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

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**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: 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
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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)
Genotoxicity / Mutagenicity: Comet assay
B.13/14  Reverse mutations in bacteria (Ames test) (OECD 471)
B.10  Chromozomomal 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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