



Europe goes alternative... contributions to reduce animal testing

Thomas Hartung & ECVAM Team

*Joint Research Centre, European Commission
Institute for Health and Consumer Protection (IHCP)
Ispra (Va), Italy*

<http://ecvam.jrc.it>





ECVAM



- Animal welfare directive 1986 (86/609/EEC)
- Established 1991, 61 staff members
- 16 alternative methods validated until 2002
- Business plan and reorganization 2003 responding to **7th amendment of the cosmetic directive 2003** emerging **REACH legislation 2007**
- 9 methods validated 2006
- 5 methods expected April 27th 2007
- Focus FP7: more drug, vaccine, food plus **CORRELATE**



Purposes of animal experiments in 2002 (EU-15, statistics DG Environment)

Total number	10,700,000	100%
Safety evaluations	1,060,000	10 %
Agricultural chemicals	123,000	1 %
Industrial chemicals	136,000	1 %
Cosmetics	2,700	0.025%



**Cosmetics' ingredients are tested
as chemicals**



Often forgotten: there was good reason to introduce animal experiments, e.g. Draize eye test

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This is the manufacturer's version of the effect of this aniline eyelash dye.

The New and Improved Eye, Brow and Eye Lash Dye

LASH LIFE

Radiates Personality

Total blindness was its actual effect in at least one instance.

Before

After



3R Success stories



OECD acceptance of ECVAM validated methods:

- **1999-2001**
 - **Refine:** Painless test for skin sensitisation
 - **Reduce:** Animal numbers for acute tox. from 45 to 8 (REACH: 1.1 million saved)
- **2004**
 - **Replace:**
 - phototoxicity
 - skin corrosion



Cosmetics industry and the 7th amendment



- **EU: 2.000 companies, 60 billion € turnover**
- **EU: 5.000 new products per year, 25% turnover with products released within last 6 months**
- **Marketing ban if testing finished products or not using ECVAM-validated methods since 2003**
- **Phasing out ingredient testing with test and marketing bans in 2009 and 2013**
- **Critical need for alternatives**



Chemical industry and REACH

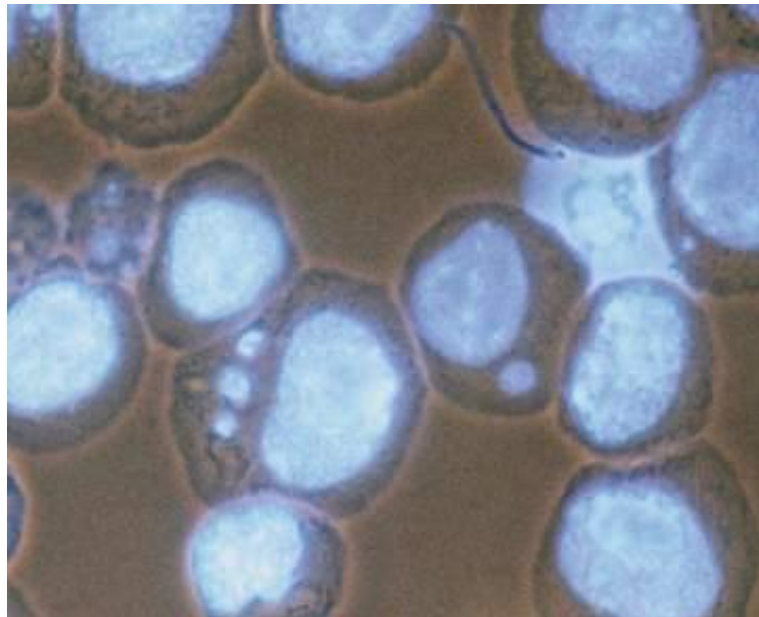


- EU: 27.000 companies (96% SME), 590 billion € turnover = 33% of world market, 1,7 million employees
- EU: occupational skin disease cost 3 million work days per year, i.e. about 600 million €
- 86% of toxicological data on 'old' chemicals are lacking
- REACH will assess 30.000 chemicals marketed >1 ton/year
- Expected 180.000 preregistrations 2009, 70% of testing 2011-2017
- Alternatives increase test throughput and reduce costs and animals



Validated 2006: Mutagenicity

- **Micronucleus test improves in vitro assessment for mutagenicity / genotoxicity**
- **First validation based only on a compilation of existing data, no new study**
- **Completed in two years, within one month included in REACH legislation**
- **Currently considered by OECD and ICH (International Conference on Harmonisation)**



- **Accelerated validation**



Validated 2006: Acute Ecotoxicology



- Test strategy developed and validated by ECVAM and European Chemical Bureau within two years
- Saves 60% of fish
- Implemented for REACH saving 170.000 fish and 23 million € testing costs
- Submitted to OECD, EMEA etc.



Expected validity: Skin irritation

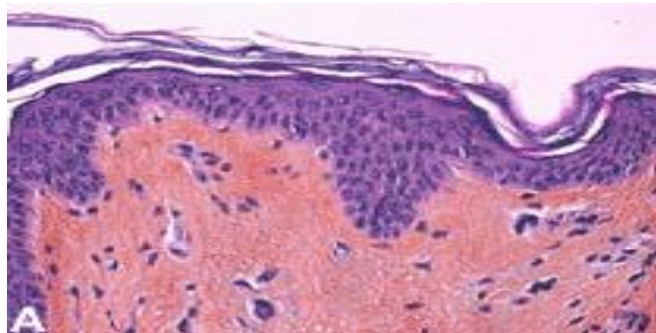
- Rabbit test for drugs, chemicals and cosmetics introduced 60 years ago
- Validation study 2003-2006 of three models with 9 labs (2 U.S.), 58 test chemicals
- Best model (Episkin), optimized in an FP4 DG RTD contract, **represents a full replacement**



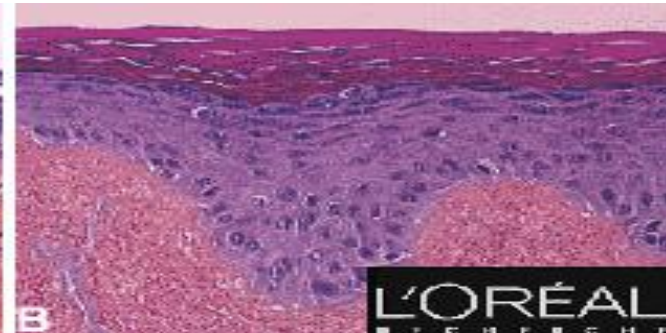


Artificial human skin

- Biotechnology product originally to treat burn patients
- 5 European and 1 American producer
- Forerunner Episkin opens the avenue for others to follow
- 2009 deadline of cosmetics directive, 10.000 REACH substances



Skin



Reconstructed epidermis EPISKIN



Expected validity: Eye irritation



- Retrospective evaluation with U.S. ICCVAM
- 4 tests analyzed, 2 qualify for the detection of severe eye irritants confirming an ECVAM analysis of 2003
- 8 other assays and the suitability for mild irritants currently under evaluation
- Intense collaboration with COLIPA
- REACH 10.000 substances; critical for cosmetics 2009



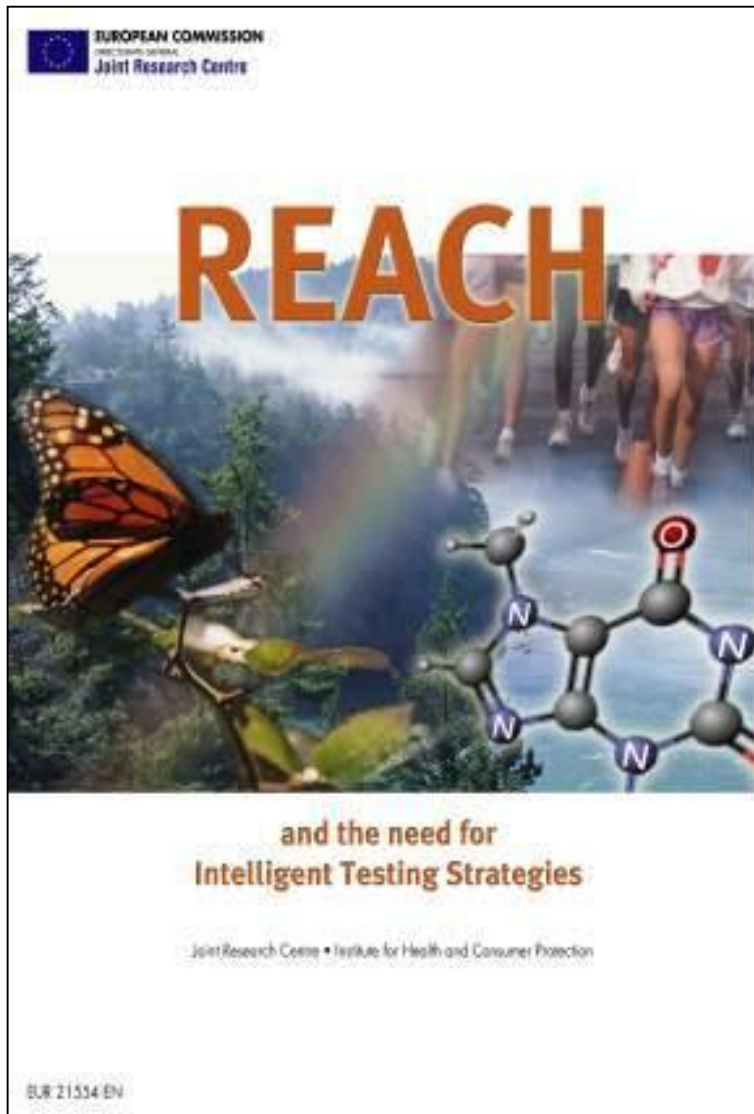
Expected validity: Skin allergy



- OECD accepted, validated alternative method (Local Lymphnode Assay) is the reference method for 30.000 REACH chemicals
- Test strategy to test only highest dose results in 50% less animals with <1% of substances missed
- Concept by ECVAM task force 2006
- Foreseen already in REACH test strategy (saves 240 thousand mice)



Test strategy development for REACH

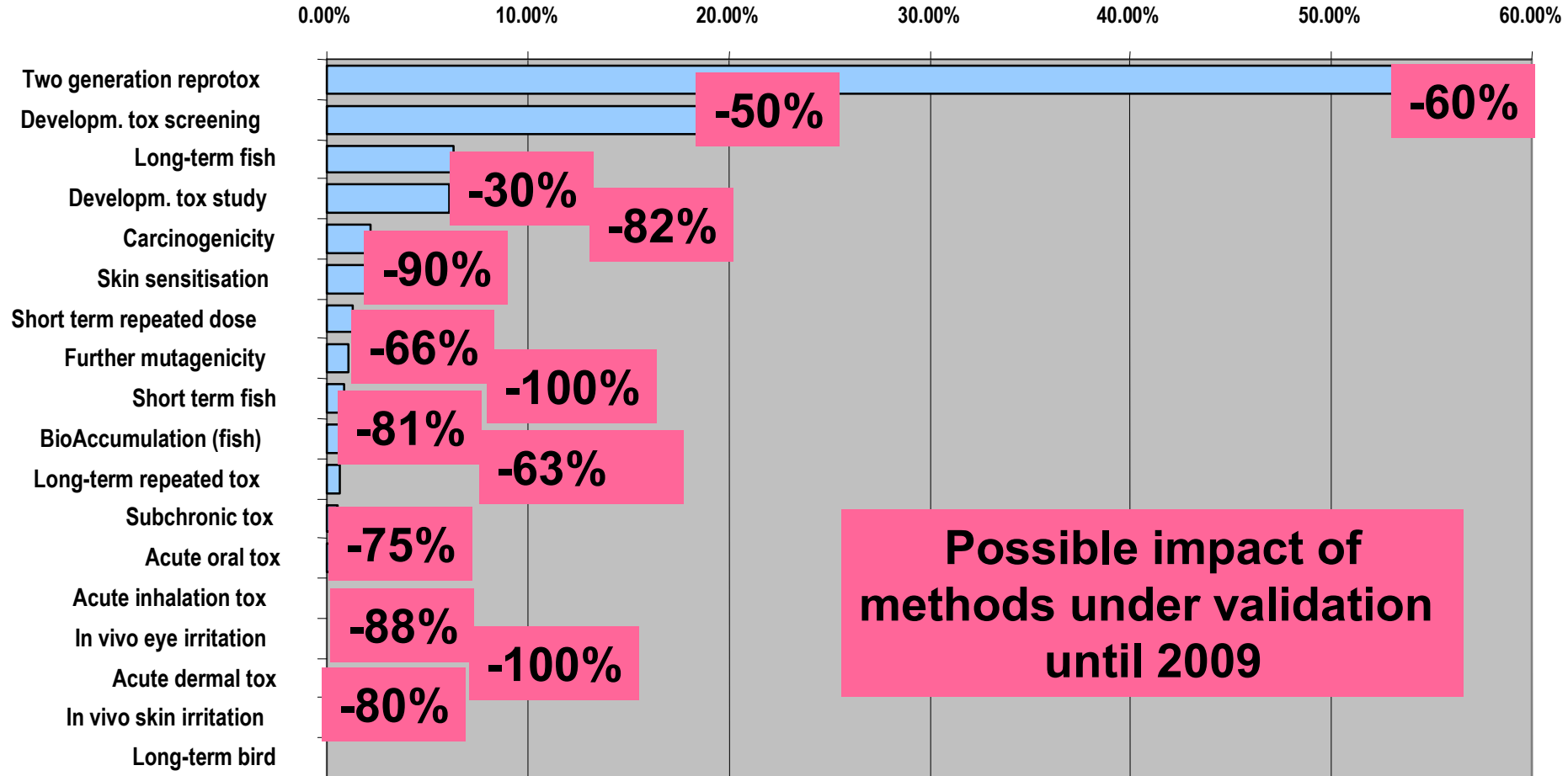


- Key contribution to REACH implementation process
- CEFIC management, strong regulator and industry involvement, >200 experts
- ECVAM as coordinator for Commission
- About 2.000 pages ready May 2007
- Many methods under validation already foreseen

Estimated test animal need for the different endpoints

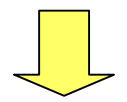
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% of total test animals needed



Possible impact of methods under validation until 2009

In silico methods

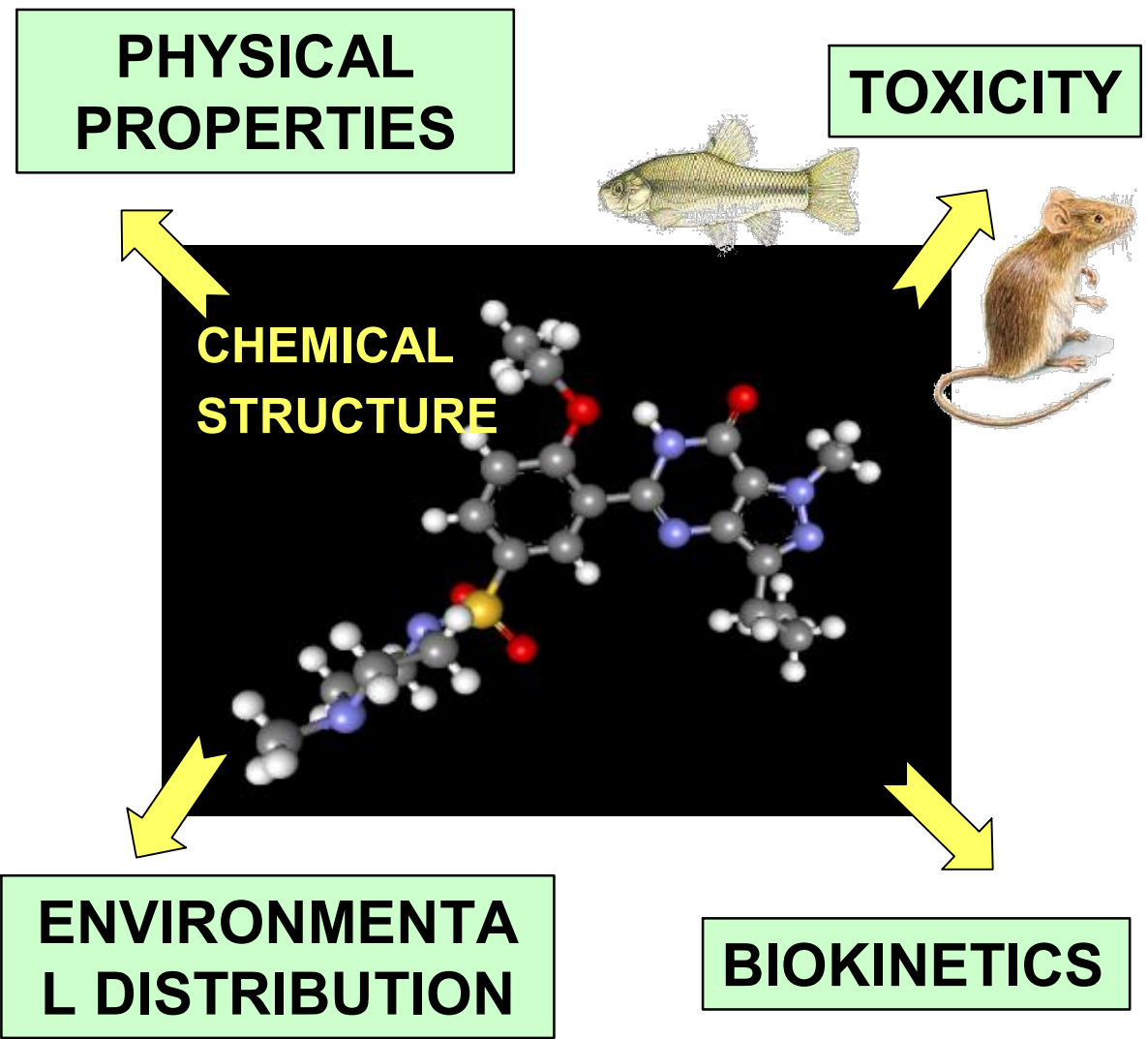


➤ SARs: Structure-Activity Relationships

AND

➤ QSARs: Quantitative Structure Activity Relationships

... are theoretical models that relate the structure of chemicals to their properties



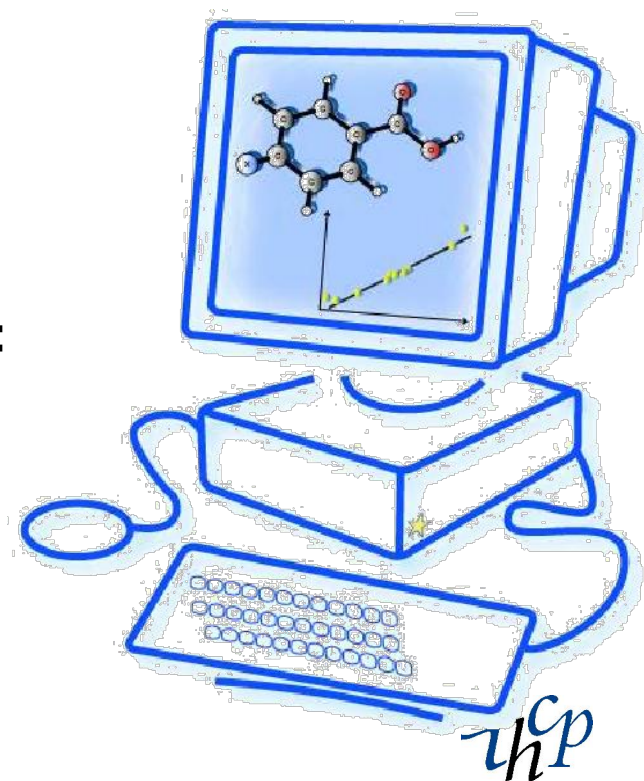


Computational Toxicology and Environmental Risk Modelling (European Chemicals Bureau)

Promoting the availability for regulatory use of valid computer-based methods

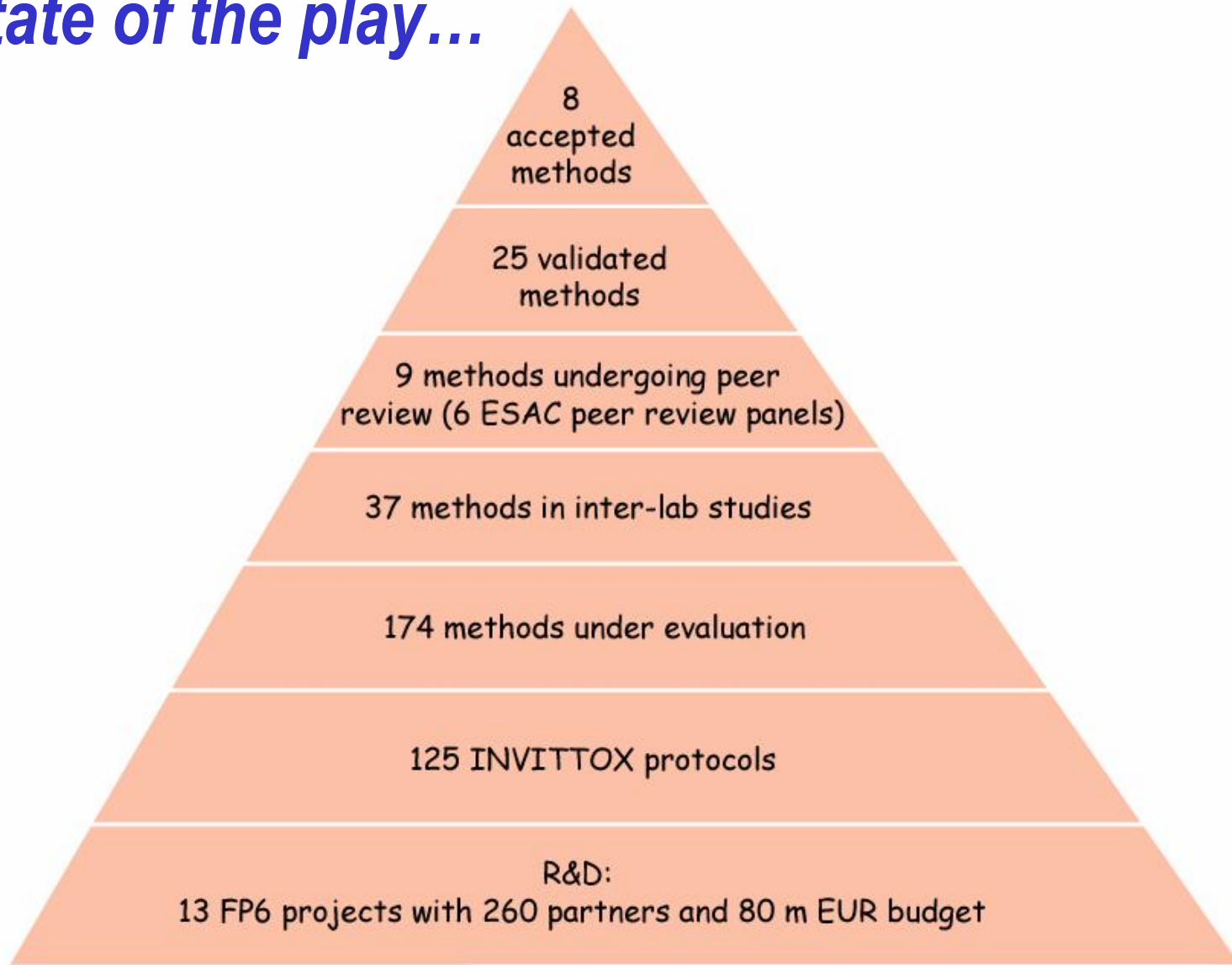
ACTIVITIES:

- **QSAR software tools for regulatory purposes (downloadable or accessible from the ECB website: <http://ecb.jrc.it/qsar/>).**
- **Case studies on QSAR validation and guidance document on QSAR validation.**
- **REACH guidance on grouping of chemicals and regulatory use of QSARs.**





State of the play...





ECVAM DATABASE SERVICE
ON ALTERNATIVE METHODS TO
ANIMAL EXPERIMENTATION

Current Activities & Prospects

- Online availability since 29th October 2006
- Protocols for alternative methods (“cook book”)
- Continuously extended data collections for all toxicological areas
- Extension to computational toxicology
- ECVAM website: <http://ecvam.jrc.it>

<http://ecvam-dbalm.jrc.it>



Europe goes alternative

1st Conference, Brussels, 7th Nov 2005

2nd Conference, Brussels, 18th Dec 2006

3rd Conference, planned 5th Nov 2007



- Hosted by Commissioners G. Verheugen (DG ENTR) and J. Potočník (DG JRC / DG RTD)
- **European Partnership** (7 trade associations, 27+ companies)
- Action programme



Thank you!