3Rs Center
at the National Institute of Public Health
Czech Republic

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MINISTRY OF EDUCATION,
YOUTH AND SPORTS

3Rs Center at the NIPH
at the Centre of Toxicology and Health Safety

History

- **Begun to form since 1999** - World Congress on Alternatives in Bologna
- **Developed** in connection with the anticipated **ban on animal testing for cosmetics and their ingredients** – safety of cosmetics / consumer products is the main task of the Centre of Toxicology

  - 7th Amendment to the Cosmetics Directive (Dir. 2003/15/EC):

  11.9.2004 ban for finished products, 11.3.2009 ban for ingredients

  CZ.- testing ban for cosmetics and ingredients (both) already in 2004

  (Act No.246/1992 Coll., updated by No.77/2004, on protection of animals)

  - Regulation No.1223/2009: 11.3.2013 final testing / marketing ban
- **Activities primarily aimed at Replacement** of animal tests by other procedures (in vitro, QSAR, Read Across ….) for the hazard and risk assessment of consumer products / ingredients

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History

- **2001** experts initiated **establishment of CZECOPA**, registered 10.5.2003
- **2004**, May 1, CR the EU member, experts repeatedly elected for **ESAC,** Scietific Advisory Committee to ECVAM (European Center for Validation of Alternative Methods, est. in 1991 due to the Dir. 86/609/EEC on protection of animals)
- **Directive 2010/63**, on protection of animals used for scietific purposes, replaced Dir. 86/609/EEC
- **2011,** according to Dir. 2010/63/EU the **Union Reference Laboratory EURL-ECVAM** was established**.**
- **2013 - NRL at the Centre of Toxicology** nominated by Ministry of Agriculture as **qualified laboratory and single contact point in the CR for alternative methods**

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Current Functions according to the Dir.2010/63/EU

- **National single contact point** to provide advice on the regulatory relevance and suitability of alternative approaches proposed for validation (Directive 2010/63/EU, Article 47) in 2013
- **PARERE** (Preliminary Assessment of Regulatory Relevance), the network of regulators to get early advice about the relevance of *in vitro* methods and the impact on the 3Rs principles
- **EU-NETVAL** - EURL ECVAM's European Union Network of Laboratories for the Validation of Alternative Methods (03/07/2013)

  - validation trial participation 2018: (1b) TSH receptor mediated activation, non-radioactive method

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Current Tasks

- Participation in EU - NETVAL validation trials
- Ethical mission to industry - Promotion of extended use of alternatives in testing of chemicals / toys / cosmetics / MD in routine practice of testing labs, Demonstrations / training for industry / NGOs / Academia
- Spread of knowledge: pre- and post-gradual education, Ph.D. students
- Cooperation with scientific institutions and universities in the CR
- Sharing of information on 3Rs towards general public via mass media
- Scientific support for responsible authorities and legislation (authorization of proposals for animal experiments for Ministry of Health)
- Expert is a member of Central Commission for Animal Welfare
- Experts involved in legislative actions, Peer Reviews, OECD, ECVAM … etc.

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Routine Testing Agenda

NIPH is a health care establishment and research institution

- **Testing facility** for control authorities, manufacturers, NGOs, individuals
- **Scientific projects – to verify predictive capacity of in vitro methods for hazard prediction and risk assessment for man**

Main task: Public health promotion and protection /
Basic and applied research

Comprises: Hazard identification of chemicals, pharmaceuticals and safety assessment of consumer products

(MD, cosmetics, toys, children products, chemical preparations, others...)

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Legislative Frame

- **Directive 2010/63/EU** on protection of animals used for scientific purposes
- **Regulation No.440/2008/EC - OECD TG – ISO – DB-ALM**
- **Regulation (EC) No. 1223/2009** on cosmetics
- **Regulation (EC) No. 1907/2006 (REACH)** on chemicals
- **Regulation (EC) No 1272/2008 –** CLP
- **EP Resolution of 14 March 2013** on the protection of public health from endocrine disrupters (2012/2066(INI)), (2016/C 2016/C 036/14)

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In vitro methods

Regulation No.440/2008/EC - OECD TG – ISO - ESAC

Skin corrosion: B.40 EpiSkin/ EpiDerm models of epidermis (OECD 431)

Skin irritation: B.46 EpiDerm, SkinEthic RHE models (OECD 439)

Phototoxicity: B.41 3T3 NRU test (OECD 432), 3D skin models

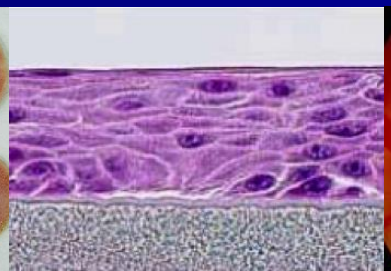
Eye irritation: Cytotoxicity test - 3T3 NRR
Organotypic model HET-CAM
3D cornea models: EpiOcular, HCE SkinEthic (OECD 492)

Inflammation markers: ELISA – IL1α, IL6, IL8, TNFα

Skin absorption / penetration: B.45 (OECD 428) ex vivo porcine skin

Skin sensitisation: DPRA (OECD 442C), LuSens (OECD 442D)



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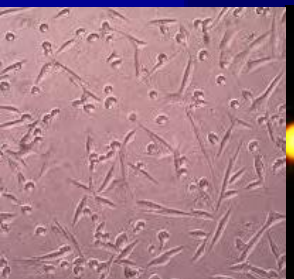
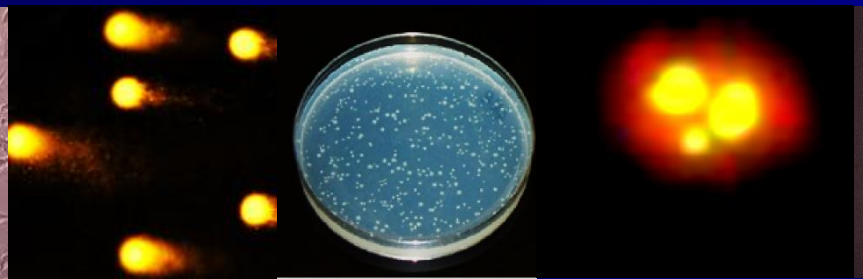
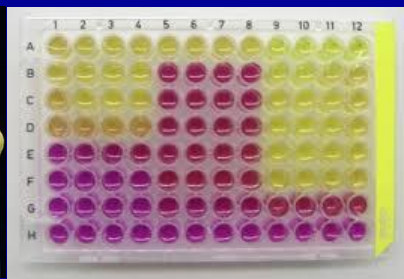
In vitro methods

Regulation No.440/2008/EC - OECD TG – ISO – DB-ALM

Genotoxicity / Mutagenicity: Comet assay
B.13/14 Reverse mutations in bacteria (Ames test) (OECD 471)
B.10 Chromozomal aberations in mammals in vitro (OECD 473)
Clastogenicity + aneugenicity: In vitro micronucleus test (OECD 487)
Acute tox.: Cytotox.test LD50 est.>2000 mg/kg (OECD Rec.129, DB-ALM 139)
Cytotoxicity test: EN ISO 10993-5 for medical devices
Estrogen receptor transactivation: OECD 455 / 457
Estrogen and Androgen receptor transactivation: YES/YAS
assay using S. cerevisiae strains with stably transfected hERα, hAR
Ecotoxicity / genotoxicity: Allium cepa test



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Thank you for your attention.

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