



# **SEURAT-1**

## **a first step towards animal-free methods for better human safety assessment**

Ruxandra Draghia-Akli, MD, PhD  
DG RTD Health

**SEURAT-1 symposium, Brussels, 4 December 2015**

# Animal welfare is enshrined in the Lisbon Treaty

- *Article 13 of the TFEU states*
  - "In formulating and implementing the Union's agriculture, fisheries, transport, internal market, research and technological development and space policies, the Union and the Member States shall, **since animals are sentient beings, pay full regard to the welfare requirements of animals,** while respecting the legislative or administrative provisions and customs of the Member States relating in particular to religious rites, cultural traditions and regional heritage."

# Legislative context of alternatives to animal testing in the EU

- *3Rs encouraged in:*
  - 2004 Regulation on detergents
  - 2007 REACH Regulation
  - 2009 Regulation on plant protection products
  - 2010 Directive on protection of animals used for scientific purposes
  - 2013 Regulation on biocides
  - **2013** Complete ban on animal testing in the Cosmetics Directive/Regulation

# The "STOP VIVISECTION" European Citizen's Initiative\* – EC Response

- *4 actions to speed up progress in 3Rs*
  - Knowledge sharing in the field of the 3Rs
  - Development, validation and implementation of new alternative approaches
  - Enforcement of compliance with 3Rs principle and alignment of relevant sector legislation
  - Stakeholders conference

\* <http://ec.europa.eu/citizens-initiative/public/initiatives/finalised/details/2012/000007>

# EC initiatives towards the 3Rs

- *RTD*
  - **Research & Innovation through FPs, H2020**
- *EURL-ECVAM (EU Reference Lab for alternatives)*
  - **Validation & guiding development of alternatives**
- *EPAA (EU Partnership for Alternative Approaches)*
  - **Promotes development & implementation of alternatives**

# FP7-H2020 research in animal-free safety testing

*More than €400 million from RTD- and IMI-funded research projects, examples:*

- **SEURAT-1**: repeated dose systemic toxicity
- **HeCaToS**: drug-induced liver and heart toxicity
- **e-Tox**: *in silico* toxicology & database
- **SAFE-T**: new tests based on biomarkers

**13 EFPIA companies; 12 Public organizations; 5 SME**  
**Total Budget: €19 million**

# E-TOX

- Largest database on preclinical safety data providing access to unpublished safety data
- 90 in silico models for safety prediction delivered
- Regulatory dialogue on the use of the database and in silico tools
- First early candidate assessment based on eTOX database in member company allowed more targeted development process
- *Links with SEURAT-1 and EU-ToxRisk*

**Novartis, AstraZeneca, Boehringer Ingelheim, Bayer Schering Pharma, Laboratorios del Dr Esteve, GSK, J&J UCB Pharma, H. Lundbeck A/S, Pfizer, F. Hoffmann-La Roche, Sanofi-Aventis, Les Laboratoires Servier SA**

**11 EFPIA companies; 5 Public organizations; 4 SME**  
**Total Budget: €36 million**

**SAFE-T**

- **improved tools for drug-induced injuries to the kidney, liver, vascular system**
- **identify sets of biomarkers in blood and/or urine**
  - 153 potential BM evaluated; 30 BMs to be included in validation studies; 20 clinical studies for biomarker qualification completed; 24 clinical studies for biomarker validation ongoing
- **gain regulatory acceptance for routine use of these biomarkers in drug development**
  - Set of novel safety biomarkers progressed towards an aligned EMA/FDA qualification; Guidelines for qualification and validation of biomarkers discussed with EMA and FDA

**Novartis, Laboratorios Almirall, Amgen, AstraZeneca, Bayer Schering, Boehringer Ingelheim, Eli Lilly, GSK, Pfizer, F. Hoffmann-La Roche, Sanofi-Aventis**



# Challenges for SEURAT-1

- *New form of a flexible Public-Private Partnership EC/industry*
  - **each contributing €25 million cash**
- *Addressing complex scientific issues, for which no alternative methods exist*
- *6 complementary projects and 70 partners requiring high level efficient coordination*

## Open Science

# SEURAT-1 impact



- *Scientific knowledge*
  - on underlying mechanisms of adverse health effects
  - **>300 scientific publications**
- *New tools & techniques*
  - **liver bioreactor, differentiated iPS cells, predictive biomarkers, *in silico* models, etc.**
- *Huge amount of -omics and toxicity data*
  - **open access in Cosmos database and ToxBank**

## Open Innovation



## SEURAT-1 impact (2)

- *Validation of the approach in cross-cluster case studies*
- *Oriented towards regulatory needs*
- *Sustainable partnership with industry*
- *Approach valid for all human safety assessment application sectors*
- *Leverage for innovation potential*

## Open to the World



# SEURAT-1 impact (3)

- *International research collaboration*
  - **approach complementary to US programmes (ToxCast/Tox21)**

- *Flagship EU initiative "an international driver"*

# Political context at the end of SEURAT-1

- *Paradox*
  - Increasing pressure to ban **all** animal experiments
  - Higher demand for better safety assessment for humans
- *Continued political priority for EU research*
  - **H2020 & IMI**
- *SEURAT-1 to be followed up & extended in H2020*
  - **EU-ToxRisk**

**€28 million**

## EU-ToxRisk

- *6 years – start: January 2016*
- *Mechanism-based safety testing strategy*
  - **Repeated dose toxicity in 4 organs (liver, lung, kidney and nervous system)**
  - **Developmental and reproductive toxicity (incl. ED)**
  - **200 compounds**
- *Test systems - single cells to 4 organs-on-a-chips*
- *Participation of large industries, SMEs, regulators*
  - ROCHE, BASF, Unilever, L’Oreal, Cosmetics Europe, SimCyp, CAAT-EU
- *Built on FP7 and IMI projects*

# Perspectives

## ***Still needed***

- *More top science in the alternative field*
- *More exchange & partnerships*
  - **IMI, EPAA, regulatory bodies**
- *EC open to future PPPs with industry sectors*
- *Faster validation & uptake of new scientific developments*
- *Public outreach*



Musées Royaux des Beaux-Arts de Bruxelles

## **Information on H2020 workprogrammes 2016-2017**

[http://ec.europa.eu/research/participants/portal/desktop/en/funding/reference\\_documents.html#h2020-work-programmes-2016-17](http://ec.europa.eu/research/participants/portal/desktop/en/funding/reference_documents.html#h2020-work-programmes-2016-17)

## **Information on EU support for alternatives to animal testing**

[http://ec.europa.eu/research/health/biotechnology/alternative-testing-strategies/index\\_en.html](http://ec.europa.eu/research/health/biotechnology/alternative-testing-strategies/index_en.html)

## **Information on IMI-2**

<http://www.imi.europa.eu/>

## **Information on EPAA**

[http://ec.europa.eu/growth/sectors/chemicals/epaa/index\\_en.htm](http://ec.europa.eu/growth/sectors/chemicals/epaa/index_en.htm)

# **So long SEURAT-1**