The Chemical Strategy for Sustainability: a Game Changer for NAMs?

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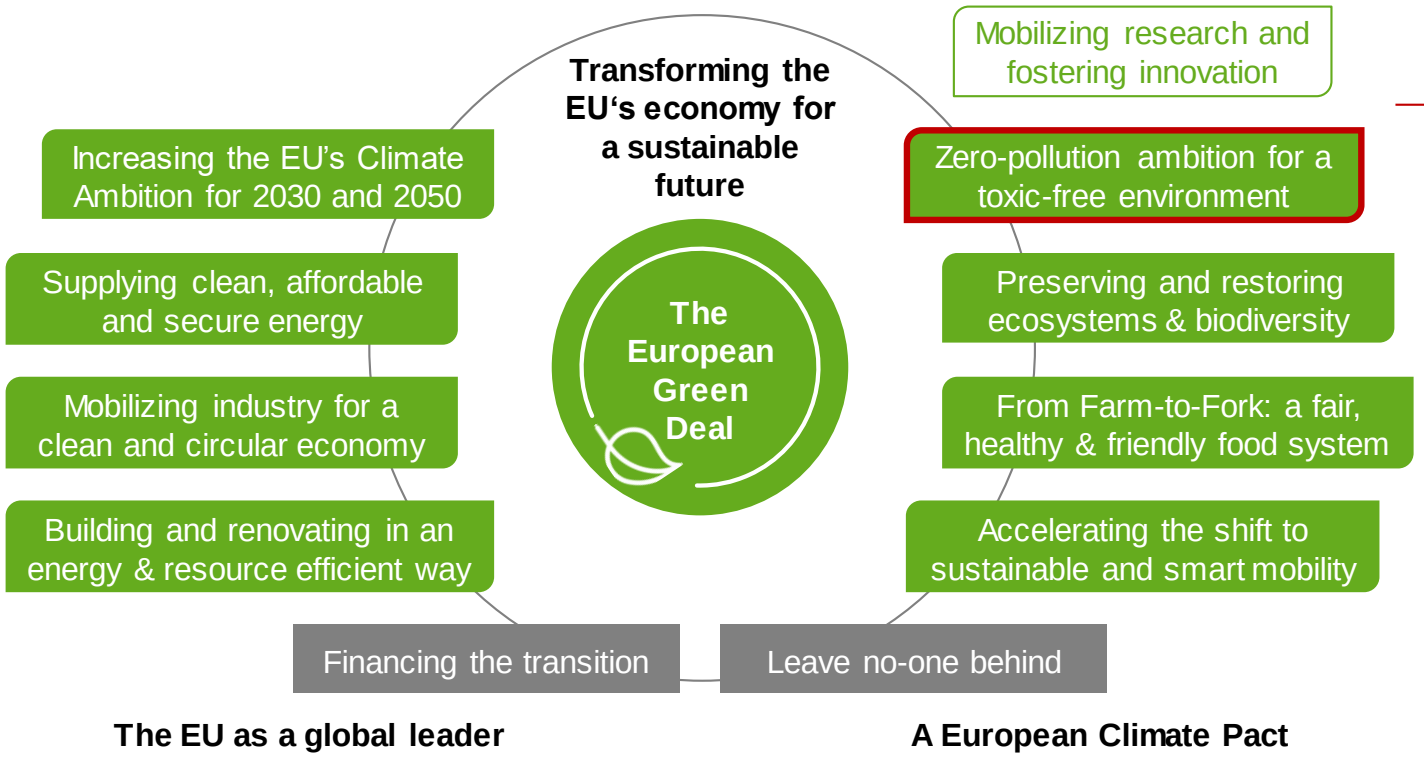
Ludwigshafen am Rhein, Germany, 10/27/2021

Chemicals Strategy for Sustainability as part of the GREEN DEAL

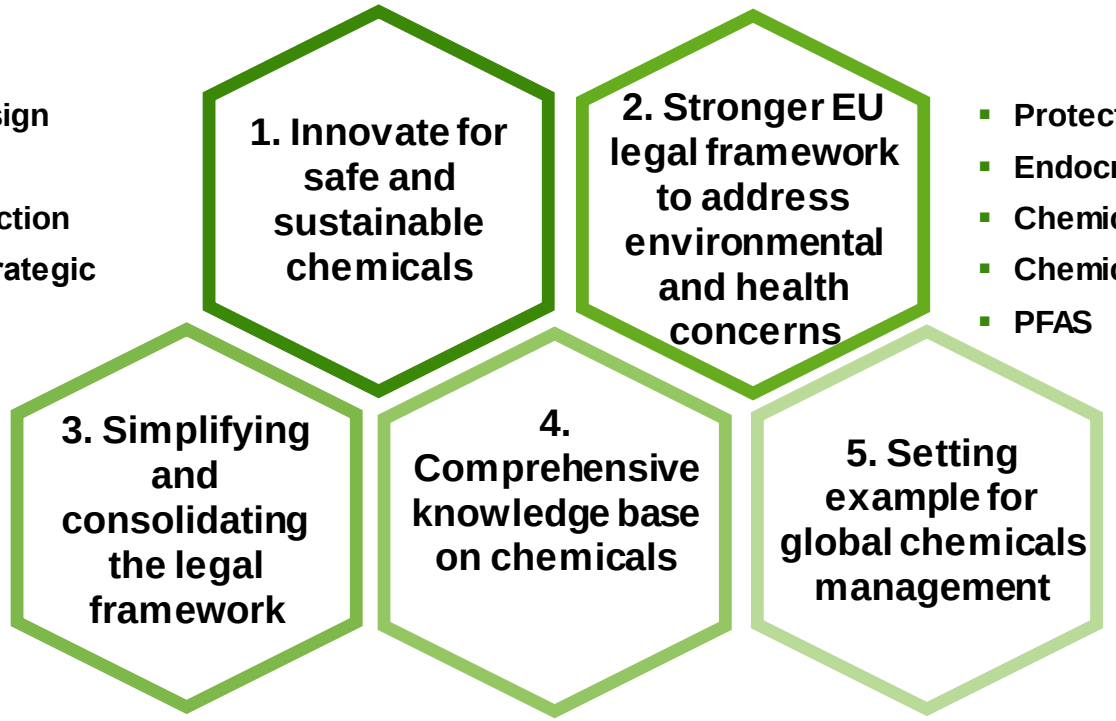


Includes Chemicals Strategy for Sustainability

Two Objectives:

1. Enhancing protection of human health and the environment
2. Boost innovation to enable transition to safe and sustainable chemicals

CSS's five building blocks and 16 measures



- Safe and Sustainable-by-design
- Non-toxic material cycles
- Innovating industrial production
- Strengthening EU's open strategic autonomy

- Protection against harmful chemicals
- Endocrine disruptors
- Chemical mixtures
- Chemical pollution in the environment
- PFAS

- Coordinate and simplify actions across institutions and EU chemical legislation
- Methodologies and Data
- Zero-tolerance for non-compliance

- Lead internationally, where improvement is most needed
- Cooperation with third countries

- Information requirements
- Inclusion of science into policy

More than 80 changes to chemicals legislations are set out by the Chemicals Strategy for Sustainability to be implemented between 2021 and 2024

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The role EPAA could play in CSS

- BASF is a founding member of EPAA since 2005
- We believe in its effectiveness as a unique collaboration platform between industry and regulators
- The users' scientific knowledge and practical perspective can contribute in the implementation of CSS

Main Challenges and Opportunities presented by CSS

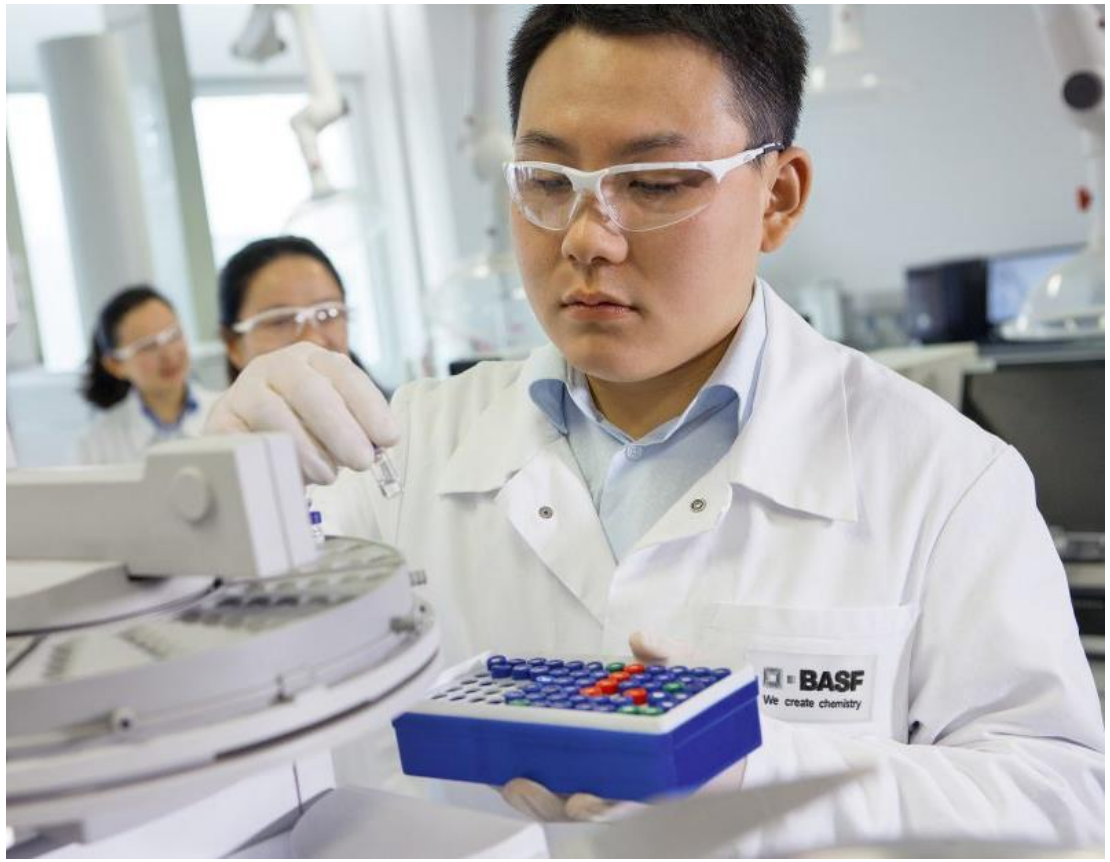
- Innovate chemical products and production for safety and sustainability;
  include safety and sustainability considerations early in product development

- Use best science to guide these innovations;
  utilize and further improve modern risk assessment tools

Dedicated and faithful collaboration of regulators, industry and NGOs to achieve this
→ EPAA is an effective platform to ensure this dialogue and collaboration

Chemical assessment under REACH

- Data requirements are driven by tonnage
- Requirements mainly based on animal studies
- Regulatory acceptance of limited number of NAMs, incl. waiving, read across and grouping

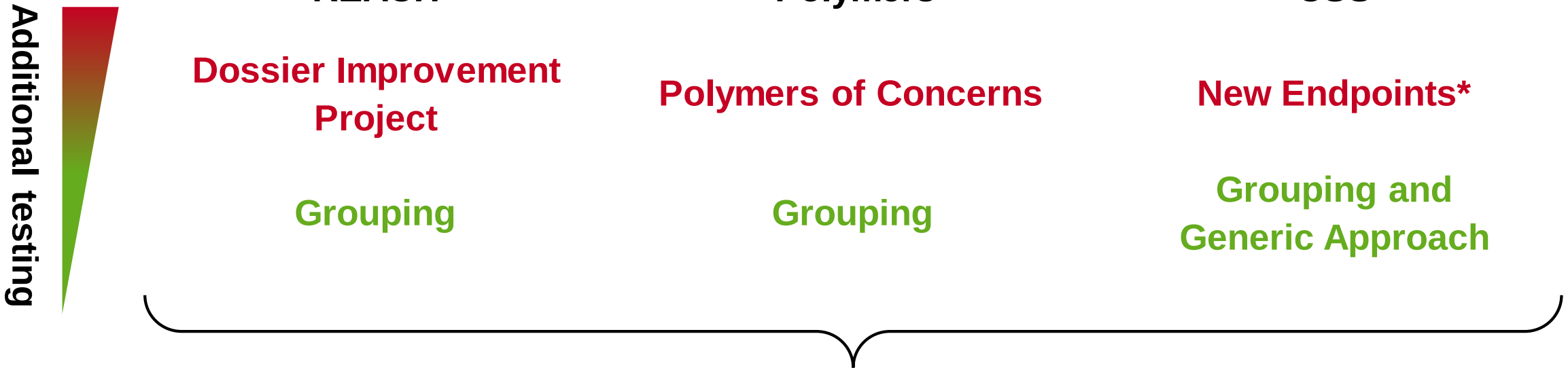


Still, most toxicological data are generated by animal studies

- Skin irritation and corrosion
- Eye irritation
- Skin sensitization
- Acute systemic toxicity
- Repeated exposure organ toxicity
- Reproductive toxicity
- Mutagenicity
- Carcinogenicity

- Animal study
- Non-animal study

Future development of regulatory data requirements

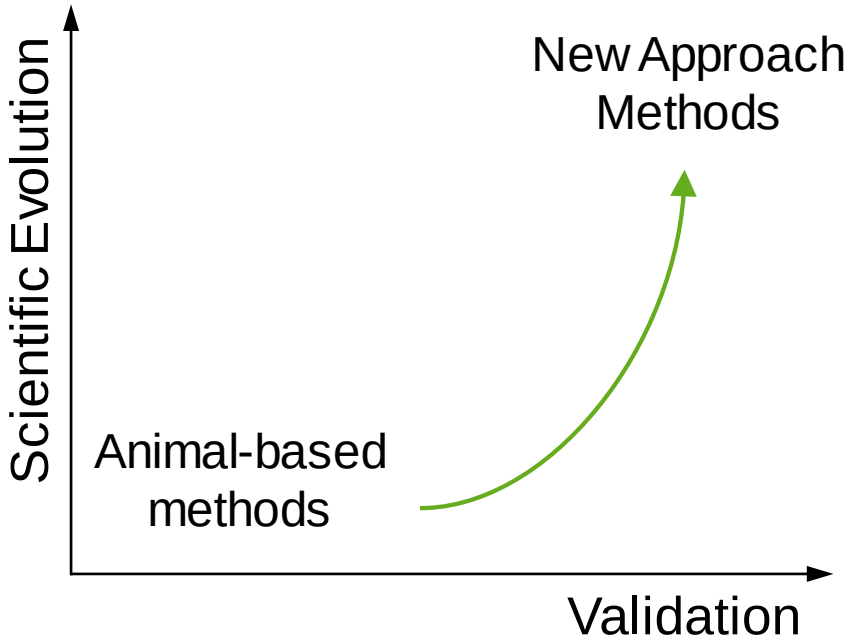


>2 millions of additional animals will be consumed for testing**

TIME TO REVISIT OUR TESTING STRATEGIES

* e.g. Endocrine Disruptors, immuno- and neurotoxicity **Estimate by Cruelty Free Europe

Benefits of NAMs: validation matters

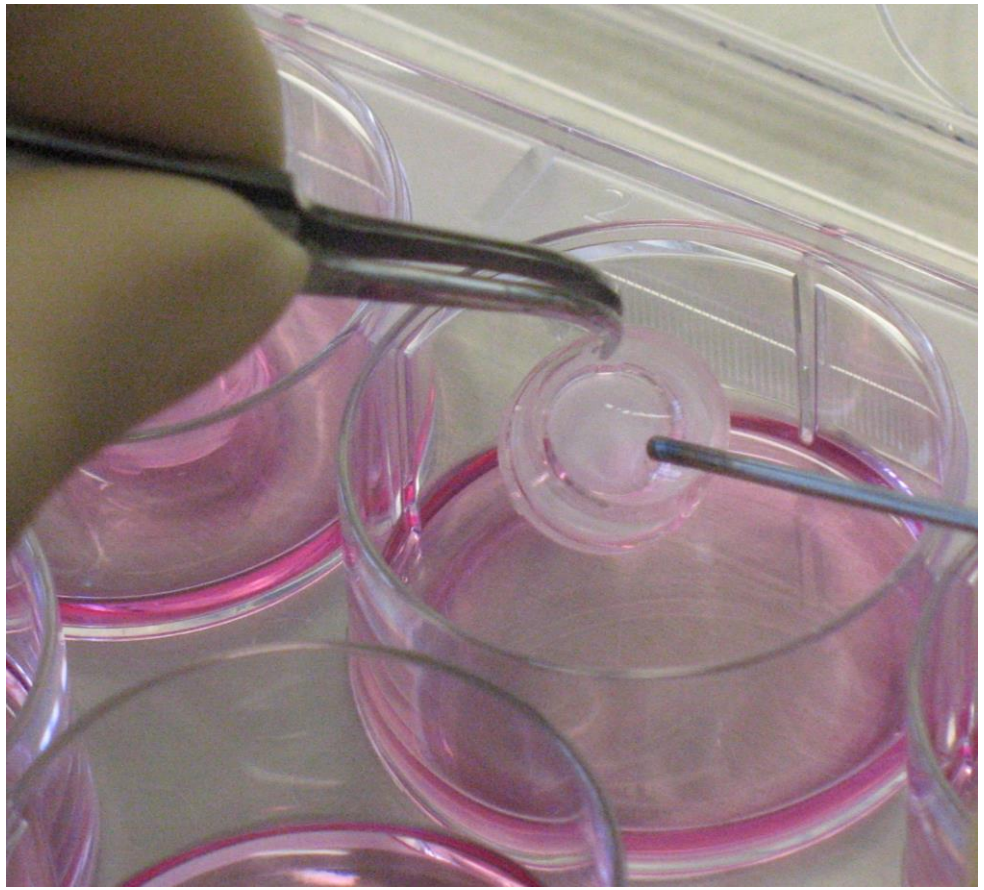


- All modern NAMs have undergone scientific validation
- Example skin sensitization:
  - LLNA* one of the rare, validated animal test methods
  - *In vitro / in chemico* test methods adopted by OECD
  - Human data available from patch tests

***In vitro / in chemico* tests demonstrate higher predictive quality for skin sensitization in humans**

* Local Lymph Node Assay, OECD TG 429

Benefits of NAMs: More robust and less variable data



NAMs not bound by animal welfare regulations, allowing for:

- Ring-trials to validate test methods
- Proficiency testing to ensure competence of the performing labs
- More test concentrations to obtain veritable concentration-response curves
- More controls to obtain robust results
- Sufficient data to define and consider uncertainties (borderline ranges)

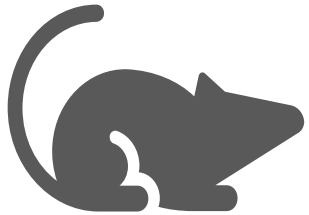
Example: *in vivo* rabbit eye irritation test

- Variability between experiments: 73-94%*
- 1 positive animal sufficient to conclude on a positive test
- High overprediction rate**

* Luechtefeld *et al.*, ALTEX, 2016 ** Adriaens *et al.*, Arch. Toxicol., 2014

Further comparison demonstrates additional advantages …

New Approach Methods



Animal-based Methods

New Approach Methods	Animal-based Methods
▪ Focus on key events in the AOP	▪ Focus on observing adverse effects in non-human species
▪ Test system may include human material	▪ Interspecies extrapolation always required
▪ Well defined applicability domain	▪ No or limited definition of the applicability domain
▪ Less test substance required, lower costs and faster results*	▪ Higher-tier studies may take years and generate costs up to €1 mn
▪ Adaptable to high throughput screening and automation	▪ Not suitable for automation

* Compared to higher-tier animal tests

Shortcomings of NAMs

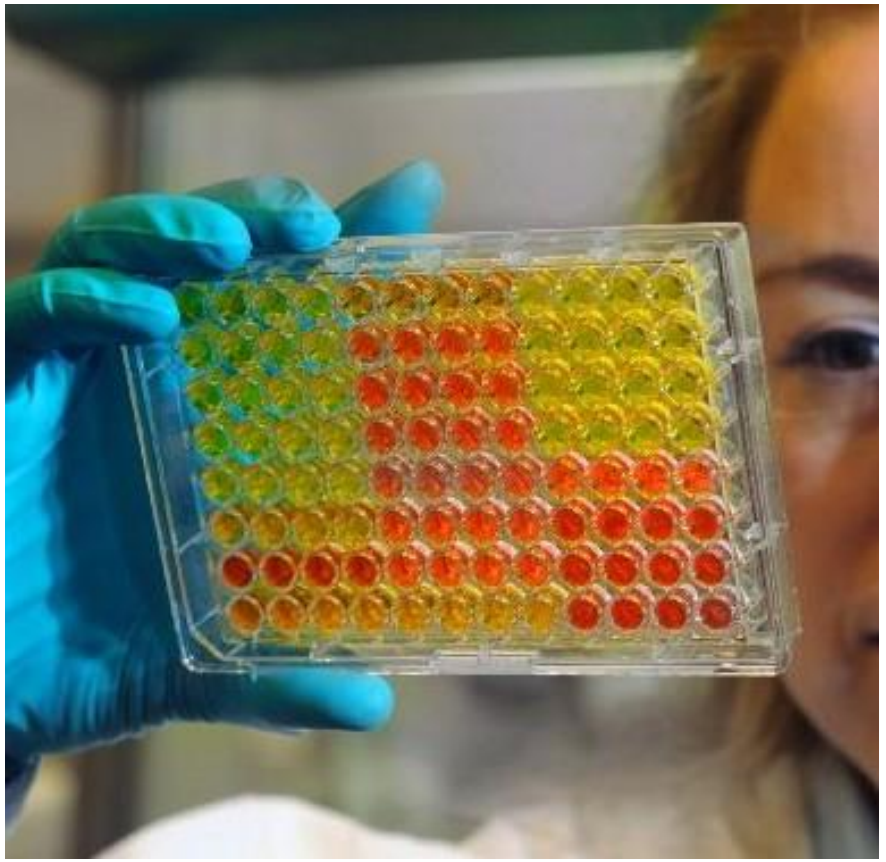
- NAMs **do not (yet)**
  - Provide an alternative for higher-tier animal studies
  - Cover all adverse effects observed in a complete organisms
  - Easily correlate with actual external exposure to humans

Prioritization of research and funding needed to close the gap

What‘s needed for the future under CSS

- Prioritization and funding of development and validation of NAMs
- Faster adaptation of NAMs at OECD level to fuel regulatory acceptance globally
- Scientific dialogue to modernize testing strategies with smarter and state-of-the art approaches
- Enhancing regulatory implementation of NAMs in the EU regulations and other major jurisdictions

→ EPAA offers opportunities for identifying and pursuing new science-based approaches



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