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

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The European Green Deal

1. Enhancing protection of human health and the environment
2. Boost innovation to enable transition to safe and sustainable chemicals
More than 80 changes to chemicals legislations are set out by the Chemicals Strategy for Sustainability to be implemented between 2021 and 2024.

CSS’s five building blocks and 16 measures:

1. Innovate for safe and sustainable chemicals
   - Safe and Sustainable-by-design
   - Non-toxic material cycles
   - Innovating industrial production
   - Strengthening EU’s open strategic autonomy

2. Stronger EU legal framework to address environmental and health concerns
   - Protection against harmful chemicals
   - Endocrine disruptors
   - Chemical mixtures
   - Chemical pollution in the environment
   - PFAS

3. Simplifying and consolidating the legal framework
   - Coordinate and simplify actions across institutions and EU chemical legislation
   - Methodologies and Data
   - Zero-tolerance for non-compliance

4. Comprehensive knowledge base on chemicals
   - Information requirements
   - Inclusion of science into policy

5. Setting example for global chemicals management
   - Lead internationally, where improvement is most needed
   - Cooperation with third countries
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

TIME TO REVISIT OUR TESTING STRATEGIES

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

* 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 …

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