

In This Issue

- **Project news**
- **Keynote**
- **Achievements**
- **Publications**
- **Report-o-meter**
- **Upcoming Events**

Prof. Goldman views about eTOX

Professor Michel Goldman, Executive Director of the Innovative Medicines Initiative (IMI), has been [interviewed](#) by the National Centre for Replacement Refinement & Reduction of Animals in Research (NC3Rs), about **eTOX**.

Prof. Goldman summarises his views about the eTOX project and hopes that regulatory agencies (such as EMA) will include some output of the project in their own guidelines for the assessment of the safety of new drugs.



Season's Greetings from the eTOX team, with best wishes for 2015!

PROJECT NEWS

11th Consortium Meeting, Basel, Switzerland

The meeting was hosted by Roche on October 15th and 16th. Key topics were the progress in ontologies, the verification procedures for the *in silico* models and the presentations on eTOX database use cases from EFPIA companies. In addition, progress on the two ENSO topics (roadmap for including human safety data into eTOXsys, SEND readiness of eTOX) was presented.

eTOX Hackathon

eTOX will be organizing a 4-day Hackathon between EFPIA experts (toxicologists and bioinformaticians) and public modellers to be held during the first months of 2015, in Barcelona. Goal of this exercise will be to mine the collected eTOX data in order to derive new *in silico* models.

eTOX collaboration with iPIE

The IMI project iPIE, covering the topic of pharmaceuticals in the environment has signed the Grant Agreement. One key objective is to build an ecotoxicological database using the eTOX platform and its experience in safe data sharing, ontologies and controlled vocabulary.

KEYNOTE

IMI2, an open door for eTOX

Message from Dr. Salah-Dine Chibout, Global Head Discovery & Investigative Safety, Novartis Pharma

The unprecedented levels of data sharing between public and private partners in the IMI1 **eTOX** project has resulted in the launch of a rich preclinical database (eTOXdb) and a new *in silico* toxicology prediction system (eTOXsys), which when fully validated will significantly improve our ability to predict the safety of new medicines and therefore, play a direct role in reducing attrition rates.

Achieving a sustainable interoperable solution that consistently and reliably allows for safety prediction will be critical to this IMI-driven effort. The IMI2 program, with some of its improved features over IMI1, might be able to provide perspective activities to potentially build on the successes of eTOX.

IMI2 will aim at delivering tools, methods and prevention and treatment options, directly or indirectly, that will progress the vision of personalized medicine and prevention. It is not purely focused on the development of new medicines, but on solutions that provide a holistic, personalized healthcare package. The Strategic Research Agenda (SRA) for IMI2 is set to achieve the vision of delivering 'the right prevention and treatment to the right patient at the right time' for priority diseases. IMI2 will put a spotlight on excellence in data management and data transparency, encouraging the engagement of all stakeholders to educate on science of clinical trials and translational research and inclusion of these groups via knowledge management platforms in clinical and translational research in such aspects as sample collection, data sharing, collaborative study design and analysis.

IMI2 introduces some improvements over IMI1:

- Idea generation will be open to proposals from third parties (with final decision with EFPIA) final decision to submit to IMI JU but not on the calls.
- Focus will be on health outcomes and patient access, not on attrition rate only.
- Strategic Advisory Groups will be implemented to ensure a program approach over opportunistic projects.
- Simplified reporting process will be introduced.
- Global budget 3.45€ billion (2014 – 2020). Non-EU in kind will be allowed with 30% across the IMI2 program.
- Funding will be available for companies up to 500€ million.
- Processes with short time to grant will be implemented.

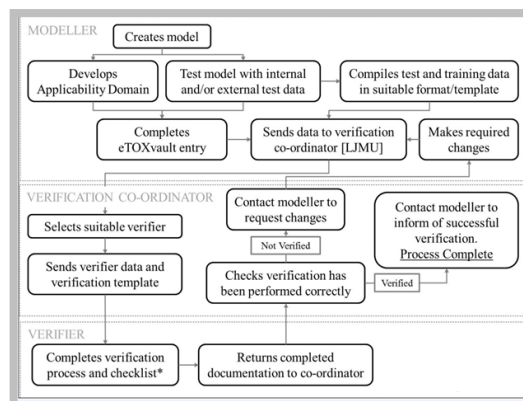
Overall, IMI2 appears to provide an excellent perspective for a follow up projects in the area of safety prediction of new medicines.



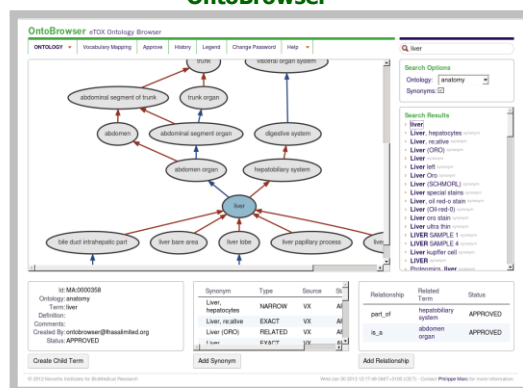
ACHIEVEMENTS

- Between 2014.2 (August 2014) and 2015.1 (January 2015) **eTOX database** releases, a revision of the database schema has been carried out to afford collection of Safety pharmacology and DMPK data, and as well *in-vitro* and *in-vivo* Genotoxicity, Reproductive-developmental and Carcinogenicity studies in the future.
- As a pilot study, the **Model Verification workflow** has been already tested for a small subset of models implemented in the **eTOXsys** by three current active verifiers. LJMU will take advantage of their feedback to fine tune the protocol before it goes live in the system.
- This month, the **eTOXsys** version 2.0 has been released (boxed and online). A beta testing phase is under way at Novartis and BHC site in advance of other EFPIA members in the consortium.
- Novartis is in the process of open-sourcing the [OntoBrowser](#) software. The source code will be released under the [Apache License Version 2.0](#) and will be available from [GitHub](#) in early 2015. The OntoBrowser tool was developed to manage ontologies and controlled terminologies (e.g. [CDISC_SEND](#)) used within the scope of the **eTOX** project. The primary objective of the tool is to provide an online collaborative solution for expert curators to map report terms (accessed from the **eTOX database**) to preferred ontology (or controlled terminology) terms. Additional features include: visualisation of ontologies in hierarchal/graph format, advanced search capabilities, peer review/approval workflow and web service access to data. The initial release will include an installation guide to facilitate deployment of the software within various environments. Visit the [OntoBrowser youtube channel](#) for tutorial videos.

Model Verification workflow



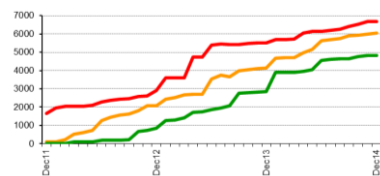
OntoBrowser



REPORT-O-METER

6659

After 3 years of data processing, 6056 reports of the 6659 cleared have finished the extraction data process and are available in the **Vitic Nexus eTOX database**.



Cleared Reports submitted to CROs or in-house facilities for data extraction
Extracted Reports with processing by CROs or in-house facilities completed
Vitic Reports with data available at Vitic Nexus database

PUBLICATIONS

A full list of publications is available on <http://www.etoxproject.eu>

- ARTICLE-(FIMIM): [The eTOX Data-Sharing Project to Advance in Silico Drug-Induced Toxicity Prediction](#). Cases M, Briggs K, Steger-Hartmann T, Pognan F, Marc P, Kleinöder T, Schwab CH, Pastor M, Wichard J, Sanz F. *Int J Mol Sci* 2014 Nov 14; 15(11): 21136-54.
- ARTICLE-(DTU): [Identification of Odorant-Receptor Interactions by Global Mapping of the Human Odorome](#). Audouze K, Tromelin A, Le Bon AM, Belloir C, Petersen RK, et al. *PLoS ONE* 2014; 9(4): e93037.
- ARTICLE-(LL): Value of shared preclinical safety studies - the eTOX database. Briggs K, Barber C, Cases M, Marc P, Steger-Hartmann T. *Toxicology Rep.* 2015; *in press*.

UPCOMING EVENTS

- **10-12.02.15** | OpenTox. Johns Hopkins, Baltimore (USA). Info: <http://goo.gl/WNNI82>
- **22-26.03.15** | SOT 2015. 54th Annual Meeting and ToxExpo. San Diego (California). Info: <http://www.toxicology.org/AI/MEET/am2015/>
- **19-24.04.15** | KESA 2015. The International Workshop on Knowledge Extraction and Semantic Annotation. Barcelona (Spain). Info: <http://www.iaia.org/conferences2015/KESA.html>
- **23-26.04.15** | 8th International Biocuration Conference. Beijing (China). Info: <http://biocuration2015.tilsi.org/>