The European Partnership
for Alternative Approaches to Animal Testing

Regulatory Acceptance and Implementation of 3R Approaches

Activities of The European Partnership for Alternative Approaches to Animal Testing (EPAA)

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Introduction

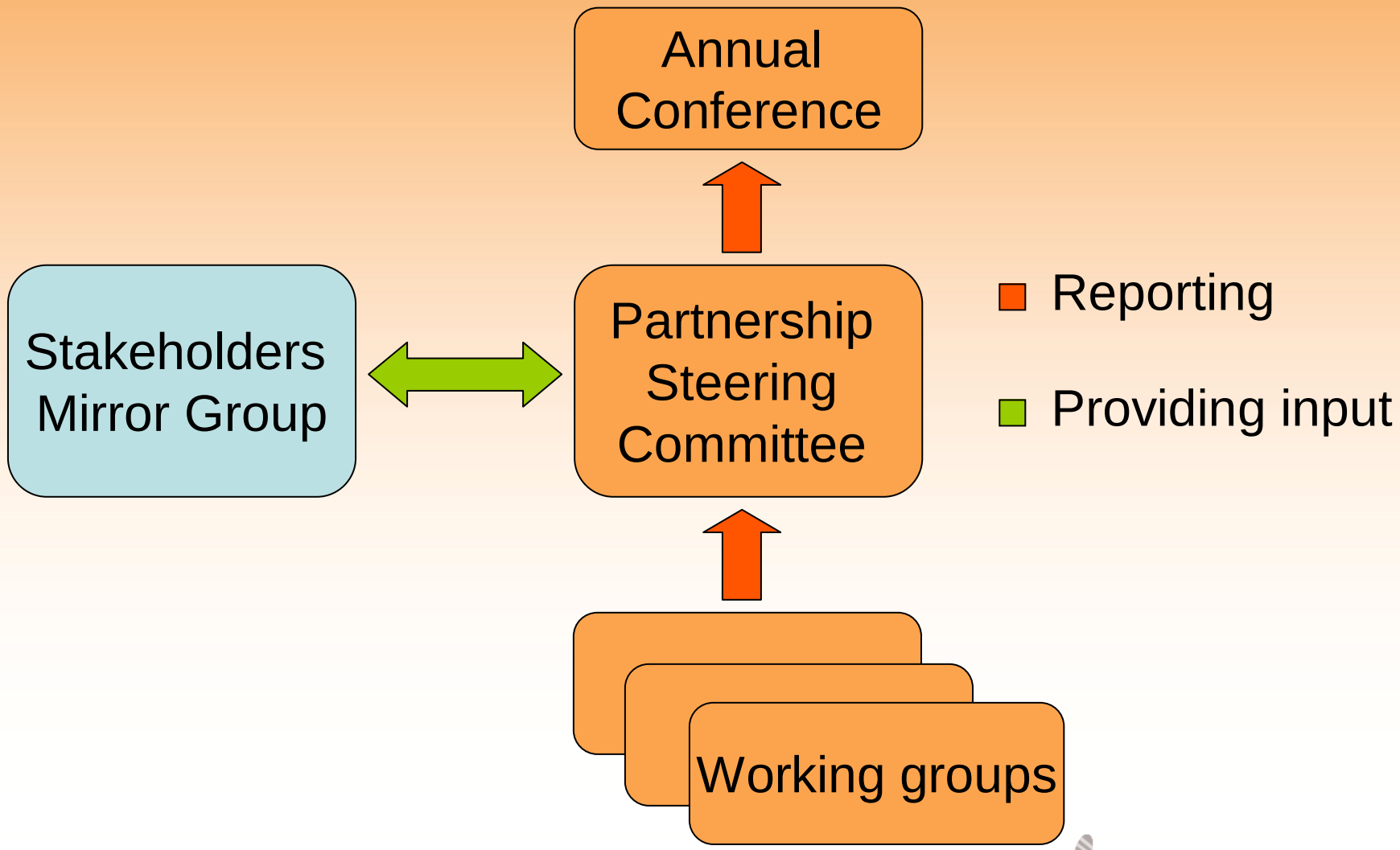
- 3R approaches can only be successfully implemented if the results are accepted by regulatory authorities worldwide

- Therefore, EPAA is dedicated to identify and overcome hurdles of the acceptance of methods and their regulatory implementation

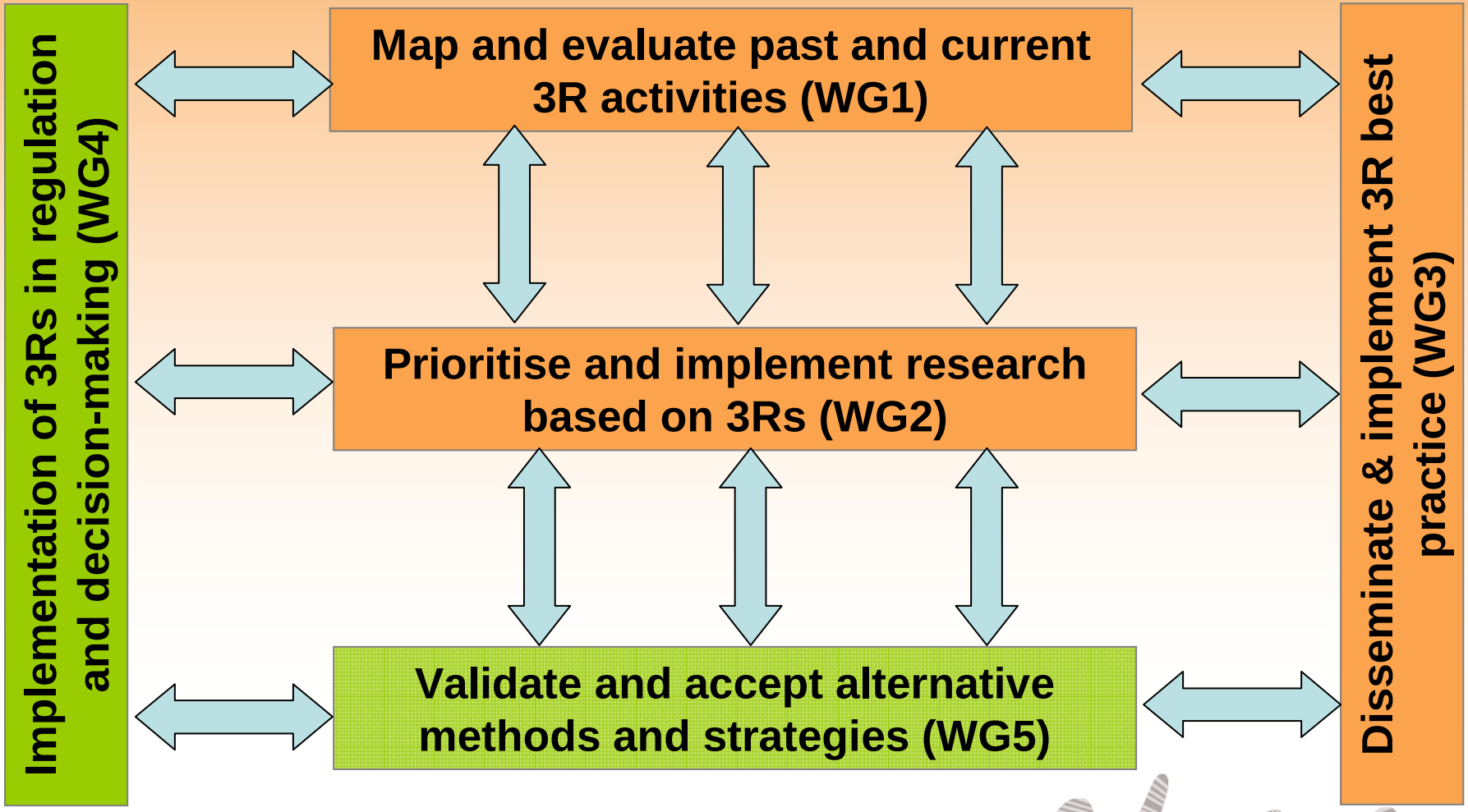
EPAA: Partnership for Alternative Approaches to Animal Testing

- Launch in November 2005
- **Partners**:
  - A joint initiative between the Commission services, more than 35 individual companies and 7 trade federations
- **Objective**:
  - To promote research, development, validation, dissemination, regulatory acceptance and implementation of 3Rs, based on the "Brussels 3Rs declaration"
- **Scope**:
  - Regulatory testing in currently seven industry fields (chemicals, human and veterinary medicines, cosmetics, hygiene products, crop protection, biotechnology)
- More information: **www.epaa.eu.com**

The EPAA Structure



The EPAA Action Programme:
5 Interlinking Themes Dealt by 5 Working Groups



Regulatory Acceptance and Implementation of 3R Approaches

- Analysis of **regulatory requirements** and **major drivers** behind regulatory testing: potential hot spots and issues for further discussion in various sectors
- Identification of potential **hurdles** for uptake of 3Rs techniques, e.g. precautionary principle, liability issues
- **Statistical reporting** of animals in regulatory testing: May it facilitate and confirm the implementation of the 3Rs?

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- Identifying and promoting opportunities to facilitate and accelerate the **validation and acceptance** procedures
- Understanding sector-specific **acceptance criteria**
- Analysing **case studies** to identify barriers and delays to validation and regulatory acceptance
- Enhanced collaboration between industry and ECVAM to prioritise and facilitate the validation of alternative methods/strategies

Different Sectors and a Plethora of Regulations

Chemicals: 67/548/EEC, REACH, GHS …

Human and Veterinary Pharmaceuticals: 2001/83/EC, 2001/20/EC, ICH Guidelines…

Animal protection: Directive 86/609/EC

Cosmetics: 76/768/EEC, 7th amendment …

Agrochemicals/ Crop Protection: 91/414/EEC…

Food&Feed: EC/178/2002, 89/107/EEC …

Product liability: 85/374/EC…

Activities in 2007 Involving Relevant Stakeholders

- Workshop on Regulatory Acceptance

  http://ec.europa.eu/enterprise/epaa/wg_5_1.htm

- Meeting on Statistical Reporting

  http://ec.europa.eu/enterprise/epaa/wg4_statistical_reporting_3rs.pdf

- EPAA Annual Conference: Regulatory Acceptance as Main Theme

  http://ec.europa.eu/enterprise/epaa/conf_2007.htm

Major Outcomes were Related to

I. Analysis of sector-specific requirements: regulation, acceptance criteria

II. Linking validation and acceptance

III. Usefulness of current statistical reporting

IV. Relation between legal issues and scientific criteria

V. International dialogue

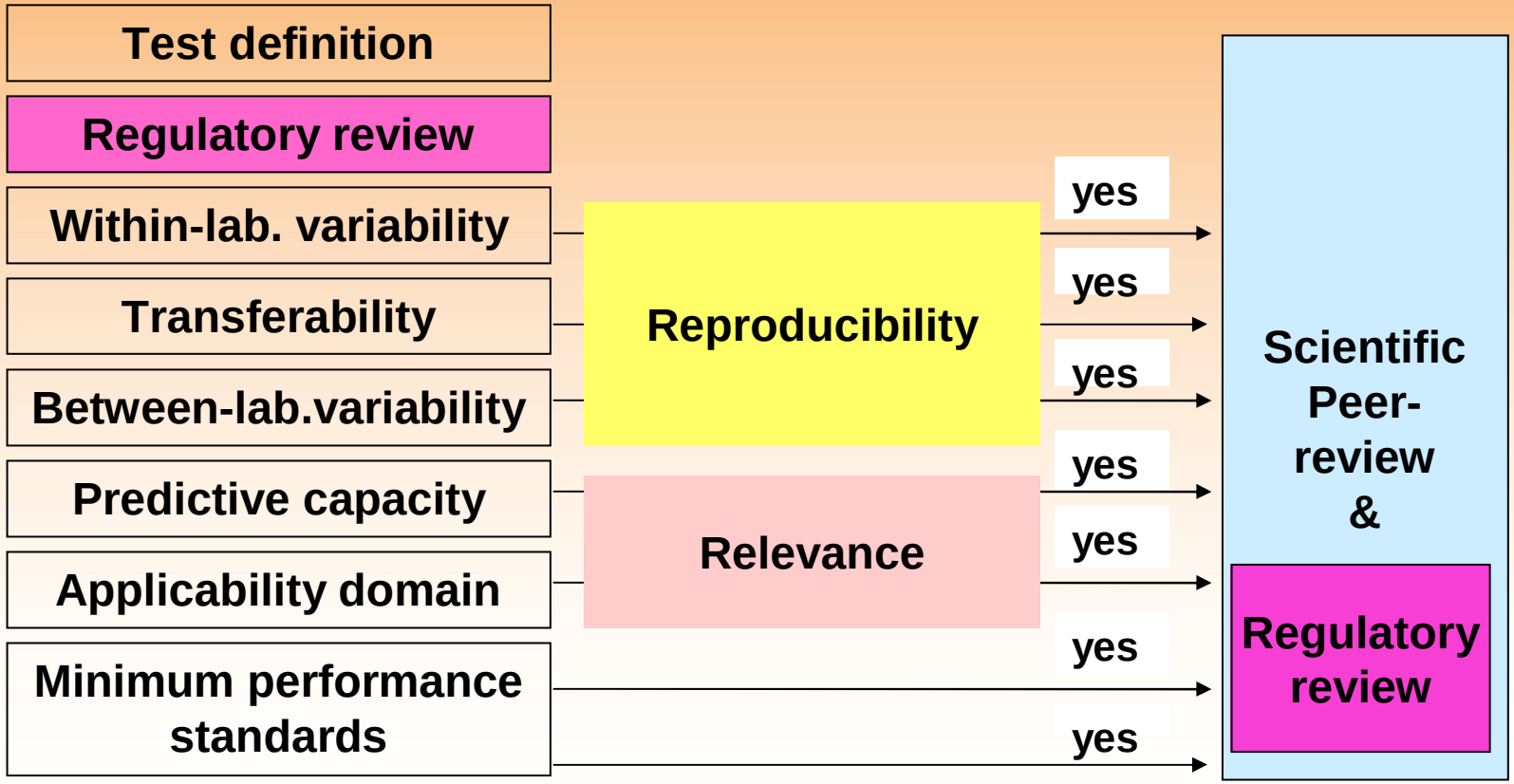
I. Sector-specific Requirements

- Requirements differ depending on the respective legal framework
- Mandatory (regulation) and flexible elements (guidelines/guidance) may exist
- Some sectors benefit already from an international process like ICH, as well as from an integration of regulators, industry and academics

II. Linking Validation to Acceptance and Implementation

- In order to enable efficient uptake and acceptance of 3R methods, validation and acceptance should go hand in hand
- Scientifc robustness is a main driver for acceptance
- Regulators, and also other potential users of a method should be involved already in early stages of the process: dissemination, training, feedback

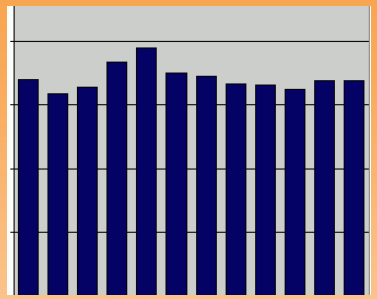
Suggested Expanded Modular Approach to Validation: element of building trust in a method



Securing regulatory relevance and acceptance to trigger more support from all stakeholders : ECVAM's proposal for ERAP (European Regulatory Advisory Panel)

III. Statistical Reporting of Animals:

Suitability of Current Statistics



- Statistics are not the appropriate tool to measure the success of alternative approaches in general
- Only limited aspects of the 3Rs might be detected: changes in the use of specific methods, changes in testing per product type, switch from “higher” to “lower” species, severity where it is reported
- Revision of Directive 86/609/EEC ongoing including the requirements for statistical reporting
- **EPAA to identify other ways of assessing the uptake of 3R approaches**

IV. Legal Issues and Scientific Criteria

- „Duty of Care“- safety needs to be ensured in the first place (precautionary principle referred to e.g. in REACH)
- „Burden of Proof“- sufficient data and justification is required: Methods need to be scientifically acceptable / accepted
- Which data is acceptable or is the best data?
- **Liability is linked to the state of scientific and technical knowledge**

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State of Scientific and Technical Knowledge - Toxicology Paradigms at Stake

- Following the current paradigm, animal tests in many cases are seen as the “gold standard”, but might also lack validation
- There is less experience with data from alternative methods in risk assessment
- Regulators and safety assessors might not accept a method as such, but as a precaution only acknowledge positive results

V. International Dialogue

- Cross-sectoral exchange useful (data, experience)
- Global dimension: Regional implementation of 3R methods usually impossible - authorities from different countries often require different data
- More transparency and efficient communication between regulators, industry and “xCVAMs” required
- Interlinked processes and efficient mechanisms needed
- **An international regulatory dialogue is essential for global acceptance**

Conclusions

Industry and regulators have a common challenge: Securing best safety for human health and at the same time applying alternative approaches wherever possible

EPAA's role is to provide a platform for communication and information exchange in order to accelerate acceptance and implementation, with a specific emphasis on cross-sectoral links.

→ Further actions will be identified and reviewed with appropriate key players

Outlook

- Follow-up on WS on regulatory acceptance and Annual Conference outcomes: Addressing barriers to acceptance
- EPAA workshop at ECVAM addressing barriers to validation
- Setting up new “horizontal”, cross-sectoral case studies, e.g. on acute toxicity testing requirements throughout sectors
- Monitoring implementation of existing and new regulation: scope for optimisation of 3Rs uptake (e.g. REACH)

Thank you for your attention!