3Rs Center at the National Institute of Public Health
Czech Republic
3Rs Center at the NIPH at the Centre of Toxicology and Health Safety

**History**

- **Began 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**, Scientific 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 scientific 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 during pre- and post-gradual education
- 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
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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 430)

**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 - ESAC

**Genotoxicity / Mutagenicity:** Comet assay
B.13/14  Reverse mutations in bacteria (Ames test) (OECD 471)
B.10 Chromozomal aberrations in mammals in vitro (OECD 473)

**Clastogenicity + aneugenicity:** In vitro micronucleus test (OECD 487)

**Acute toxicity:** Cytotoxicity test for LD50 estimation (>2000 mg/kg)

**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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