

The Joint Research Centre

The scientific arm of the European Commission

Clemens Wittwehr

European Commission, Joint Research Centre (JRC)
Ispra, Italy

RepRefRed Seminar, 2025-05-06

A green ribbon graphic with rounded ends, featuring the word AGENDA in white capital letters.

AGENDA

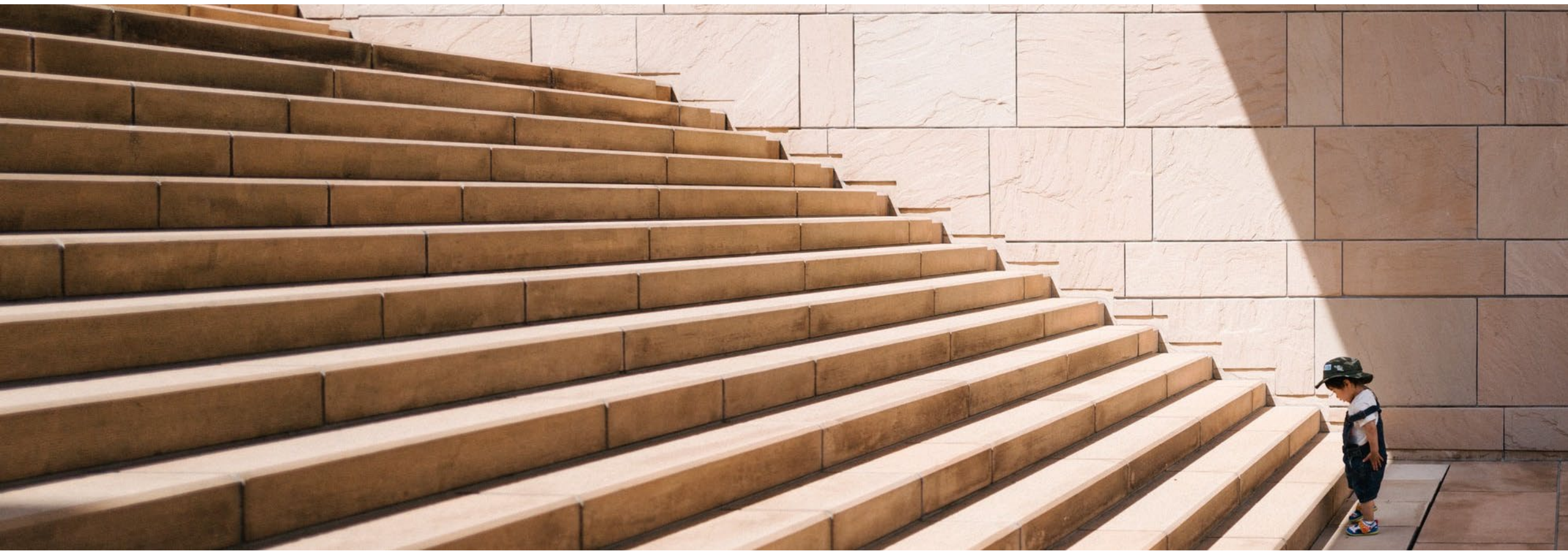
- The Joint Research Centre
- EURL ECVAM
- Adverse Outcome Pathways

A green ribbon graphic with rounded ends, featuring the word AGENDA in white capital letters.

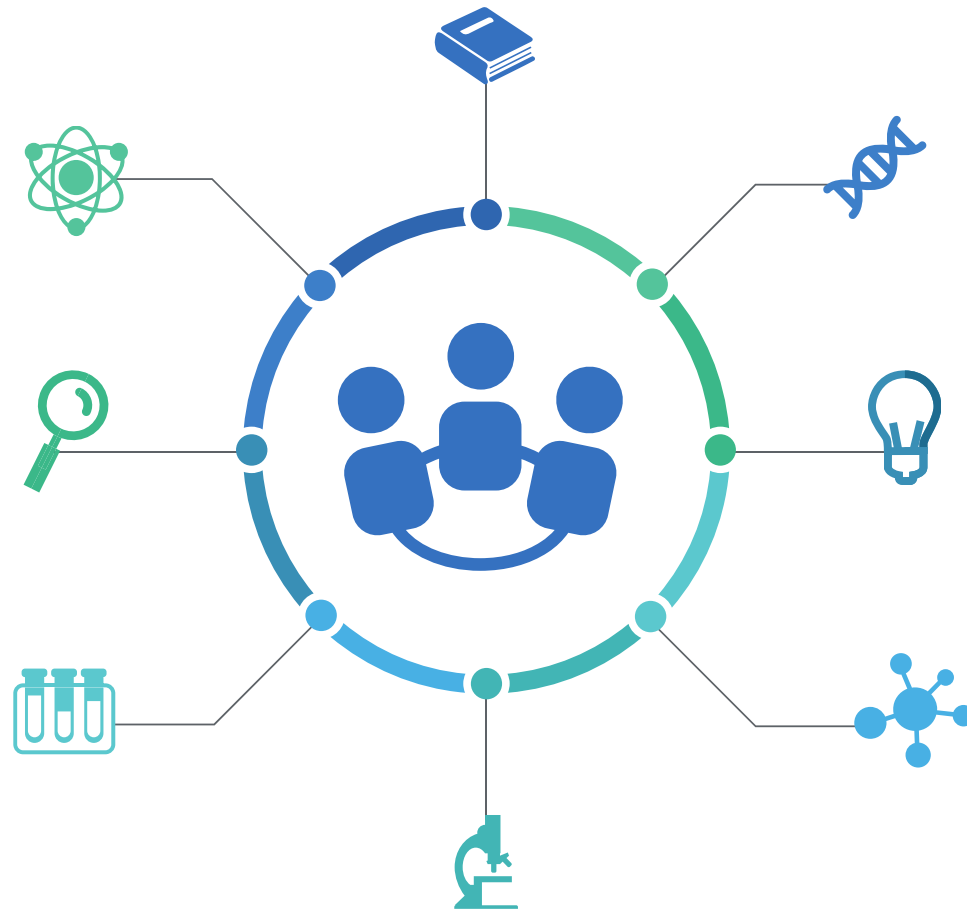
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Society is facing many challenges



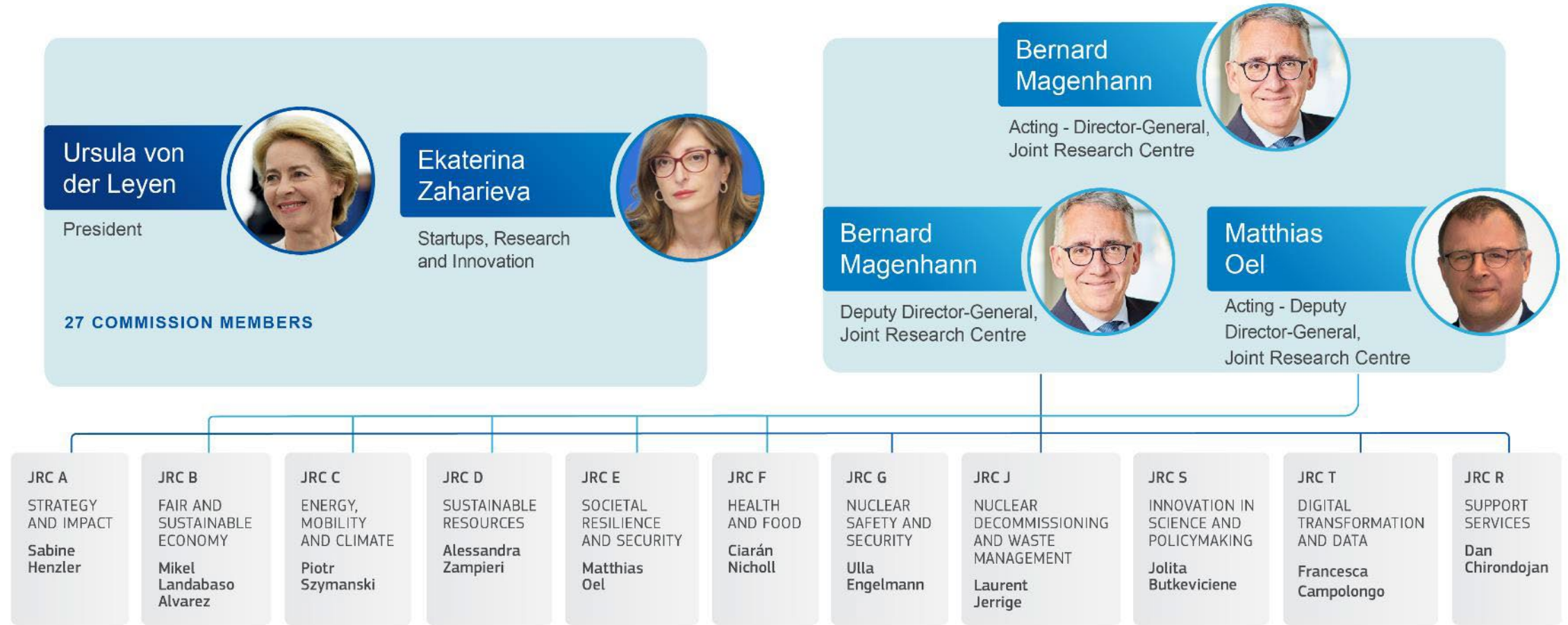
The need for evidence to inform policy



The European Commission's political leadership

 Ursula von der Leyen President	 Teresa Ribera Rodríguez Executive Vice-President <i>Clean, Just and Competitive Transition</i>	 Henna Virkkunen Executive Vice-President <i>Tech Sovereignty, Security and Democracy</i>	 Stéphane Séjourné Executive Vice-President <i>Prosperity and Industrial Strategy</i>	 Kaja Kallas High Representative/ Vice-President <i>Foreign Affairs and Security Policy</i>	 Roxana Minzatu Executive Vice-President <i>People, Skills and Preparedness</i>
 Raffaele Fitto Executive Vice-President <i>Cohesion and Reforms</i>	 Maroš Šefčovic Vice-President <i>Trade and Economic Security / Interinstitutional Relations and Transparency</i>	 Valdis Dombrovskis Commissioner <i>Economy and Productivity Implementation and Simplification</i>	 Dubravka Šuica Commissioner <i>Mediterranean</i>	 Olivér Várhelyi Commissioner <i>Health and Animal Welfare</i>	 Wopke Hoekstra Commissioner <i>Climate, Net Zero and Clean Growth</i>
 Andrius Kubilius Commissioner <i>Defence and Space</i>	 Marta Kos Commissioner <i>Enlargement</i>	 Jozef Sikela Commissioner <i>International Partnerships</i>	 Costas Kadis Commissioner <i>Fisheries and Oceans</i>	 Maria Luís Albuquerque Commissioner <i>Financial Services and the Savings and Investments Union</i>	 Hadja Lahbib Commissioner <i>Preparedness and Crisis Management Equality</i>
 Magnus Brunner Commissioner <i>Internal Affairs and Migration</i>	 Jessika Roswall Commissioner <i>Environment, Water Resilience and a Competitive Circular Economy</i>	 Piotr Serafin Commissioner <i>Budget, Anti-Fraud and Public Administration</i>	 Dan Jørgensen Commissioner <i>Energy and Housing</i>	 Ekaterina Zaharieva Commissioner <i>Startups, Research and Innovation</i>	 Michael McGrath Commissioner <i>Democracy, Justice and the Rule of Law</i>
 Apostolos Tzitzikostas Commissioner <i>Sustainable Transport and Tourism</i>	 Christophe Hansen Commissioner <i>Agriculture and Food</i>	 Glenn Micallef Commissioner <i>Intergenerational Fairness, Youth, Culture and Sport</i>	#vdLcommission		

The Joint Research Centre within the Commission



Science for policy



ANTICIPATE



INTEGRATE

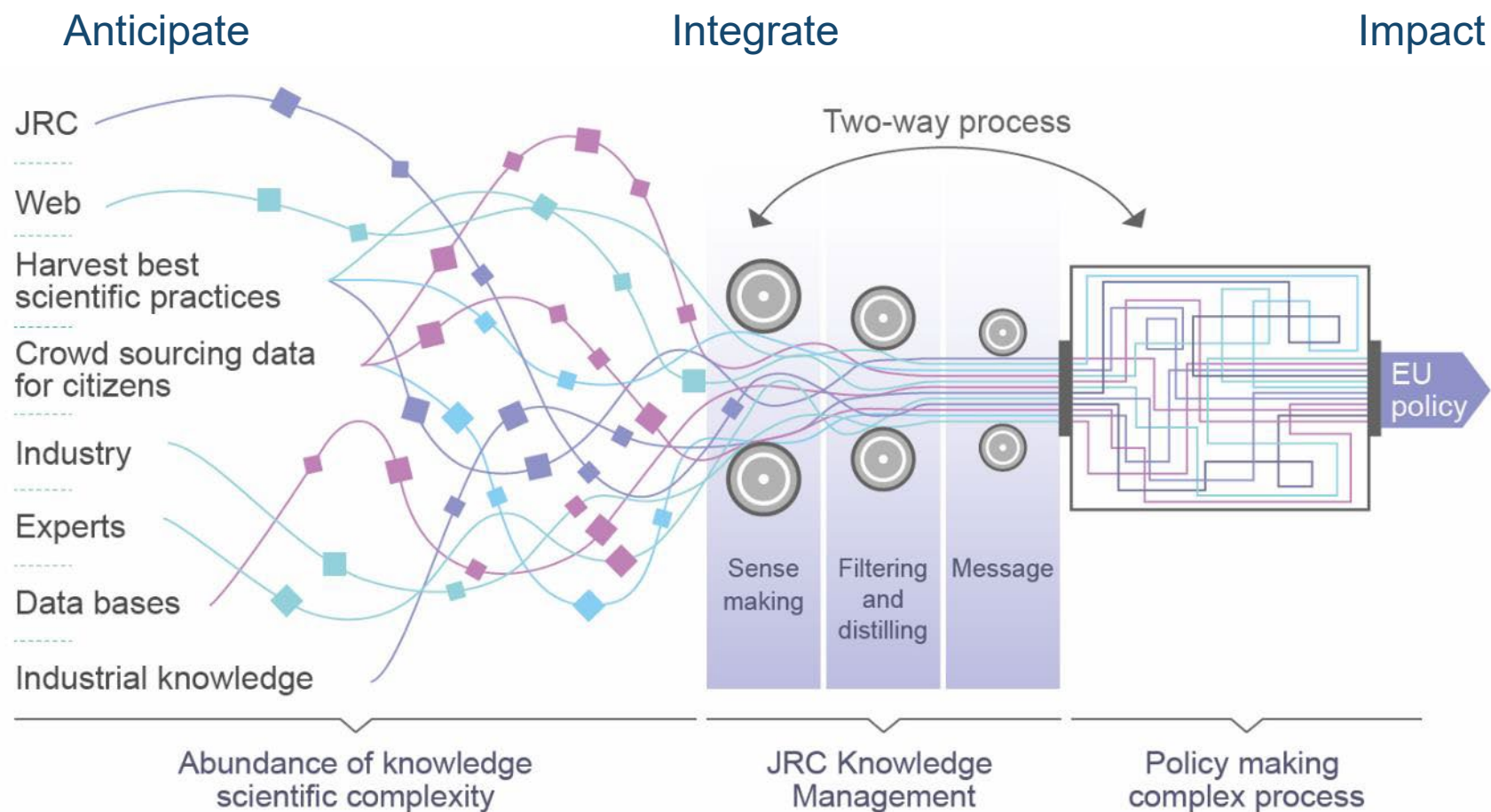


IMPACT

Our purpose

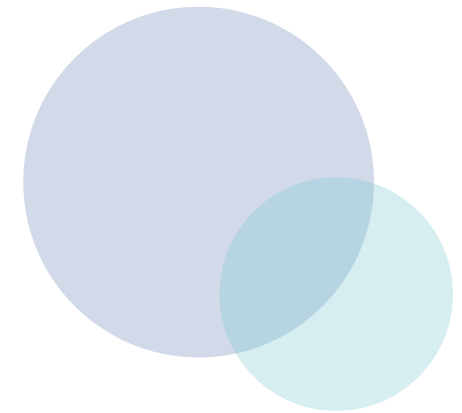
The Joint Research Centre provides independent, evidence-based knowledge and science, supporting EU policies to positively impact society.

Dealing with the information overload



Keeping the pace with the development of research

- Fully **policy-relevant** and world class **knowledge production**
- Priorities driven **knowledge and competence management**
- One JRC – **anticipating** emerging issues, **understanding** complexities and **bridging** silos
- **Addressing challenges of research**
(information deluge, multidisciplinary, integrity, reproducibility)



Our role

- **Independent** of private, commercial or national interests
- Works for more than **40 European Commission policy departments**



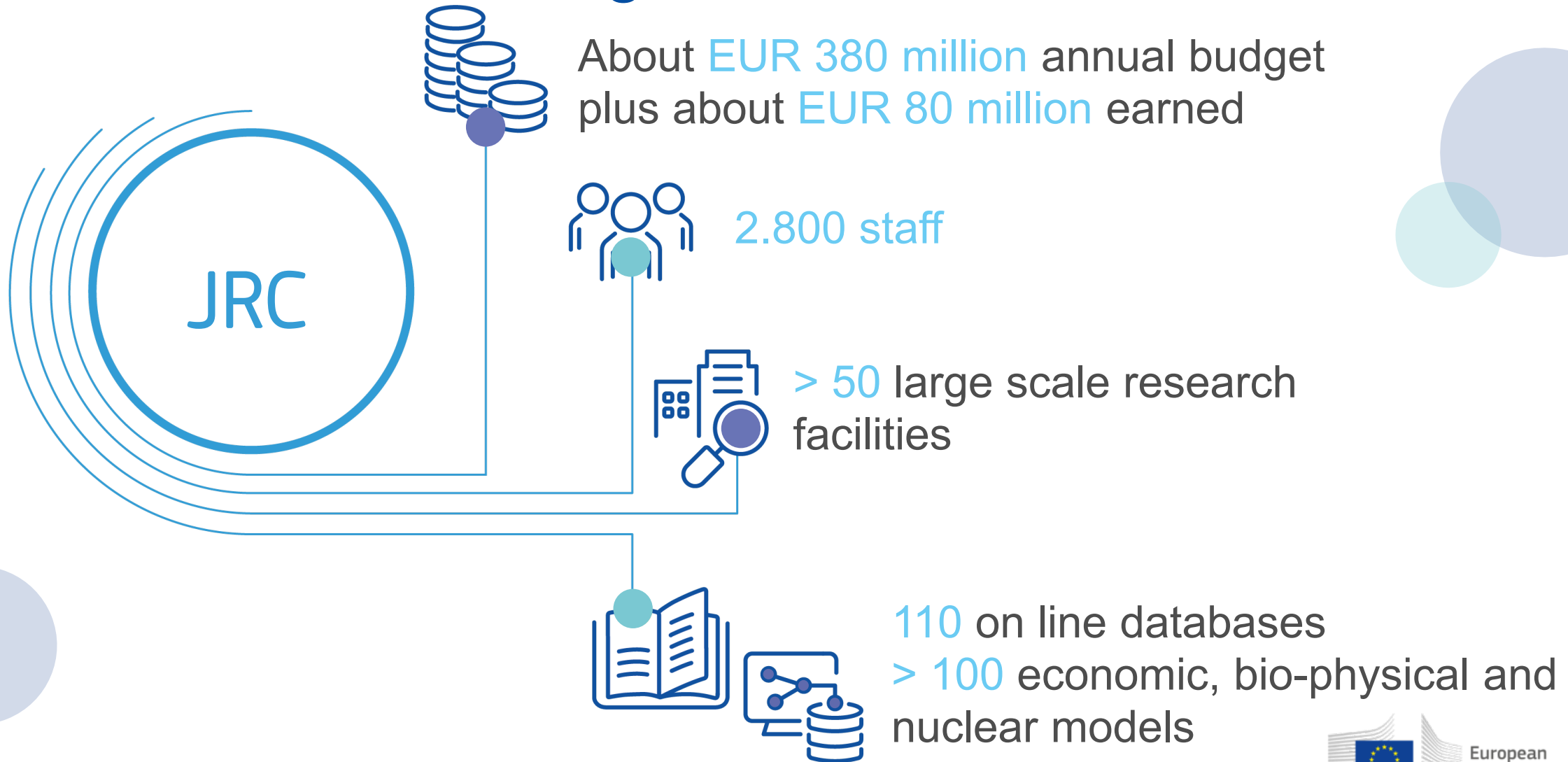
JRC sites

Headquarters in **Brussels**
and research facilities located
in **5 EU Countries**:

- Belgium (Geel)
- Germany (Karlsruhe)
- Italy (Ispra)
- The Netherlands (Petten)
- Spain (Seville)



JRC – Facts and figures



Portfolios to improve collaboration!

A **cross-disciplinary approach** that:

- creates new insights, knowledge and methods
- ensures better integration across scientific and policy domains
- maximises our capacity to anticipate new challenges
- provides 'calling cards' for outreach and for managing our relations with external partners



Portfolios: the main building blocks of our multiannual work programmes

01. SHAPING THE GREEN TRANSITIONS FOR A SUSTAINABLE AND FAIR EUROPE

02. SUSTAINABLE, CLEAN, INNOVATIVE AND COMPETITIVE ENERGY SOLUTIONS

03. CLEAN HYDROGEN AND OTHER DECARBONISED GASES

04. SAFETY OF NUCLEAR TECHNOLOGY IN SUPPORT OF THE TRANSITION TOWARDS CLIMATE NEUTRALITY

05. SMALL MODULAR REACTORS

06. DECARBONISED, SMART AND SAFE MOBILITY

07. CITIES AND BUILDINGS FOR BETTER LIVES

08. PATHWAYS TO CLIMATE NEUTRALITY: THROUGH LOW-CARBON ENERGY AND LAND USE MANAGEMENT

09. ZERO POLLUTION FOR PLANETARY HEALTH - INTEGRATED RESPONSES

10. HEALTHY BIODIVERSITY AND NATURAL CAPITAL ACCOUNTING

11. TRANSITION TO SUSTAINABLE FOOD SYSTEMS IN A EUROPEAN AND GLOBAL CONTEXT

12. SUSTAINABLE MATERIALS AND PRODUCTS FOR A CIRCULAR AND RESILIENT EUROPE

13. INDUSTRIAL TRANSFORMATIONS FOR SUSTAINABILITY, COMPETITIVENESS AND OPEN STRATEGIC AUTONOMY

14. MONITORING AND SHAPING THE DIGITAL TRANSITION

15. TRUSTWORTHY ARTIFICIAL INTELLIGENCE FOR A FAIR AND DEMOCRATIC EUROPE

16. CYBERSECURITY OF SOCIETY AND INDUSTRY

17. EXPLOITING DATA AS A STRATEGIC RESOURCE FOR SCIENCE AND POLICY

18. OBSERVING THE EARTH FOR POLICY

19. GALILEO NEXT GENERATION AND SECURE CONNECTIVITY

20. TOWARDS AN INCLUSIVE AND RESILIENT SOCIETY: SOCIAL JUSTICE AND FAIR TWIN TRANSITIONS

21. EDUCATION, SKILLS AND EMPLOYMENT FOR A FAIR TWIN TRANSITION

22. ECONOMIC GOVERNANCE AND STRUCTURAL REFORMS

23. TERRITORIAL INTELLIGENCE FOR EU POLICIES

24. SCIENCE FOR THE GLOBAL GATEWAY AND THE INTERNATIONAL GREEN DEAL

25. ENHANCED SITUATIONAL AWARENESS FOR CRISIS MANAGEMENT

26. UNDERSTANDING AND ACTING ON FUTURE RISKS AND OPPORTUNITIES

27. BETTER PREPAREDNESS AND RESPONSE TO HEALTH CRISIS

28. INNOVATION IN LIFE AND HEALTH SCIENCES

29. TACKLING CANCER AND OTHER NON-COMMUNICABLE DISEASES

30. SCIENCE FOR SECURITY

31. SUPPORT TO NUCLEAR COMPLIANCE ASSURANCE

32. CHALLENGES AND OPPORTUNITIES OF POPULATION DYNAMICS AND MIGRATION

33. INNOVATIVE POLICYMAKING IN A COMPLEX WORLD: SCIENCE, FORESIGHT AND EVALUATION FOR POLICYMAKING AND DEMOCRACY

A European Green Deal

A Europe fit for the digital age

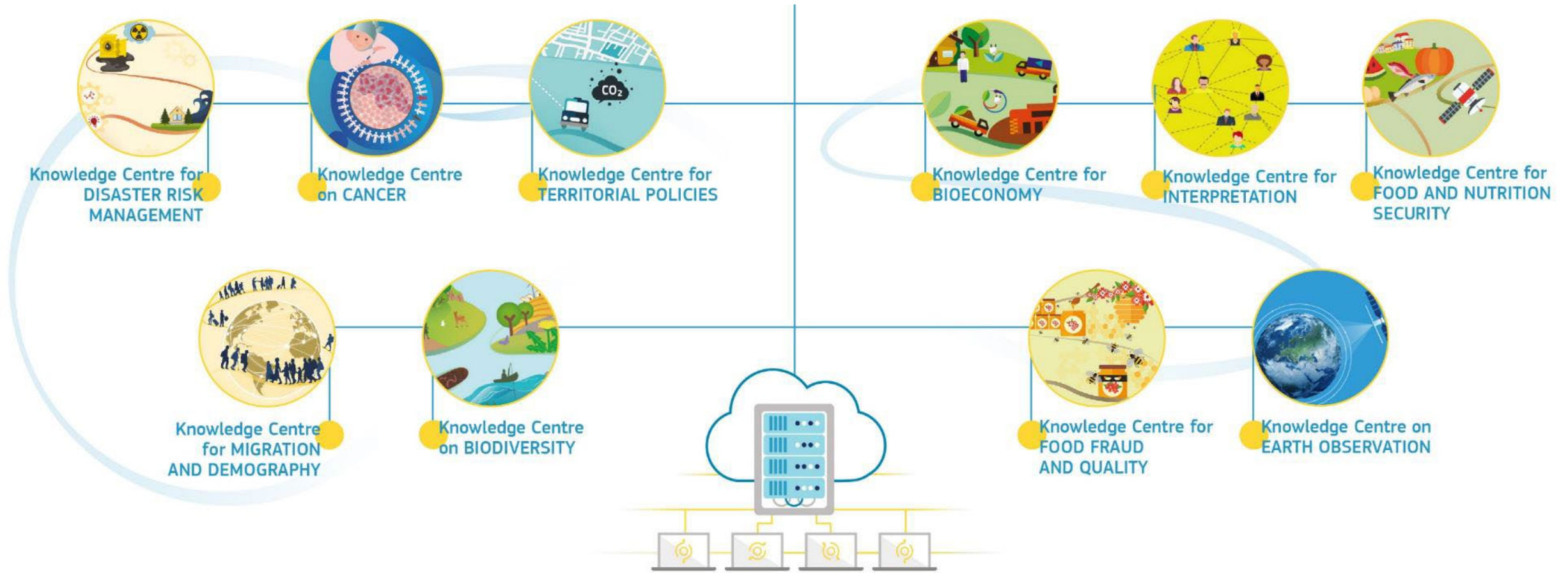
A stronger Europe in the World

An economy that works for people

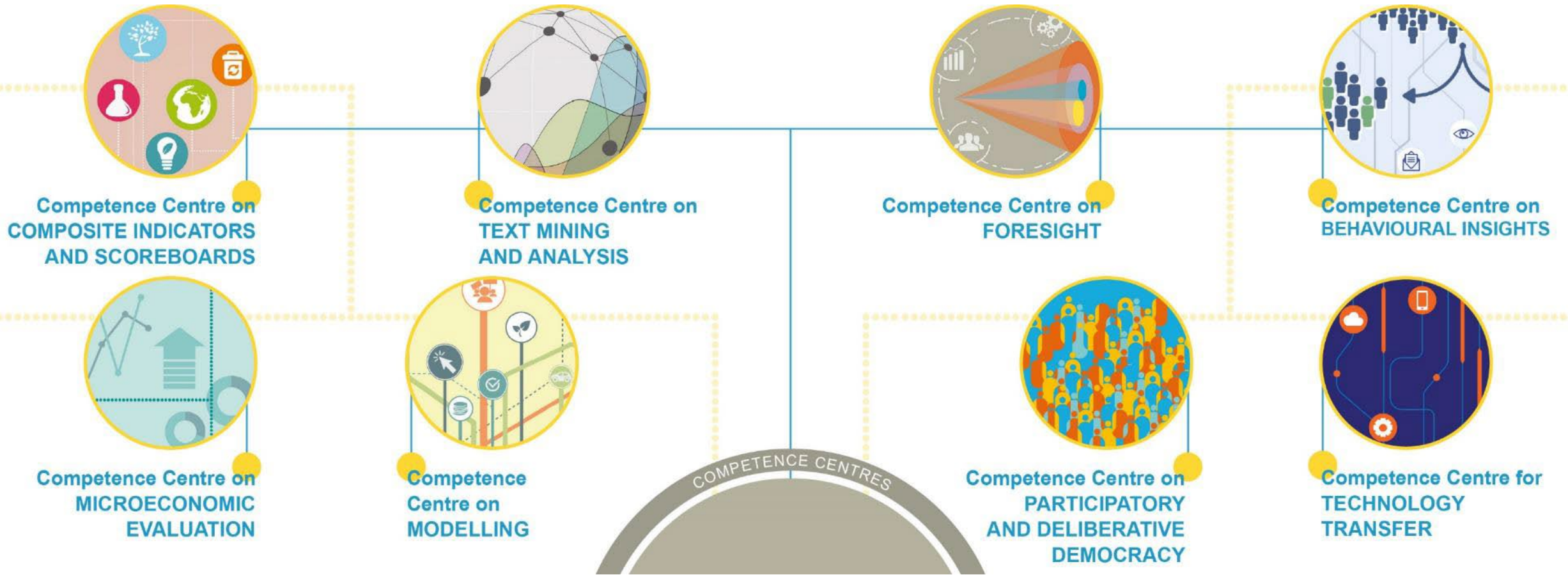
Promoting our European way of life

A new push for European democracy

Knowledge Centres



Competence Centres



We are on par with Oxford and Cambridge

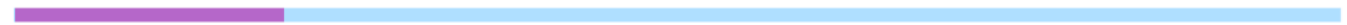
3.7% publications

in the top 1% most
cited worldwide

24.5% publications

in the top 10%

International Institute for Applied Systems Analysis – AT



University of Oxford – UK



Joint Research Centre



University of Cambridge – UK



Max Planck Society – DE



National Institute of Standards and Technology – US



Chinese Academy of Sciences – CN



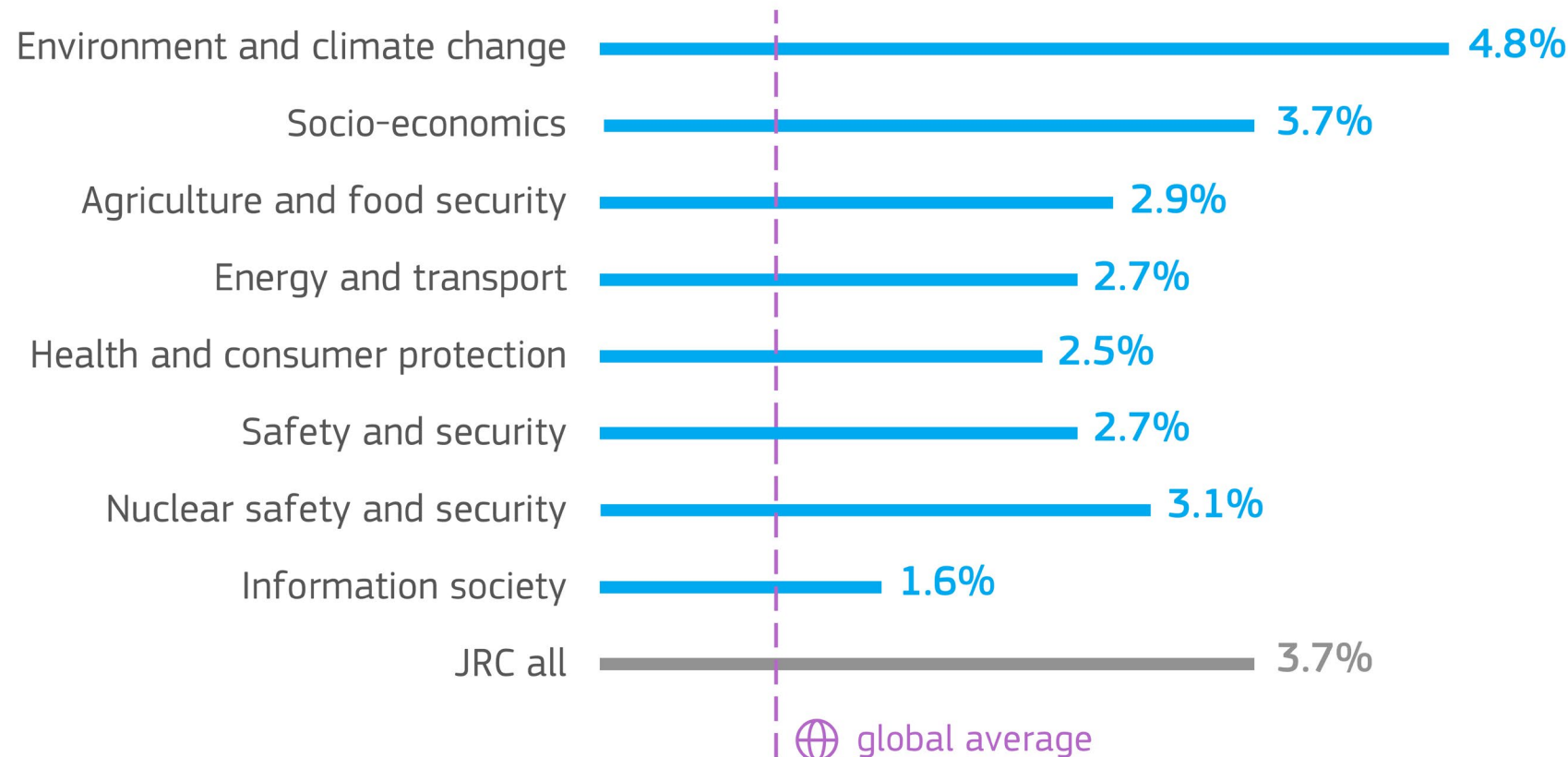
National Centre for Scientific Research – FR



5% publications

We perform well across all of our research fields

Percentage of JRC publications among the globally most cited 1% (2018-2022)



We lead on European policy impact

Joint Research Centre

International Institute for Applied Systems Analysis, AT

University of Oxford, UK

University of Cambridge, UK

National Institute of Standards and Technology, US

Max Planck Society, DE

National Centre for Scientific Research, FR

Chinese Academy of Sciences, CN

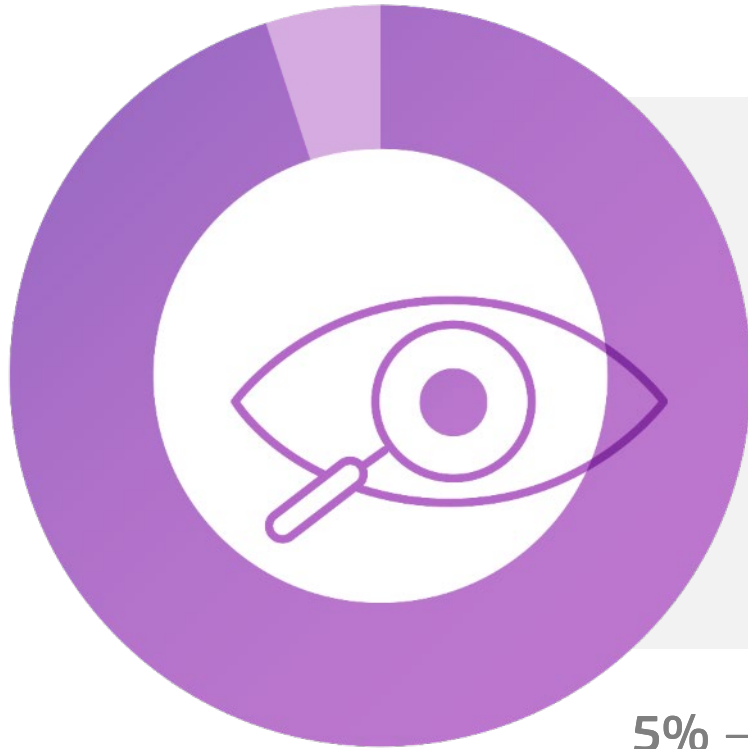
0.1 citations / article

0.43 citations by EU policy documents
per publication

>350 EU policy documents
cited JRC science in 2020.

**The JRC leads on policy
impact per publication.**

We are close to a 100% open access



We believe in transparency
and strive for open science.

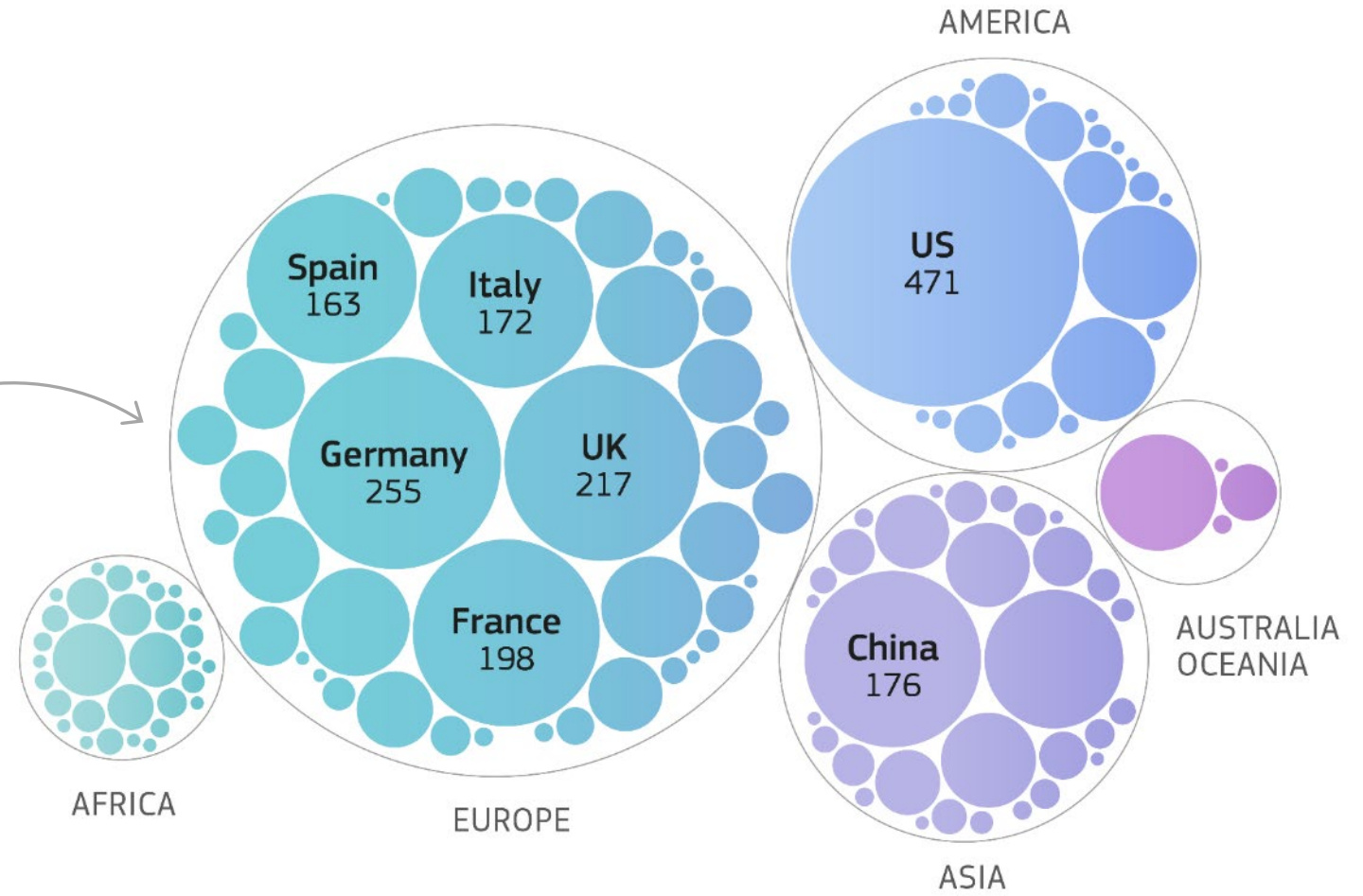
95% of our studies were
published open access in 2022.

5% — no suitable open access journal found

We cooperate across the whole world

82% of JRC publications were co-authored with scientists from

>3200 organisations in 134 countries



Data for JRC publications (2018-2022)

JRC facilities – some examples

Virtual tour at <https://visitors-centre.jrc.ec.europa.eu/en/media?type=8>

Neutron beams
to explore
the femtoscale
(MONNET)



Food Contact
Materials
(EURL FCM)



Nanobiotechnology
Laboratory



JRC neutron
time-of-flight
facility (GELINA)



Reference Material
Processing Hall



Water Laboratory



JRC facilities – some examples

Virtual tour at <https://visitors-centre.jrc.ec.europa.eu/en/media?type=8>

European
Laboratory for
Structural
Assessment
(ELSA)



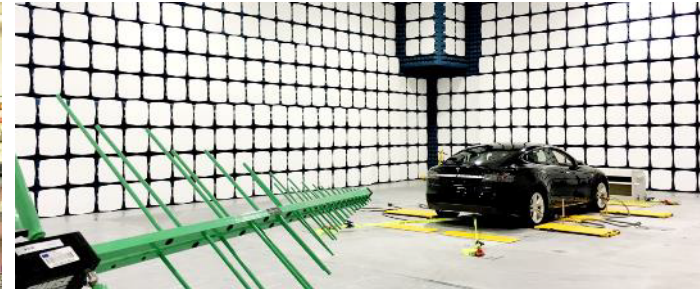
Hopkinson
Bar facility
(HOPLAB)



Vehicle Emission
Laboratory (VELA)+
vehicle Market
Surveillance
Laboratory



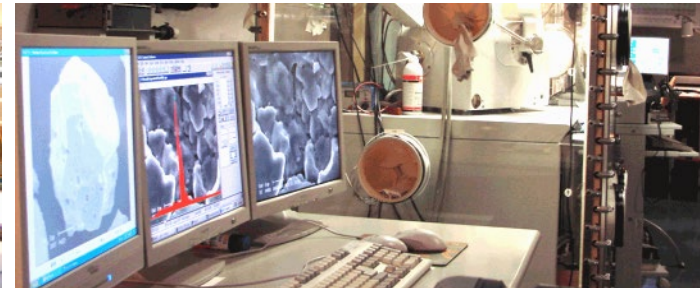
European
Interoperability
Centre for Electric
Vehicles and
Smart Grids



Battery Testing
Facility Laboratory



Nuclear Forensic
Laboratory



JRC facilities – some examples

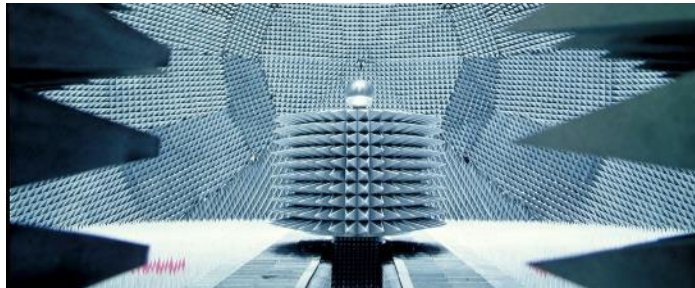
Virtual tour at <https://visitors-centre.jrc.ec.europa.eu/en/media?type=8>

JRC ultra low-background gamma-ray spectrometry facility (HADES)



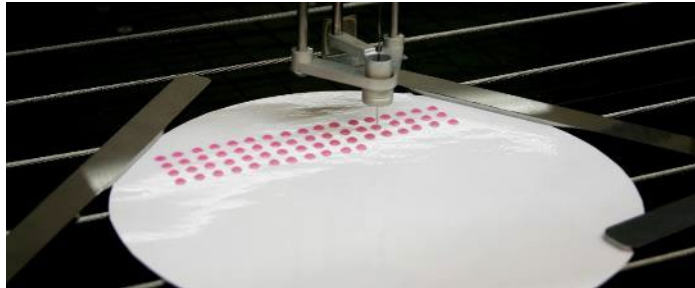
European Solar Test Installation (ESTI)

European Microwave Signature Laboratory (EMSL)



Gas Testing Laboratory

JRC radionuclide metrology laboratory (RADMET)

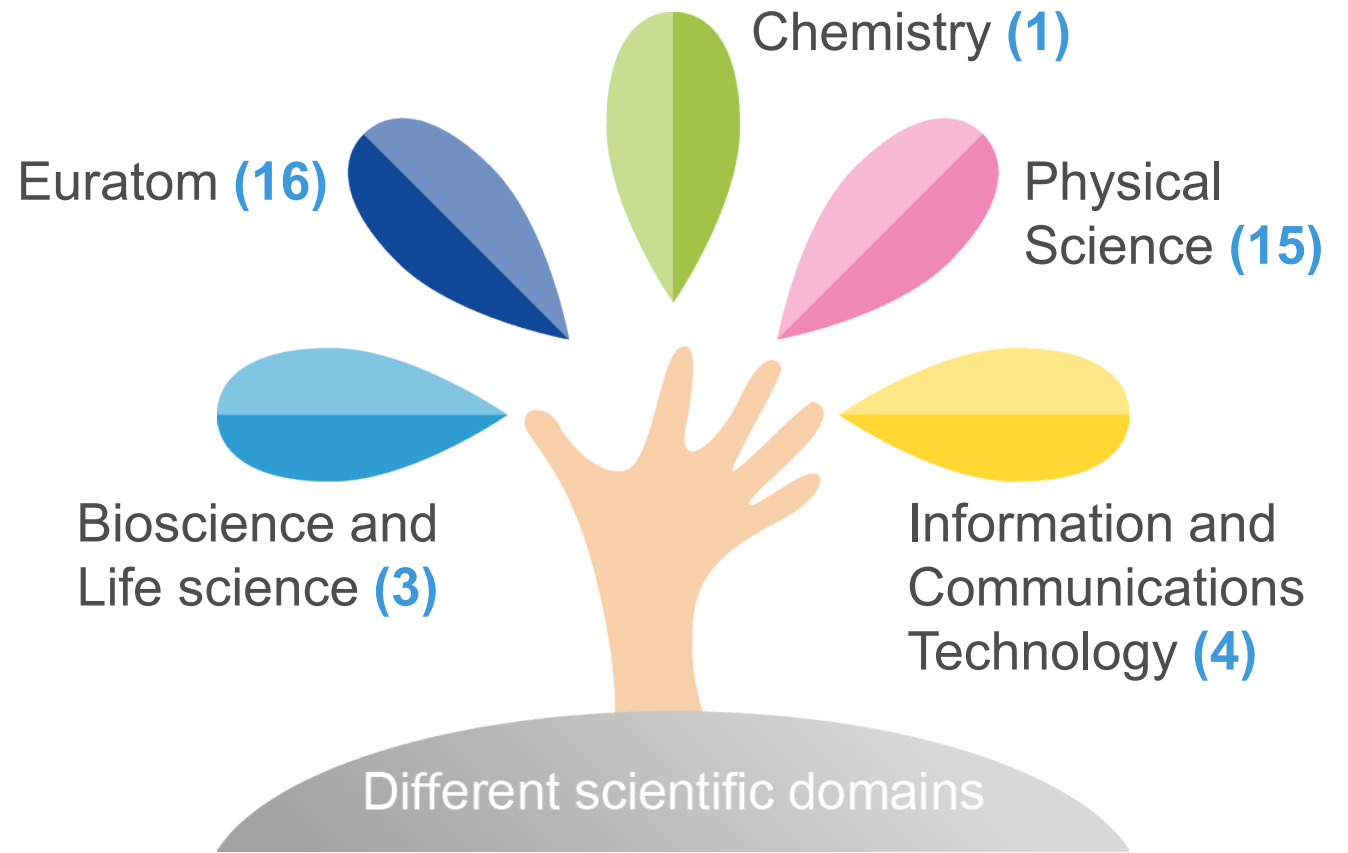


European Crisis Management Laboratory (ECML)

Open access to JRC Research Infrastructures

The JRC hosts **39 physical Research Infrastructures (RI)** with a potential of **opening to external users** (out of a total of **56**)

<https://europa.eu/!CM63UK>



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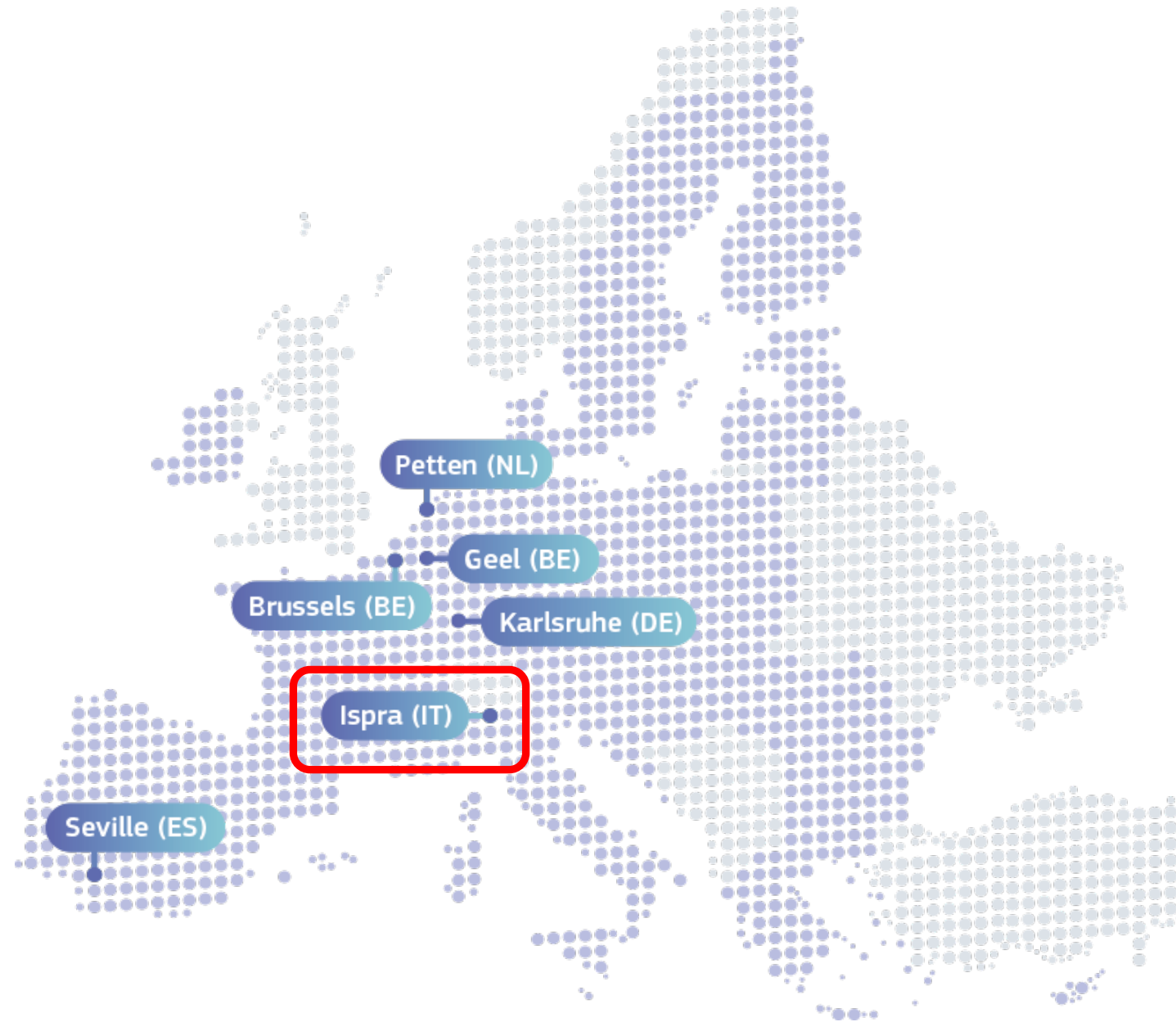
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- **EURL ECVAM**
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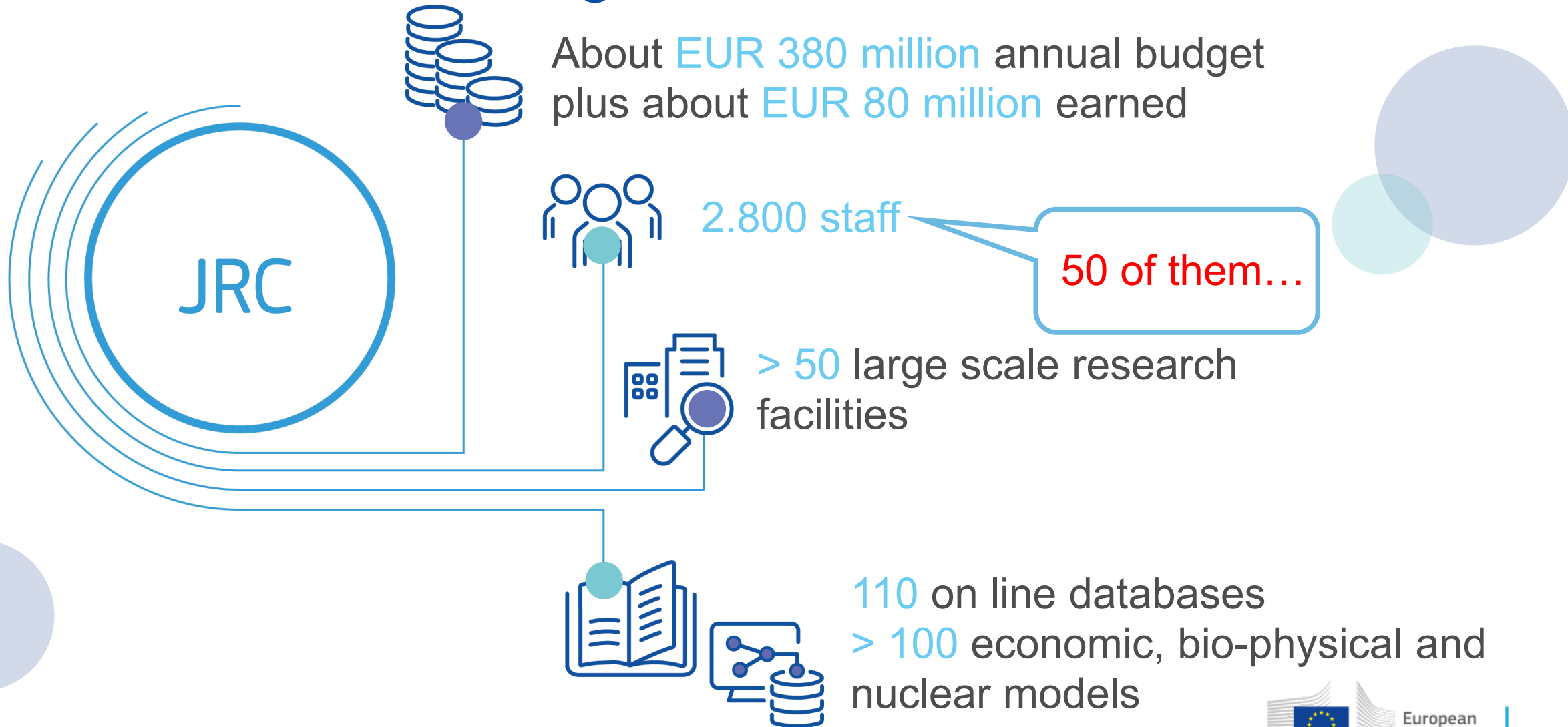
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JRC – Facts and figures



The European Union Reference Laboratory for alternatives to animal testing

Research and development of alternative methods

Validation of alternative methods for chemical safety assessment

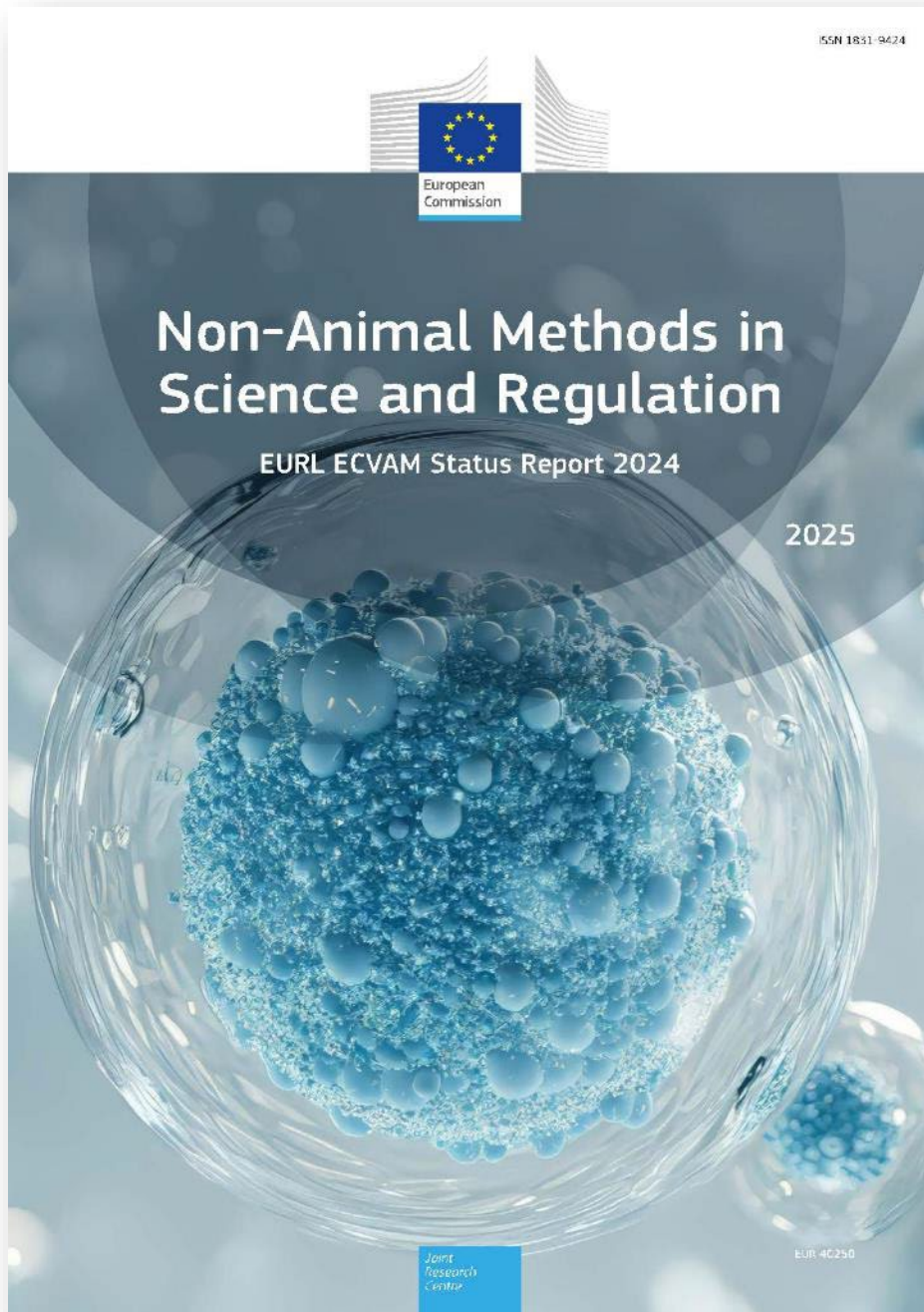


Dissemination of information on the 3Rs

Promotion of non-animal approaches in science



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



Our Annual Report 2024

- Development
- Validation
- Regulatory Application
- Alternatives in Research and Education



JRC SUMMER SCHOOL ON NON-ANIMAL APPROACHES IN SCIENCE

Towards
sustainable innovation
23-26 May 2023

Challenges
& Future Directions
21-24 May 2019

VIRTUAL EVENT
The Three R...evolution
17-21 May 2021

The path from science
to protection of human health
and the environment
16-19 May 2017

32
methods

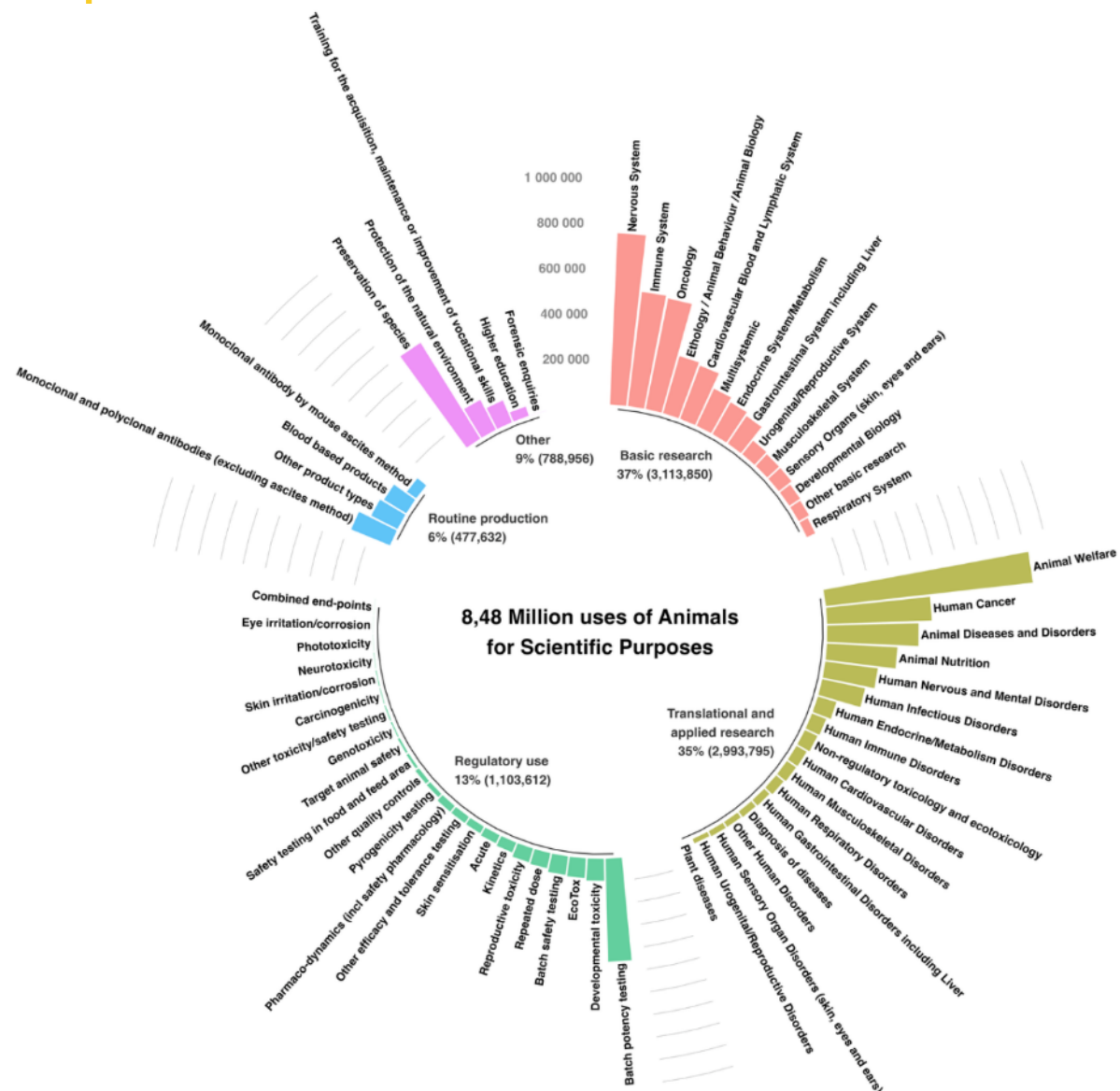
Summer school

NEXT EDITION May 2025

JRC SUMMER SCHOOL ON NON-ANIMAL APPROACHES IN SCIENCE CHANGING THE PARADIGM



Statistics on the use of animals in science



Statistics on the use of animals in the EU27 + Norway (2022)

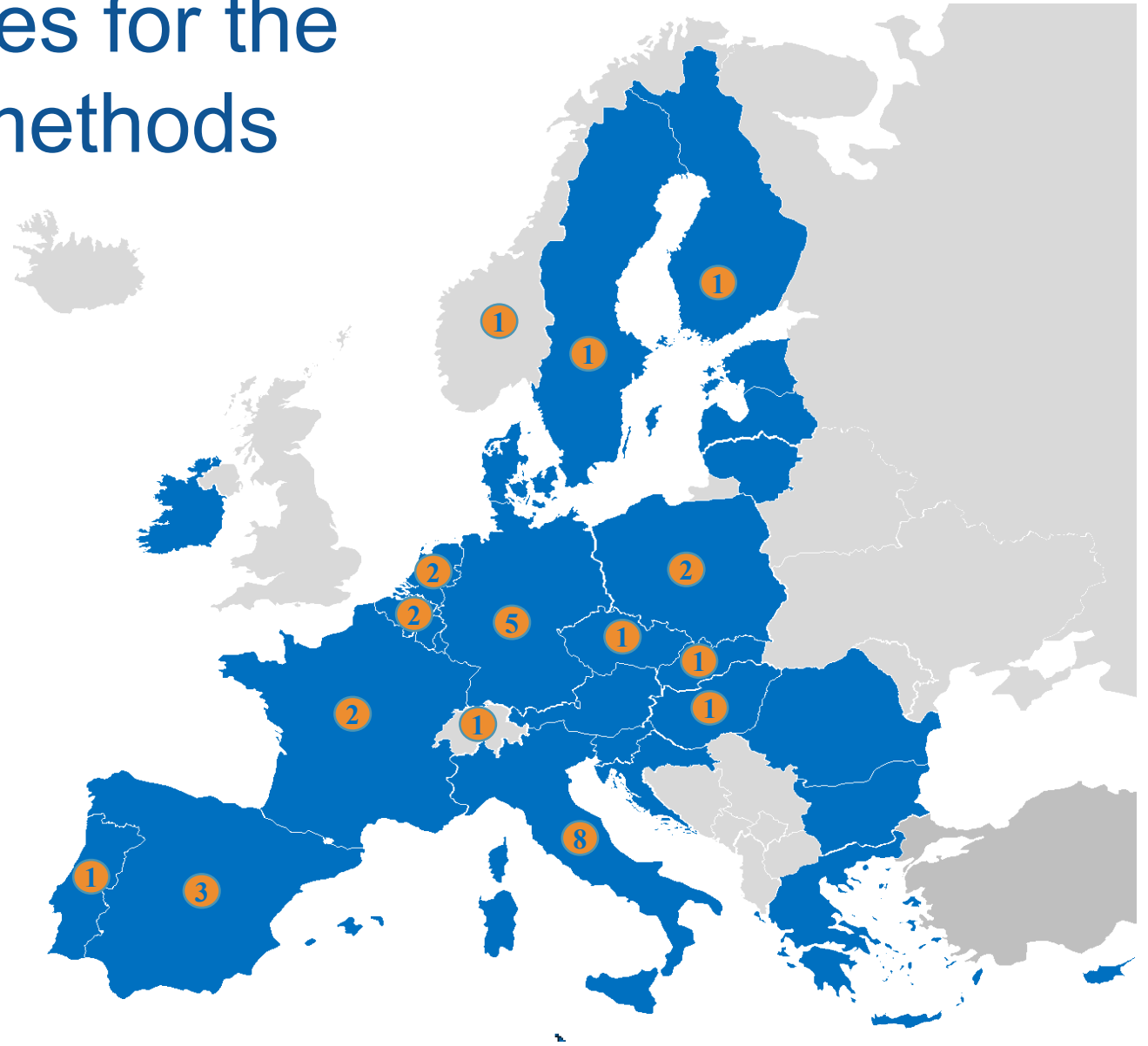
- 72% of animal uses are in research
- 4.1 million uses are for human centred research
- Trend
 - 2020 -> 2021: **+18.5%**
 - 2021 -> 2022: **-10.9%**
 - Regulatory procedures since 2018: **-32%**

EU Network of laboratories for the validation of alternative methods

Belgium	2
Czech Rep	1
Finland	1
France	2
Germany	5
Hungary	1
Italy	8
Netherlands	2
Norway	1
Poland	2
Portugal	1
Slovakia	1
Spain	3
Sweden	1
Switzerland	1
EC-JRC	1
Total	33

EU-NETVAL

Facilities either fund themselves or receive some support from their respective Member States as foreseen in Directive 2010/63/EU



JRC biomedical reviews of non-animal models (2013-2019)



1. Respiratory tract diseases
2. Breast cancer
3. Neurodegenerative diseases
4. Immuno-oncology
5. Immunogenicity testing for ATMP
6. Cardiovascular diseases
7. Autoimmune diseases

- 322,827 abstracts screened
- 89,446 full texts analysed
- 3049 non-animal methods

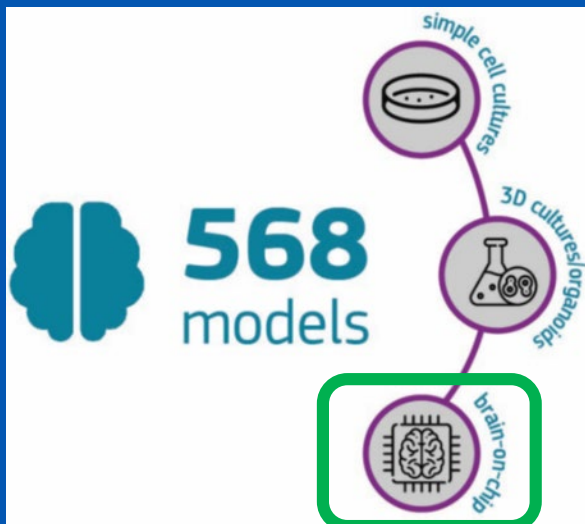
**Access all model details in
the JRC Data catalogue**



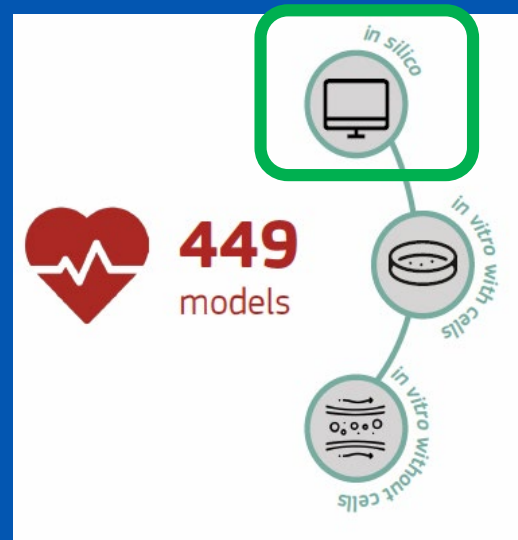
GENERAL FINDINGS

- Preferred methods differ among research areas
- Those involving cells are the most common
- Steady increase in the use of Organ-on-Chip in certain areas

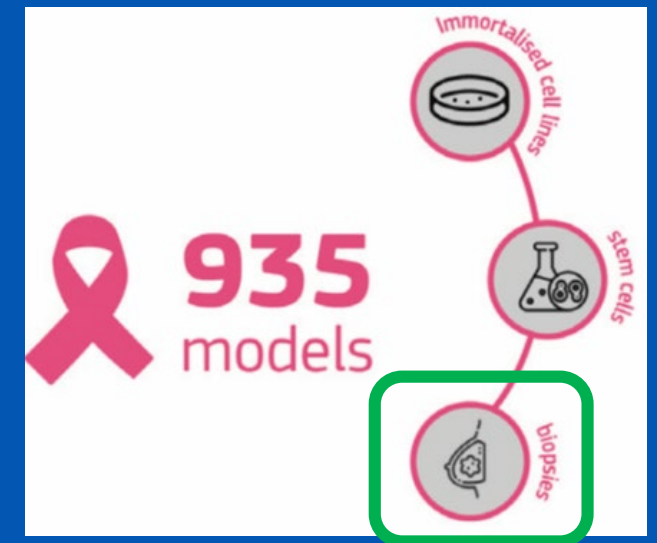
Neurodegenerative Diseases



Cardiovascular diseases



Breast Cancer



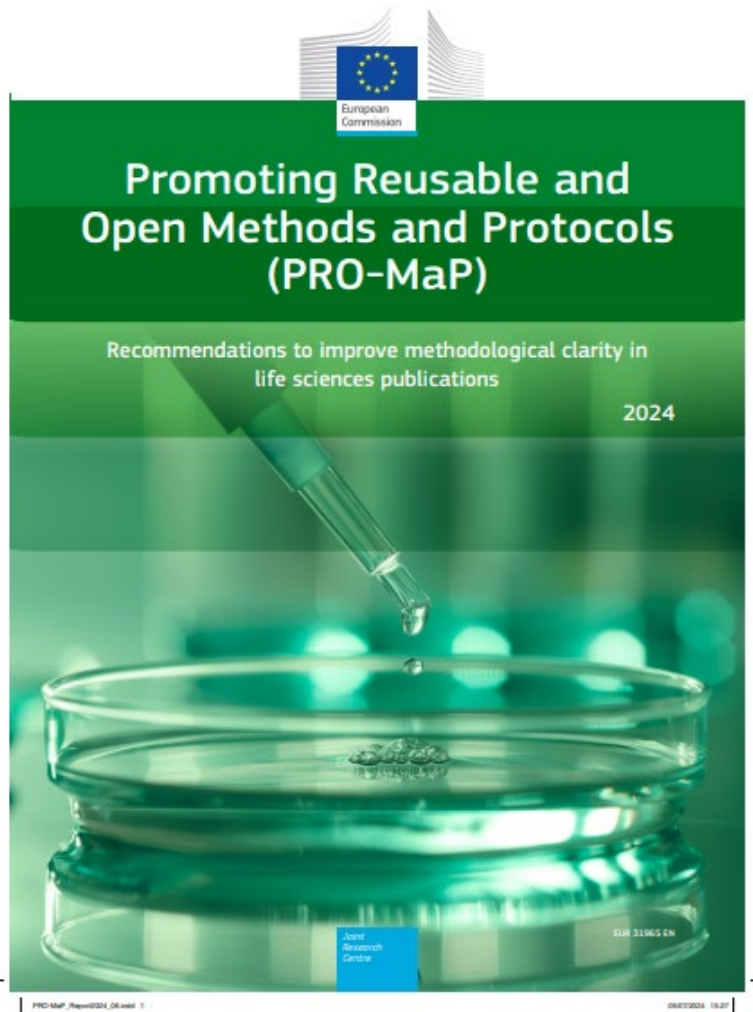
AI-based automated database

Pilot Project: Initiative or scheme designed to test and explore the feasibility, effectiveness, or usefulness of a particular idea, concept, policy, or program within a limited scope or timeframe.

- **AI-powered system** to curate PubMed titles and Abstracts as well as analyse Open access articles:
 - Literature **categorisation** in: Animal-based, Human and Animal-based, Human-based
 - **Continuous** monitoring for new literature
 - **Data extraction and visualisation.**
- **Automated approaches** to mine published literature that can be **searched by anyone.**
- **Extension** of already collected models both in time and in scope (10 disease areas).

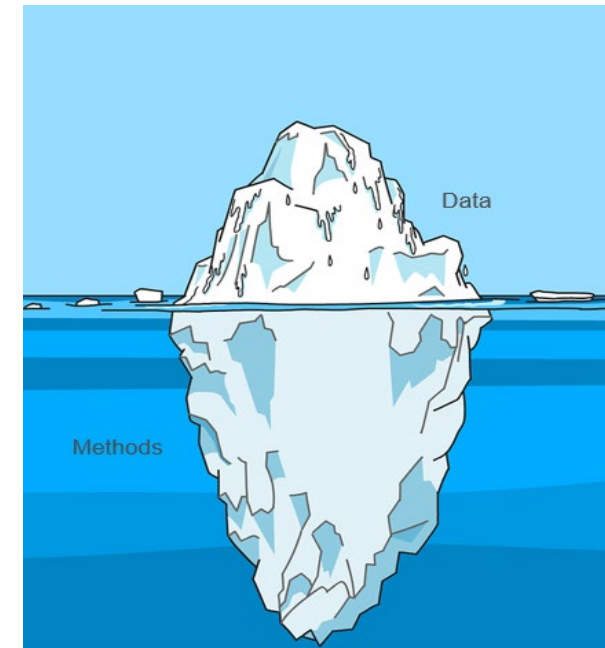


Coming soon!!



Improving the way scientific methods & protocols are reported to increase:

- **Reproducibility**
- **Trust**
- **Transparency**
- **Translation**
- **Impact**



RECOMMENDATIONS *for Researchers*

- Document, share and follow protocols within your research group
- Follow reporting guidelines
- Link to dynamic protocols
- Responsible shortcut citations
- Availability statement
- Support a change in culture

RECOMMENDATIONS *for* Research institutions

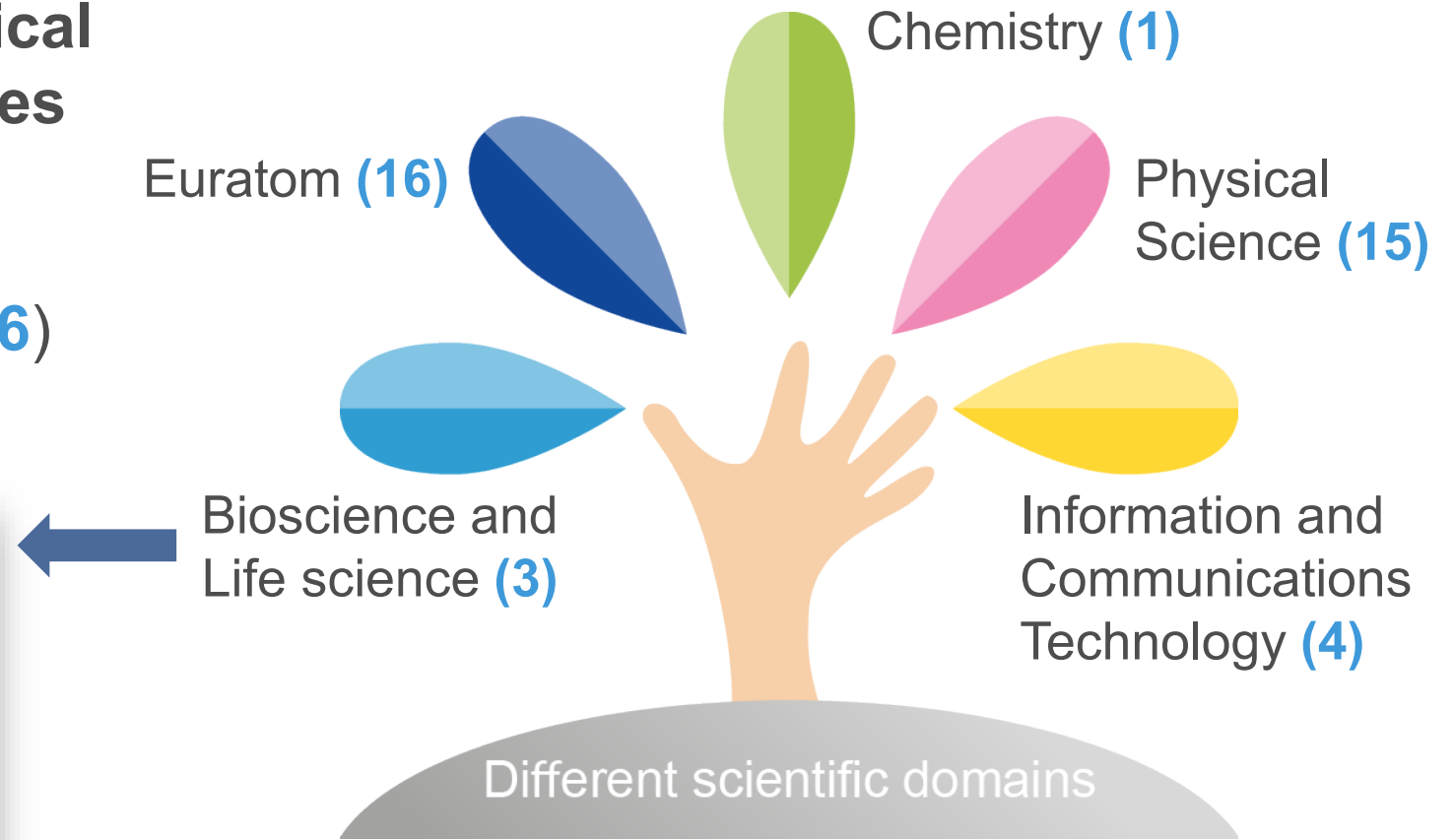
RECOMMENDATIONS *for* Funders

RECOMMENDATIONS *for* Publishers & Editors

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<https://europa.eu/!CM63UK>



Open Access to JRC Research Infrastructure

High Throughput Testing (HTT) Laboratory for In Vitro Methods

EURL ECVAM

The European Union Reference Laboratory for alternatives to animal testing



Closed Call: <https://europa.eu/!PVvGP7>

Opening date: 5 February 2025

Deadline date: 31 March 2025

Stay tuned for a new call!



JRC-OPEN-ECVAM@ec.europa.eu

Why we are interested in opening access to our lab

- Assess and improve the transferability of in vitro methods with regulatory relevance



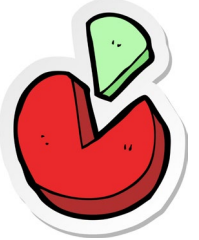
- Use automation and high throughput testing to accelerate aspects of validation

- Scout for promising methods and assess their performance with libraries of reference chemicals



- Facilitate scientific and technical knowledge sharing and provide hands-on training

What we offered (in the first call):

- Access to HTS platform free from additional costs to users 
- The Open lab activities will occupy less than 10% of the lab activities 
- The call will give access to two experimental studies where the users (coming from 1 or more Institutes/SMEs) can assist the experiments in person or remotely.



- Each experimental study will consist of a maximum of 16 access unit corresponding for example to 5 experiments on the HTS (= cell seeding + treatment + output measurement)





Robotic platform quiz

0/3



Cell cultures quiz

0/3



Organ-on-chip quiz

0/2



Explore the ECVAM laboratory in 360°

Virtual Reality training for (school) students



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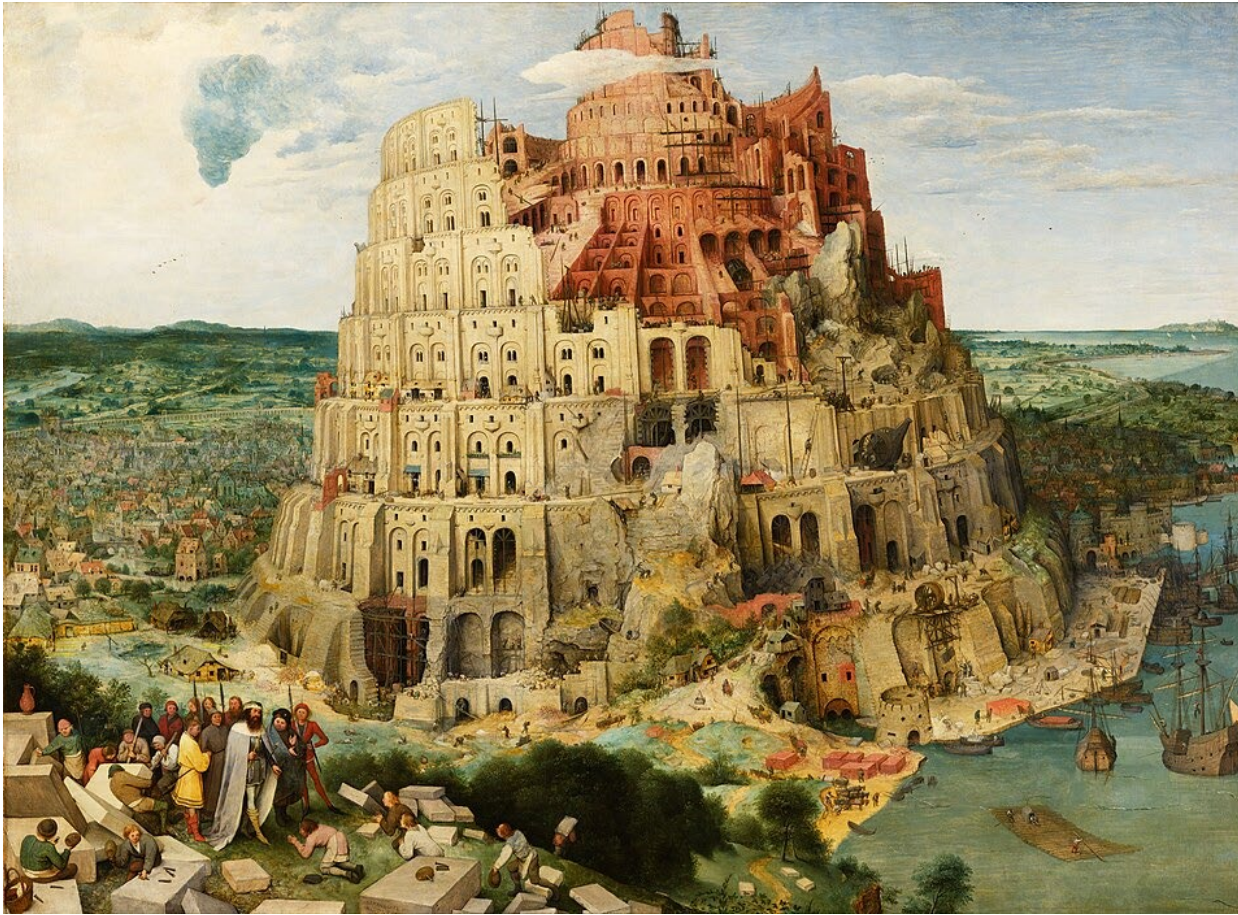
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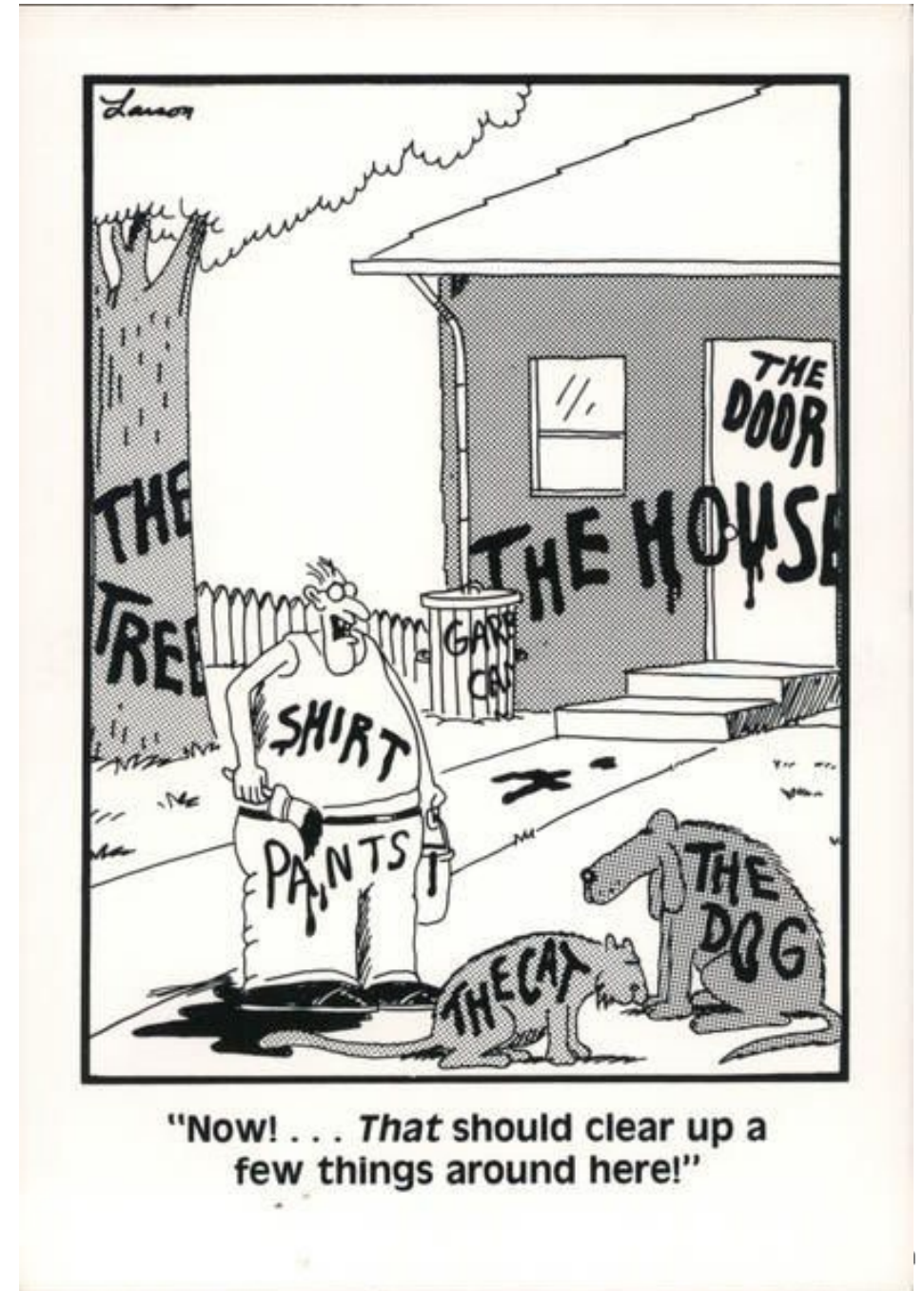


*"We now have unprecedented ability to collect data about nature but there is now **a crisis developing in biology**, in that completely **unstructured information does not enhance understanding**. We need a framework to put all of this knowledge and data into - that is going to be the problem in biology. We've reached the stage where we can't talk to each other - we've all become highly specialized. ... driving toward that framework is really the big challenge."*

The Tower of Babel, Pieter Bruegel, 1563
Kunsthistorisches Museum, Vienna



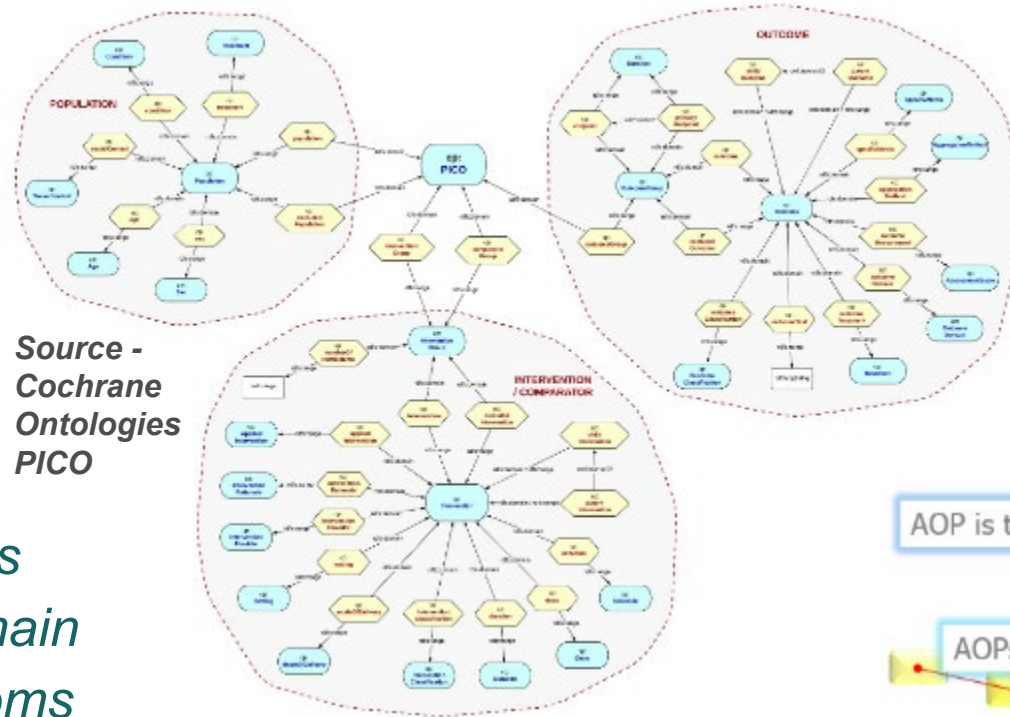
- In science, we seem to have a “**Babylonische Sprachverwirrung**” (*Babylonian language confusion*)
- **Let's find a common language!**



Gray Larson: The Far Side

Ontologies

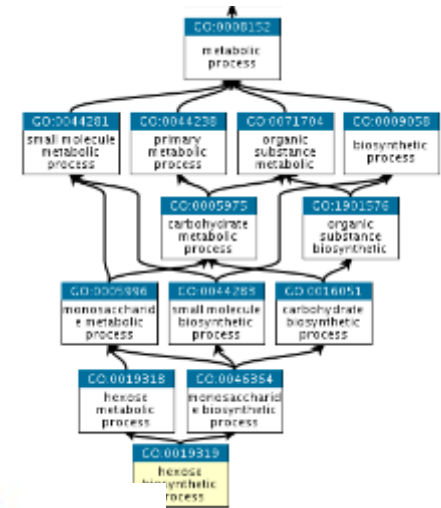
.... a way of showing the properties of a subject area and how they are related, by defining a set of concepts and categories that represent the subject



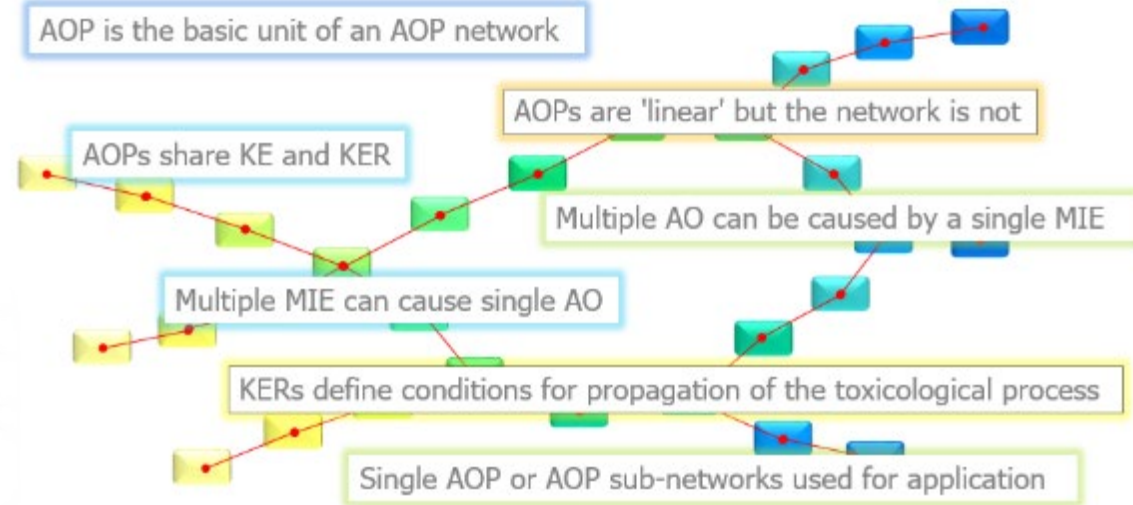
rules
domain
axioms
relations
attributes
restrictions
vocabulary
objects/concepts
classes/categories



3 related ontologies covering
molecular function,
biological processes and
cellular components



AOP is the basic unit of an AOP network

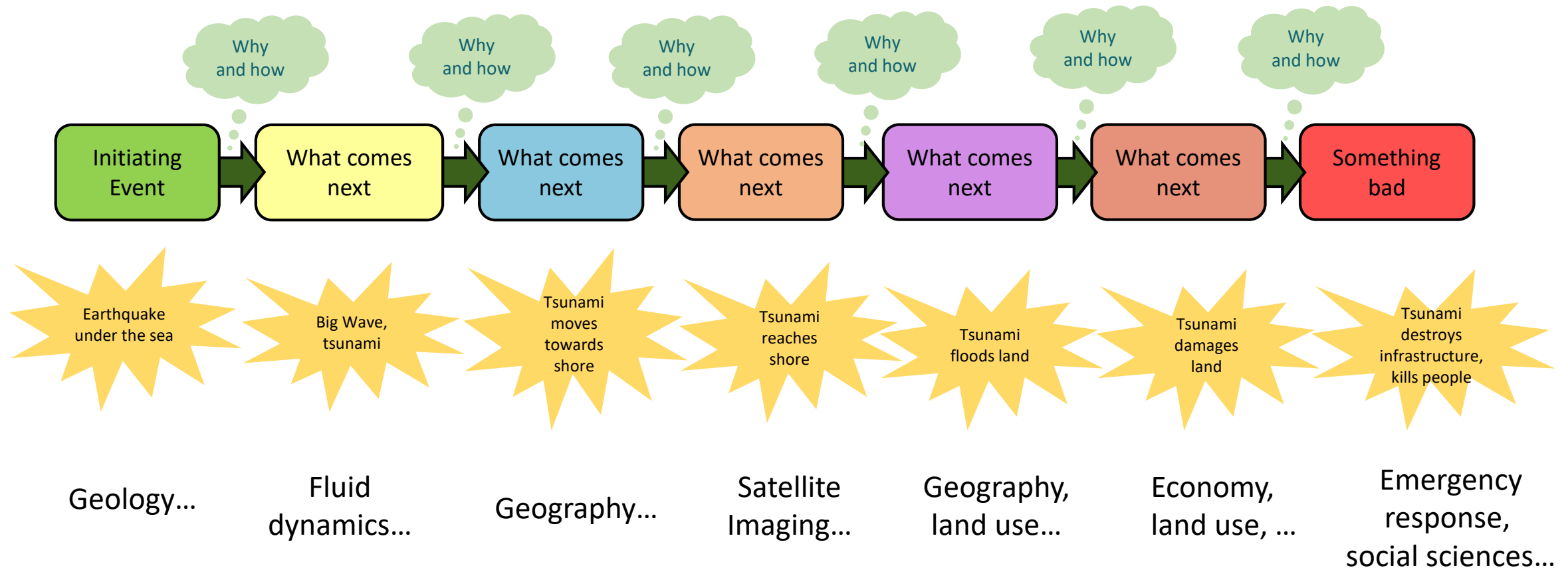


Adverse Outcome Pathways

Adverse Outcome Pathways (AOPs)

General
concept

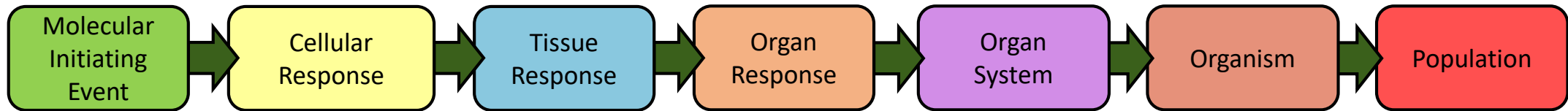
An **AOP** links, in a **linear way**, **existing knowledge** along one or more series of **causally connected key events** between two points — an *initiating event* and an *adverse outcome* that occur at a level of science accessible to risk assessment. The **linkage** between the events is described by **key event relationships** that describe the **causal relationships** between the key events.



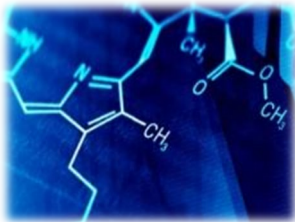
Adverse Outcome Pathways (AOPs)

Real life

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In silico modeling



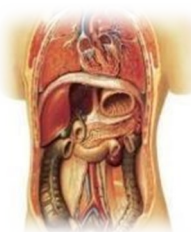
Biochemistry



Molecular biology



Cellular biology



Physiology



Ecology



Epidemiology

Why AOPs?

- Promote International Collaboration

- The AOP framework encourages sharing of data and methodologies, promoting consensus and standardization across borders.



- Enhance Predictive Capacity

- By mapping out the biological pathways, AOPs improve the predictive accuracy of toxicological assessments, reducing reliance on animal testing and improving human relevance.



Why AOPs?



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- **Guide the Development of NAMs**
 - By understanding the key events in an AOP, scientists can develop targeted in vitro assays and computational models.



AI generated

- **Facilitate Regulatory Acceptance**
 - AOPs provide a scientifically credible basis for regulatory decisions, helping to justify the use of alternative methods.

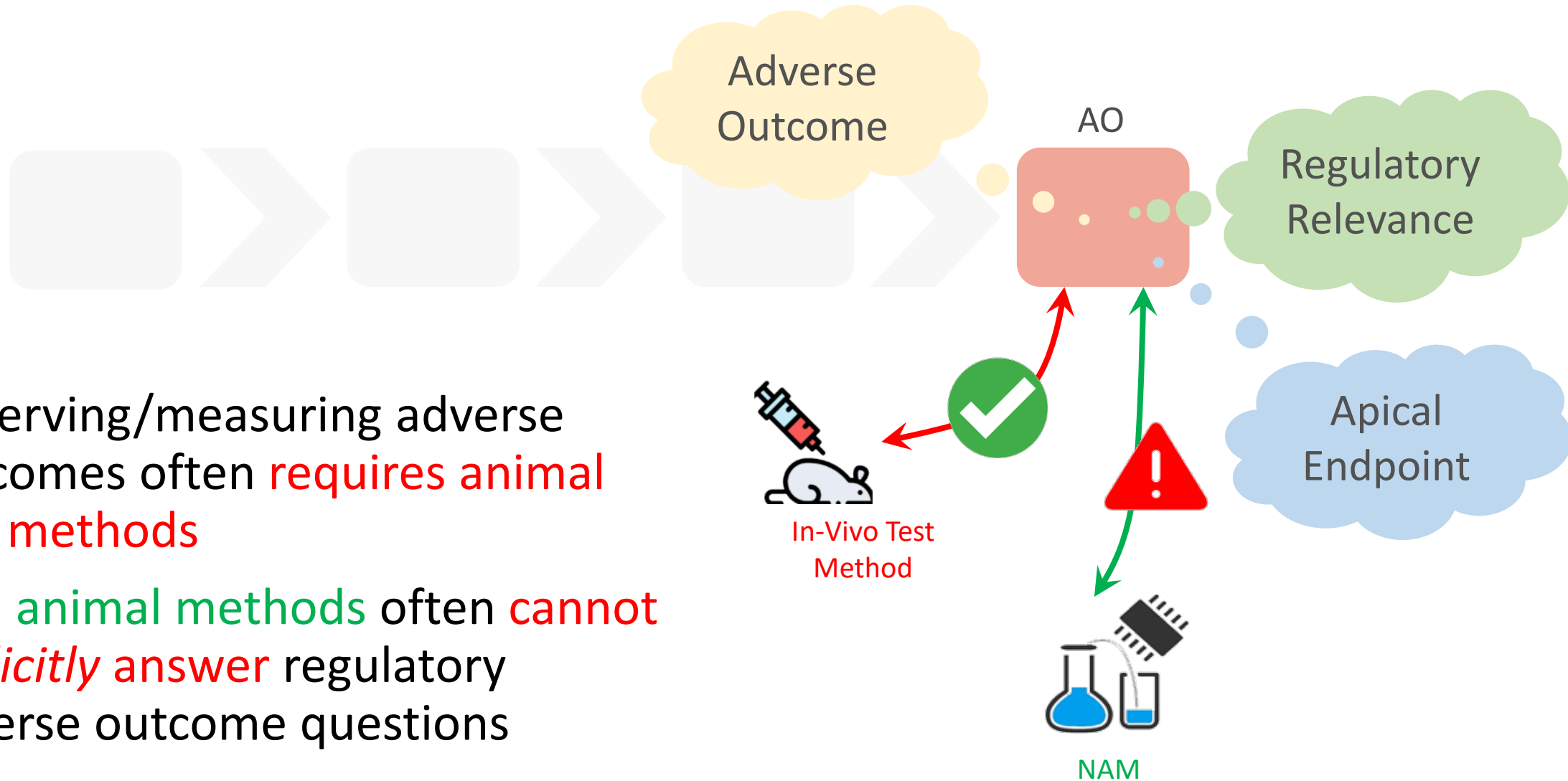
Observed correlation turns into **explainable causality**

Plausibility

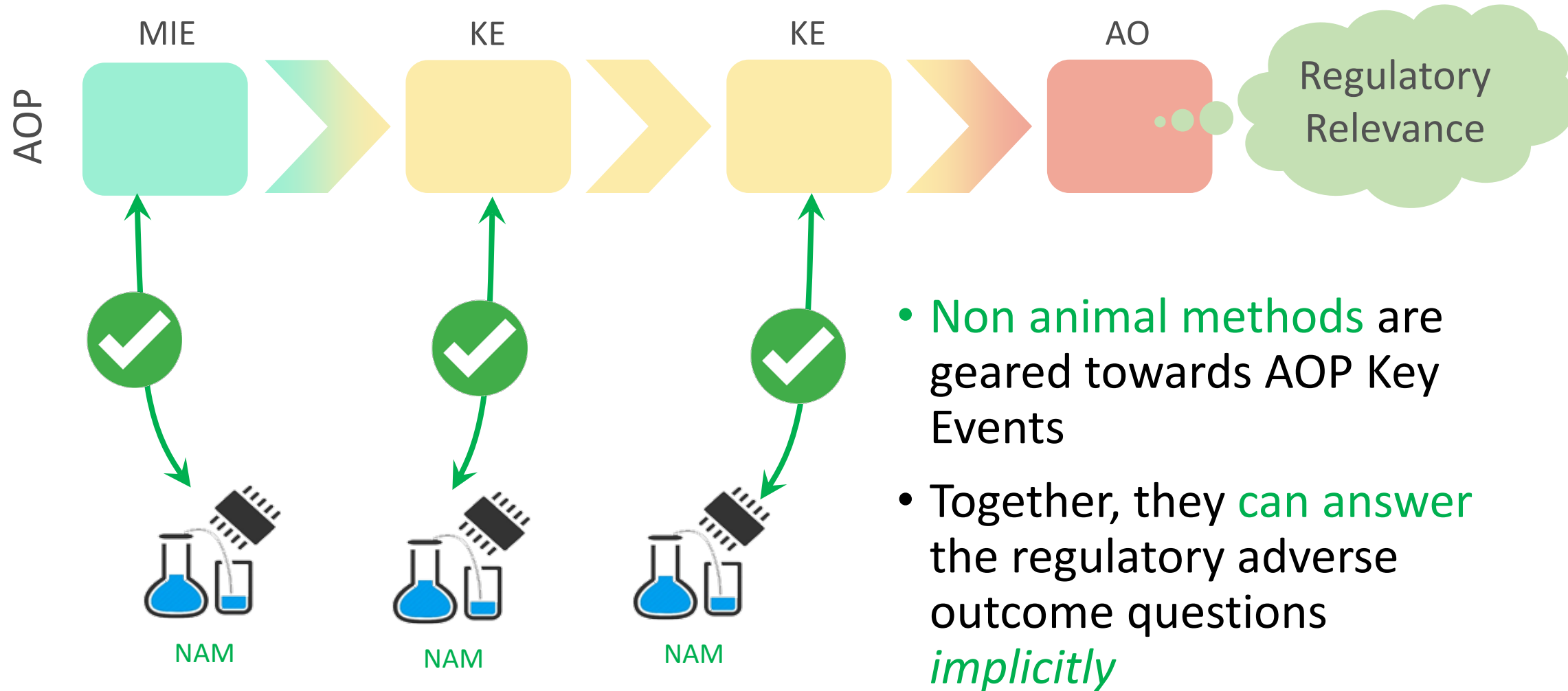


Conventional way to ask and answer toxicological questions

- Observing/measuring adverse outcomes often **requires animal test methods**
- **Non animal methods** often **cannot explicitly answer** regulatory adverse outcome questions



The **AOP way** to ask and answer toxicological questions



AOP networks



AOP is the basic unit of an AOP network

AOPs are 'linear' but the network is not

AOPs share KE and KER

Multiple AO can be caused by a single MIE

Multiple MIE can cause single AO

KERs define conditions for propagation of the toxicological process

Single AOP or AOP sub-networks used for application

Nodes represent Key Events (KE)
Edges represent Key Event Relationships (KER)



Main page

AOPs Key Events KE Relationships Prototypical Stressors Developers' Handbook Login Register

Welcome to the Collaborative Adverse Outcome Pathway Wiki (AOP-Wiki)

Version 2.7 was released on March 30, 2024. More details regarding the new release are available here: [Release 2.7](#).

Interested in helping plan for Version 3.0? Please submit your ideas on the AOP Forum [here](#).



View Content

AOPs

Key Events

KE Relationships

Prototypical Stressors

Get access to the main elements of an Adverse Outcome Pathway managed in the AOP-Wiki

Download Content

Download Options

Download our content and use it in your own tools



Contribute

Register

Start a new AOP

Developers' Handbook

You can do so much more once we get to know you - register

Browsing through existing AOPs is great - adding your own is even better!

View up to date guidance, tips, and best practices for AOP development



Get Information

Get started here...

Who are we?

Announcements

AOP Training

What is an AOP? How will AOPs change Chemical Risk Assessment?

Find out more about the people behind the AOP-Wiki and the AOP Framework

Don't miss our regular announcements and news!

Learn about training materials and opportunities



Community

AOP Help

AOP Forum

Third Party Tools

Get AOP related help - it's free!

Discuss AOP-related topics with other stakeholders! Click [here](#) to learn more.

Explore AOPs using tools developed by AOP community partners

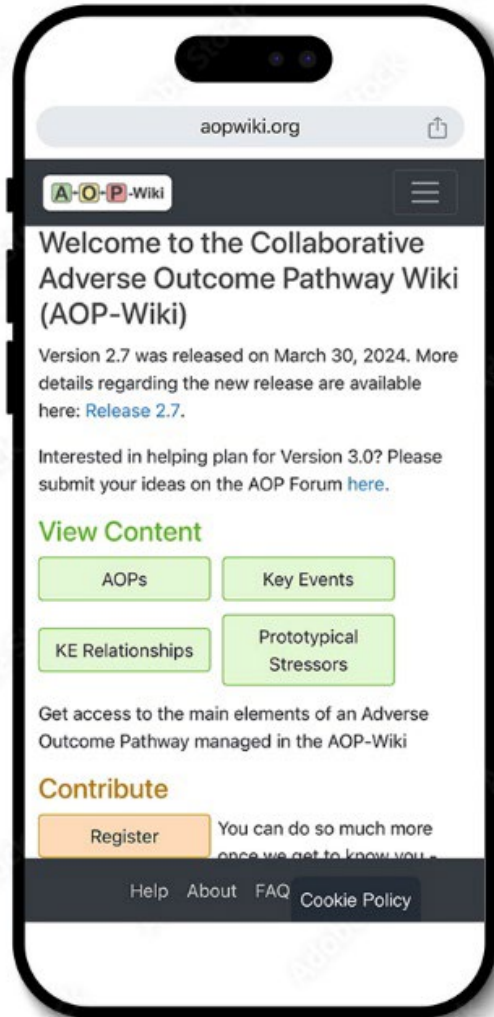
Help About FAQ Download Options Metrics



<https://aopwiki.org/>



Main page



- Also available on mobile devices
 - Same URL
 - Same content
 - Same functionality



<https://aopwiki.org/>

Communities building AOPs



Toxicological Sciences

TOXICOLOGICAL SCIENCES, 163(2), 2018, 346–352

doi: 10.1093/toxsci/kfy047

FORUM

Representing the Process of Inflammation as Key Events in Adverse Outcome Pathways

Daniel L. Villeneuve,^{*,1} Brigitte Landesmann,[†] Paola Allavena,[‡] Noah Ashley,[§] Anna Bal-Price,[†] Emanuela Corsini,[¶] Sabina Halappanavar,^{||} Tracy Hussell,^{|||} Debra Laskin,^{|||} Toby Lawrence,[#] David Nikolic-Paterson,^{**} Marc Pallardy,^{††} Alicia Pains,[†] Raymond Pieters,^a Robert Roth,^b and Florianne Tschudi-Monnet^c



Tanabe, S., et al. (2022)
39(2), pp. 336–338..

Report of the 1st and 2nd Mystery of Reactive Oxygen Species Conferences

frontiers
in Public Health

PERSPECTIVE
published: 19 May 2021
doi: 10.3389/fpubh.2021.638605

Systematic Organization of COVID-19 Data Supported by the Adverse Outcome Pathway Framework

Penny Nymark^{1*}, Magdalini Sachana², Sofia Batista Leite³, Jukka Sund³, Catharine E. Krebs⁴, Kristie Sullivan⁴, Stephen Edwards⁵, Laura Viviani⁶, Catherine Willett⁶, Brigitte Landesmann³ and Clemens Wittwehr^{3*}

CIAO: Modelling the pathogenesis of COVID-19 using the **A**dverse **O**utcome Pathway framework

<https://ciao-covid.net/>

... how about ...

Beneficial Outcome Pathways (BOPs)?!

We are hiring



Check our vacancies
recruitment.jrc.ec.europa.eu

Thank you !

Clemens Wittwehr

Systems Toxicology Unit, Directorate for Health and Food,
European Commission, Joint Research Centre (JRC).

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<https://www.linkedin.com/in/clemenswittwehr/>



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