosterbosch, Petra Kern, Pilar Prieto, Raffaella Corvi, Raphaël Tremblay, Sofia Batista, Stephane Dhalluin, Tina Mehta, Tomasz Sobanski, Zsuzsanna Koenig, Zvonimr Zvonar

EPAA website: https://ec.europa.eu/growth/sectors/chemicals/epaa_en
E-mail: GROW-EPAA@ec.europa.eu