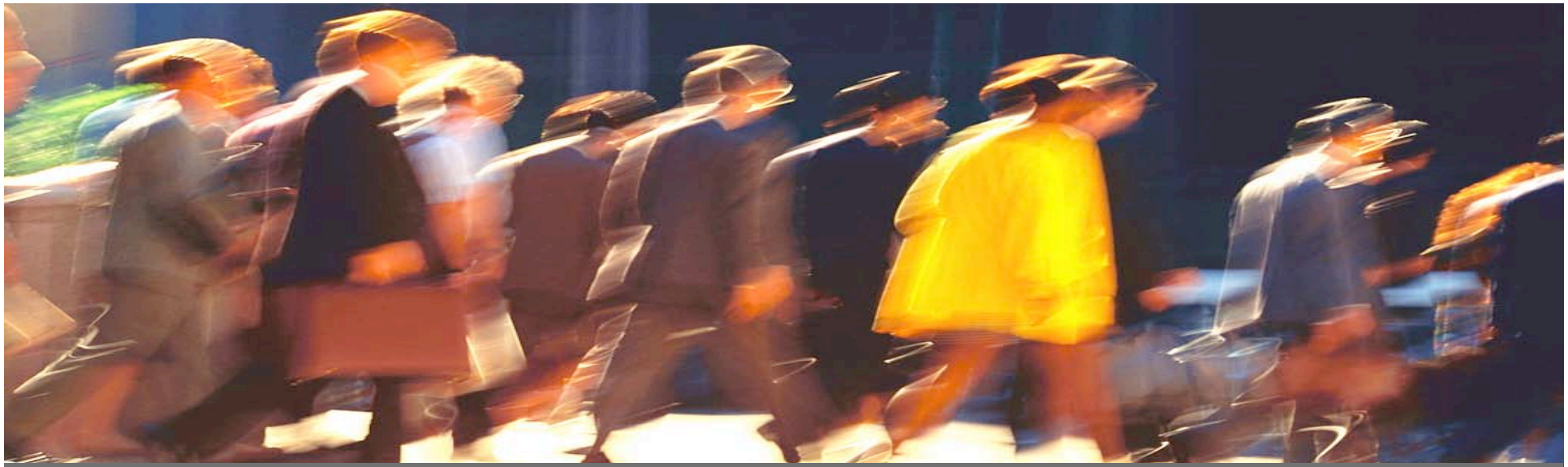


9th Annual ECOPA Workshop

Improved REACH implementation using new science based tools?

29 November, 2008

Bruessel

Gernot Klotz
CEFIC Executive Director for Research&Innovation
gkl@cefic.be

The Challenges

1

1 Substance → Consortia > 1000 participants → X 100 customers → X 10 **Or 100 Or 1000 customers**

2

REACH is about information, not testing!


cefic


10 YEARS
LRI
The Long-range
Research Initiative

Increased acceptance of high quality industry research as basis for policy making

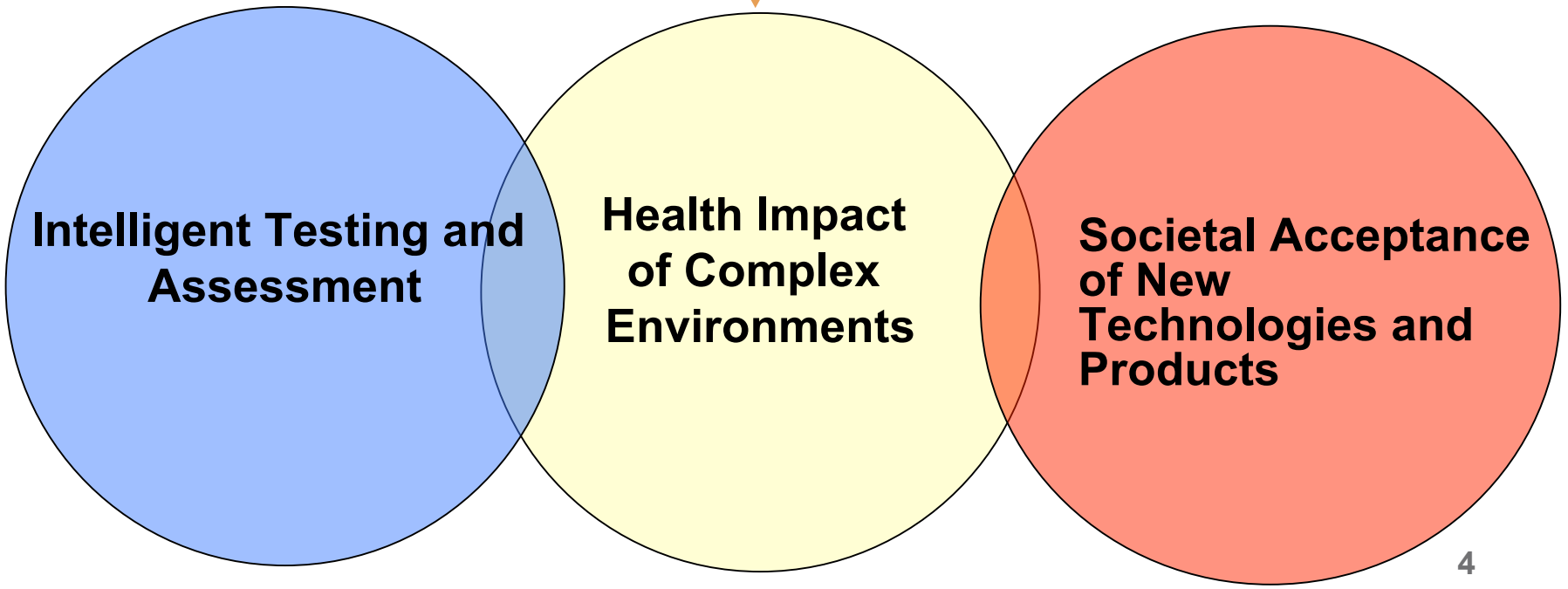
New policy scenario - increased complexity; less animal tests =>diffuse results => increased precaution

- ease if data generation => lack of understanding => media attacks

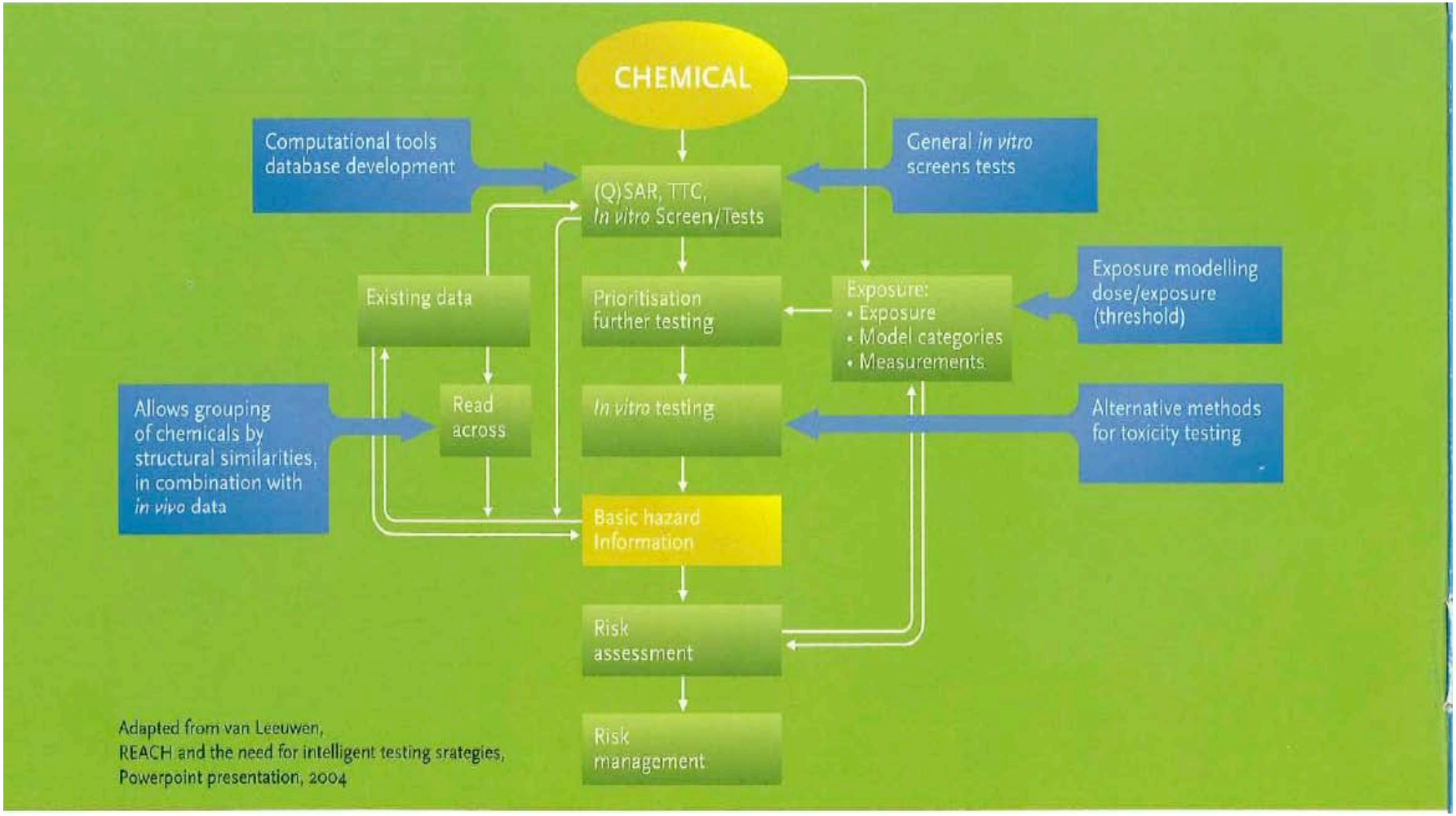
- bias in science today towards identifying additional adverse effects of chemicals

=> challenge to risk based decision making, impact on innovation

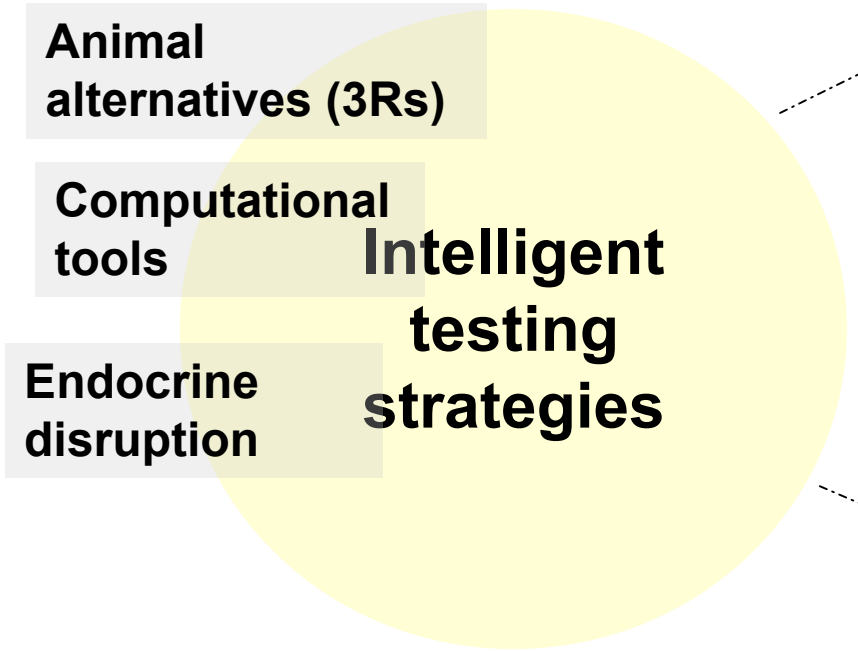
Refocus of LRI in 2007



Map of LRI sponsored research on the Intelligent Testing flow chart

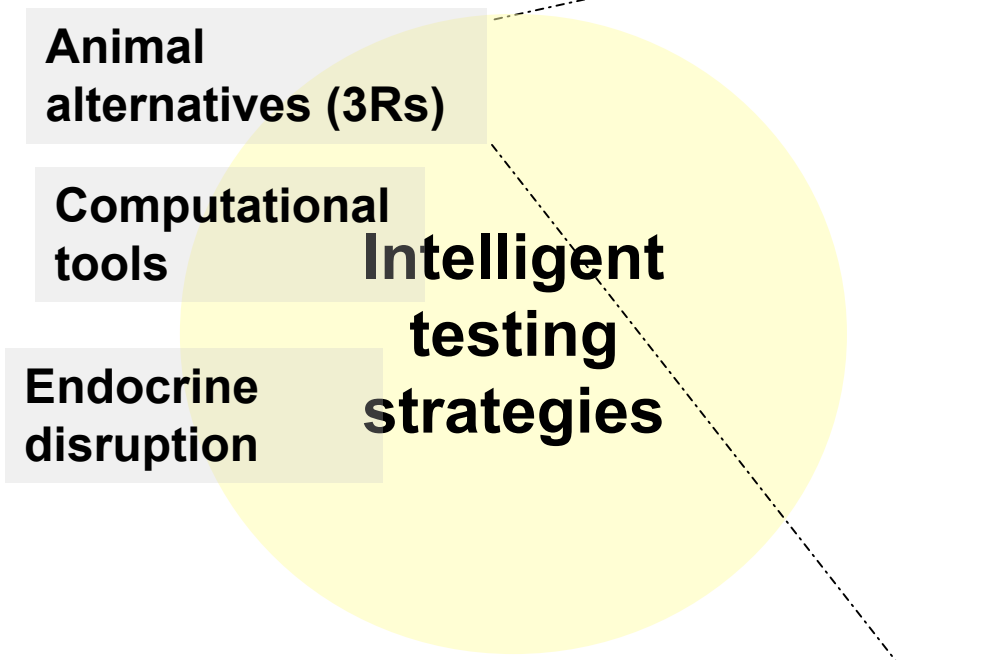


Cefic LRI projects 2007



- New design for reproduction toxicty studies in mammals (replace standard 2-gen reprotox study –TG416
- Work with OECD on computational toolbox
- Contributions within OECD Endocrine disrupter Testing and Assessment framework (e.g. hershberger, uterotrophic, OECD 407))

Cefic LRI projects 2007



- Reduction on number of animals by means of innovative technologies and computational tools (AMBIT data management and OECD tool box)
- Results used by the European Chemicals Bureau (ECB) to build tools such as ToxTree and ToxMatch.
- New design for reproduction toxicty studies in mammals (replace standard 2-gen reprotox study –TG416
- Through Cefic LRI, REACH Implementation Projects (RIPs) have integrated the 3Rs principle

Computational Tools

CEFIC LRI

- Validition criteria for (Q)SARs (Setubal, 2002)
- AMBIT Discovery (Joanna Jaworska & IdeaConsult)
- AMBIT XT (Joanna Jaworska & IdeaConsult)
- Gold-Standard bioconcentration database and repeat-dose toxicity database

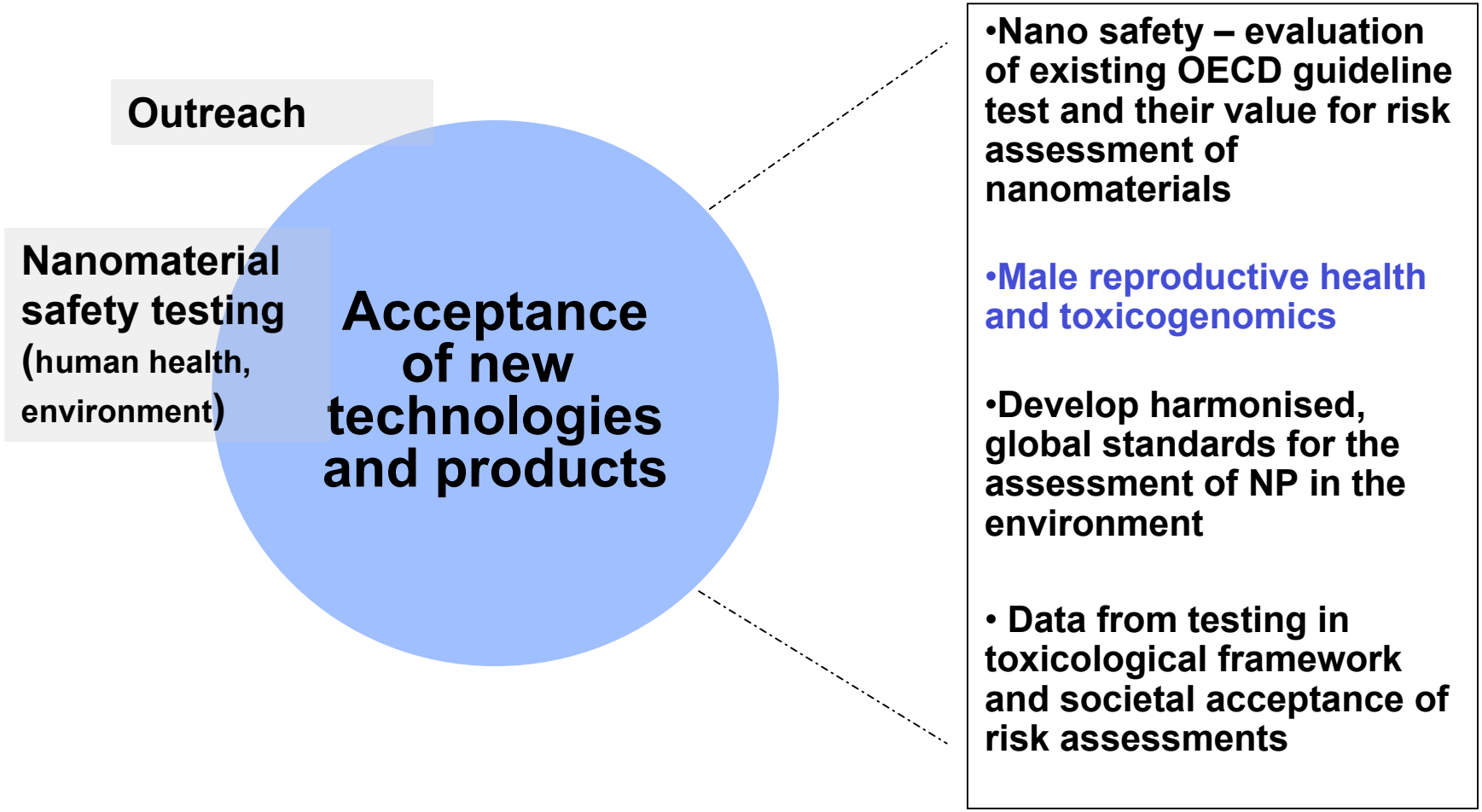
ECB

- TC NES (Q)SAR Ad hoc Working Group
- (Q)SAR Work Programme (Andrew Worth)
  - e.g. ToxMatch & ToxTree (w/ IdeaConsult)
- Reporting formats: (Q)SARs and (Q)SAR predictions
- (Q)SAR database

OECD

- Existing Chemicals (Bob Diederich, Gill Veith)
- Validation criteria (Q)SARs
- Read Across and Categories guidance documents
- Proof of principle Toolbox

Cefic LRI strategic themes 2008



Reprotoxicity studies: current status

- Requirement under REACH for higher tonnages

- New design of mammalian reprotoxicity studies, the « Extended 1-generational vs 2-generational study» was proposed:
  - Cooperation with EPAA, OECD and government bodies
  - Development of triggers/waivers by ECETOC Task Force (www.ecetoc.org)
  - Posibility of approximate reduction of 1500 animals per compound

Current Draft 5 inclusions

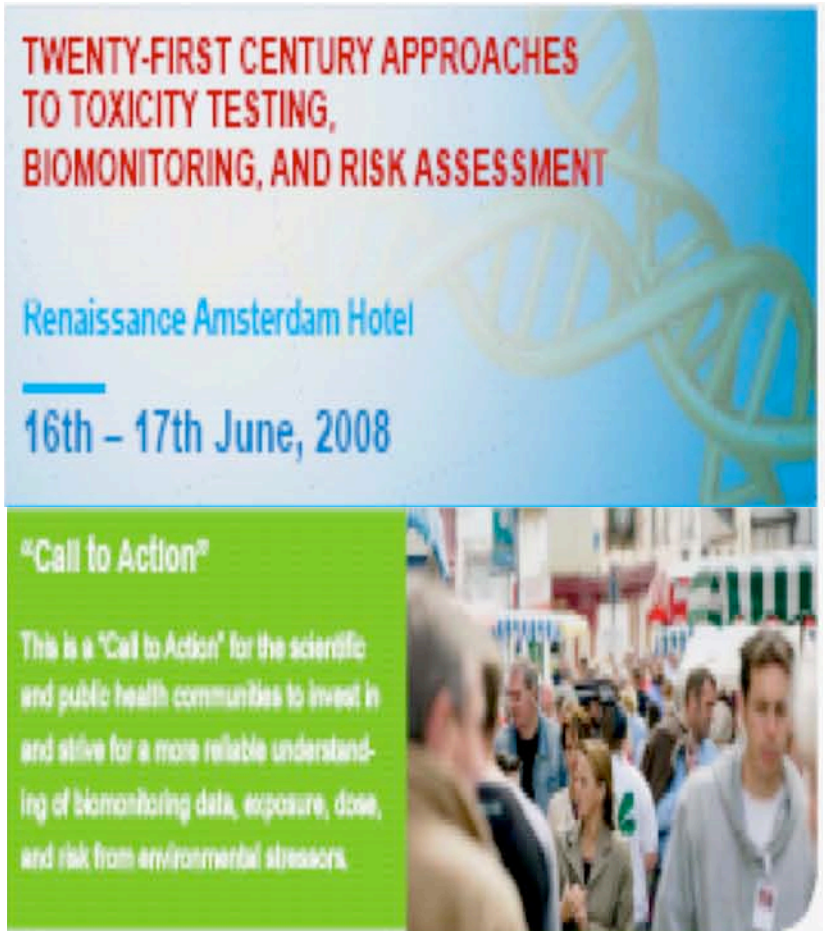
- Default of cohort 1, 2 and 3 for pesticides and for industrial chemicals are mandatory, ignoring tiered assessment approach.

Draft 5 remains to be discussed at the WNT OECD.

Drawbacks of Draft 5:

- **Inclusion of endpoints suggested would result in a complex design for routine evaluation of industrial chemicals (e.g. > 2800 tier 1 chemicals). Only a small number of laboratories would be capable of conducting such a study.**
- **It would increase the potential for additional animal usage in further studies**
- **It will increase the cost for Annex X reproductive testing (currently OECD 416) per substance from 350.000 Euro to approximately. 700.000 - 800.000 Euros**

Twenty-first century approaches to toxicity testing, biomonitoring and risk assessment



ICCA-LRI Global Research Strategy

- **Continuation and extension of biomonitoring conferences**
- **Refocus risk assessment framework to understanding of environmentally relevant doses, enabled by new technologies (e.g. toxicogenomics)**

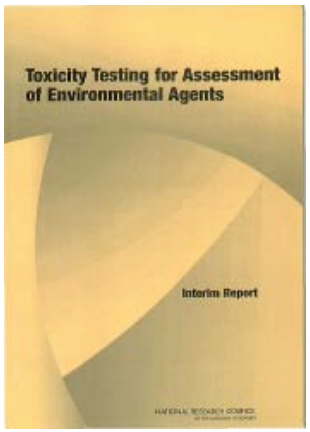
Outcomes

- **Role of new molecular biology techniques on the assessment of impacts of various environmental stressors in relation to human health**
- **Awareness within the industry of innovations in toxicology testing**

Message

- **To engage academics, regulators, government and industry in the appropriate application of innovative toxicology**

The Future Paradigm: Integrating Technology and Risk Assessment



Exposure

Tissue Dose

Biological Interaction

Perturbation

Thinking from Biological Perturbations to Responses

Higher yet

Biological Inputs

Normal Biological Function

Altered Cellular Responses

Adaptive Stress Responses

Cell Injury

Disease

Speakers affiliations

Government bodies

- **Connecticut Department of Health, USA**
- **Environmental Protection Agency (EPA), USA**
- **European Commission, JRC, Italy**
- **Federal Environment Agency (UBA), DE**
- **National Institutes of Health, USA**
- **Centers for Disease Control and Prevention, USA**
- **The National Institute for Public Health and the Environment (RIVM), The Netherlands**
- **Flemish Institute for Technological Research (VITO), BE**

Research Institutions

- **University of Erlangen-Nürnberg, DE**
- **The Hamner Institutes for Health Sciences, USA**
- **University of Ottawa, CA**
- **University of Maastricht, NL**
- **Children's Hospital Osnabrück, DE**

21st Century Approaches

Janus Challenge for risk assessment

opportunity to improve
Less testing through clustering of chemicals activating similar pathways

threat of hazard-based decisions
More testing or by-pass of risk assessments by scare and media

Science has one question and one answer plus 2 new questions

- **Next requests for testing are around the corner beyond 2010**

… next requests for testing are currently developed

Next 5-year cycle

WHO Children Environment & Health - 2009

Next 5-year cycle

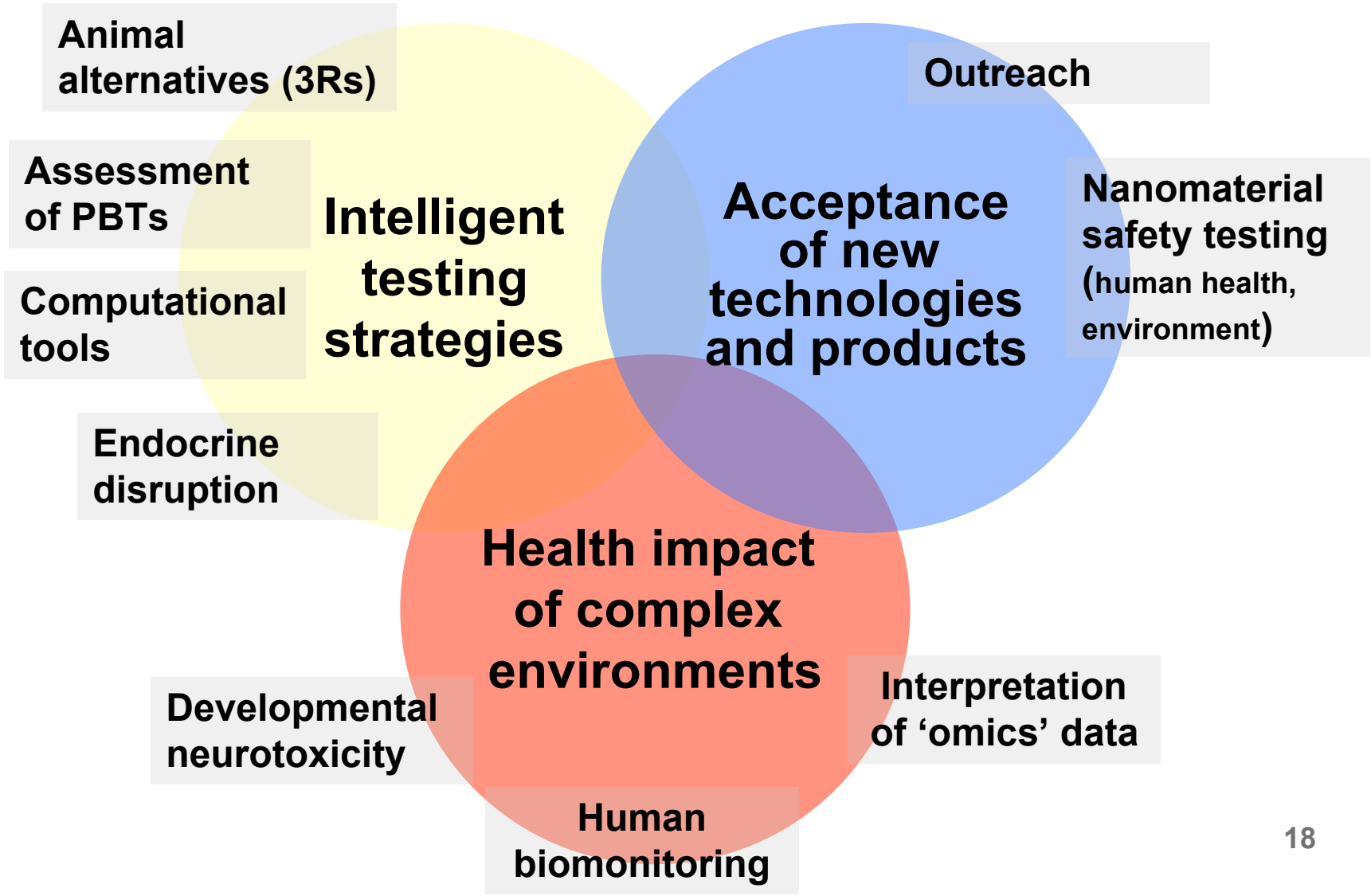
EU Environment and Health Action Plan - 2010

Major points:

- Indoor air policy: focus on chemicals and products
- Human Biomonitoring, new risk assessment methods
- Precautionary principle extended
- Refocus on vulnerable population

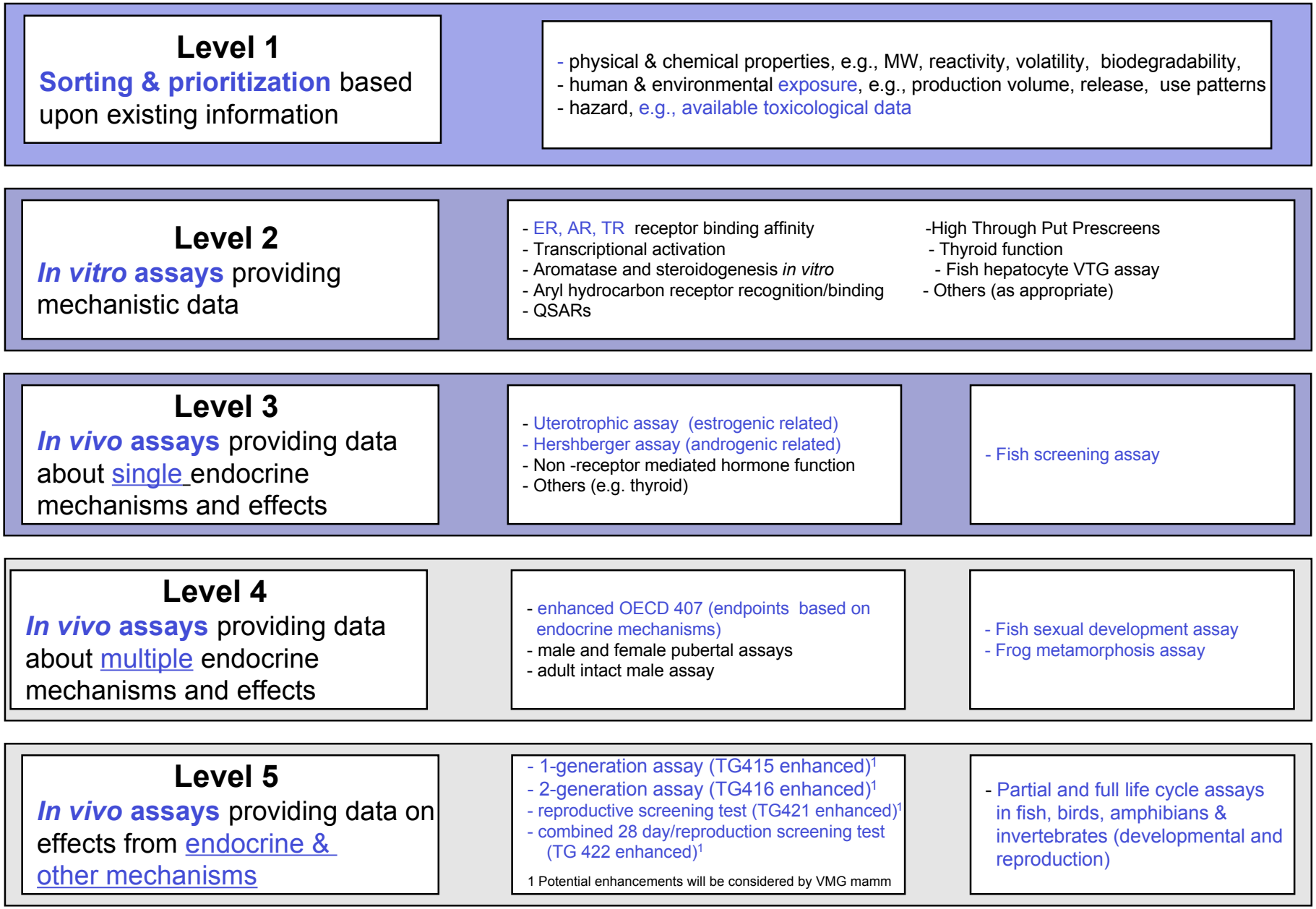
Plus scientists are pushing for mixtures, late effects and low doses

Cefic LRI strategic themes 2008/2009



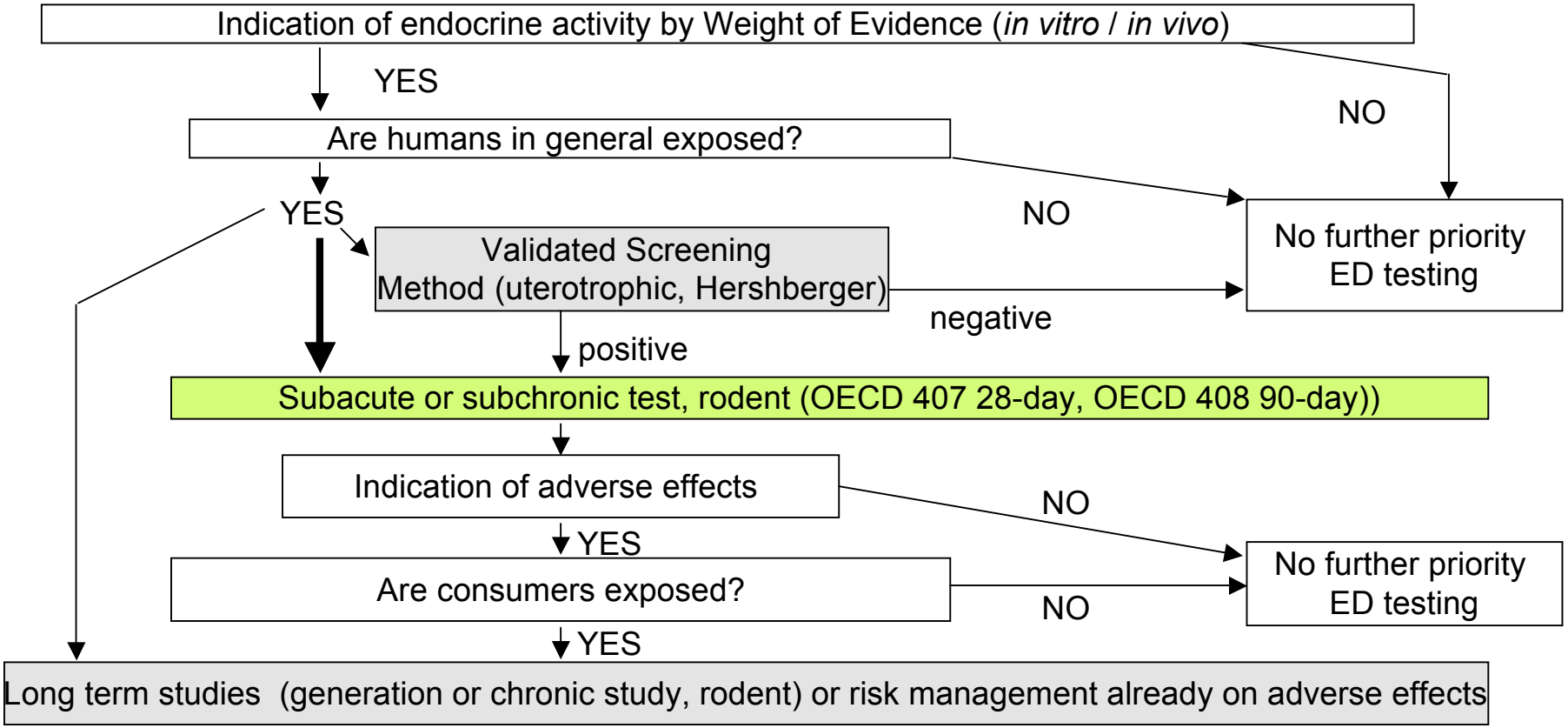
OECD Conceptual Framework* for the Testing and Assessment of Endocrine Disrupting Chemicals

Industry-sponsored development and validation activities



* Framework based on 6th meeting of OECD EDTA Task Force, see www.oecd.org

Decision tree for toxicological testing of substances with indication of endocrine activity



Part of REACH and other regulations

Exact timing is part of the solution