



A future chemicals regulation embracing ZeroPM

Presenter Elisabet Berggren, JRC – European Commission

Achieving Zero Pollution of Persistent and Mobile Substances: Prioritization through Substance Grouping and Risk Assessment, Dessau-Roßlau, 20 September 2024

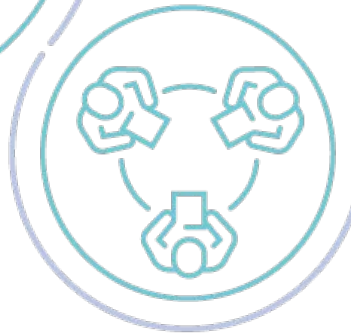
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Unit F3: Systems Toxicology

EURIL
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European Union Reference Laboratory for alternatives to animal testing

3Rs

mandate under Directive 2010/63

- research & evaluation
- validation
- dissemination
- promotion





July 2024

Policy Brief

Achieving zero pollution by 2050 needs regulatory change: a call for policy support of New Approach Methodologies (NAMs)

Authors: Martin Paparella, Sarah Hale, Iseult Lynch, Julia Hartmann
 Illustrations: Alexandra Schaffert

<https://projects.research-and-innovation.ec.europa.eu/en/strategy/strategy-2020-2024/environment-and-climate/european-green-deal/green-deal-projects-support/green-deal-resources/policy-brief-achieving-zero-pollution-2050-needs-regulatory-change-call-policy-support-new-approach>

MANAGE CHANGE

BASE SAFETY ASSESSMENT ON LEVEL OF PROTECTION

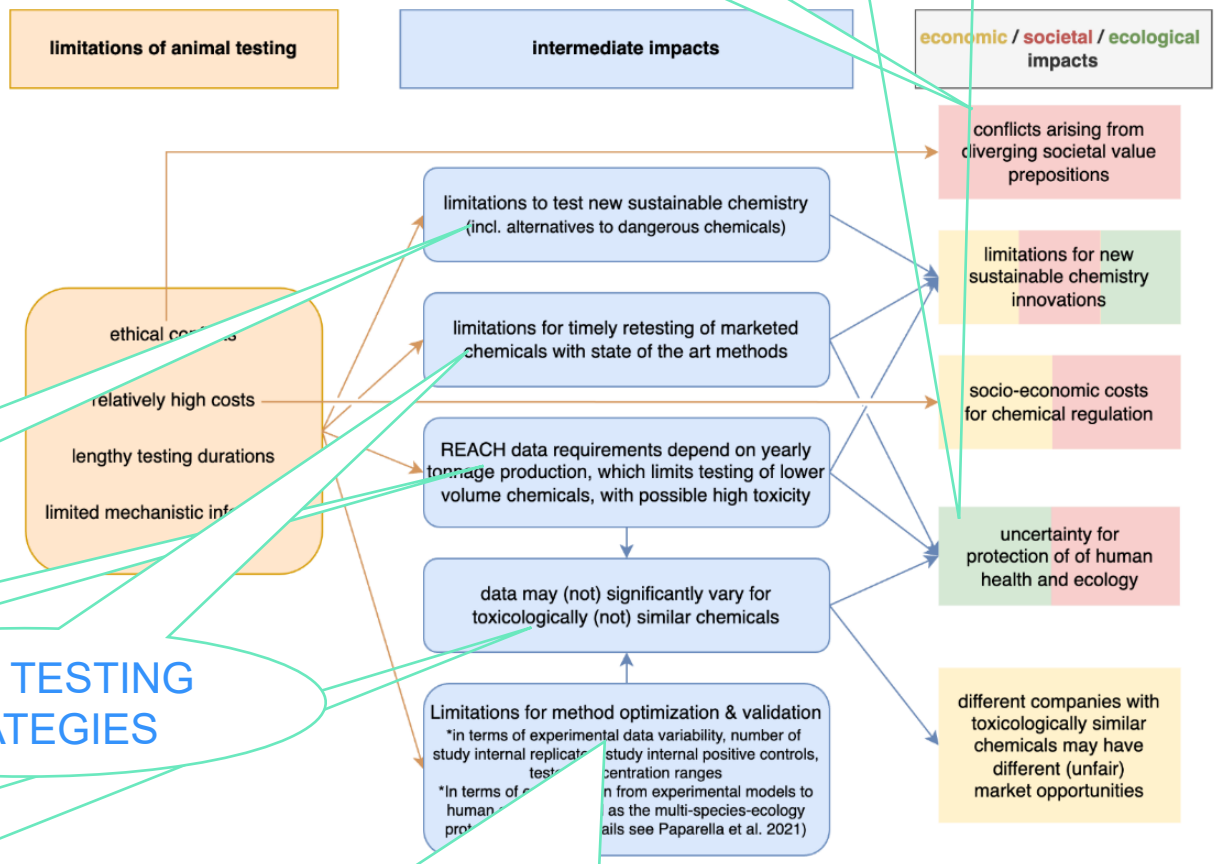


Figure 2: The... result in economic, social and ecological

GREEN ENOUGH

1S1A & TESTING STRATEGIES

START TO KNOW A BIT ABOUT EVERYTHING

RECOGNISE UNCERTAINTY FOR BUILDING BETTER EVIDENCE

STANDARDISE, QUALIFY & VALIDATE – KEEPING FLEXIBILITY, EMBRACE INNOVATION & FOCUS ON IMPACT



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Regulatory Toxicology and Pharmacology

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

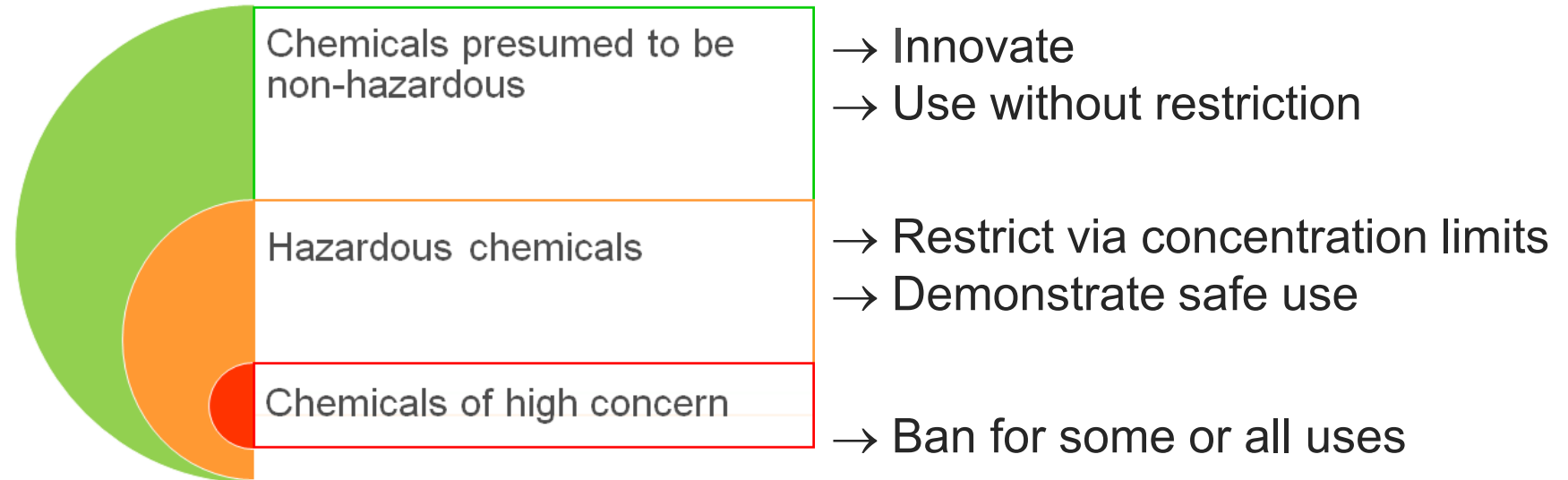


Towards a future regulatory framework for chemicals in the European Union – Chemicals 2.0

Elisabet Berggren, Andrew P. Worth*

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PRINCIPLE OF EQUIVALENT PROTECTION: MAKE THE SAME DECISIONS, NOT NECESSARILY THE SAME PREDICTIONS



DEVELOPING A NEW CLASSIFICATION SCHEME

- A generic risk matrix is developed to assign chemicals to groups 1-3 (low, medium & high concern)
- Existing data for already classified chemicals (high & medium concern) are used to calibrate the classification scheme resulting in **equivalent protection**

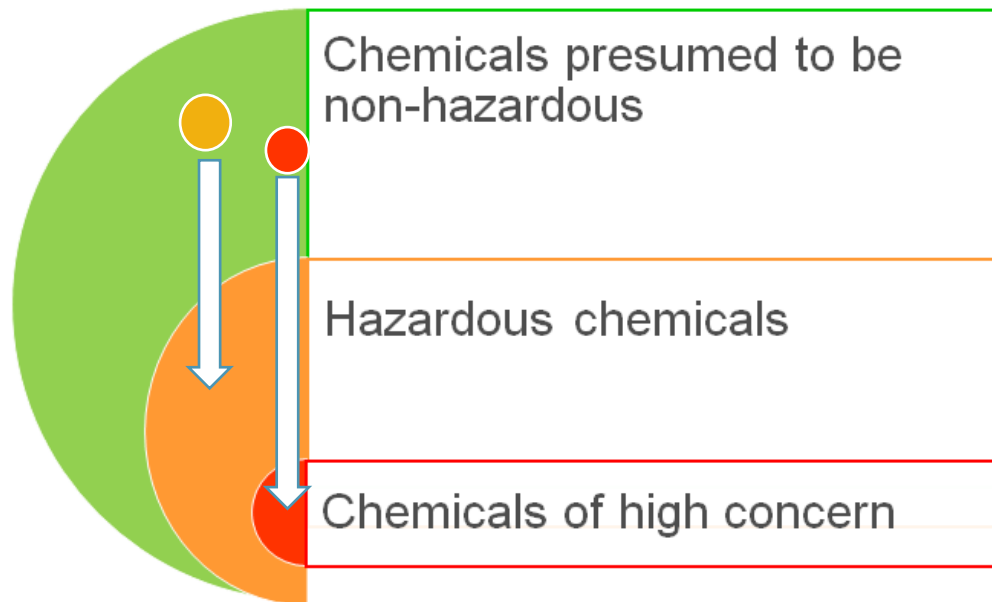
		Activity (NAM-based toxicodynamics)		
		High	Medium	Low
Potential Systemic Availability (NAM-based toxicokinetics, based on ADME properties)	High <i>(vPvM)</i>	H	H	M
	Medium <i>(PM)</i>	H	M	L
	Low	M	L	L



https://single-market-economy.ec.europa.eu/epaa-launches-designathon-human-systemic-toxicity_en

NAMS CAPTURE CHEMICALS CURRENTLY TREATED AS GREEN, BUT BASED ON NO OR LIMITED INFORMATION

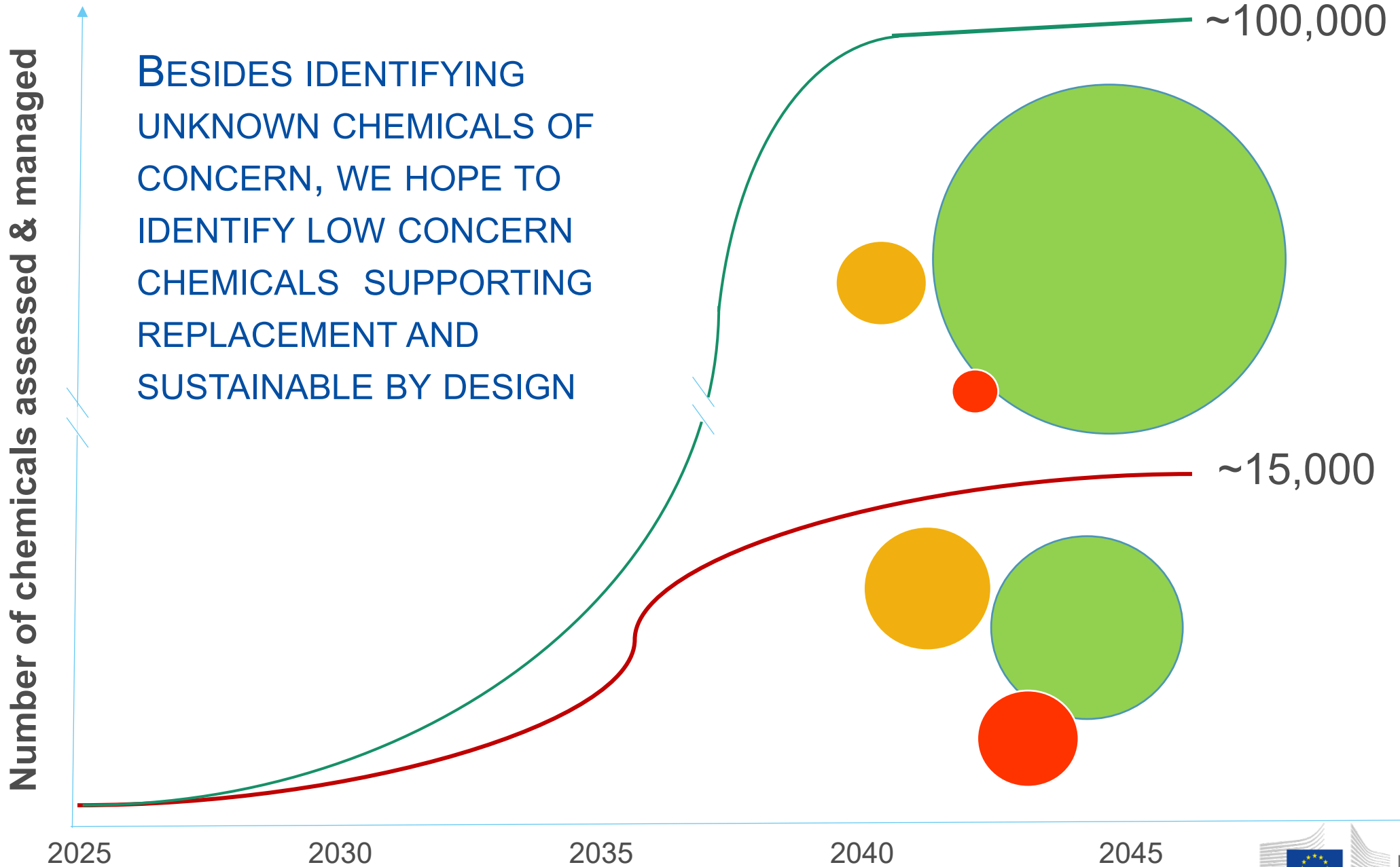
- Application of the new classification scheme to chemicals in the current low concern group will result in some additional classifications and thus an **overall higher level of protection**



→ Demonstrate safe activity/systemic availability profile

→ Classification & Labelling +
→ Risk assessment

→ Classification & Labelling



GHS & SYSTEMIC HEALTH EFFECTS

Acute Tox	Muta	Carc	Repro	STOT SE	STOT RE	(ED, not GHS)

Current GHS classes for Systemic Toxic effects:

- Criteria based on non-animal methods increases with time
- Current criteria based on human evidence and animal methods remains to avoid obligation to re-evaluate already classified chemicals and allow for use of existing data

Future class “Systemic Toxicity”:

- Criteria only based on non-animal methods, providing same protection level as other classes combined

Non-animal methods overlapping but not identical to the ones introduced under the current classes



Systemic Toxicity

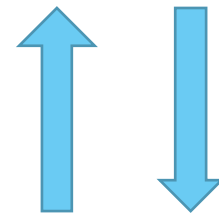
FROM ANIMAL-BASED CRITERIA TO NON-ANIMAL BASED CRITERIA

Expected development of current classes

Criteria based on non-animal methods increases step by step

- to provide partial replacement solutions to current criteria, and
- to cover additional health concerns (not currently considered)

Acute Tox	Muta	Carc	Repro	STOT SE	STOT RE	(ED, not GHS)

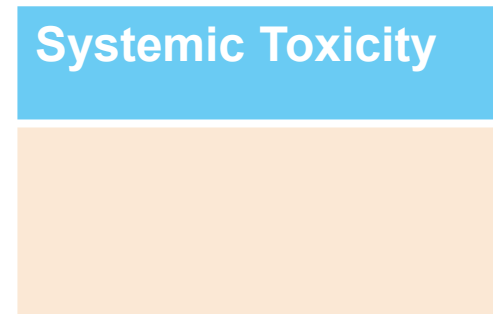


Continuous mutual exchange of progress in non-animal methodologies during parallel development

Future class “Systemic Toxicity”

New classification system based on only non-animal criteria

- developed on the matrix concept
- calibrated on already classified chemicals to achieve equivalent protection



A FUTURE CLASSIFICATION SYSTEM FOR SYSTEMIC HEALTH EFFECTS

Acute Tox	Muta	Carc	Repro	STOT SE	STOT RE	(ED, not GHS)	Systemic Toxicity

- New GHS class “Systemic Toxicity” is introduced in parallel to current classes applying the GHS building block principle
- There is a choice when to implement the new class and stop applying the current classes for systemic toxicity as same protection is achieved
- When the new class solely based on non-animal methods will become the class of choice, because supporting a less complex and therefore less information requiring system, information related to chemicals classified in the current system, will become a historical archive, and the classification for systemic health effects will include only the one generic class

HOW TO CAPTURE RELEVANT RISK MANAGEMENT BASED ON CONCERN

	Activity (NAM-based toxicodynamics)		
	High	Medium	Low
Potential Systemic Availability (NAM-based toxicokinetics, based on ADME properties)	High	H	M
	Medium	H	L
	Low	M	L



Cat. 1
DANGER

Carc Cat. 1
Muta Cat. 1
Repro Cat. 1
ED Cat. 1
STOT-RE Cat. 1

Classes covered & used to calibrate the new class to capture same protection

Carc Cat. 2
Muta Cat. 2
Repro Cat. 2
ED Cat. 2
STOT-RE Cat. 2



Cat. 2
WARNING

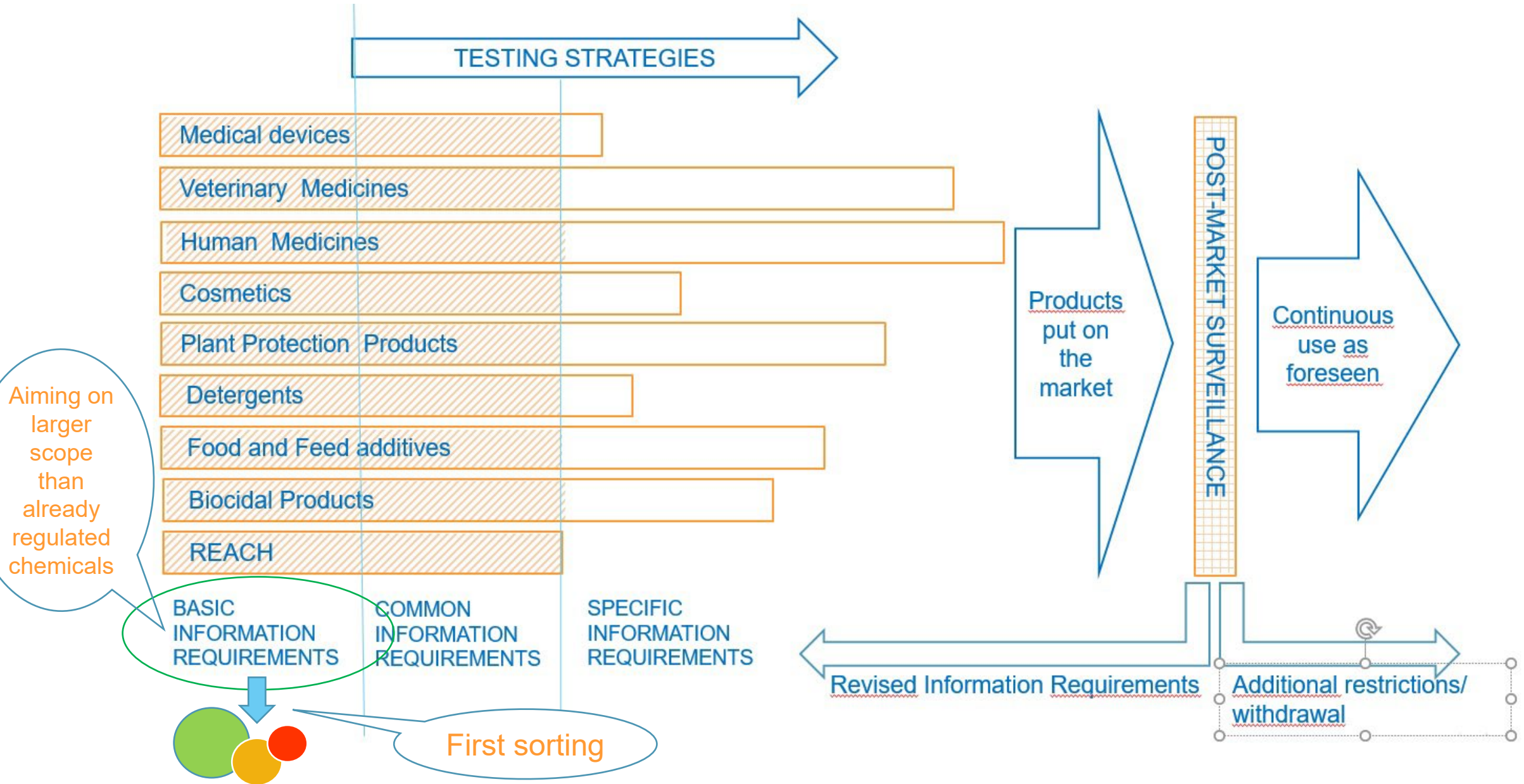
Systemic Toxicity

Acute Tox Cat. 1-3
STOT SE Cat. 1

Classes not *a priori* covered but might include elements useful to capture same protection

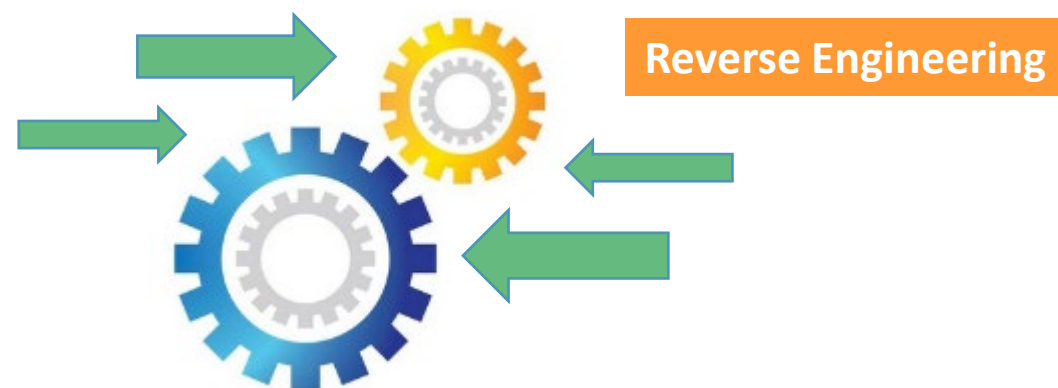
Acute Tox Cat. 4
STOT SE Cat. 2

INFORMATION REQUIREMENTS IN EU CHEMICAL LEGISLATION

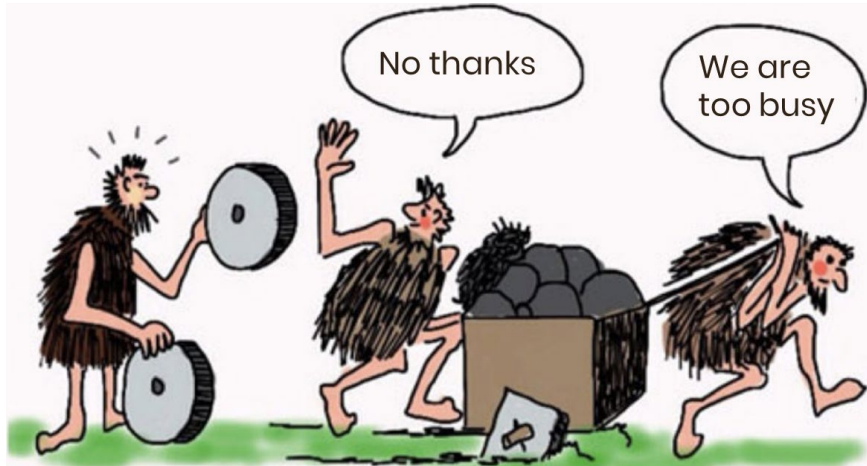


RISK ASSESSMENT & THE PRINCIPLE OF EQUIVALENT PROTECTION

- Group chemicals based on their current risk management measures – **risk categories**
- Identify relevant physicochemical, NAM-based toxicokinetic/dynamic and possibly use-related properties
- Identify a quantitative measure of similarity - similarity metric (e.g. cut-off limits for certain properties)
- Decide a grouping algorithm for the properties and similarity metric to form the **risk categories**
- Group non assessed chemicals in risk categories and apply the corresponding risk management measures



THE STATUS QUO BIAS – WE DO NOT LIKE CHANGE



<https://precisiontox.org/wp-content/uploads/2024/02/D6.1-Report-on-Socio-Technical-Barriers-26Jan.pdf>


Wellcome Open Research

Wellcome Open Research 2024, 9:167 Last updated: 02 SEP 2024



RESEARCH ARTICLE

REVISED **Chemicals regulation and non-animal methods: displacing the gold standard [version 2; peer review: 2 approved with reservations]**

Annamaria Carusi 

<https://doi.org/10.12688/wellcomes.20581.2>

Interchange Research, London, E5 8JW, UK



“What if we don’t change at all ... and something magical just happens?”

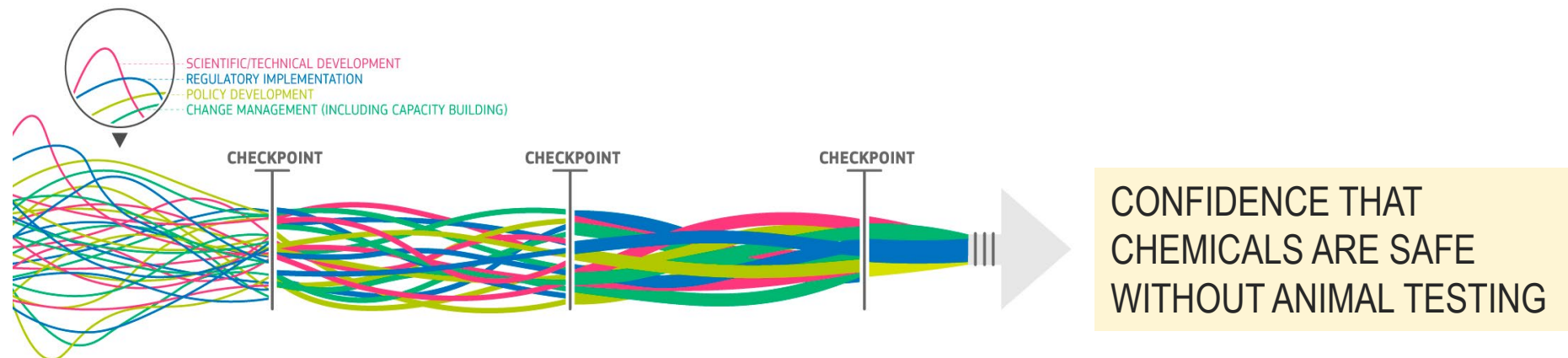
MANAGE CHANGE & BUILD TRUST

To prepare for the European Commission roadmap towards phasing out animal testing for chemical safety assessment 3 working groups are established:

- Human Health (Chair: Katrin Schutte, ENV)
- Environmental Safety Assessment (Chair: Georg Streck, GROW)
- Change Management (Chairs: Elisabet Berggren, JRC, Marco Fabbri, GROW)

Aim of the Change Management Working Group:

To identify principles and practices that will facilitate the structuring of the roadmap as well as the subsequent transition to animal-free safety assessment.



Thank you



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