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German Federal Institute for Risk Assessment

Towards “Next-Generation” Chemical Risk Assessment (NGRA) in EU chemicals legislation

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Matthias Herzler
Unit 71 - Coordination and Assessment Strategies
Dept. 7 - Chemical and Product Safety

Disclaimer

The views expressed in this presentation solely represent those of the author and not necessarily an official view of the BfR.

Focus of this presentation

EUROPEAN COMMISSION

Brussels, 1.6.2026
C(2026) 3497 final

COMMUNICATION FROM THE COMMISSION

Roadmap towards phasing out animal testing for chemical safety assessments

{SWD(2026) 144 final}

EUROPEAN COMMISSION

Brussels, 1.6.2026
SWD(2026) 144 final

COMMISSION STAFF WORKING DOCUMENT
Accompanying the document

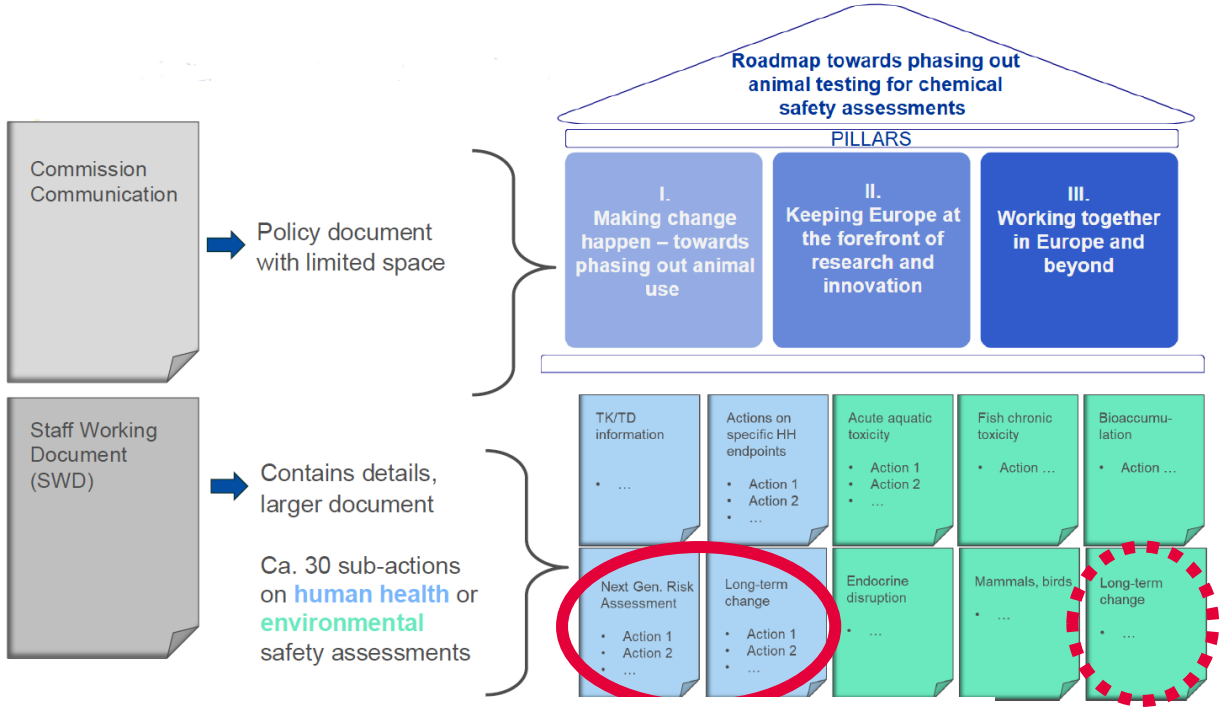
Communication from the Commission

Roadmap towards phasing out animal testing for chemical safety assessments

{C(2026) 3497 final}

Communication,
26 pages,
general policy document

SWD
258 pages,
detailed description of framework and actions



2.2. Preparing for the transition to animal-free chemical safety assessment

2.2.1. The long-term shift towards "Next-Generation Risk Assessment" (NGRA) in EU chemicals legislation

Terminology

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2.2.2. Characterising the protection level and level of confidence associated with next-generation risk assessments

Introduction – the concept of adequate level of protection

A future animal-free Next-Generation Risk Assessment[35] (NGRA) framework should allow to determine whether an "adequate level of protection" (as defined by the regulatory context and problem formulation) for human health and the environment is attained. One of the most frequently heard requirements for NGRA is that, compared to the current system, it needs to provide "the same or a higher level of protection for human health and the environment."

What is NGRA?

Although the “original“ from **US EPA** in 2014 sketches out a **broad, generic NGRA framework**, a more **limited, context-dependent** definition is often used:

*“In this context, a Next Generation Risk Assessment (NGRA) is defined as an **exposure-led**, **hypothesis driven** **risk assessment approach that incorporates one or more NAMs** to ensure that use of a cosmetic product does not cause harm to consumers.”* (Dent et al., 2018)

BUT this definition is **not flexible enough**:



Review

All *EHP* content is accessible to individuals with disabilities. A fully accessible (Section 508–compliant) HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1307260.

A Framework for the Next Generation of Risk Science

Daniel Krewski,[1,2] Margit Westphal,[1] Melvin E. Andersen,[3] Gregory M. Paoli,[2] Weihsueh A. Chiu,[4] Mustafa Al-Zoughool,[1] Maxine C. Croteau,[1] Lyle D. Burgoon,[4] and Ila Cote[4]

[1]McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Ottawa, Ontario, Canada; [2]Risk Sciences International, Ottawa, Ontario, Canada; [3]Institute for Chemical Safety Sciences, The Hamner Institutes for Health Sciences, Research Triangle Park, North Carolina, USA; [4]National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, DC, USA

Many typical risk assessment workflows
(e.g. under REACH, PPP, BP)
are **hazard-led (≠ hazard-based!)**,
i.e. the assessment starts on the hazard side.

Computational Toxicology 7 (2018) 20–26

Contents lists available at ScienceDirect

Computational Toxicology

journal homepage: www.elsevier.com/locate/comtox

ELSEVIER

Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients

Matthew Dent[a,*], Renata Teixeira Amaral[b], Pedro Amores Da Silva[b], Jay Ansell[c], Fanny Boisleve[d], Masato Hatao[e], Akihiko Hirose[f], Yutaka Kasai[g], Petra Kern[h], Reinhard Kreiling[i], Stanley Milstein[j], Beta Montemayor[k], Julcemara Oliveira[l], Andrea Richarz[m], Rob Taalman[n], Eric Vaillancourt[o], Rajeshwar Verma[l], Nashira Vieira O'Reilly Cabral Posada[l], Craig Weiss[p], Hajime Kojima[f]

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What does the Roadmap SWD say about it?

Section 2.2.1, The long-term shift towards “Next-Generation Risk Assessment” (NGRA) in EU chemicals legislation

*“… the eventual full phasing out of animal testing for chemical safety assessments requires the transition to a **“New Safety Paradigm”** characterised by the following elements:*

- ***Human**-centric safety assessments using alternatives to animal testing*
- ***Mechanistic** understanding to distinguish relevant from irrelevant substance effects*
- *Utilisation of **up-to-date science***
- *High **throughput** and **efficiency***
- *A high level of **protection and confidence**, demonstrated explicitly and transparently*
- ***Consistency** across regulatory sectors in line with the **One Substance, One Assessment (OSOA)** principle”*

*“For the purpose of this document, **“NGRA” then refers to chemical risk assessment conceptual frameworks or practical workflows implementing one or more elements of this paradigm.**”*

The need for an integrated, overarching NGRA framework

Roadmap main document, section 3.1.2

*"[…] **both the methods and the overall safety assessment framework must change.** The transition to a new scientific framework for integrating non-animal information represents a **paradigm shift**. […]*

*It also presents an opportunity to **harmonise assessments** across sectors consistent with the 'One Substance, One Assessment' (OSOA) approach* […]."

(Roadmap main document, section 3.1.2)

*"Such framework will help to recognise **knowledge gaps**, prioritise future **research funding** and identify any **needs for possible changes**."*

(Roadmap SWD, section 2.2.1)

But how to implement this?



Image generated with generative AI

The Roadmap provides concrete ideas for how to get there!

No need to reinvent risk assessment as such

Large variety of regulatory programs - **limited number of basic risk assessment problem formulations** addressed across all sectors with **similar, modular workflows**, e.g.

- screening/prioritisation, ADME/fate, **hazard** identification/characterisation, **exposure** assessment, full **risk/safety** assessment (hazard- or exposure-driven)

Current risk assessment workflows rely on a number of **standardised (intermediate) outputs**, e.g.

- an estimate of internal or external **exposure**, a "**point of departure",** a **hazard classification,** a **safe dose** for humans and the environment, a **risk metric** for humans and the environment

Methods/approaches may change, but
similar standardised outputs will still be needed in the future!

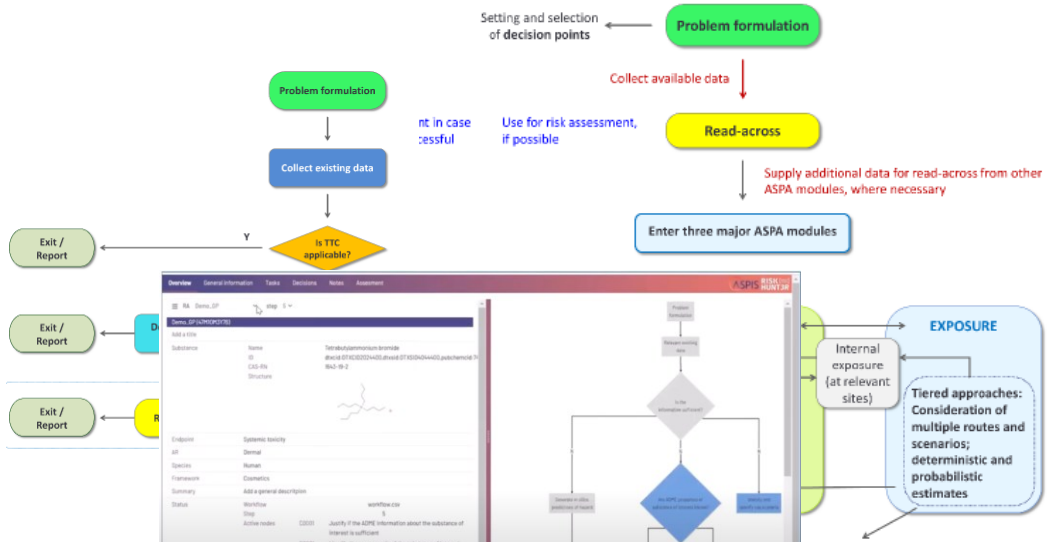
Practical application

https://aspis-cluster.eu

A future unified NGRA framework should in the end be able to **integrate** **all relevant** human health and environmental safety assessment **workflows** into a **modular** scheme providing all **required** **regulatory (intermediate) outputs**.

Balancing standardisation with flexibility
will be key to regulatory acceptance,
in view of practicalities

Example: Alternative Safety Profiling Algorithm (ASPA), developed by the ASPIS cluster



Concept Article

An Alternative Safety Profiling Algorithm (ASPA) to Transform Next Generation Risk Assessment into a Structured and Transparent Process

Marcel Leist[1,2,#], Silvia Tangianu[1,2,#], Femke Affourtit[3], Hedwig Braakhuis[4], John Colbourne[5], Eike Cöllen[1], Nadine Dreser[1], Sylvia E. Escher[6], Iain Gardner[7], Stefan Hahn[6], Barry Hardy[8], Matthias Herzler[9], Barira Islam[7], Hennicke Kamp[10], Viktoria Magel[1], Philip Marx-Stoelting[9], Martijn J. Moné[11], Patrik Lundquist[12], Ilse Ottenbros[4], Gladys Ouedraogo[13], Giorgia Pallocca[14], Bob van de Water[11], Mathieu Vinken[15], Andrew White[16], Manuel Pastor[17$] and Mirjam Luijten[18$]

ALTEX 43(1), 158-175. https://doi.org/10.14573/altex.2509081

Long-term change – we do not start from scratch

Proposed stepwise approach to testing and assessment, SWD section 2.2.1

Step 1: **Existing data** for substance in question

Step 2: **Read-across** from existing data for similar substances (read-across)

Step 3: Exclude **relevant exposure**, if possible (ADME in silico info)

Step 4: Sensitive („protective“) **screening step with broad biological coverage** to focus further testing

Step 5: Specific („predictive“), **targeted follow-up testing *in vitro***

Step 6: Follow up ***in vivo*** on any remaining concerns, after case-specific evaluation **(during transition only)**

Hypothesis building

Hypothesis testing

Spells out „animal testing as the last resort“,
could be applied immediately, if legislation would allow.

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The stepwise approach not only drives a mindset change, it also lays out important work areas for gradually achieving the transition, e.g.

- curate, machine-readable **high-Q reference datasets**, more in-depth work on interspecies transferability across a wide range of taxa (see e.g. PrecisionTox), AI-supported data retrieval and processing p
- promote **NAM-enhanced read-across** (see e.g. EU-Toxrisk, new Texas A&M Complement-ARIE NAMs Decision Centre“) integrating „biological similarity“, also as a means to gain more practical experience with NAMs under comparatively flexible regulatory conditions
- develop criteria for **„insignificant/negligible“** (internal) **exposure** (e.g. TTC concept)
- develop/benchmark **broad screening approaches** with sufficient biological coverage, e.g. test batteries, omics
- develop/benchmark **targeted predictive methods** endpoint by endpoint, use for „positive“ prediction in the beginning
- …

Considerable progress has been achieved in many of these areas in recent years!

Major challenges

(the solution of which will be central to success)

*"Non-animal chemical safety assessments will mostly rely on a mechanistic understanding of toxicity rather than on observing adverse effects in animals. This entails determining whether molecular-level changes **predict adverse outcomes**, and can, if necessary, describe them **quantitatively**."* (Roadmap, section 3.2.1)

Quantitative link to **adversity** is a strong regulatory requirement!

→ Chemicals regulation interferes with legal rights, e.g. market freedom, etc.

→ Work on qKERs and qAOPs is very important.

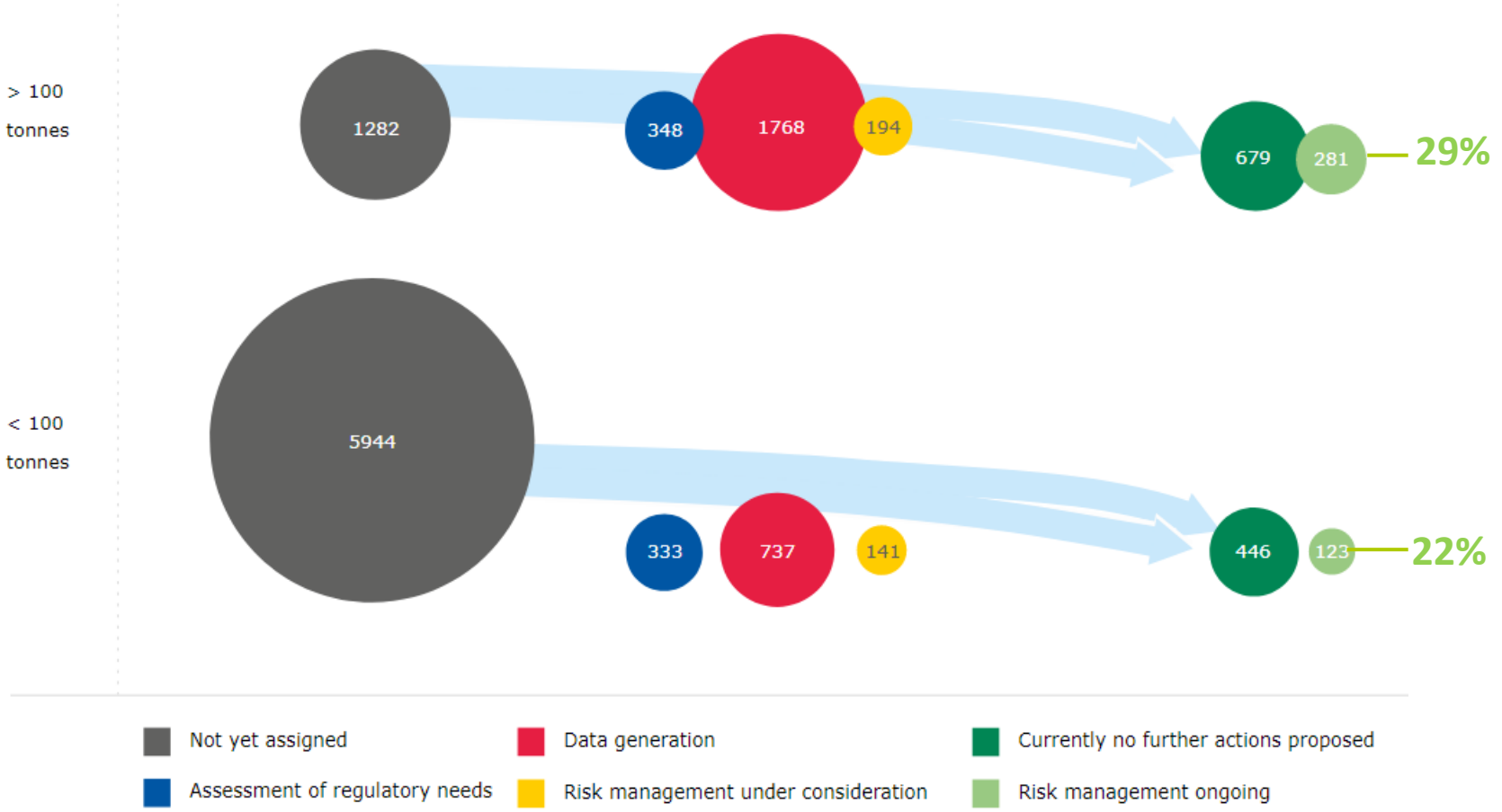
Define „sufficient" **biological coverage** to make sure **no adverse outcomes are missed**

→ When to accept „negative" results?

→ Qualitative and quantitative aspects, e.g. discuss maximum required test concentrations

Incentives to engage in the transition

Figure: REACH chemical universe: substances with active registrations above 1 tonne/year.



Acc. to current knowledge...

... ~25% of the chemicals in the database need (further) risk management ...

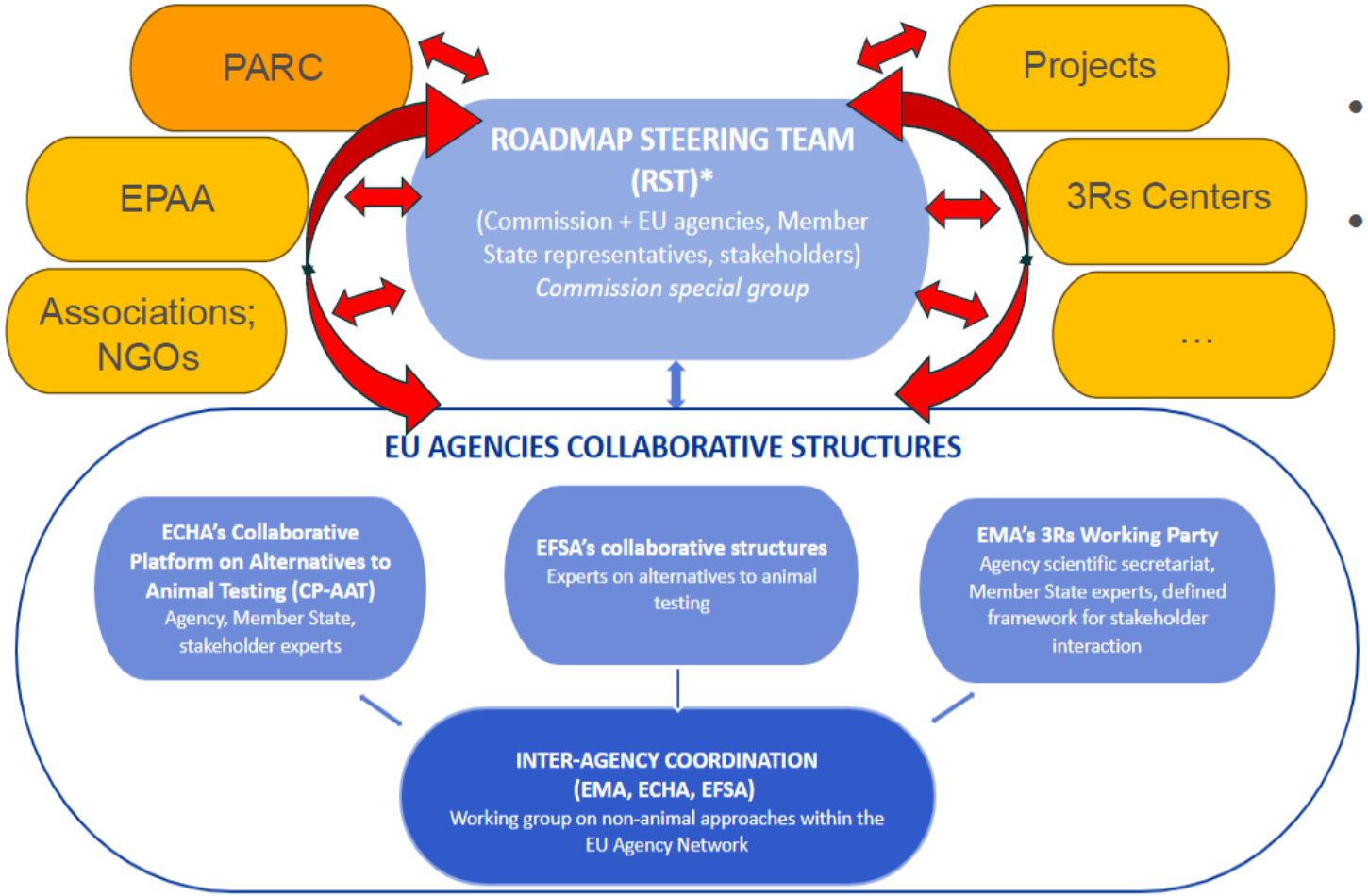
... ~75% don‘t.

Incentives for actively engaging in the transition

- **Inefficiency** of current processes
- Need to ascertain **adequate level of protection** of the new system
  → Define **benchmarks**, both from the scientific and political / risk management side
- Chance to **overcome methodological deficiencies of the current system**
  → More **consistent and transparent assessments** as well as regulatory decisions
- Have a say to help **steer developments** in the right direction
- **Train and prepare** for new methods
- …

Efficient organisation of collaboration will be key, too

(Roadmap section 3.3 „Pillar III – Working together in Europe and beyond“)



- Implementation will have to be a collaborative effort
- Exchange and coordination as key element of the organisational set-up

OSOA group

European Commission

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PARCopedia.eu - a collaborative online resource

https://parcopedia.eu



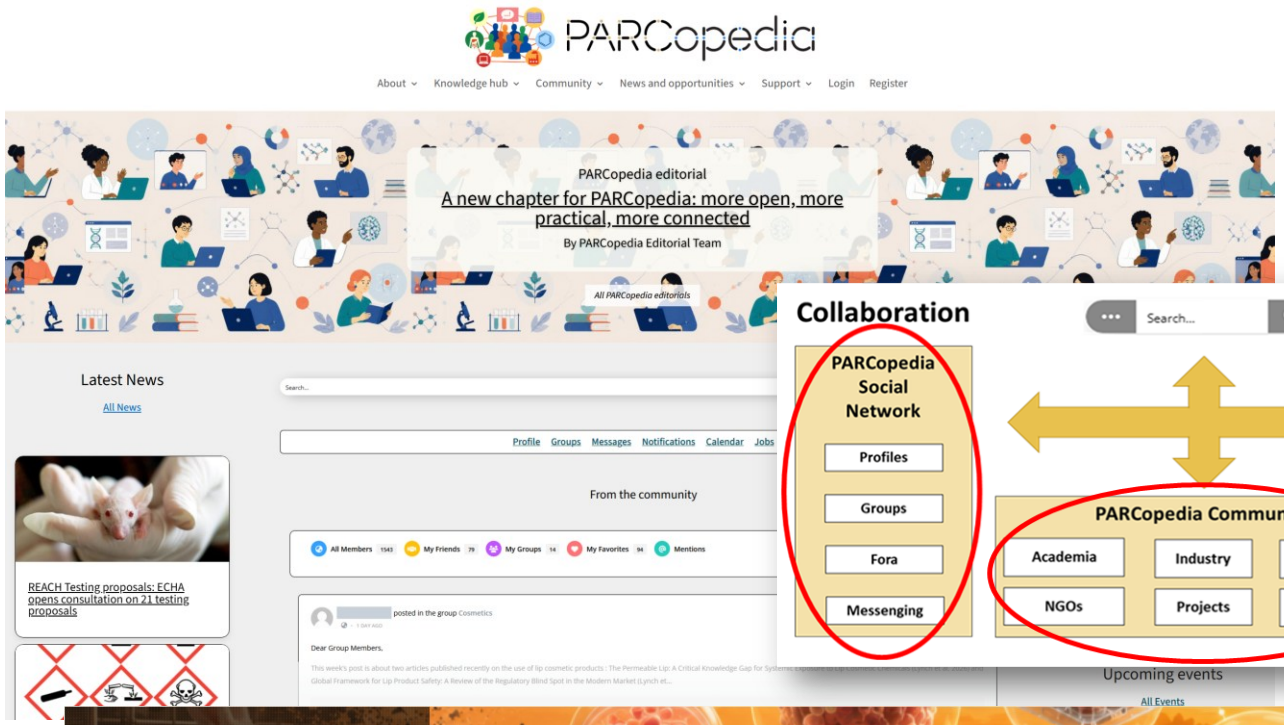
A **knowledge repository**



An opportunity for **knowledge sharing**



A **community space** for **networking** and **discussion**







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Consumer health protection to go

BfR2GO – the BfR Science Magazine

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