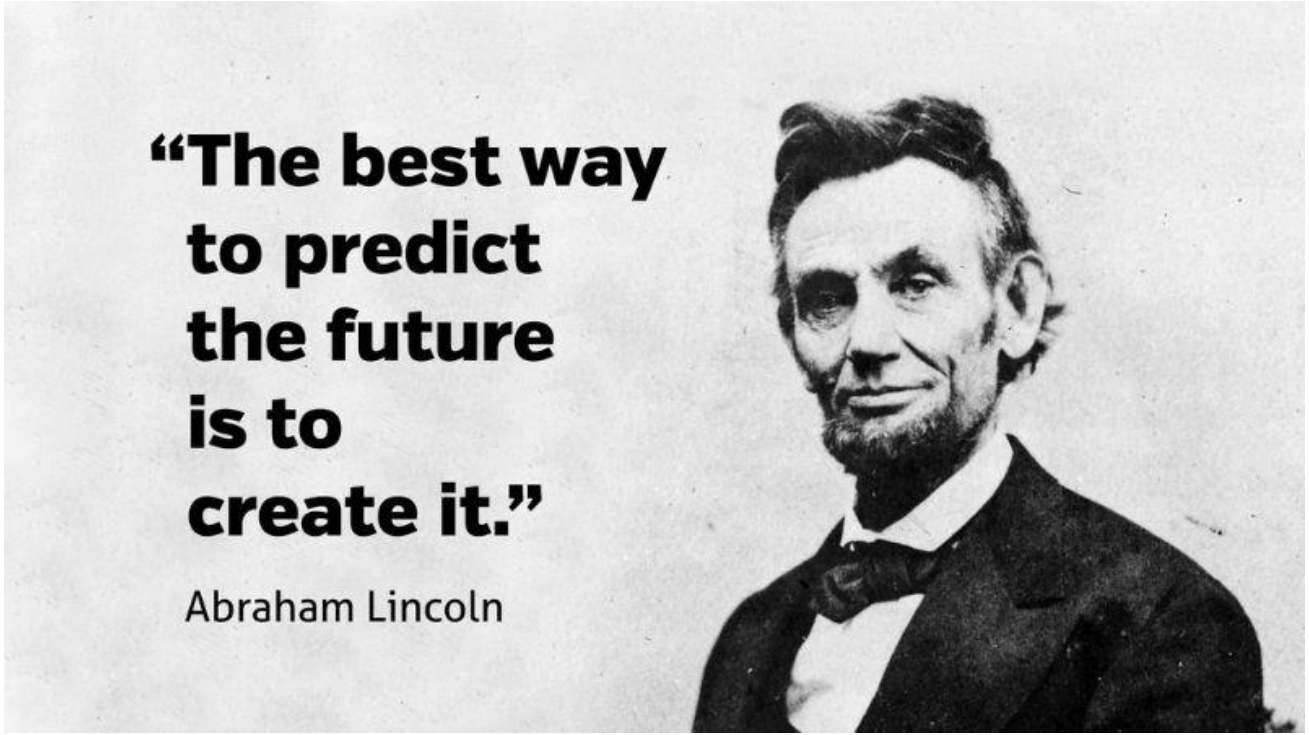
Computational modelling for sustainable chemicals management

Andrew Worth
European Commission – Joint Research Centre

19° Congresso Nazionale Società Italiana di Tossicologia – SITOX
11 February 2020, Bologna



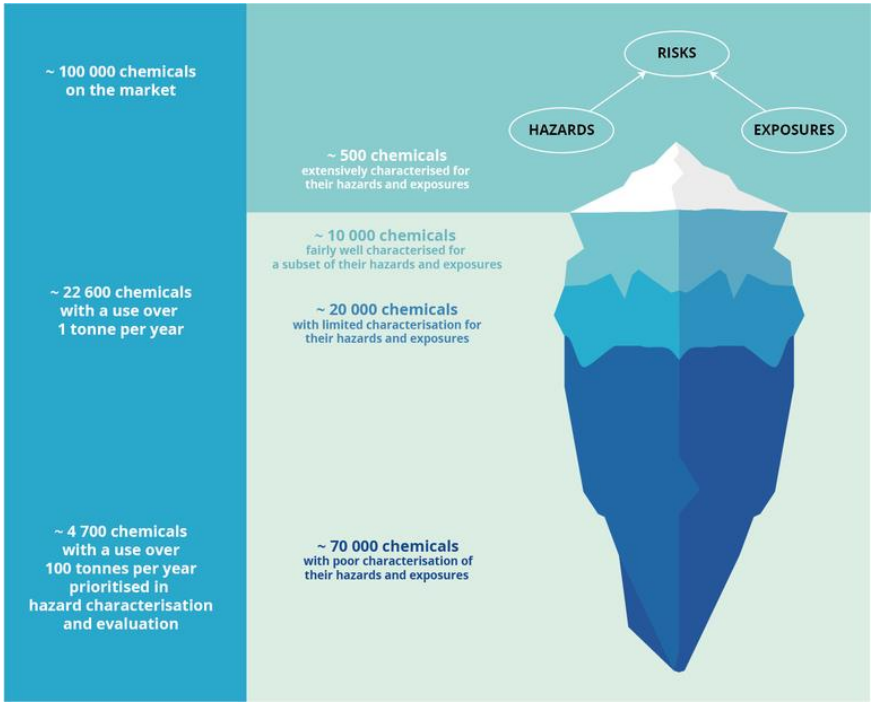
European Commission

State of the European Environment

"Europe's environment is at a tipping point. We have a narrow window of opportunity in the next decade to scale up measures to protect nature, lessen the impacts of climate change and radically reduce our consumption of natural resources."

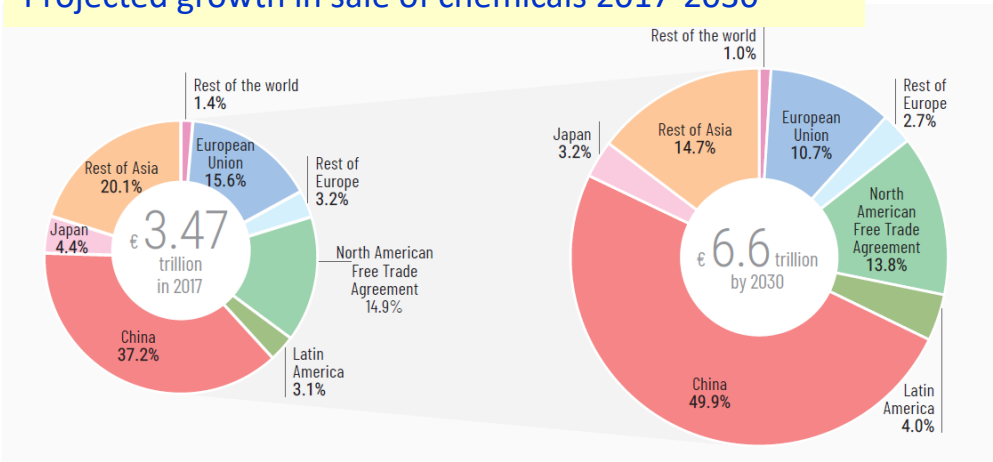
Hans Bruyninckx, EEA Executive Director, December 2019

Evolving chemical environment



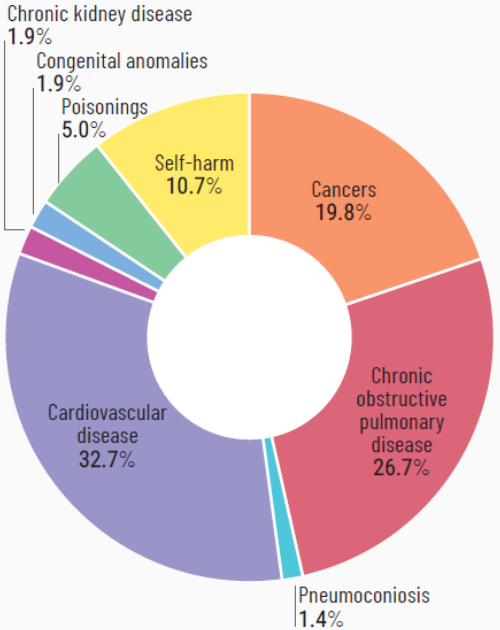
What we know – tip of the iceberg

Projected growth in sale of chemicals 2017-2030



Contribution of chemicals to burden of disease

Deaths (total: 1.6 million) attributed to selected chemicals (per cent), 2016 (adapted from WHO 2018a, p. 2)



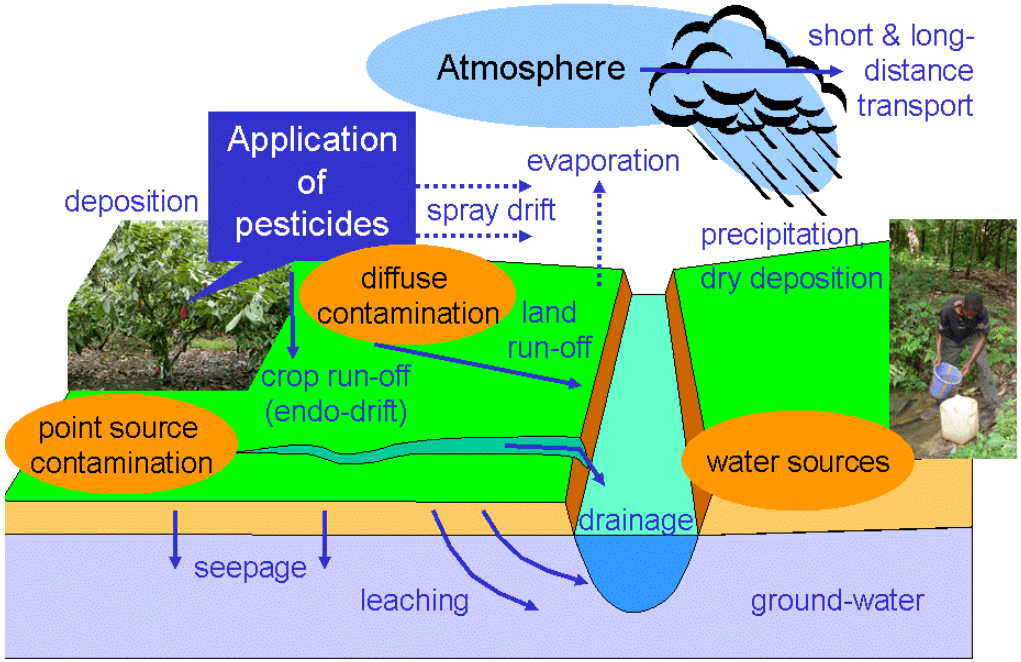
Estimates for 2016

- 1.6 million deaths
  - 2.7% of total global deaths
- 45 million disability-adjusted life years (DALYs)
  - 1.7% of total global burden of disease

World Health Organization (2018)

European Commission

Environmental fate and impacts of chemicals



European Commission

The European Commission's 6 political priorities

A European Green Deal

I want Europe to strive for more by being the first climate-neutral continent

An economy that works for the people

I want Europe to strive for more when it comes to social fairness and prosperity

A Europe fit for the digital age

I want Europe to strive for more by grasping the opportunities from the digital age within safe and ethical boundaries

Protecting our European way of life

I want Europe to strive for a Union of equality and diversity, building consensus on migration and enhancing resilience to hybrid threats

A stronger Europe in the world

I want Europe to strive for more by strengthening our unique brand of responsible global leadership

A new push for European democracy

I want Europe to strive for more in nurturing, protecting and strengthening our democracy

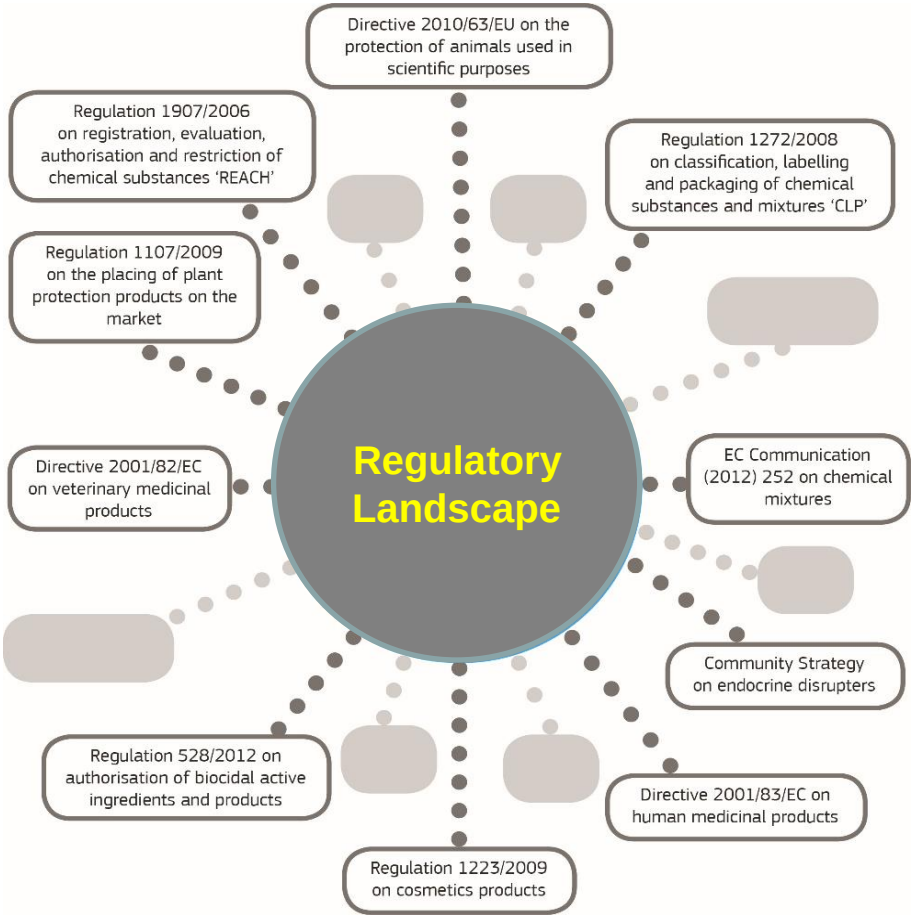
European Commission

The EU Green Deal

Towards a toxic-free environment

Chemicals and the UN Sustainable Development Goals

The EU Chemicals Acquis



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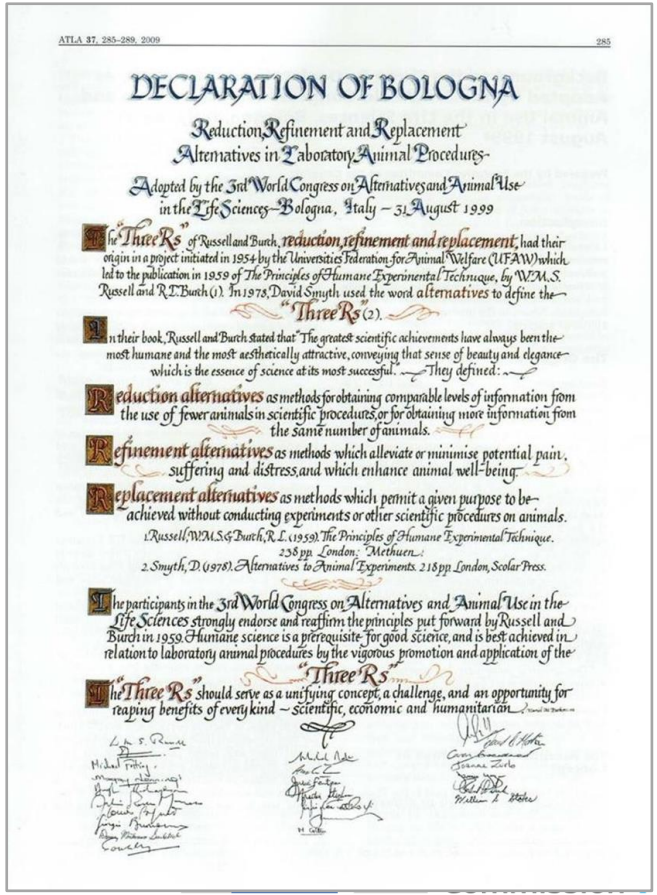
Animal welfare as an underpinning policy

Article 13 of the Treaty on the Functioning of the European Union (TFEU)

"In formulating and implementing the Union's … policies, the Union and the Member States shall, since animals are sentient beings, pay full regard to the **welfare requirements of animals**,…"

Directive 2010/63/EU on the protection of animals used for scientific purposes

"… an important step towards achieving the **final goal of full replacement** of procedures on live animals for scientific and educational purposes **as soon as it is scientifically possible** to do so."



ATLA 37, 285–289, 2009 285

DECLARATION OF BOLOGNA

Reduction, Refinement and Replacement
Alternatives in Laboratory Animal Procedures

Adopted by the 3rd World Congress on Alternatives and Animal Use in the Life Sciences—Bologna, Italy – 31 August 1999

The "Three Rs" of Russell and Burch, reduction, refinement and replacement, had their origin in a project initiated in 1954 by the Universities Federation for Animal Welfare (UFAW) which led to the publication in 1959 of The Principles of Humane Experimental Technique, by W.M.S. Russell and R.L. Burch (1). In 1978, David Smyth used the word alternatives to define the "Three Rs" (2).

In their book, Russell and Burch stated that "The greatest scientific achievements have always been the most humane and the most aesthetically attractive, conveying that sense of beauty and elegance which is the essence of science at its most successful." They defined:

Reduction alternatives as methods for obtaining comparable levels of information from the use of fewer animals in scientific procedures or for obtaining more information from the same number of animals.

Refinement alternatives as methods which alleviate or minimise potential pain, suffering and distress, and which enhance animal well-being.

Replacement alternatives as methods which permit a given purpose to be achieved without conducting experiments or other scientific procedures on animals.

1. Russell, W.M.S. & Burch, R.L. (1959). The Principles of Humane Experimental Technique. 238 pp. London: Methuen.
2. Smyth, D. (1978). Alternatives to Animal Experiments. 218 pp. London, Scolar Press.

The participants in the 3rd World Congress on Alternatives and Animal Use in the Life Sciences strongly endorse and reaffirm the principles put forward by Russell and Burch in 1959. Humane science is a prerequisite for good science, and is best achieved in relation to laboratory animal procedures by the vigorous promotion and application of the "Three Rs".

The "Three Rs" should serve as a unifying concept, a challenge, and an opportunity for reaping benefits of every kind – scientific, economic and humanitarian.

Towards a circular economy for chemicals

SCIP database:

Substances of **C**oncern **I**n articles as such or in complex objects (**P**roducts)

Europe fit for a Digital Age

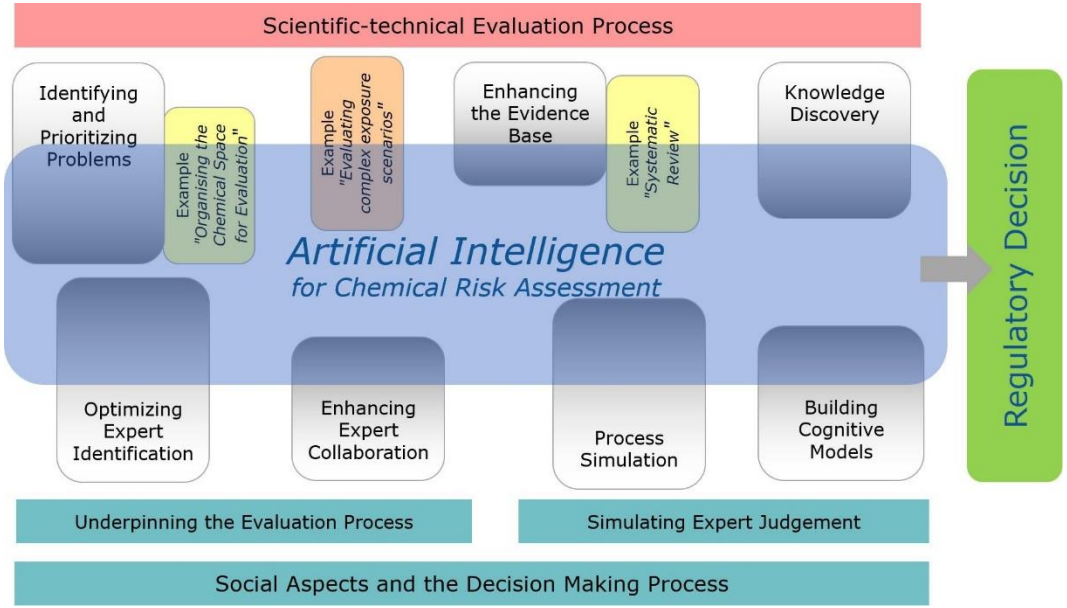
European Commission

Commission Work Programme 2020

Annex I: New Policy Objectives [1]

10.	**A European approach to Artificial Intelligence**	**White Paper on Artificial Intelligence** (non-legislative, Q1 2020); **European Strategy for Data** (non-legislative, Q1 2020); **Follow-up to the White Paper on Artificial Intelligence, including on safety, liability, fundamental rights and data** (legislative, incl. impact assessment, Article 114 TFEU, Q4 2020)

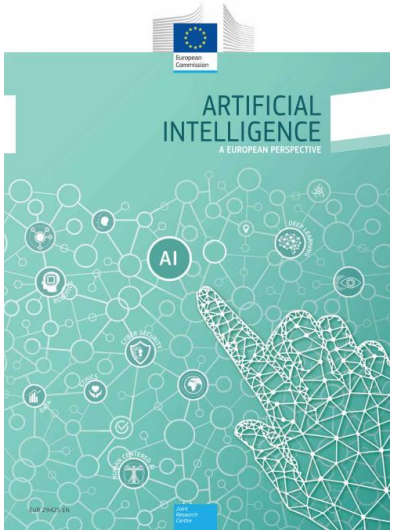
Big data and Artificial Intelligence



Artificial Intelligence for chemical risk assessment

Wittwehr *et al.* (2020).
Computational Toxicology 13, in press.

Guidelines on trustworthy Artificial Intelligence



- Ethics Guidelines for Trustworthy AI approach
  - Human agency oversight
    - Fundamental rights
    - Human agency
    - Human oversight
  - Technical robustness and safety
    - Resilience to attack and security
    - Fall back plan and safety
    - Accuracy
    - Reliability and Reproducibility
  - Privacy and data governance
    - Respect for privacy and data protection
    - Quality and integrity of data
    - Access to data
  - Transparency
    - Traceability
    - Explainability
    - Communication
  - Diversity, non-discrimination and fairness
    - Unfair bias avoidance
    - Accessibility and universal design
    - Stakeholder participation
  - Societal and environmental wellbeing
    - Sustainable and environmental friendly AI
    - Social impact
    - Society and democracy
  - Accountability
    - Auditability
    - Minimising reporting negative impact
    - Documenting trade-offs
    - Ability to redress

OECD Principles on Artificial Intelligence

AI should **benefit people and the planet** by driving inclusive growth, sustainable development and well-being.

AI systems should be designed in a way that **respects** the rule of law, human rights, democratic values and diversity, and they should include appropriate **safeguards** – for example, enabling human intervention where necessary – to ensure a fair and just society.

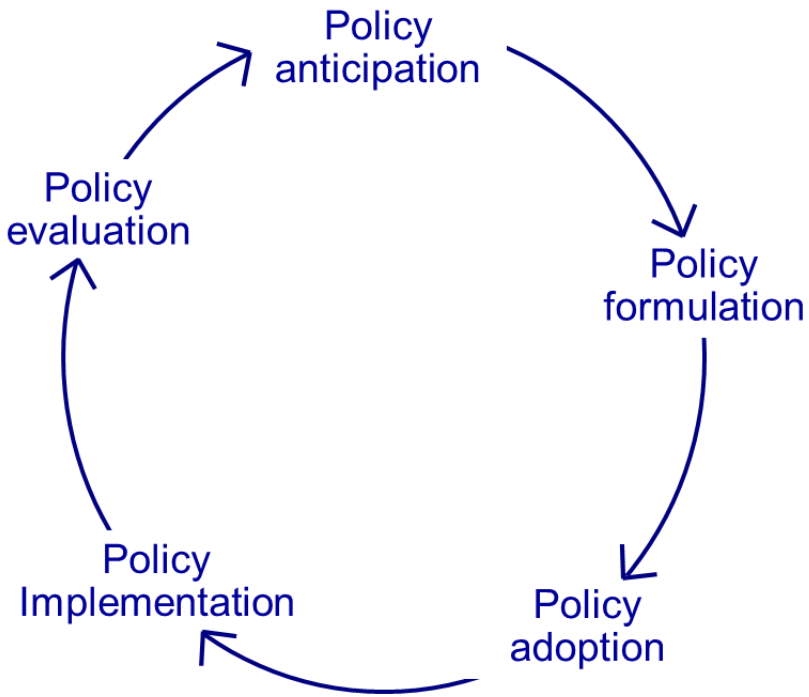
There should be **transparency** and responsible disclosure around AI systems to ensure that people understand AI-based outcomes and can challenge them.

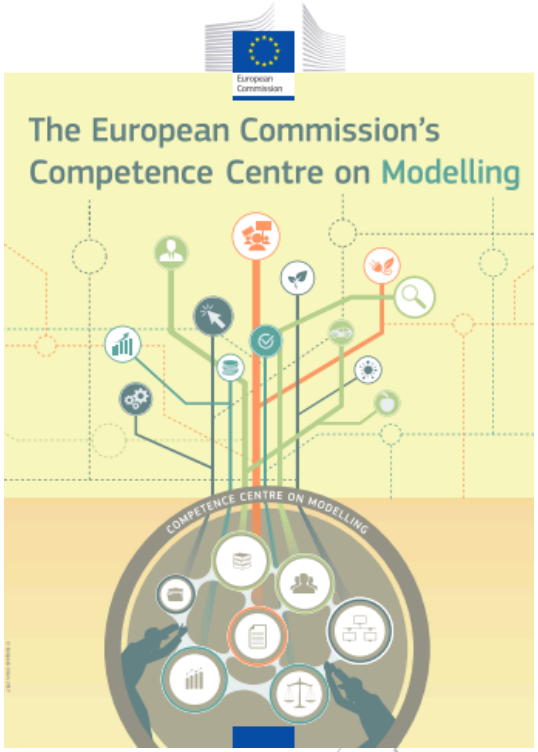
AI systems must function in a **robust, secure and safe** way throughout their life cycles and potential risks should be continually assessed and managed.

Organisations and individuals developing, deploying or operating AI systems should be held **accountable** for their proper functioning in line with the above principles

OECD Council Recommendation on Artificial Intelligence, May 2019

Modelling in the policy cycle





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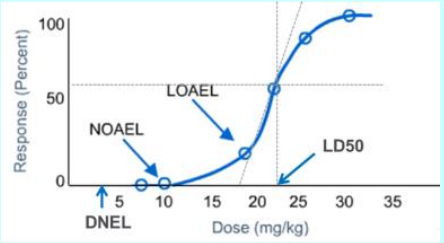
Modelling in chemical risk assessment

QSAR models

Read-across

Quantitative AOPs

3. Hazard characterisation



In vitro dose-response models

1. Problem formulation

2. Hazard identification

5. Risk characterisation

4. Exposure assessment

Environmental fate models

Physiological based kinetic models

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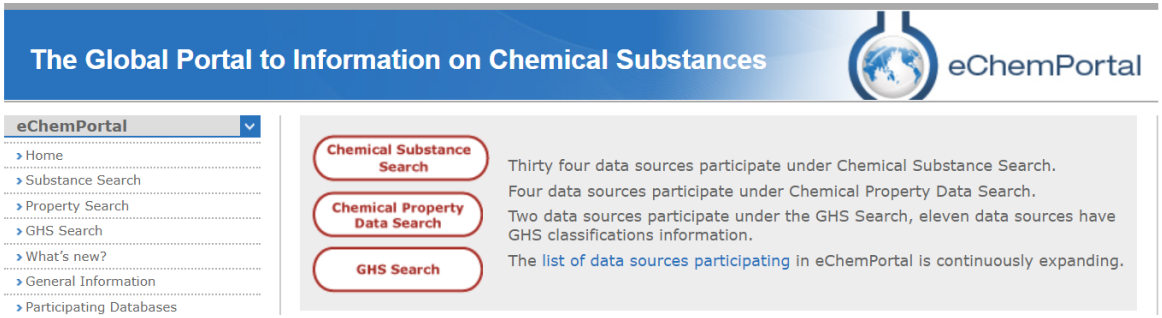
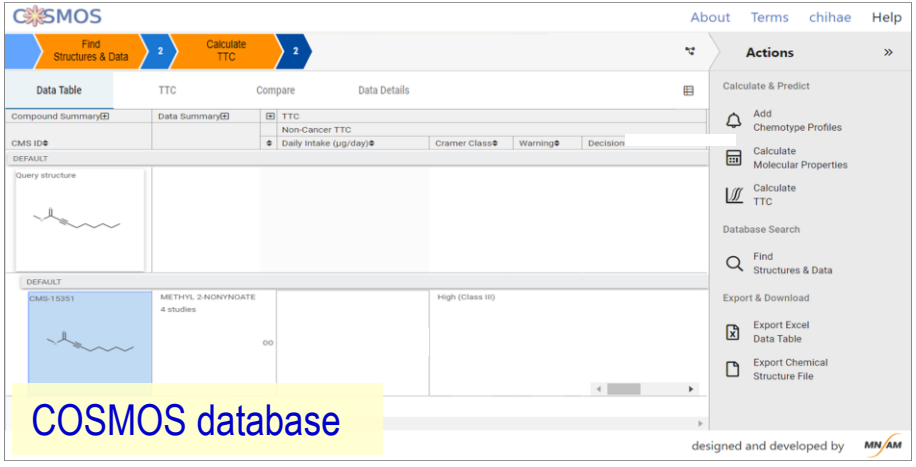
Knowledge sources for modelling

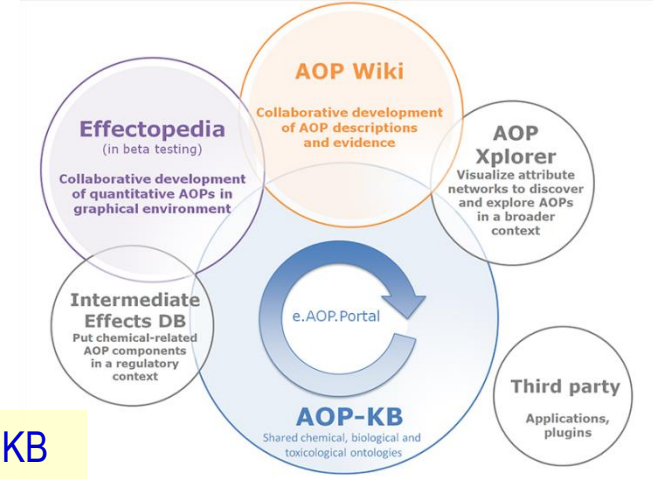


OECD eChemPortal

IPChem – (bio)monitoring database



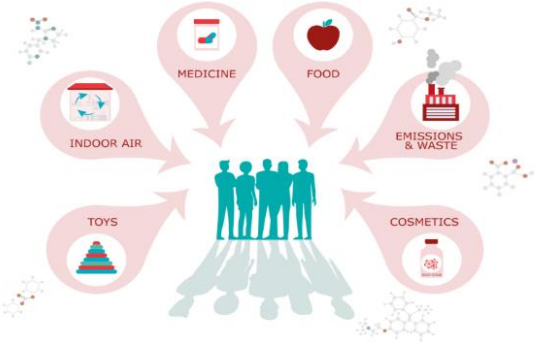
COSMOS database



OECD AOP KB

Focus areas for modelling

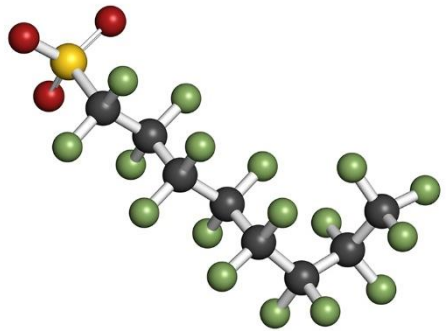
Mixtures: combined exposure effects



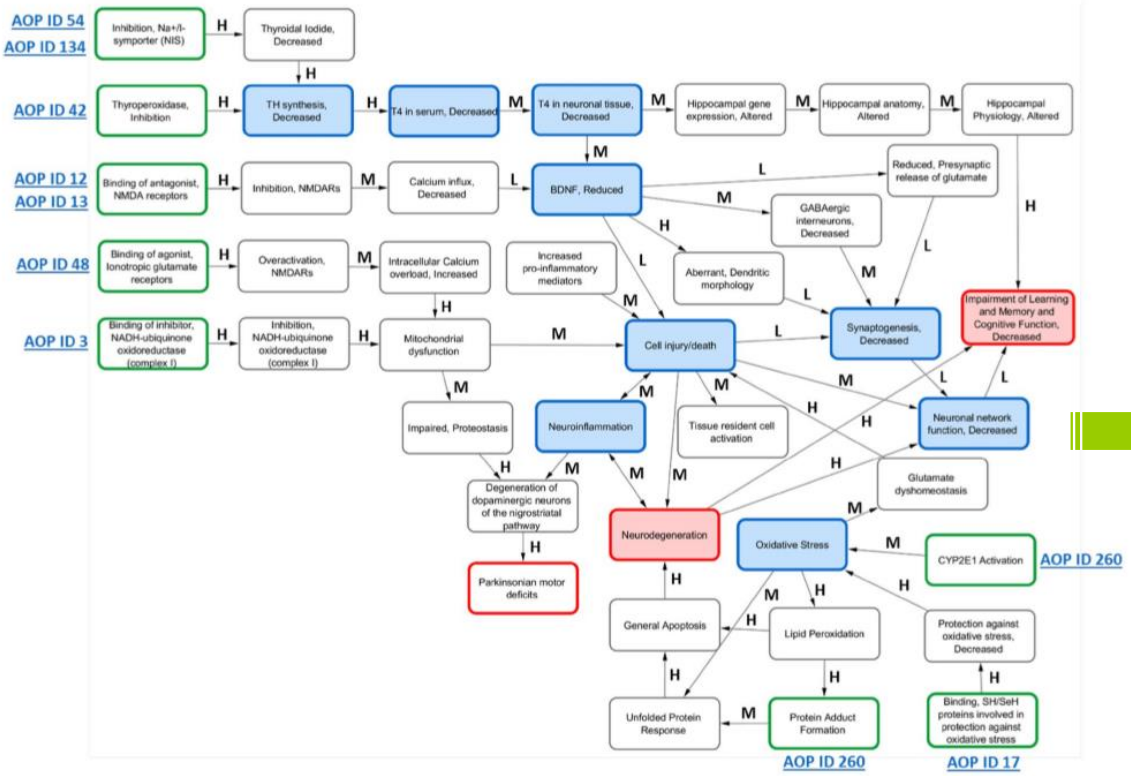
Endocrine disruptors

Non-communicable diseases

Persistent chemicals

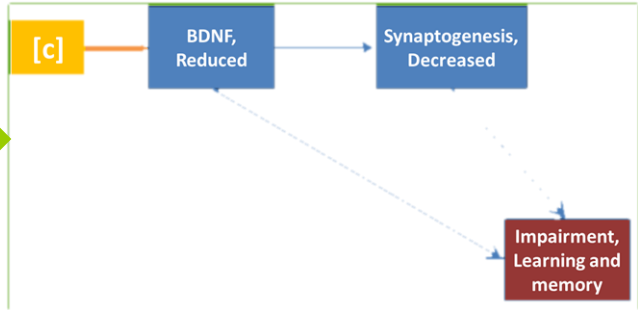


AOP networks for complex human health effects



AOP network for neurotoxicity

Spinu *et al.* (2019).
Archives of Toxicology 93, 2759–2772.



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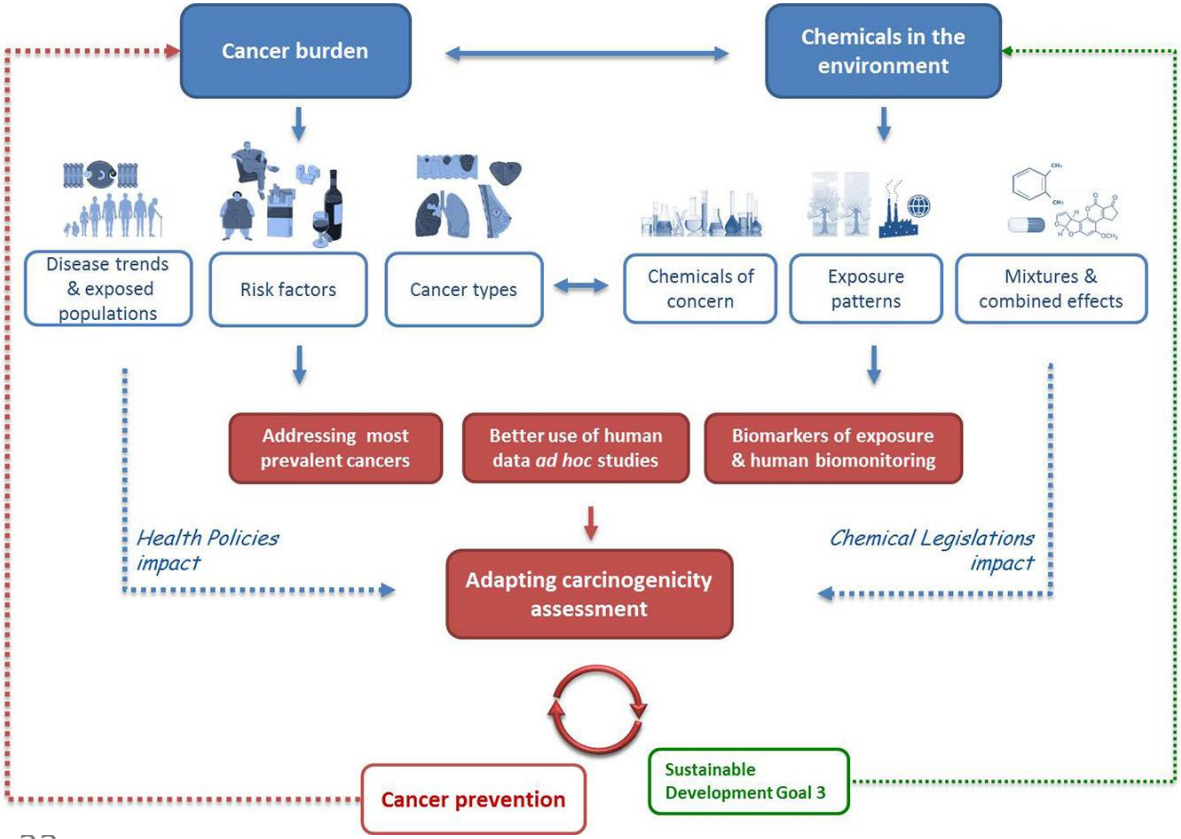
Chemicals management for cancer prevention



Carcinogenicity assessment: Addressing the challenges of cancer and chemicals in the environment.

Madia *et al.* (2019). *Environment International* 128, 417-429.

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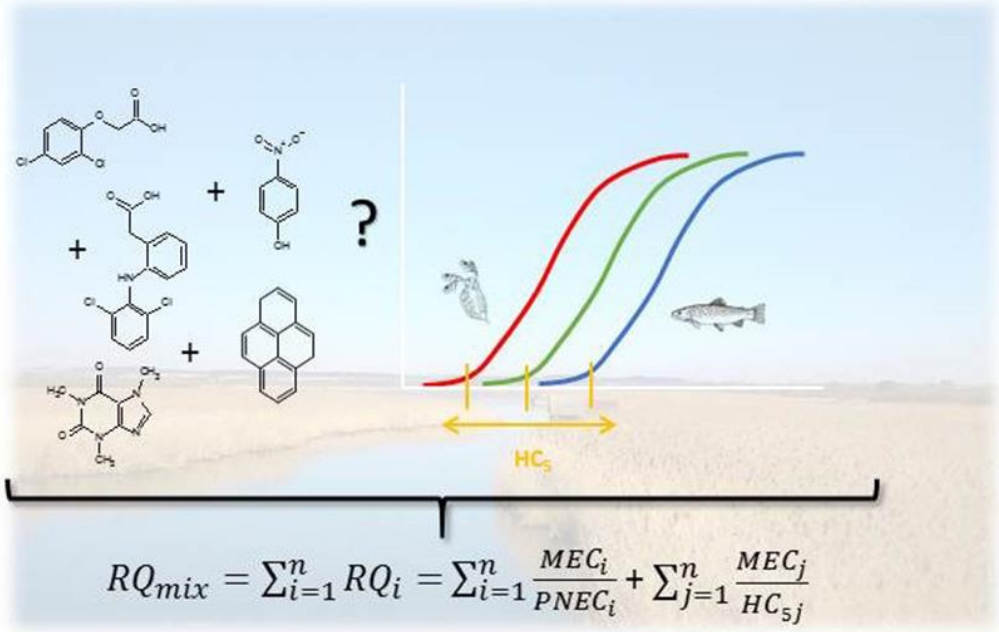
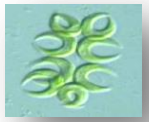
Leveraging toxicity data for ecosystem effects



EcoTTC approach

Application of new statistical distribution approaches for environmental mixture risk assessment

Kienzler *et al.* (2019).
Science of the Total Environment 693, 133510.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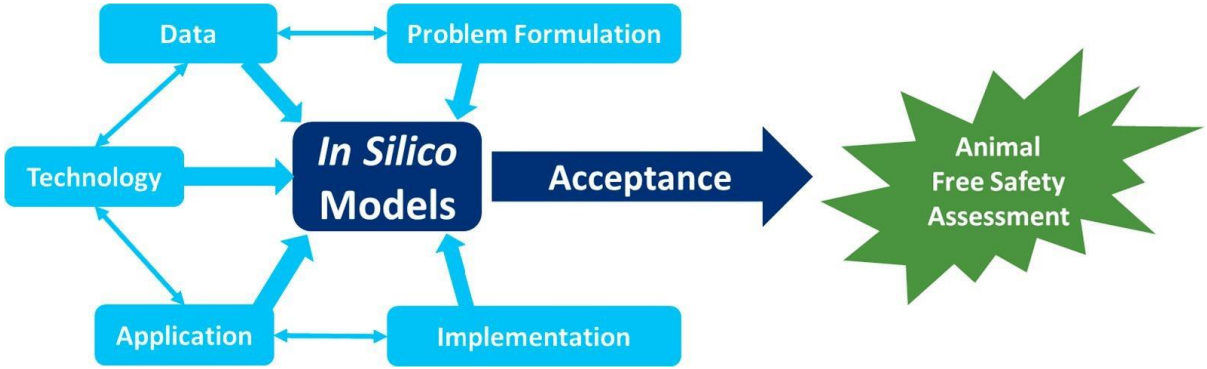
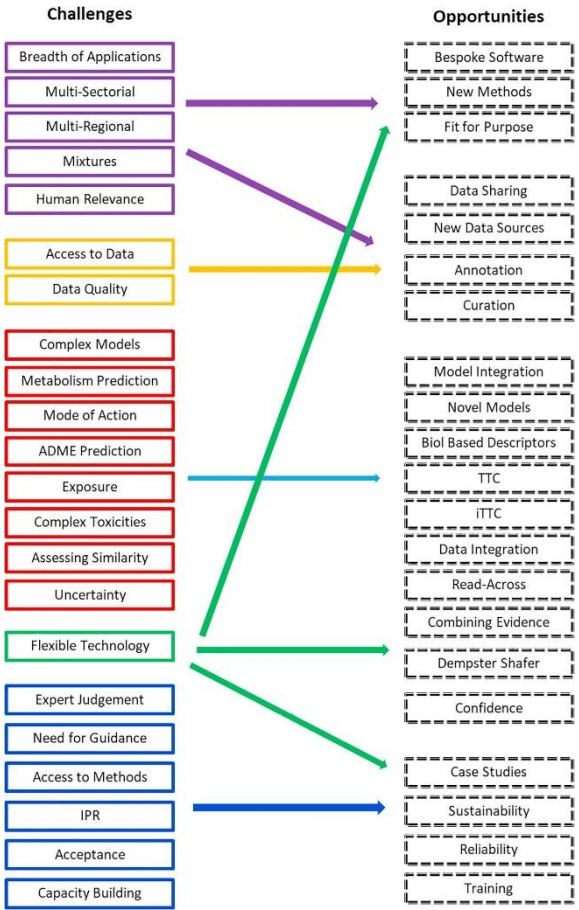
Challenges and opportunities for modelling





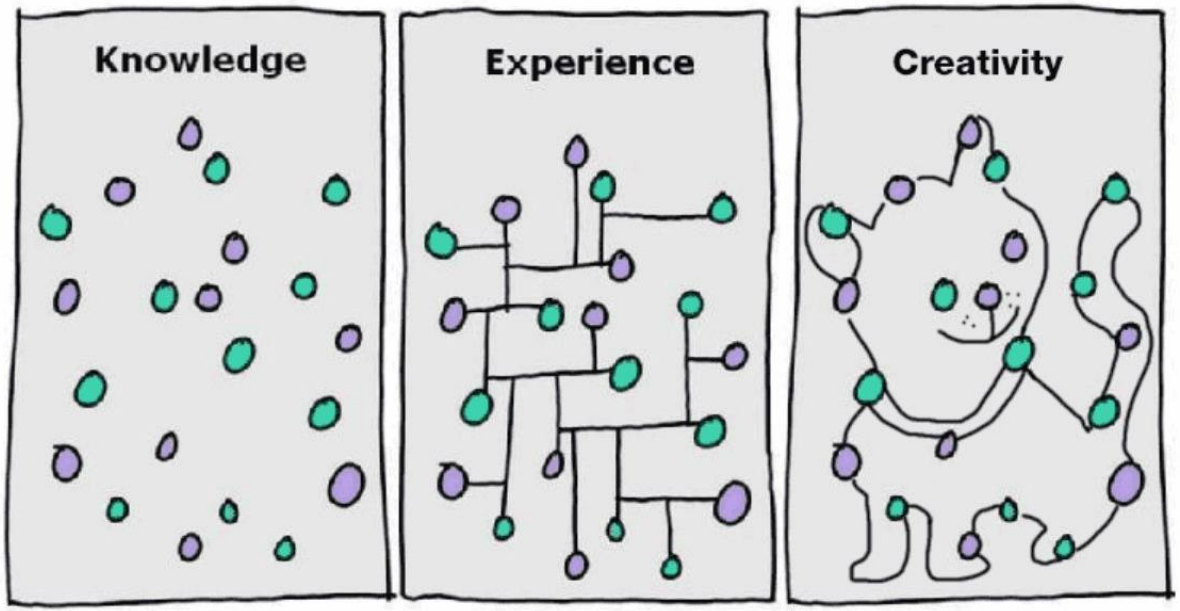
Unlocking the potential of in silico chemical safety assessment

Cronin *et al.* (2019).
Computational Toxicology 10, 38-43.

Concluding remarks

- Business as usual is not an option – “there is no planet B”
- The sustainable management of chemicals requires innovation
- Innovation in policy making, risk management and risk assessment
- Opportunities for sustainable chemistry
- Alternative methods for alternative chemicals!

The Need for Radical Thinking



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andrew.worth@ec.europa.eu

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