Review of the evolution of REACH requirements and role of the NAM (new alternative methods)

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FRANCE CHIMIE

—France Chimie in **brief**

- **A professional body that represents chemical companies in France.**
- **A network spanning the entire country.**
- **Helping companies to manage everyday operational issues and today's major transitions.**
- **Handling social dialogue for the industry, though its presence in professional bodies**

1 300
Member sites
2/3 of which are SME

representing
120 000
employees

REACH standard information requirements (SIRs)

- REACH principle « **no data, no market** » → registration when substances are imported/manufactured in EEE ≥ 1Tons/year(t/y)

  ☑ Standard Information Requirements in Annexes VII, VIII, IX and X → registration dossiers tonnage bands 1-10T/y, 10-100T/y, 100-1000T/y and ≥ 1000T/y respectively

- If there is no or not enough information to understand how a chemical impacts our health or the environment, new studies are needed to **ensure the safe use** of their chemicals and manage potential risks

  - Declarants must use non-animal testing to generate information "**whenever possible**" (art.13)

  - Methods shall be regularly **reviewed and improved** with a view to reducing testing on vertebrate animals and the number of animals involved → test methods amendments

Progress modifications of the standard REACH requirements

Example of regulations of amending REACH Annex VII as regards to :

- Skin/eye irritation (n° 2016/863)
- Skin sensitization: (n°2017/706)

→ first intent becomes *in vitro/in chemico* assay instead of *in vivo* assay

→ About 50% of the studies conducted since 1990 for skin and eye irritation available in the REACH database, are performed *in vitro*

→ About 90% for the most recent studies over the last 3 years

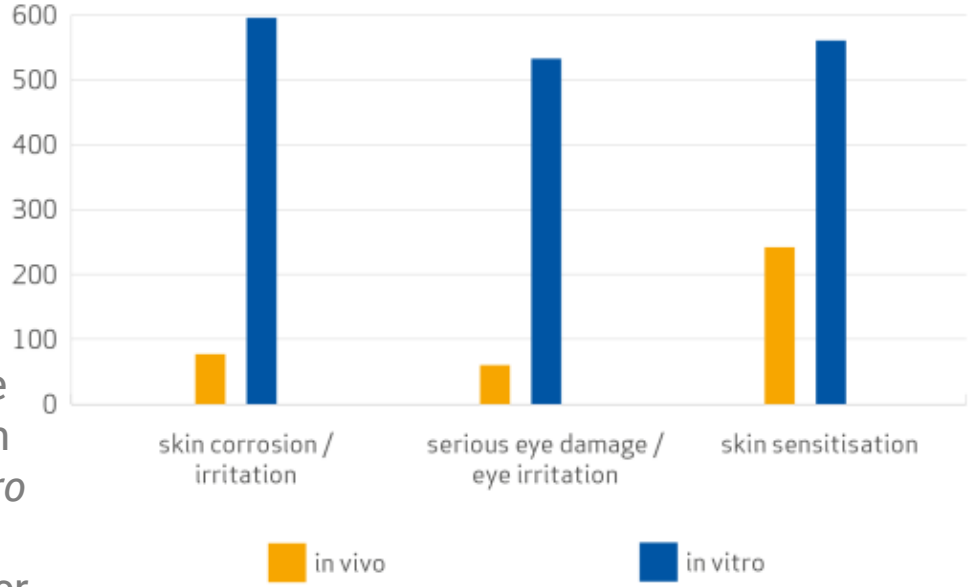
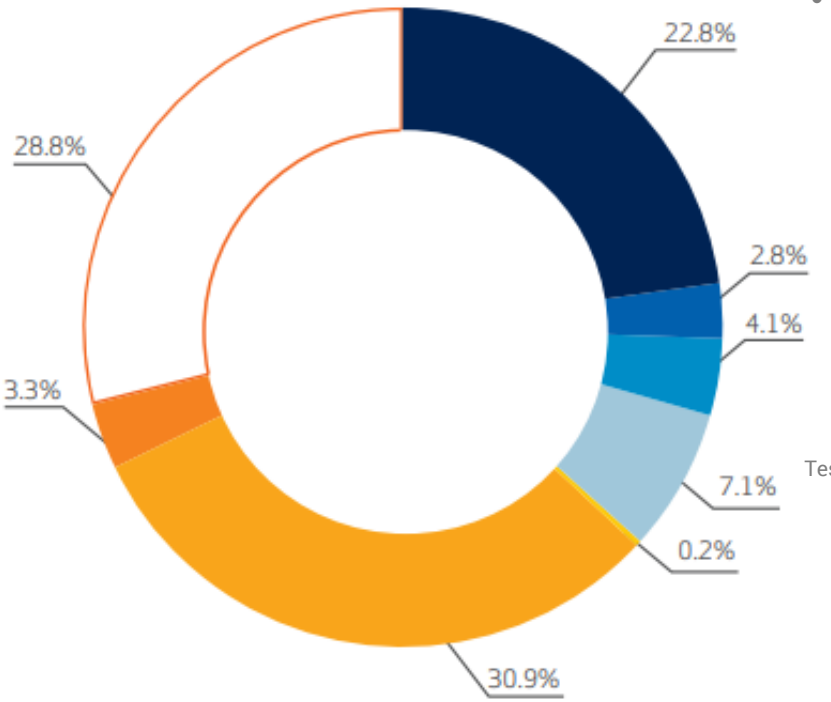


FIGURE 10: Occurrence of studies over the years 2019- 2022

Source : Fifth report under Article 117(3) of the REACH Regulation (June 2023)

The options to adapt requirements



- When additional information is required at higher tonnage bands registrants gradually use more adaptations

Testing Proposal

- Read-across
- QSAR
- WoE
- Data Waiver

Annex XI

- TP → Testing proposal relies on Article 40 and annexes IX and X (see also Regulation 2022/477)
- Experimental
- Other
- No requirement

The majority (53%) of the available experimental studies in the REACH database is legacy data generated before the entry into force of REACH

FIGURE 1: Options used to fulfil the information requirements

Source : Fifth report under Article 117(3) of the REACH Regulation (June 2023)

The EU Chemical Strategy for Sustainability (CSS)

- Global initiative within EU Green Deal, published in 14.10.2020
- Impacts REACH revision which proposal is expected by the end of 2023 → NAMs +++

SCIENCE-POLICY INTERFACE

The Commission will:

- establish and update a **research and innovation agenda for chemicals**, driven by a EU-level Coordination Group, that would also promote the regulatory uptake of research findings;
- foster multidisciplinary research and digital innovations for **advanced tools, methods and models, and data analysis capacities**[102] to also move away from animal testing;
- provide financial support for **EU-wide human and environmental (bio)monitoring capacities**, complementing ecosystem monitoring initiatives[103];
- develop an **EU early warning and action system for chemicals**[104] to ensure that EU policies address emerging chemical risks as soon as identified by monitoring and research;
- develop a **framework of indicators** to monitor the drivers and impacts of chemical pollution and to measure the effectiveness of chemicals legislation[105].

[102] E.g. predictive toxicology or virtual human platforms

https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=COM%3A2020%3A667%3AFIN

A framework for establishing scientific confidence in new approach methodologies

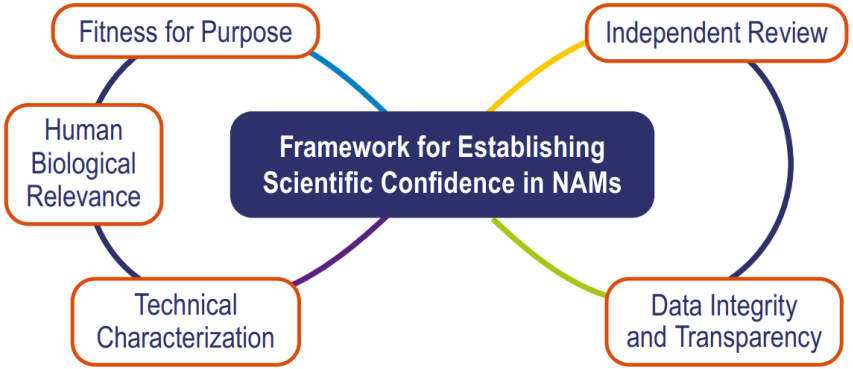
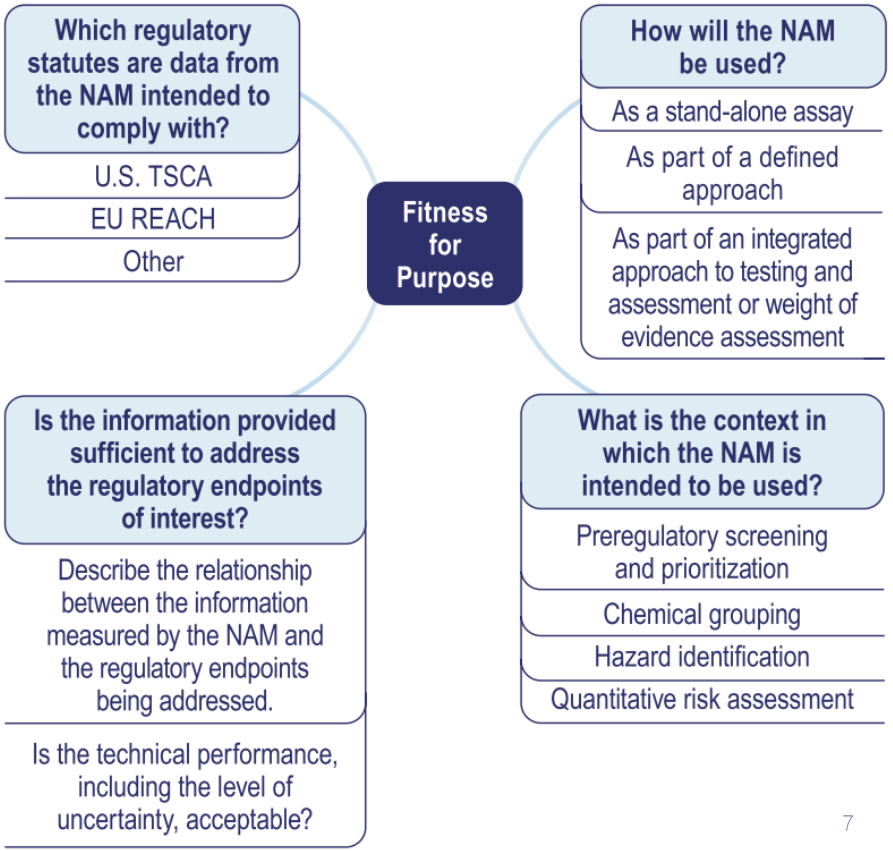


Fig. 1 Schematic illustrating the interconnectedness of the five essential elements for establishing scientific confidence in NAMs for assessing human health effects

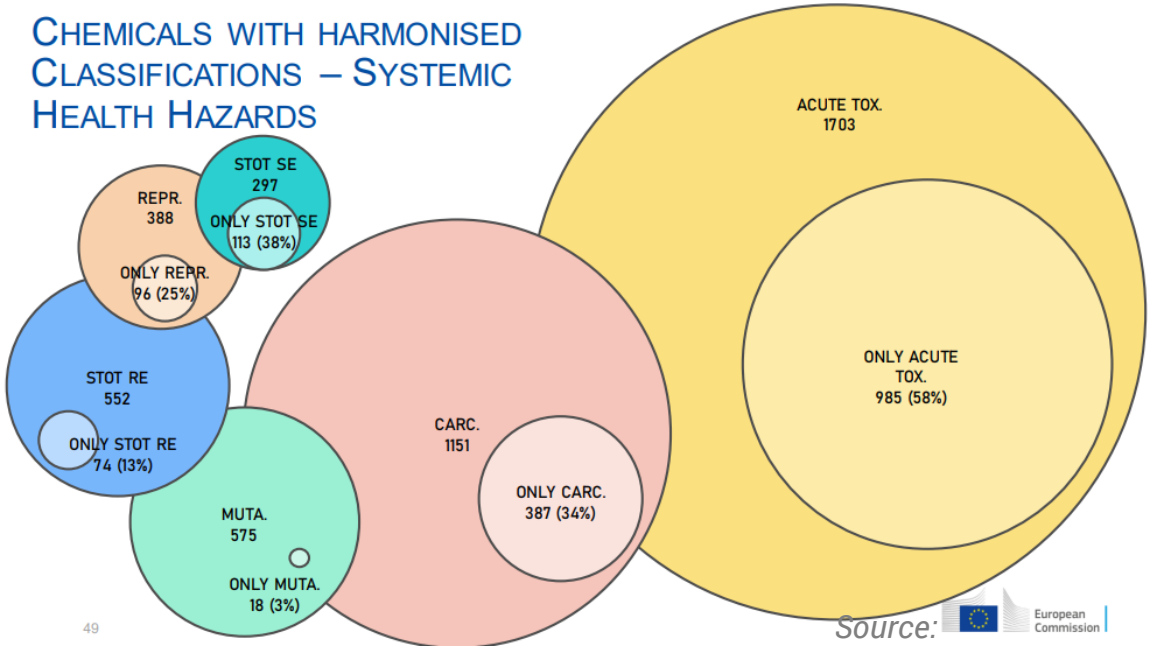
Source: J. van der Zalm et al., (2022)



Capitalise to reach our goals

Need to **acknowledge achievements** and to generate context associated with the application of NAMs, and the protection level achievable → Develop the long-term vision of the new hazard and safety paradigm, and agree on a roadmap towards it

REACH Annex	Number of substances (31 July 2022)
VII	4 901
VIII	2 857
IX	2 346
X	2 335
Total	12 439



Source: European Commission

Improve our strategy to generate (preliminary) relevant data

- Need to establish the target framework for application of NAMs which will ensure equal or higher protection levels and avoid triggering more animal testing

- **Triggers** originally derived for animal data should be re-assessed : here are some proposals made for adapting to new data type:

  - Repeated dose toxicity and screening for reproductive/ developmental toxicity (OECD TG 422) → Testing only for specific cases where the toxicokinetic assessment suggests that a chemical may have significant potential for systemic **bioavailability** or for significant **bioaccumulation ?**

  - *in vivo* **short-term fish** toxicity test → relie on *very* ***strong correlation*** *between* In vitro RTgill-W1 cell line assay (OECD TG 249) and Fish embryo toxicity (OECD TG 236, and replace *unless the in vitro tests is not applicable?*

  - in vivo tests on endocrine disruption → testing only where the weight of evidence assessment on **toxicokinetics** and **IVIVE** suggest relevant systemic **bioavailability**, compared to the bioactivity levels observed *in vitro ?*

Improve our strategy to generate (preliminary) relevant data

- Developp a standardized framework to apply quantitative *in vivo* to *in vitro* extrapolation (QIVIVE) for deriving human reference values from a combination/selection of bioactivity data and extrapolate from NAM data to *in vivo* benchmarks

- Improve selection of analogues for Read Across will be strengthened and decided on what is an acceptable low bioavailability to enable waiving/modifying data requirements
  - Need for supporting data on toxicokinetics & ADME, NAMs to enable exposure-based adaptations based on systemic bioavailability
  - Read-across is the most frequently used adaptation, then the biggest opportunities to reduce animal testing

- Progress the development and use of Bioavailability and Thresholds of Toxicological Concern (TTC) concepts for exposure-based adaptations

Our needs

Improving acceptance and confidence in New Approach Methodologies

Agreement on a framework for the current application of NAMs

Internationally harmonised application of NAM methodologies and Mutual acceptance of data

Long-term vision for a new hazard and safety paradigm, and a roadmap towards it

Better uses & exposure information governing registered substances

Source: Cefic during ECHA Workshop on NAMs , 31 May 2023
https://echa.europa.eu/fr/-/new-approach-methodologies-workshop-towards-an-animal-free-regulatory-system-for-industrial-chemicals

Thanks for your attention !

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