SEURAT-1
a first step towards animal-free methods for better human safety assessment

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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

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
Largest database on preclinical safety data providing access to unpublished safety data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
• 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
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
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

€28 million
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
Information on H2020 workprogrammes 2016-2017
http://ec.europa.eu/research/participants/portal/desktop/en/funding/reference_docs.html#h2020-work-programmes-2016-17

Information on EU support for alternatives to animal testing

Information on IMI-2
http://www.imi.europa.eu/

Information on EPAA

So long SEURAT-1