CONCERT REACH Industry Workshop «Novità e benefici attesi dall'implementazione degli "In Silico Tools" per le imprese chimiche»

Sviluppo chimica spa

"*In Silico Tools*" e *Regulatory costs*: stima dei risparmi attesi per le imprese chimiche

13 Giugno 2023

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CONCERTING EXPERIMENTAL DATA AND IN SILICO MODELS FOR REACH

LIFE17 GIE/IT/000461

Paolo Manes
SC Sviluppo chimica S.p.A.

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1. **DOVE SIAMO ADESSO**
2. DOVE VOGLIAMO ANDARE
3. QUALE IMPATTO PER L'INDUSTRIA CHIMICA
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Chemical Risk evaluation & assessment

The post-REACH Registration era

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Registration summary data

Source: Federchimica, 2019 estimates

Phase-in substances after the 3 deadlines (2010, 2013, 2018):
- 22,000 registered substances
- 95,000 registrations

In 2019 1,500 new registrations (new products).

Average costs expensed by REACH-compliant Chemical Companies:
- > 1,000,000 € (within all the 3 deadlines)

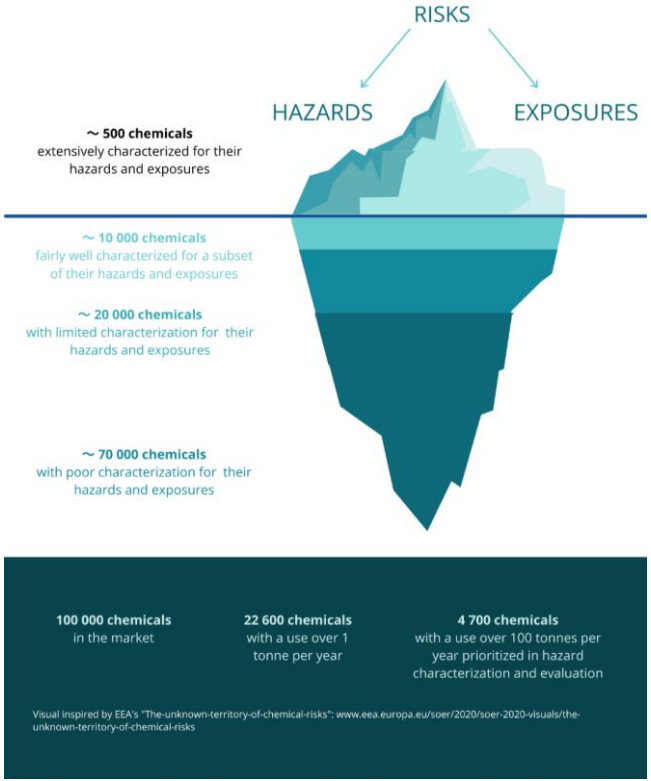
Most recurring cost components: Letter of Access (“LoA”)

Required (human) professional resources:
- 30% of declared they had to hire specific competences
- 40% reallocated internal resources
- 75% indicated the use of external support (consultancy).

Latest developments: **Dossier revision** required by ECHA to improve the quality of already provided safety data (concerning in particular chronic toxicity data with specific focus over reprotoxicity studies)
Expected associated cost within the larger tonnage band (> 10 t/y) could vary from a few tens of thousands € up to approx. 300,000 €.

14,000 registered chemicals in scope for extended Standard Information Requirements

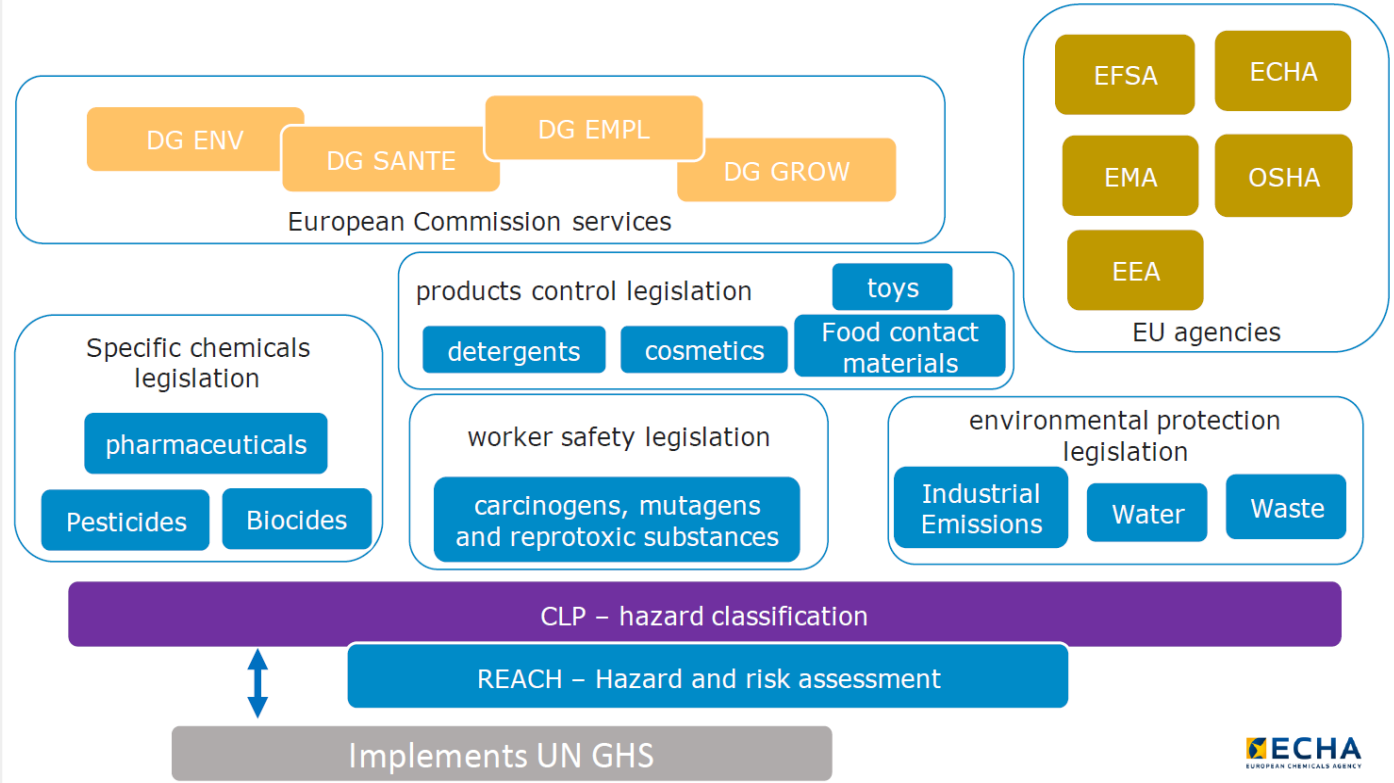
The EU example: The unknown of chemicals registration



Source: European Environmental Agency (EEA)

The European Chemicals legislation

An articulated framework



Shortcomings of “in vivo” analysis

Predictive value of certain experimental data

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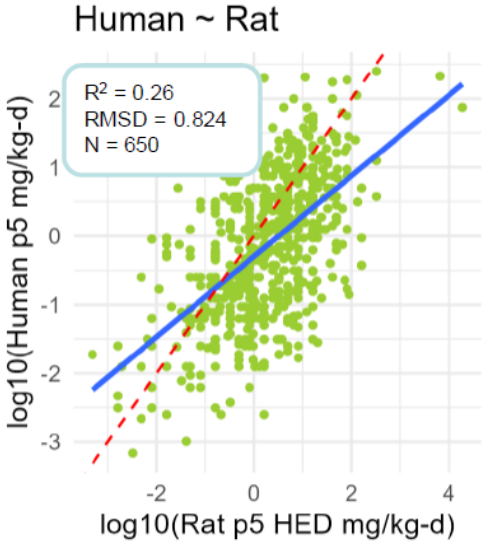
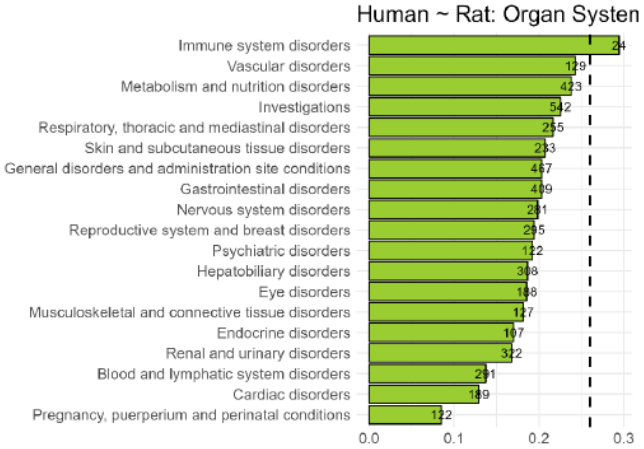
Quantitative Concordance Between Rodent and Human Toxicological Responses





R^2: log10(Human p50) ~ log10(Rat p50)

“The results of a laboratory animal can only predict the results in reproductive toxicity of another species by 60%”.

VHP4Safety project

New APCRA Case Study, Preliminary Results

Ongoing developments (1)
Transition is happening

- European Citizen's initiative (ex. "Save cruelty free cosmetics - Commit to a Europe without animal testing' submitted to EC" initiative)
- European Parliament asking for a roadmap
- Food and Drug Administration modernisation act
- European Medicines Agency 3R working party
- European Food Safety
- Authority roadmap
- European Chemicals Agency (ECHA) Report & Workshop on New Approach Methods (NAM)

Video: hiips://echa.europa.eu/it/-/new-approach-methodologies-workshop-towards-an-animal-free-regulatory-system-for-industrial-chemicals
Report: hiips://echa.europa.eu/documents/10162/23919267/230530_117_3_alternatives_test_animals_2023_en.pdf/9cfc291e-9baf-ffa2-466c-2bc2c6f06b8e?t=1685428213290

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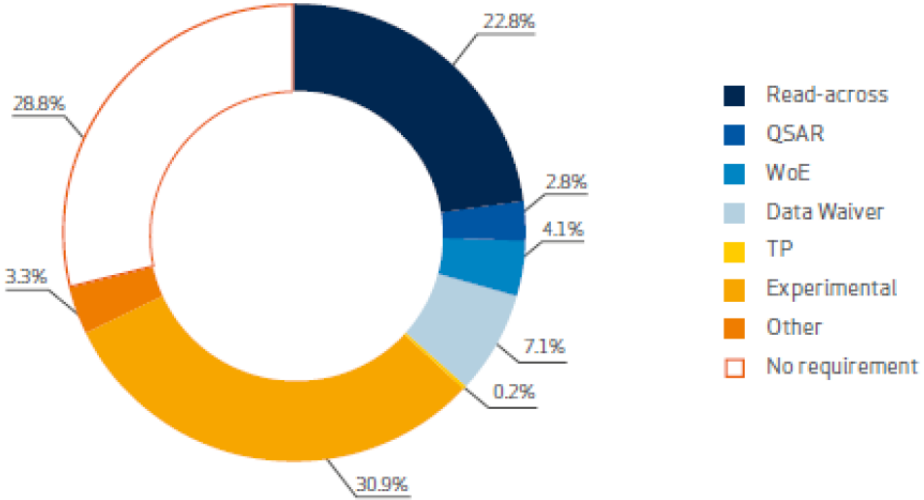
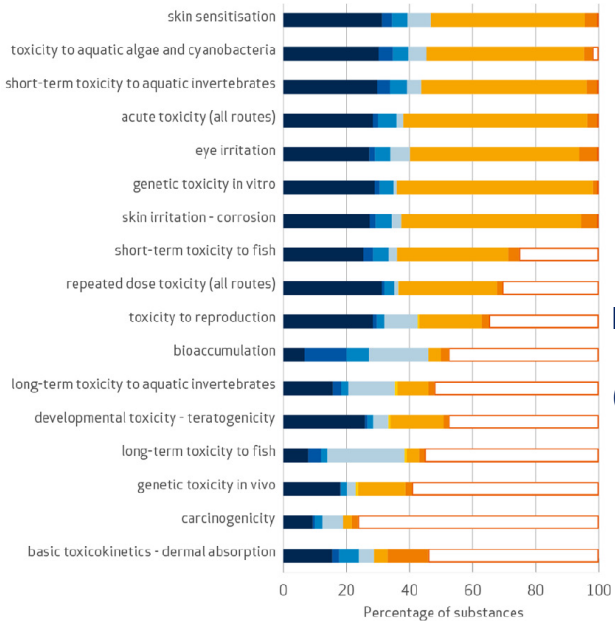
Ongoing developments (2)
Last period performance for Adaptations

ADAPTATIONS (in particular READ-ACROSS) USED MORE THAN EXPERIMENTAL STUDIES (2009-2022)





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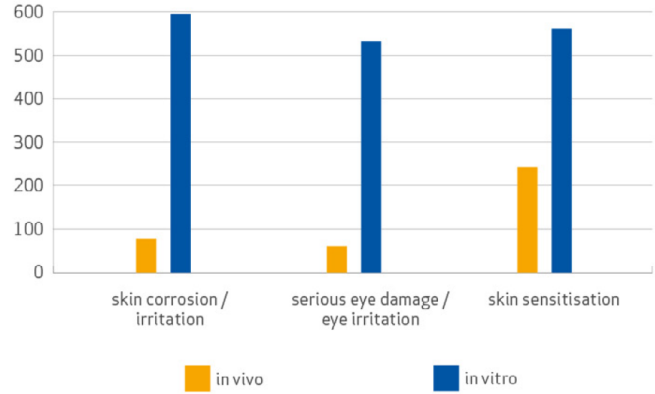
No big differences with previous periods (‘16, ‘19 and ’22)

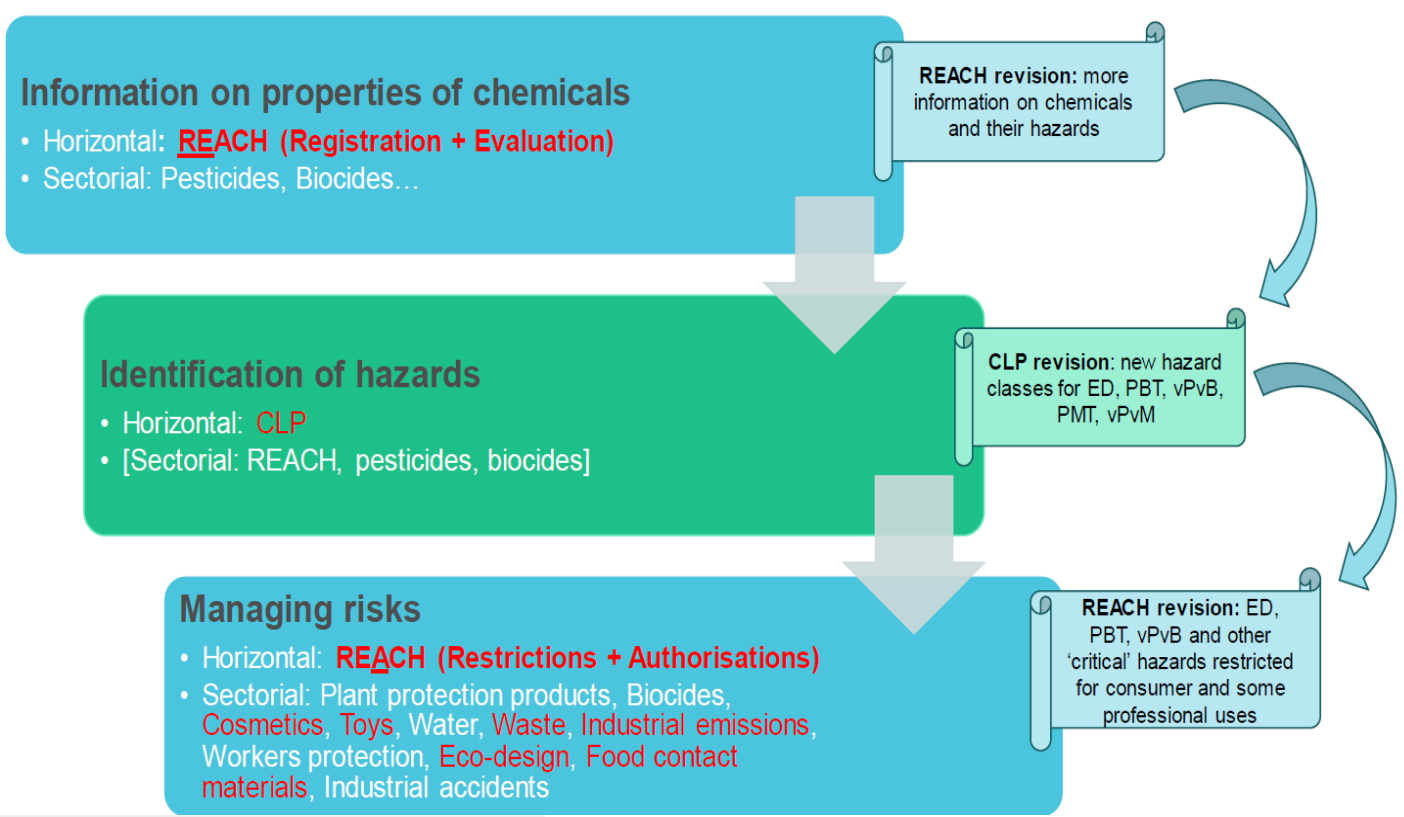
Higher tonnage bands > additional info required (higher-tier endpoints) > more adaptation

90% of executed studies within last reporting period (’19-’22) IN VITRO



Evolving Regulation for industrial chemicals

CLP & REACH revision



Source: European Commission (EC)

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Concert REACH

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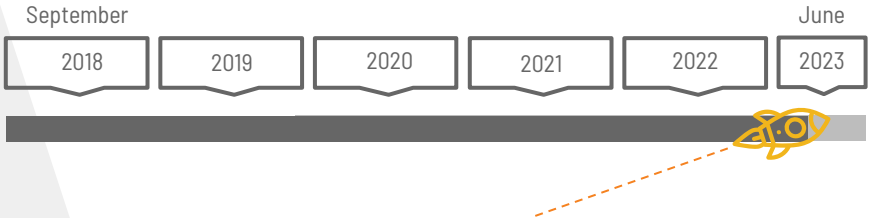
a network of **non-testing methods (NTMs)** for exploring the properties of new chemicals by using the data gathered within REACH



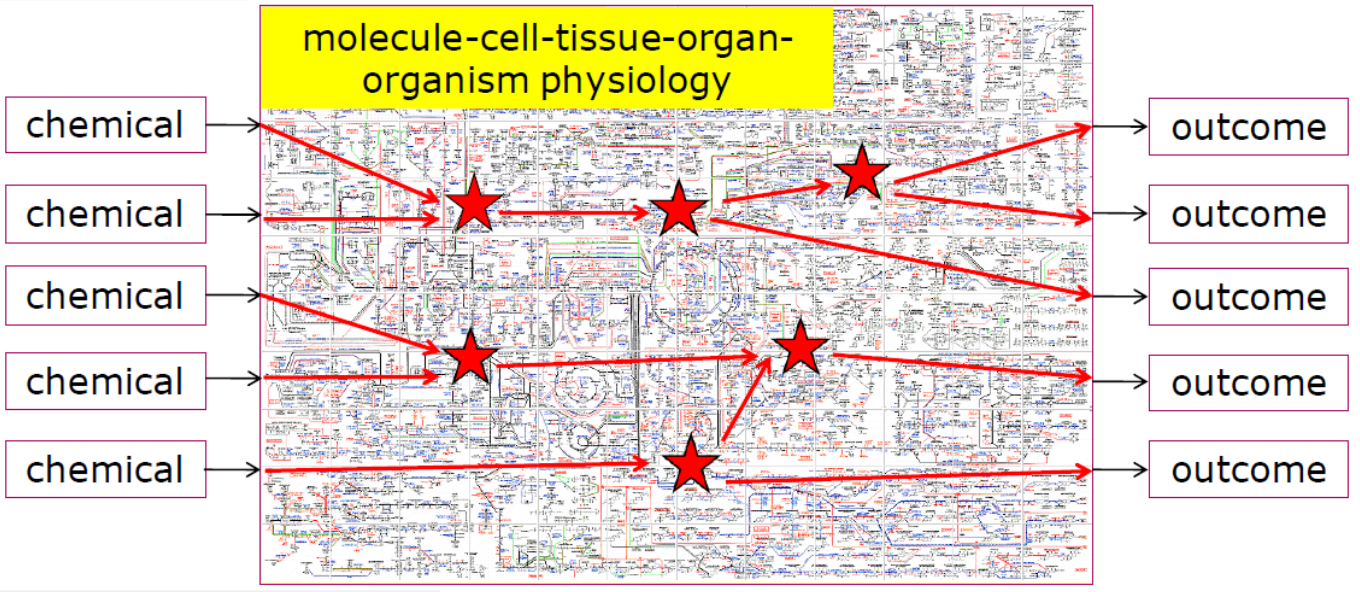
Istituto di Ricerche Farmacologiche Mario Negri, Italy
Research institute, **Coordinator**

Associated Beneficiaries

External supporting

Adverse Outcome Pathways (AOP)

Molecular Initial Event (MIE), Mode of Action (MoA) and Key Events (KE)



Source: Deloitte's report on «Chemistry 4.0: » https://www2.deloitte.com/content/dam/Deloitte/global/Documents/consumer-industrial-products/gx-chemistry%204.0-full-report.pdf

Multi level transition analysis

Identifying QSAR's barriers, leverages and opportunities

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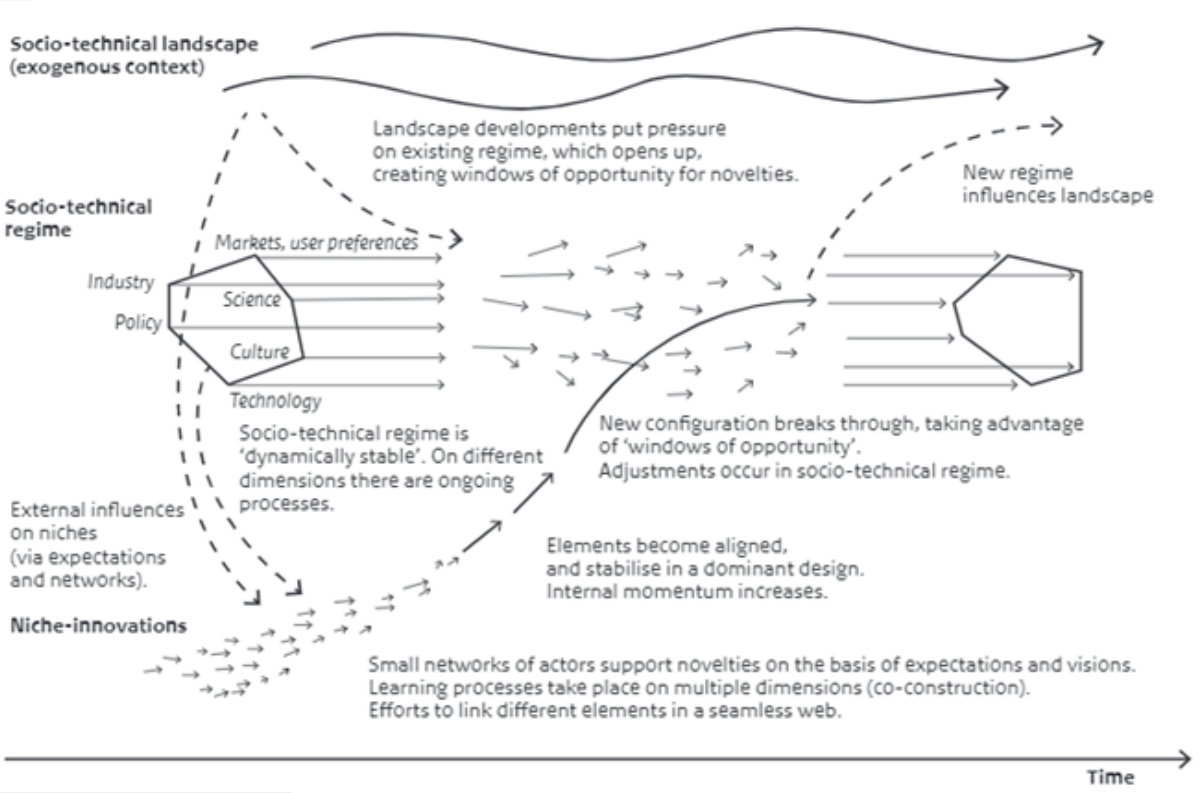
Providing scientific evidence is clearly not sufficient to make real changes

Need of flexible approach, mixed methods as well as interdisciplinary research

Societal trends

Dominant system

Alternative system



Source: Geels, F. W. (2011). The multi level perspective on sustainability transitions: Responses to seven criticisms.

Environmental innovation and societal transitions, 1(1), 24 40.

Next Generation (animal-free) Risk Assessment

THE CHALLENGE

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HUMAN-RELEVANT SCENARIOS
Current animal tox testing regimes do not reflect human-relevant scenarios, such as differences in susceptibility due to age, gender, timing of exposure, or disease state.

REPRODUCIBILITY
Only 25% of published results obtained with animal data can bereproduced.

PREDICTIVE VALUE
The results of a laboratory animal can only predict the results in reproductive toxicity of another species by 60%.

9,338,162 ANIMALS
Were still being used for research and testing in the EU in 2017 (about one third for toxicity testing).

INTERDISCIPLINARY APPROACH
Integrating data from new in vitro and in silico methods, data sciences and social sciences

SLOW DECREASE
In 10-years time, the use of animals is only decreased by 22% with the current approach to gradually refine, reduce and replaceanimal testing.

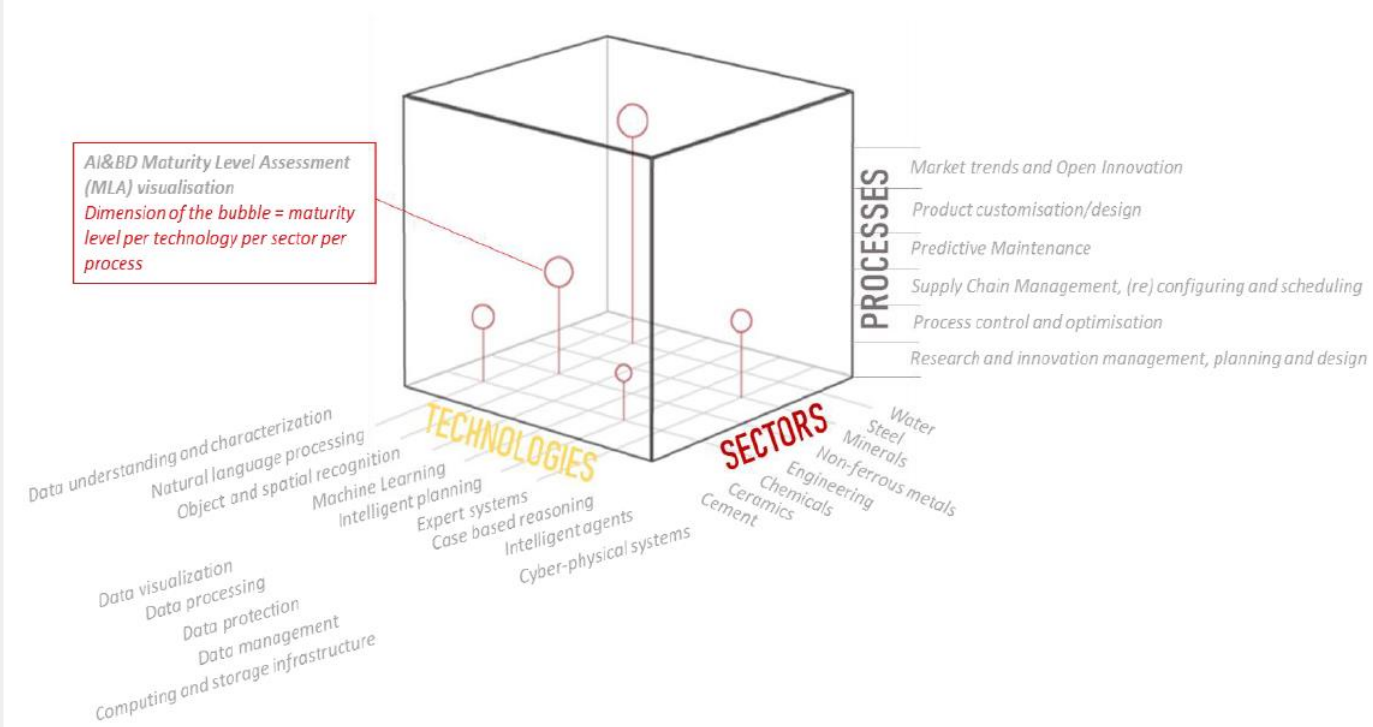
Human biology central

Science & regulations meet

Virtual human platform for safety assessment of chemicals and pharmaceuticals
VHP4Safety project NWA 1292.19.272 is part of the NWA research program 'Research along Routes by Consortia (ORC)', which is funded by Netherlands Organization for Scientific Research (NWO).

Digitalization opportunities (1)

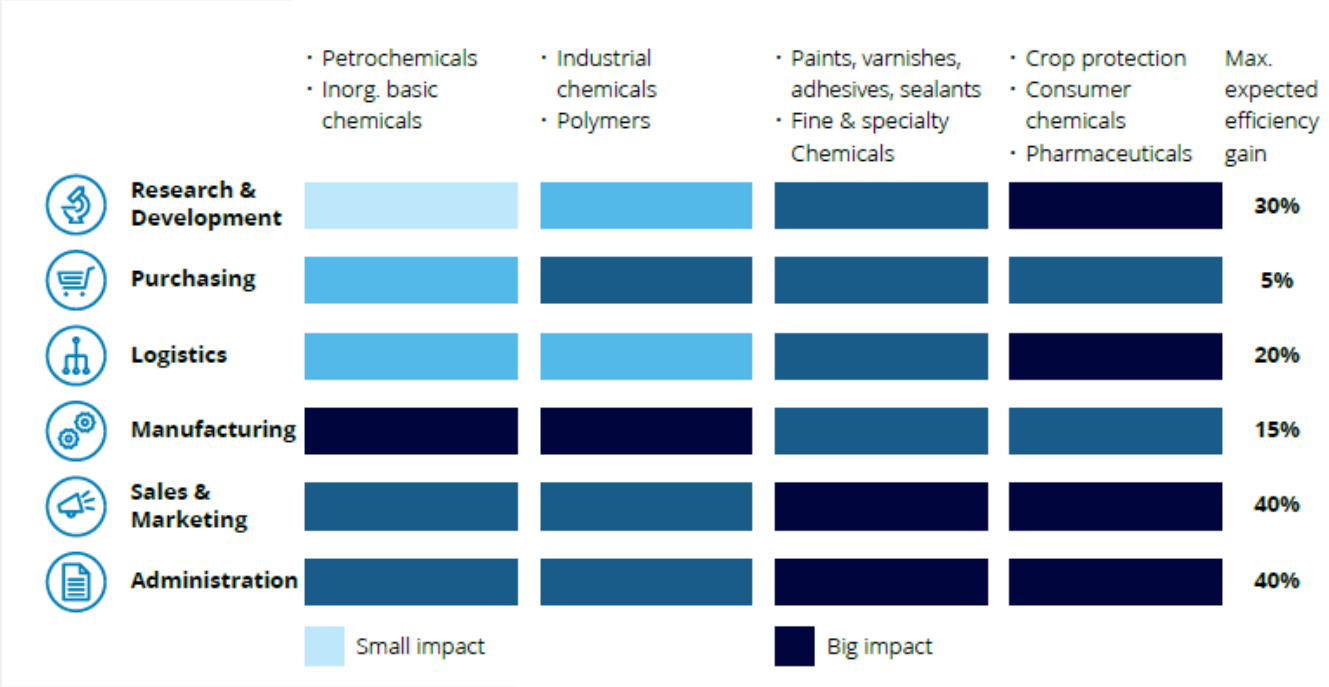
Artificial Intelligence & Big Data for Process Industries



Source: ARTIFICIAL INTELLIGENCE AND BIG DATA CSA FOR PROCESS INDUSTRY USERS, BUSINESS DEVELOPMENT AND EXPLOITATION (hiips://www.ai-cube.eu/)

Digitalization opportunities (2)

Articulated by Chemical segment & internal function



Source: Deloitte's report on «Chemistry 4.0: » https://www2.deloitte.com/content/dam/Deloitte/global/Documents/consumer-industrial-products/gx-chemistry%204.0-full-report.pdf

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REACH Compliance & CSR

Endpoints' costs of experimental testing activities

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Physico-Chemical Properties

- Boiling point
- Melting point
- Dipole moment
- Molar refractivity
- Parachor
- Octanol water partition coefficient
- Vapor pressure
- Density
- Solubility
- …

Biological activities

- Binding affinity
- Lethal dose
- Inhibition concentration
- Mutagenicity
- Carcinogenicity
- …

Unit costs estimates for individual endpoints analysis to be externally outsourced (EU labs)

Research Paper "Testing Costs and Testing Capacity According to the REACH Requirements – Results of a Survey of Independent and Corporate GLP Laboratories in the EU and Switzerland"

Appendix 1: Average prices for the tests as required by the REACH proposal: Overview by size of laboratory

Tests as specified in Appendix V-VIII of the REACH proposal	Test guide-lines: OECD / EU	No. of all labs	Avg. price: means in Euros			
			All labs	Large labs	BAuA (2004) labs	Large lab share of tot. capacity (%)
v 011 - Spectral data		10	2,094	2,626		40
v 012 - Analytical characterization		8	2,554	2,294		48
v 014 - Development of analytical method		9	5,239	9,500		85
v 5.02 - Melting point	102 / A.1	12	674	848	600	71
v 5.03 - Boiling point	103 / A.2	12	719	905	600	71
v 5.04 - Relative density	109 / A.3	11	657	829	600	72
v 5.05 - Vapour pressure	104 / A.4	8	2,779	3,211		84
v 5.06 - Surface tension	115	12	817	976	800	70
v 5.07 - Water solubility	105	11	3,813	4,508	3,900	78
v 5.08 - Partition coefficient	117 & 107	10	3,248	4,034	3,000	76
v 5.09 - Flash-point	A.9	11	809	896	800	75
v 5.10 - Flammability	A.10	9	812	912		77
v 5.11 - Explosive properties	A.14	9	2,284	1,885	3,300	76
v 5.12 - Self-ignition temperature	A.15 or 16	9	1,338	1,646	1,800	82
v 5.13 - Oxidising properties	A.17	9	2,144	2,611	2,700	74
v 5.14 - Granulometry	ECB Guidel.	6	1,328	1,318		92
vii 5.18 - Stability in organic solvents	105	5	3,496	4,427		76
vii 5.19 - Dissociation constant	112	8	3,216	4,663		76
vii 5.20 - Viscosity	114	7	860	1,281		66
v 6.1 - In vitro skin irritation/corrosion	430 & 431	4	1,645	1,893		98
vi 6.1.1 - In vitro skin irritation/corrosion	404	10	1,194	1,494	1,200	83
v 6.2 - In vitro eye irritation/corrosion		4	1,615	1,615		100
vi 6.2.1 - In vitro eye irritation/corrosion	405	12	1,343	1,650	1,100	86
v 6.3 - Skin sensitisation (LLNA)	406	8	3,959	4,668	3,200	88
v 6.4.1 - In vitro gene mutation study (Ames test)		11	3,174	3,204	2,900	91
vi 6.4.2 - In vitro cytogenicity study in mammalian cells (CA)	473	11	19,161	19,217	15,000	86

Source: Journal of Business Chemistry - Manfred Fleischer (September 2007) hiips://repositorium.uni-muenster.de/document/miami/34db8d76-be1d-4cdf-9c8e-a26c5b045d51/2007_vol4_iss3_96-114.pdf

IST implementation

Industrial, Health & Environmental expected benefits

Human Health

- public health (consumers)
- occupational health (avoidance or reduction of diseases caused by occupational exposure to chemicals: reduced costs to cure workers' ill-being by the general public - medical care; improved quality of life for the individual worker; reduced operating costs for the employer, often associated to increased working days, as well as improved Risk Management Measures-RMMs)

Environmental Benefits

- less environmental damage as well as less (public) spending for its compensation (remediation costs)
- risk reduction for dangerous chemicals (reduced exposure)
- less costs from penalties related to environmental emissions
- reduced consumption of chemicals, solvents and other lab material and resources necessary for "in vivo" and "in vitro" R&D studies

Benefits for the Business

- reduced R&D costs (all market actors have better hazard, risk and use information, while the decision basis for R&D becomes complete – provided the IST estimates prove reliable – and long-term planning easier)
- reduced Compliance costs for manufacturers and importers ("red tape")
- reduced liability claims and prevention of business risks
- increased competitiveness of EU manufacturing industries (IST as a fast tool platform allowing for efficient and cheap screening, identification and substitution of dangerous chemicals in order to prioritize safer ones etc.etc.)

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Cost-Benefit Analysis (1)

Emerging drivers for IST impact analysis

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Operational expected savings within the R&D function:

- reduced overall length-time of R&D individual product development
- reduced cost of R&D/technical internally dedicated personnel (descendent from the associated reduction of their time-effort)
- reduced consumption of chemicals, solvents and other lab material and resources necessary for “in vivo” and “in vitro” R&D studies (input: unit costs estimate of individual endpoints externally outsourced to labs)

Improved R&D productivity & performance associated to IST Regulatory investments

- REACH compliance & Chemical Safety Report (CSR dossier preparation, WoE Weight-of-Evidence)
- Improved Supply Chain communication with Suppliers and Downstream Users (product dev)

Indirect benefits and sectorial implementation:

- Safety Data Sheets - SDS elaboration (indirect benefits)
- Product Regulations (such as Product Information File within Cosmetics Supply Chain, Agropharma, FCM, etc.)

Cost-Benefit Analysis (2)

Components of Chemical Industries' R&D expenses

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Functional areas:

- Administrative (for instance, Regulatory)
- Technical (advanced dialogue within Suppliers and other stakeholders within the Supply Chain, e.g. SDS)
- Commercial (Customer "fidelization" and interaction with Downstream Users. e.g. NIAS)

Benefiting functional unit	General purpose	IST exploitation and usage	
		Expected concrete benefits	Examples and other info
Administrative Beureaucracy Compliance (Red Tape)	REACH regulatory compliance	Cheaper and faster CSR completion	
		Cheaper and faster CSR updating and modification	ECHA's request for improvement of presented (low-quality) REACH Dossiers
	Requirements for Supply Chain communication in general (often associated to existing Specific Product Regulations)	Feeding required "missing" safety data to **Cosmetics** producers	Raw Material producers feeding PIF-Product Information File
		Elaborate and present safety data within the **FCM** sector	Provision of safety data as for German ordinance's chemicals' list (anticipating EU-wide expected Regulation)
	Compliance with other "ordinary" administrative requirements in Transport & Logistics	SDS completion with missing safety data	Low tonnage chemicals (tonns/year <1)
			Lab internediates & reagents for R&D purpose
R&D and Innovation departments	R&D efficiency & productivity (streamline R&D process)	Improved general understanding of safety issues associated to specific chemicals	Prioritization
			AOP mechanism comprehension (understanding methabolic pathway of deeases)
Supply Chain Management (Operations)	Customer fidelization through provision of "supplementary" safety data and info	Feeding supplementary (but helpful) safety data to **Cosmetics** producers	Raw Material producers feeding PIF-Product Information File
		Specific info requests from Clients	NIAS (Non Intentionally Added Substance)

The EU Chemical Industry

Market dimension and internal articulation

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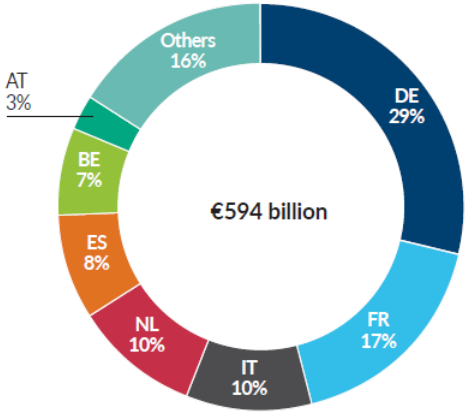
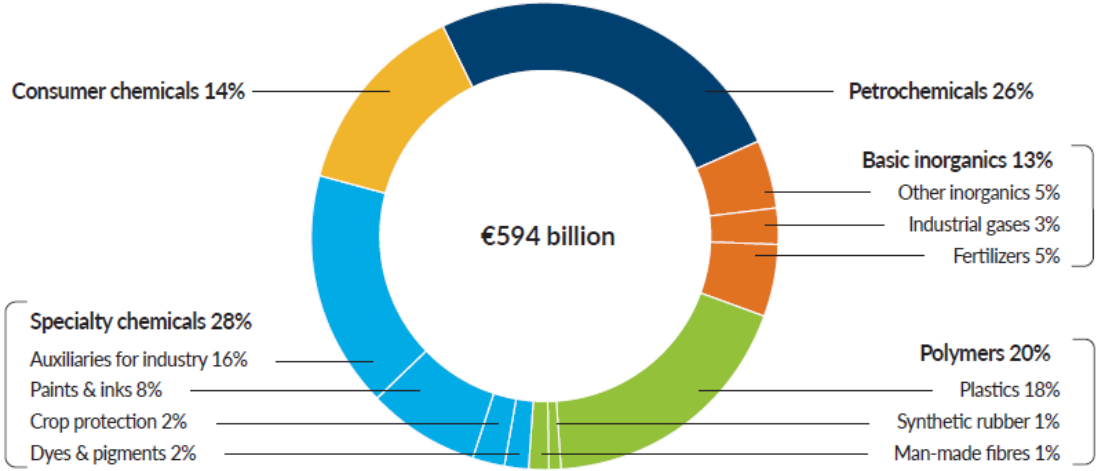
EU27 chemical sales broken down by country (2021)



EU27 chemical sales 2021 (€594 billion)

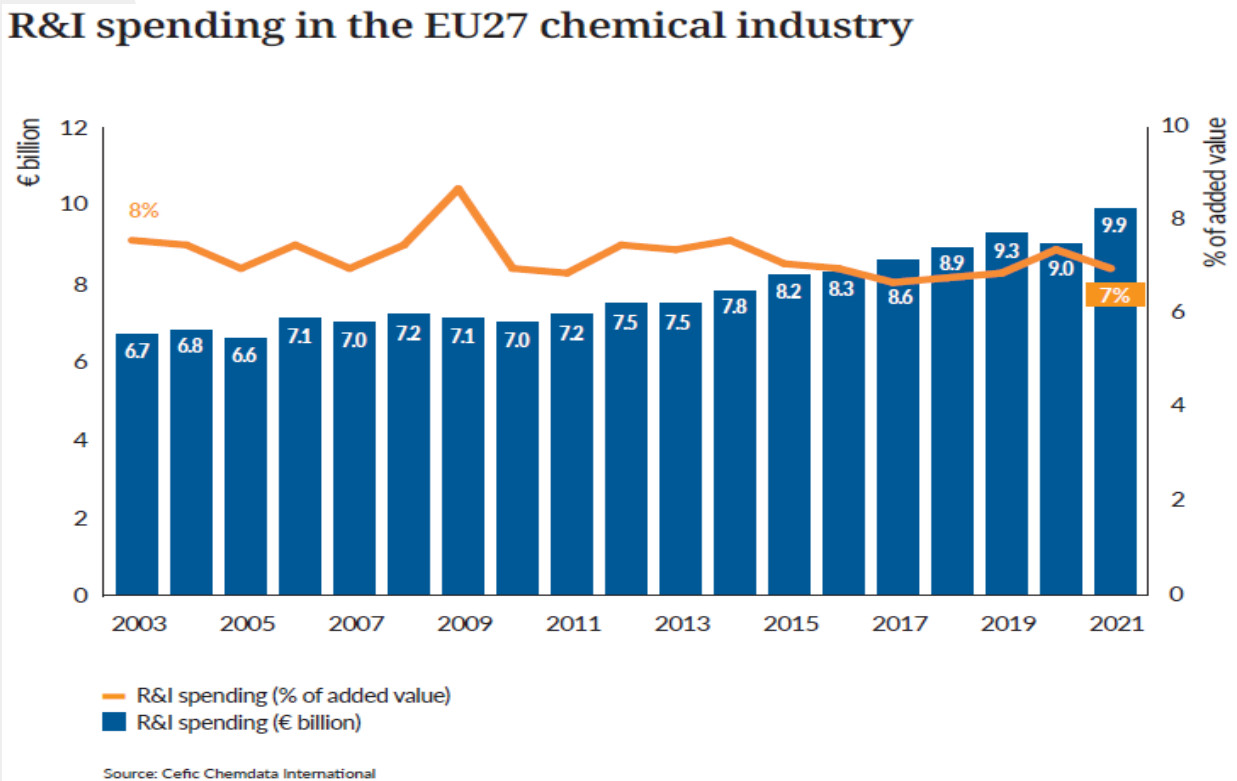


Source: Cefic Chemdata International

Source: CEFIC 2021 data (2023 Facts and Figures of the European Chemical Industry - cefic.org)

The Cost of EU Innovation & Sustainability

Increasing R&D expenses (and Regulatory costs)



R&D expenses

IST exploitation and R&D productivity improvement

Companies' Regulatory expenses	Without IST	With IST	Saving (Δ)
Internal resources (Professionals & technical assets)	2,500%	1,000%	**1,500%**
Personnel costs for R&D, Operations & Administration [1]			
Equipment & Machinery			
Laboratory materials and reagens			
Stabularium (animals for «in vivo» studies)			
External resources (Subcontracting and Assignments)	1,500%	0,500%	**1,000%**
Consultants (R&D, Operations and Administrative)			
Outsourced tests to external laboratories			
Letter of Access (LoA)			
Administrative & Marketing (Regulatory fees)			
Training expenses for dedicated Personnel	0,500%	1,000%	**-0,500%**
Regulatory costs as % of turnover	**4,500%**	**2,500%**	**2,000%**

[1] Operations & Administration require Supply Chain communication with Downstream Users and Suppliers, elaboration of SDS, verify existence of NIAS ancd comunicate it accordingly, etc. etc.

Source: SC internal calculation

Expected R&D savings (2021 data)
Impacting the EU Chemical Industry

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Product Groupings	Turnover (BLN €)	%	Sub-groupings	Turnover (BLN €)	Sub %	R&D Regulatory expenses Without IST (4,5%) (BLN €)	With IST (2,5%) (BLN €)	Potential max saving (Δ) (BLN €)	Actual expected saving Scenario 1 25,0%	Scenario 2 50,0%	Scenario 3 75,0%
Petrochemicals	**153,425**	***26,4%***		153,425	*26,4%*	6,904	3,836	3,068	0,767	1,534	2,301
Basic Inorganics	**72,348**	***13,0%***	Fertilizers	29,267	*5,2%*	1,317	0,732	0,585	0,146	0,293	0,439
			Industrial Gases	16,149	*2,7%*	0,727	0,404	0,323	0,081	0,161	0,242
			Other Inorganics	26,931	*5,1%*	1,212	0,673	0,539	0,135	0,269	0,404
Polymers	**121,660**	***18,8%***	Plastics	109,229	*16,7%*	4,915	2,731	2,185	0,546	1,092	1,638
			Man-Made fibres	7,827	*1,4%*	0,207	0,115	0,092	0,023	0,046	0,069
			Synthetic rubber	4,605	*0,7%*	0,352	0,196	0,157	0,039	0,078	0,117
Specialty chemicals	**165,999**	***28,3%***	Paints & inks	45,530	*8,1%*	0,471	0,262	0,209	0,052	0,105	0,157
			Dyes & pigments	10,465	*2,2%*	0,606	0,337	0,270	0,067	0,135	0,202
			Auxiliaries for industry	96,528	*15,5%*	2,049	1,138	0,911	0,228	0,455	0,683
			Crop protection	13,475	*2,5%*	4,344	2,413	1,931	0,483	0,965	1,448
Consumer chemicals	**80,297**	***13,5%***		80,297	*13,5%*	3,613	2,007	1,606	0,401	0,803	1,204
Total	**593,729**	***100%***		**593,729**	***100,0%***	**26,718**	**14,843**	**11,875**	**2,969**	**5,937**	**8,906**

Data source:
CEFIC Facts & Figures 2023 (data 2021)
SC internal calculations.

Chemistry & Sustainability

A central role for the Supply Chain

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Organic & Inorganic Raw Materials

↓

Base Chemicals

↓

Fine & Specialty Chemicals

Flows:
- Intermediate goods
- Research & Development & Innovation
- Competitiveness
- Sustainability

Agriculture 4,3%

Services 12,9%

Consumers 12,6%

Industry 70,2%

Plastic-rubber 19,9%	**Textile & Leather** 5,7%	**Metals** 5,3%	**Pharma** 5,0%
Food 4,6%	**Buildings** 4,4%	**Electronics** 4,2%	**Paper** 3,7%
Transport Vehicles 3,5%	**Wood & Furniture** 2,4%	**Mechanics** 2,4%	**Others** 9,1%

Source: elaboration based on ISTAT (Italian National Statistic Institute) data

INDICE DELLA PRESENTAZIONE

1. DOVE SIAMO ADESSO
2. DOVE VOGLIAMO ANDARE
3. QUALE IMPATTO PER L'INDUSTRIA CHIMICA
4. **ULTERIORI CONSIDERAZIONI**

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Final Observations and Challenges

- Reach registration costs for Industry during 2010 – 2018 ➔ around € 5 billion, most likely even higher
Source: Directorate-General for Internal Market, Industry (DG GROW)
"Entrepreneurship and SMEs Study on the impacts of the REACH 2018 registration deadline - Final report - Wood EIS GmbH – May 2021"

- ECHA Reach Registration dossier evaluation activities show 2/3 of dossiers with insufficient data

- ECHA requires dossier integration and updating, read-across to be supported by accurate WoE documentation

- ECHA dossier integration requirements are mainly for animal testing. ECHA communication in March 2023 says:

""The law requires companies to use alternative methods whenever possible – so companies should only ever test on animals as a last resort. At the moment, accepted alternative methods, as direct replacement of animal testing, only exist for acute and short-term effects, such as eye irritation, skin sensitisation, or bioaccumulation testing. Animal tests are often still essential for assessing the long-term effects, such as organ damage, weakening of the immune system, development of allergies or asthma or reproductive problems and birth defects. Unnecessary testing can, however, be avoided also in areas where no internationally accepted alternative methods exist, by sharing data or predicting the effects from what is known about similar chemicals.""

Final Observations and Challenges

Industry will have to spend further approx. € 1,0 – 2,0 billion over next 7 – 10 years only for these dossier integration activities

Will an increased and by Authorities accepted higher use of NTM/IST save at least 5 % of these additional costs = € 50 – 100 million and save a significant number of animals?

Final Observations and Challenges

Chemicals Strategy for Sustainability (CSS)

The EC adopted its Chemicals Strategy for Sustainability (CSS) on 14 October 2020 with action plan to:

- Ban the most harmful chemicals in consumer products – allowing those chemicals only where their use is essential.
- Pay attention to the cocktail effect of chemicals when assessing chemical risks.
- Phase out per- and polyfluoroalkyl substances (PFAS) in the EU, unless their use is essential.
- Boost investment and innovative capacity for the production and use of chemicals that are safe and sustainable by design throughout their lifecycle. The concept of “Safe and sustainable-by-design” intends to determine the future of not only chemical innovation but also chemical markets.
- Promote the EU’s supply and sustainability of critical chemicals.
- Establish a simpler “one substance, one assessment” process for assessing the risks and hazards of chemicals.
- Play a leading role globally by championing and promoting high chemical safety standards and not exporting chemicals banned in the EU.

All this requires a strong commitment, also financially, and definitely a wide use of NTM/tools to support this strategy

Final Observations and Challenges

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CLP Revision

ECHA will assist the EC in revising and developing new hazard criteria under the CLP Regulation for:
• persistent, mobile and toxic (PMT) and very persistent and very mobile substances (vPvM);
• terrestrial organisms;
• immunotoxicity and developmental neurotoxicity;
• endocrine disrupters (ED); and
• persistent, bioaccumulative and toxic (PBT) and very persistent, very bioaccumulative substances (vPvB).

ECHA will assess the information it has available to identify substances that qualify for the new and further hazard classes or criteria and, where possible, set up a list of these substances.

REACH Revision

ECHA will support the amendment of REACH information requirements for substances that have critical hazard properties. The Agency is involved in preparatory work for extending the registration duty to certain polymers, which currently do not need to be registered under REACH.

There are further Intentions to:
- introduce a mixture assessment factor
- develop the use of the generic approach to risk management
- develop options to reform authorisation and restrictions
- develop criteria for prioritising substances and groups of substances for restrictions
- introduce the CSR requirement also for the lowest tonnage-band 1-10 t/y

Final Observations and Challenges

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Moving towards animal free regulations

One-to-one replacement is hardly happening… but some exception is already here:

- Skin sensitisation, skin and eye irritation
- Hyalella Azteca bioconcentration test (HYBIT) instead of fish bioaccumulation test

Most often, the replacement will be assured by the combination of methods and complex approaches

- Weight of Evidence approaches

Other possibilities to reduce/phasing out animal testing

- Substance tailored exposure driven testing
- REACH Annex XI, section 3: Testing may be omitted for specific tests (OECD 421/422); 28 day repeated dose test (for <100 tonnes):
  - If no significant exposure and DNELs PNECs are available relevant for the omitted information and for risk assessment and exposure < DNELs PNECs
  - For substances not incorporated in articles: strictly controlled conditions throughout life cycle
  - For substances in articles, in which it is embedded/contained: no release during life cycle; negligible exposure; conditions for transported isolated intermediate applies
- Lower tonnages manufactured/imported might lead to lower emissions/exposure
  - For substances not incorporated in articles: strictly controlled conditions throughout life cycle
  - For environmental hazards: Relationship normally assumed
  - For human health hazards: Link between tonnage level and emission/exposure might depend greatly on uses
- Refinements possible by taking into account uses and physico chemical properties

→ Potential for reducing animal testing for lower tonnages by including waivers

Final Observations and Challenges

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Significant potential for refinement and reduction using NAMs under current system

For lower tier endpoints

- Developments of in silico methods (e.g. QSARs) with higher predictive capacity and broader applicability domain for hazard and risk assessment

For higher tier endpoints

- Better utilisation of NAMs to support read across and grouping

Problems experienced when introducing NAMs under REACH Information Requirements

- NAMs not sufficiently validated or standardised (OECD TG required?)
- Perception of “less safe” & higher uncertainty
- NAMs used to trigger additional animal testing rather than reduce animal use
- NAMs for systemic toxicity: not 1 to 1 replacement, need for IATA
- Standalone NAMs not able provide legal certainty for Classification & Labelling (C&L) (not identifying adverse systemic health effects and environmental hazards)

Final Observations and Challenges

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Other possibilities to reduce/phasing out animal testing

- Use based triggering/waiving

- Triggering of testing for uses with high potential for emissions/exposure/risks

- Triggering/waiving based on consumer/professional/industrial uses (in connection with proportionality or prioritisation considerations)

 Exposure driven, emission/exposure and use based waiving/triggering underemployed due to database architecture, challenges for checking compliance etc.
 Further analysis required of what would be needed to more often apply such approaches, overcome challenges etc.

- **Grouping**: require animal testing for some group members (+ read across or other methods, e.g. Omics)
- Need to clarify how biological information (e.g. Omics) can support grouping based on structural similarity hypothesis
- Base grouping approaches only on biological information?

→ Which group members to test, cost sharing, data sharing rules
→ Templates for reporting biological information (see OECD Omics Reporting Framework)
→ Guidance on the use of biological information

Final Observations and Challenges

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Legal certainty

- Mutual Acceptance of Data (MAD) at international level

- Clarity for industry how to fulfil their obligations and the conditions for acceptance by authorities (information requirements; waivers and adaptations; testing proposals)

- Clarity for authorities that data fulfil requirements facilitates checking of compliance/enforcement

- Importance of legal certainty for industry and authorities for
- Predictability
- Replacing/avoiding animal testing
- Avoiding delays in providing information for the assessment of chemicals

 Description of IR/classification criteria as clear as necessary
 Reporting templates, guidance

THANK YOU FOR YOUR ATTENTION

Does anyone have any questions?

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