Realistic Basis for Implementation of Legislation and Alternative Methods?!

(And what to do next?)

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Agenda

- Introduction: Deadlines, wishes
- Overview of the diverse legislation to be implemented:
  - consequences
- Realistic basis? Examples – current and previous ones
- How to deal with EU-member states, Europe, US, and the World?
- Postulation: further developing science in parallel, harmonization and internationalization

INTRODUCTION

1 - Deadlines, a political measure!

2 - Wishes, not constructive (solutions) approaches!

DEADLINES

A deadline, almost forgotten:

Goal 2000: 50% reduction of all European animal experimentation

Did not work, because…

- basic figures for 100%
- Future science not known
- Legislation such as REACH, resp. aspects such as Endocrine Disruption not included

Lesson

- Try to find the best knowledgeable basis (experts!)
- Adapt always in the course of events
- Stick to science progressing, and watch (out for) it!

And there was…

And there was…

…much more reduction in industrial early research experimentation than in regulatory / safety testing due to progress of science than during the time that goal was formulated and present in the political arena.

(Quote from the 1st START-UP Expert Workshop, Madrid, 2008)

Progress of science was not induced by the goal setting, but by academic and industrial endeavour!

(RIAs developed, HTScreening and Robotics developed, etc.)

THAT BROUGHT SOLUTIONS TO THE TABLE!

Lesson learned?!

Text quotes in Cosmetics Directive (No. 2003/15/EC)
and Opinionated Paper:

YES

Quote Cosmetics Directive:
"…2009 deadline fixed for certain testing, but 2013 adaptable/flexible: „„"

NO

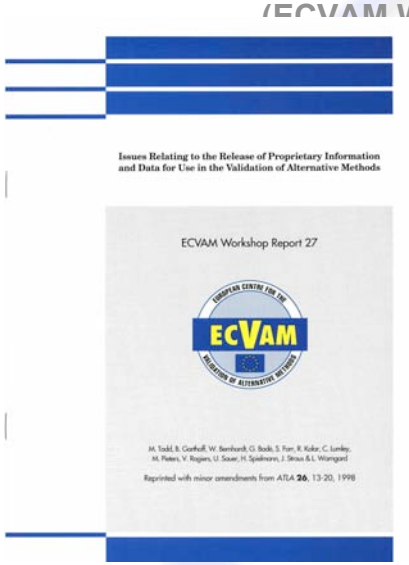
Quote from the Th. Hartung-paper (ALTEX 25, 3/08, p. 159)
"…Thus the 7th amendment represents the starting point for this important private/public partnership (i.e. the EPAA). Another reason to be happy about the political 'victim'…"

- **So, deadlines are political measures and means to satisfy requests of citizens, NGOs and own supporters!**
- **And, they have nothing to do with solid science!**
- **And, are they, and should they be enforced, NO MATTER WHAT?**

WISHES

- Issues with option to tap into original data, in-vivo e.g. (originator, IP-data, „task-force“-data)
- A problem recognized early-on:

(ECVAM Workshop Report No. 27, Munich, ATLA, 26, 1998, p 13-20):



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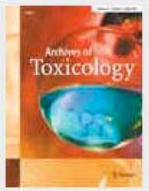
J and Spi , Archives of Toxicology, a) 75, 1-21, 2001 and b) 79, 615-626, 2005)

Rainer J. Box[1] and Horst Spielmann[1]



Use of the dog as non-rodent test species in the safety testing schedule associated with the registration of crop and plant protection products (pesticides): present status

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The use of dogs as second species in regulatory testing of pesticides. Part II: Subacute, subchronic and chronic studies in the dog. [Journal Article]
Arch Toxicol 2001 Mar; 75(1):1-21.

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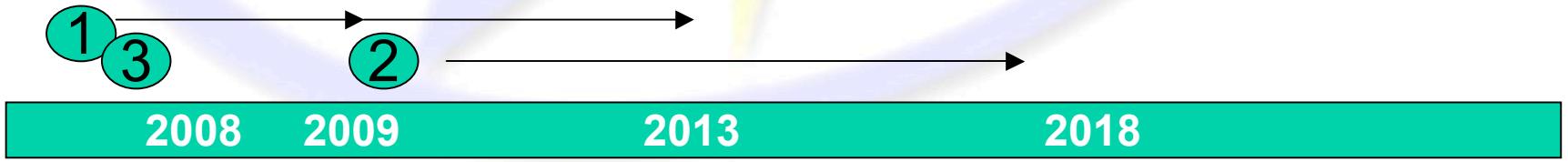
esp. in a.i. industry

LESSON

- Wishes that do not take into account realities/legislation (IP patent laws, antitrust laws) will not be heard and followed
- Rather go for a world-wide harmonized approach (and add solutions to the formulated wish!)

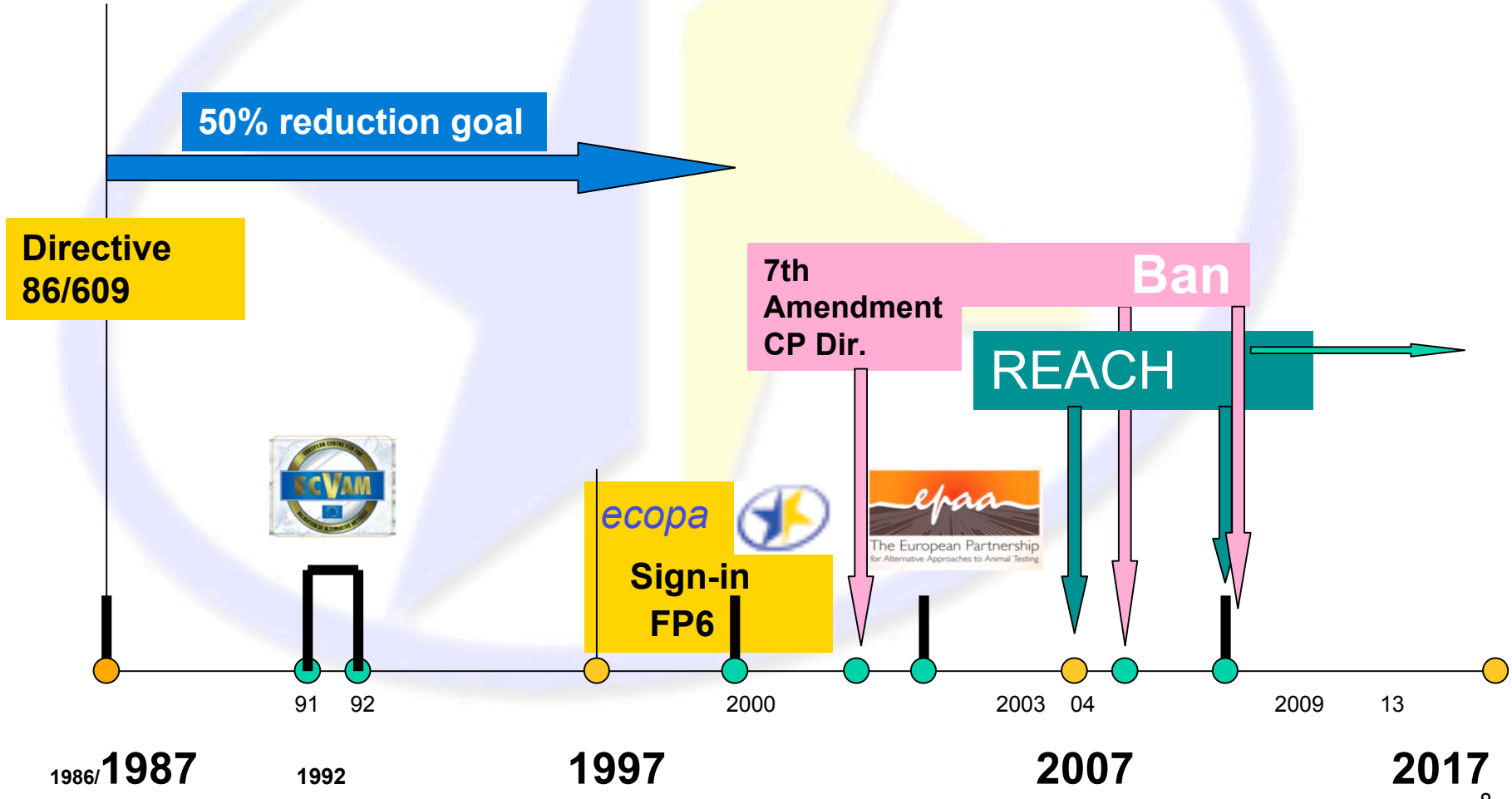
Overview of the diverse legislation/timelines to be implemented

- **1 (Novel of) Cosmetics Directive: 7th Amendment**
- **2 (Novel of) Animal Welfare Directive 86/609**
- **3 REACH legislation, timelines**
- **4 Others, such as PPP ("Pesticides") Directive 91/414**



Dir 86/609

Time to check and think – two decades



Overview of the diverse legislation/timelines to be implemented

- **Consequences**
- **Changes**
- **Parliamentary discussions and decisions in the EU**
- **However, not all hindrances, costs and implications such as EChA workload was / could be foreseen...**

  ...nor the intermediate progress in regard to science / research and development of alternatives, though important (REACH para on adaptation e.g.)
- **Introduction of waiving (Annex XI)**

Learning curve

- New ideas about waiving animal safety-testing- experiments:

  - REACH Legislation, Annex XI
  - "Testing does not appear **scientifically** necessary

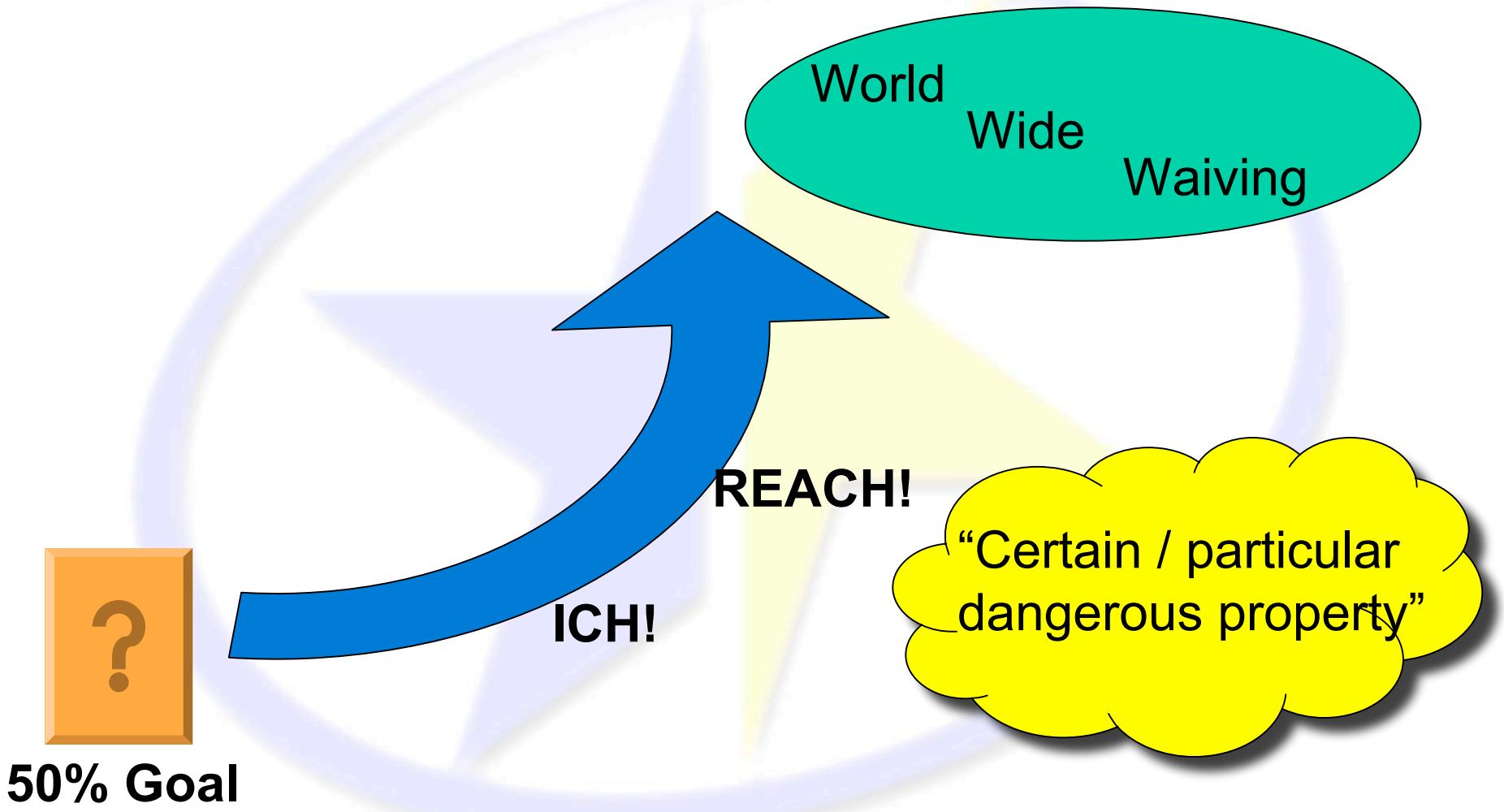
    - Use of existing data …
    - Weight of evidence …
    - Qualitative or Quantitative Structure-Activity Relationship ((Q)SAR)
    - In-vitro-methods …
      - .."suitable* in-vitro methods" …
    - Grouping of substances and read across approach

  2./3. "Other reasoning: technically not possible, exposure scenario,.."

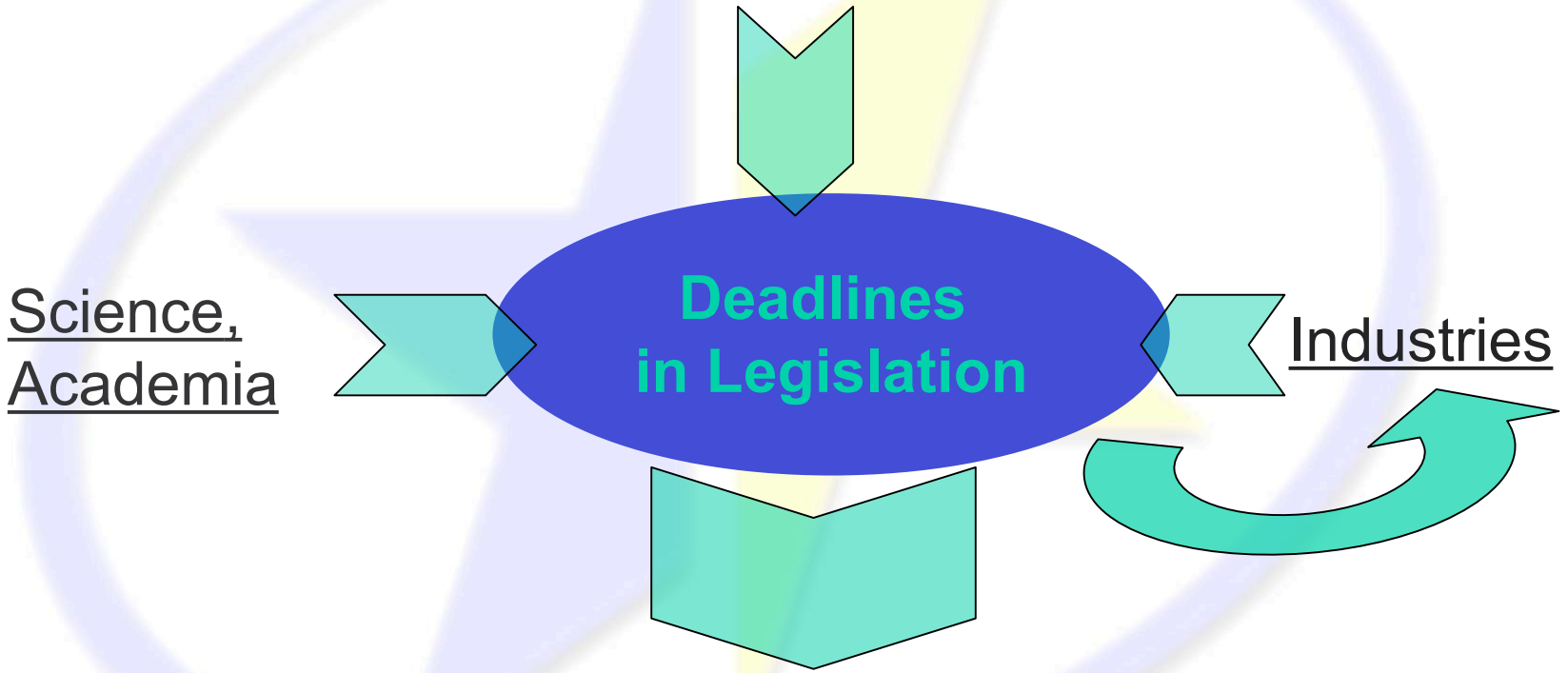
"Certain / particular dangerous property"

* suitable: i.e. sufficiently well developed according to **internationally** agreed test development criteria (e.g. ECVAM entry)

Learning curve - 2



Public/European Citizens
NGOs
Legislators (MS, EP, et al)



Regulatory Authorities
(worldwide)
Compared to the „former“ basis

Realistic Basis?

Examples for „typical“ obstacles in the development and final acceptance:

- **Extended** „one-generation study“: the case of OECD now in „typical“ OECD battle,
  Remember? Case of „AcuteTox“-refinement strategies
- **Skin tests:** the case of “colours/dyes” ,worldwide approach, but was it sound science?
  Basis questionable!
- **EST:** the case of ‘ambition’
  validated, but limited to certain areas, claims, but user-experience neglected!

Realistic Basis?

Are we asking too much from the regulators?

(given, the basic data are sometimes too shaky, or not yet sufficiently familiar to them)

And then request them to accept in vitro because of the deadlines? Though the basis is not there, yet

Quote from the carcinoGENOMICS FP6-project:

„Requirements

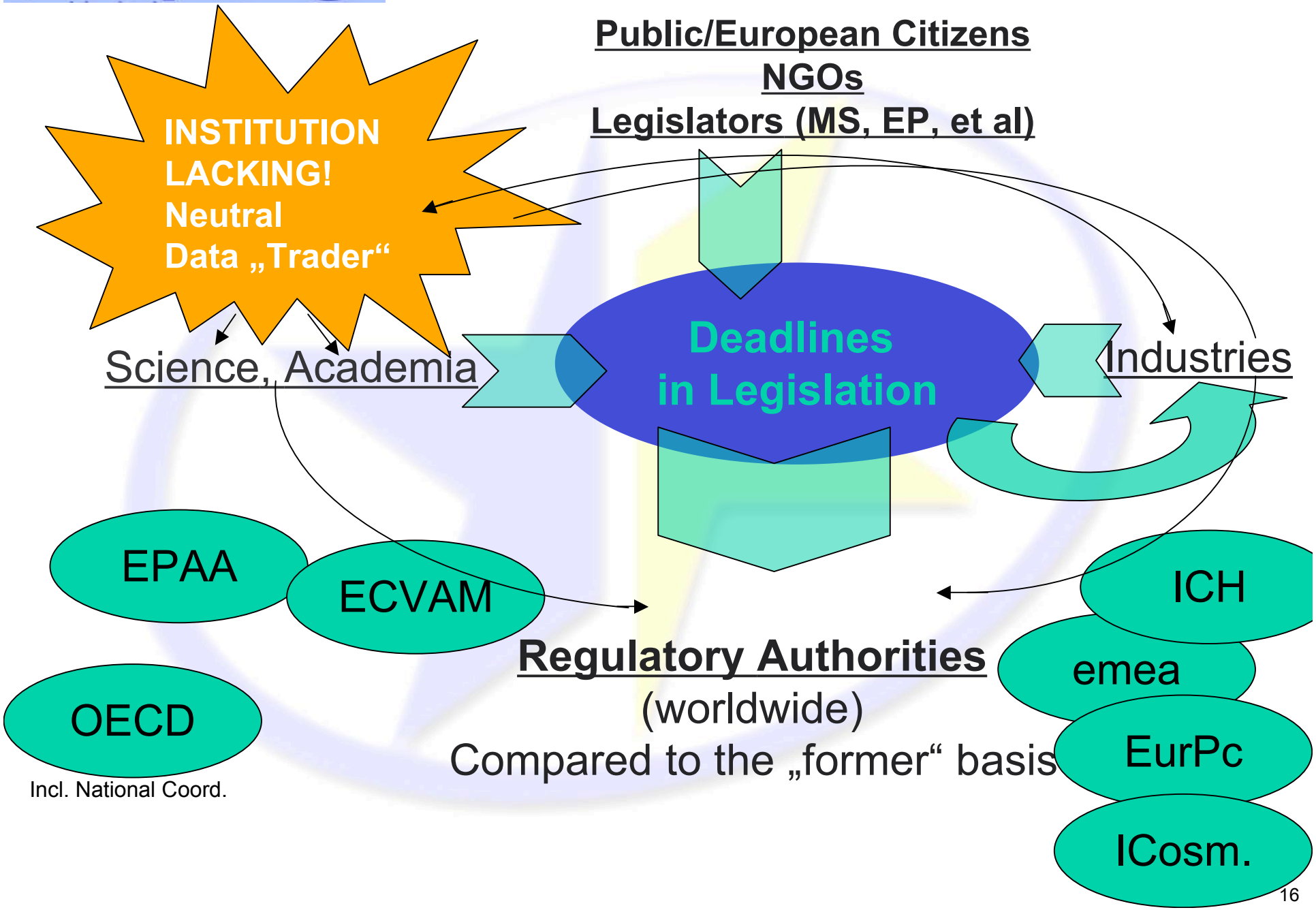
•In order to enter a new phase in the developmental process, in which regulatory authorities can be involved, we need newly developed models that are robust and have proven to be acceptable for some classes of chemicals
• The new models must be well defined and the area of application must be clear
• Clarity on what is expected from the regulatory authorities“

How to deal with the EU member states, Europe (E.C.), US, and the World?

- **Work on a worldwide scale!**
  Best example of the past, certainly saving most animals lifes in pharmaceuticals:
  International Conference on Harmonization ICH
- **Basis must be: solid scientific, undisputable data, supplied by potential users**

- **Comparative data** (of former decision basis) for waiving e.g.
- **To be supplied:** how to do?

Develop / Implement a neutral institution
that can assist in codifying and disseminating, e.g. existing in-vivo-data


Public/European Citizens
NGOs
Legislators (MS, EP, et al)
INSTITUTION
LACKING!
Neutral
Data „Trader“
Science, Academia
Deadlines
in Legislation
Industries
EPAA
ECVAM
OECD
Incl. National Coord.
Regulatory Authorities
(worldwide)
Compared to the „former“ basis
ICH
emea
EurPc
ICosm.

Postulation

- **Given the experience of the past,**
  accepting some of the lessons of the past,

  - Legislation should not „operate“ only on wishful deadlines
  - Rather „bet“ on science developing, enforce ww-harmonization, and for the benefit of all
  - Put much more emphasis on internationalization (when „talking“ alternative 3 Rs methods“)

Postulation no. 2

ecopa always proposed solutions with their requests (EU Chemical legislation and FP projects), therefore, here the next step

For potential international exchange of data,
create a neutral institution, legally independent
and a non-for-profit-organization:

INTERXALT

International Institute for Exchange of Data for Alternative Method Development

Should be followed-up in a FP7-project!

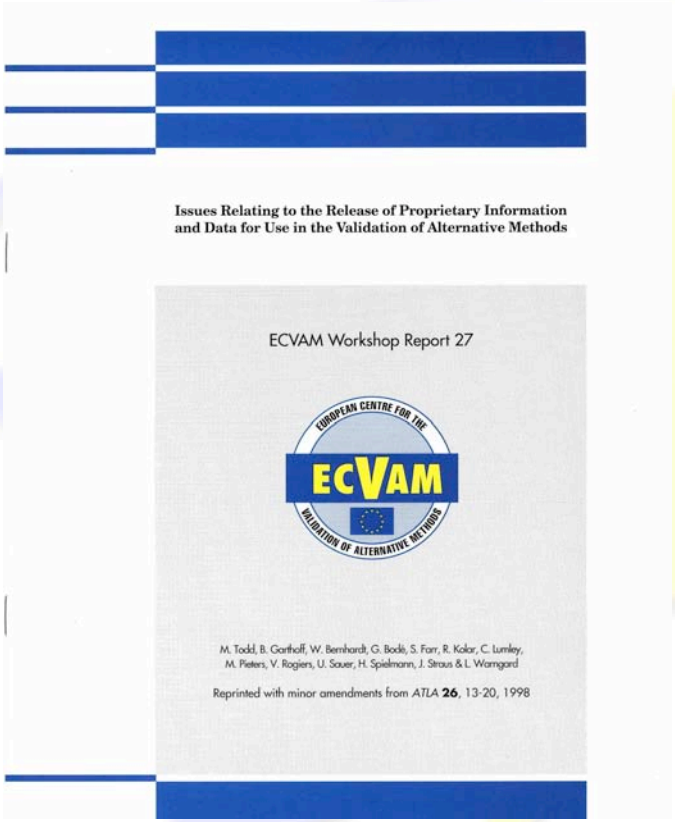
Thank you for your attention!

Let me wish you

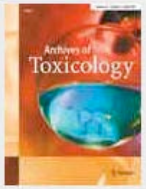
- a Merry Xmas and

- a Happy New Year!

- Back-Ups


Issues Relating to the Release of Proprietary Information and Data for Use in the Validation of Alternative Methods
ECVAM Workshop Report 27
EUROPEAN CENTRE FOR THE
ECVAM
VALIDATION OF ALTERNATIVE METHODS
M. Todd, B. Garthoff, W. Bernhardt, G. Bode, S. Farr, R. Kolar, C. Lumley, M. Pieters, V. Rogiers, U. Sauer, H. Spielmann, J. Straus & L. Warngard
Reprinted with minor amendments from ATLA 26, 13-20, 1998

Rainer J. Box[1] and Horst Spielmann[1]



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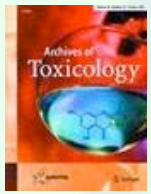

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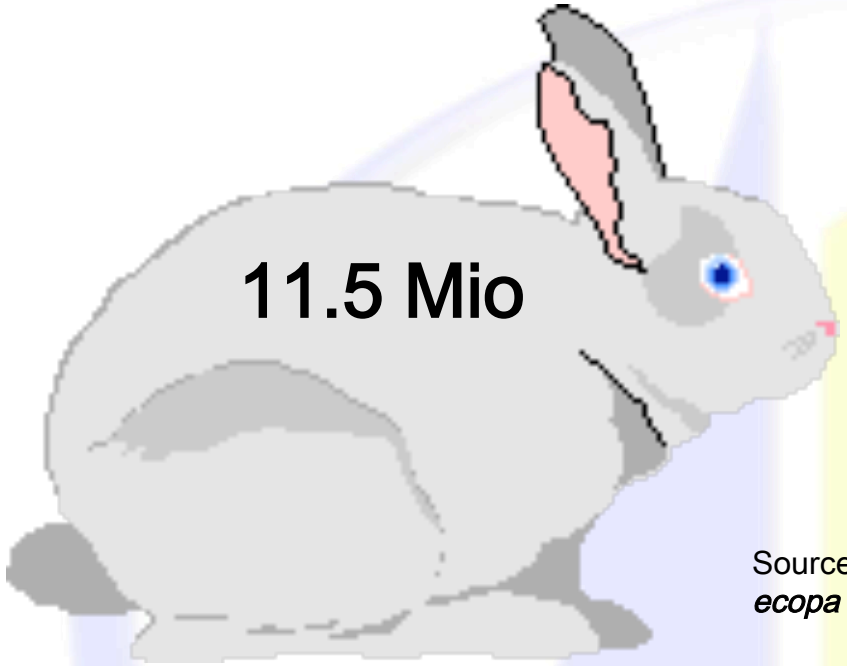
Numbers in hind sight:



The Numbers' Game…

Source: J. Vogelgesang, DG XI
ecopa Workshop 2001

ecopa statement in regard to EU Chemical Policy:

„…DGs involved immediately initiate a thorough analysis on potential animal experiments induced by the regulations, and on the realistic availability of alternative tests, under neutral guidance and chairmanship by an organisation such as *ecopa* ."

Source: *ecopa* website 2003

Learned the lesson!

Directive 2003/15/EC of the European Parliament and of the Council of 27 February 2003

"(2.3) The Commission shall study progress and compliance with the deadlines as well as possible technical difficulties in complying with the ban. […]
If these studies conclude, at the **latest two years** prior to the end of the maximum period referred to in paragraph 2.1, that for **technical reasons one or more tests** referred to in paragraph 2.1 **will not be developed** and **validated** before the expiry of the period referred to in paragraph 2.1 it shall inform the European Parliament and the Council and shall put forward a legislative proposal in accordance with Article 251 of the Treaty."