eTOX Newsletter

Issue Num. 9 - December 2013

In This Issue

eTOX gets international echo

eTOX has been mentioned at the Financial Times on the 6th of December in an article entitled *Science: High-tech drug research gives us a fuller picture*. The article highlights that 13 pharmaceutical companies have joined forces with academic institutions under the umbrella of IMI.

Season's Greetings from the eTOX team, with best wishes for 2014!

PROJECT NEWS

Managing Knowledge about Tissues meeting, Brussels, Belgium

Ending October, partners on the IMI projects (DDMoRe, OpenPHACTS and eTOX) jointly organized an event to address the challenge of maximally exploiting and sharing knowledge about tissue in support of pharmaceutical R&D. Particularly, it focused on the semantic interoperability between R&D resources across IMI projects to enable cross-linking, querying and visualization of tissue knowledge.

9th eTOX Consortium meeting, Frankfurt, Germany

The meeting was held at the Sanofi site in Frankfurt November, 5-6th 2013. One topic was the kick-off of the new ENSO work packages, which includes expanding eTOX's vision from animal to human data. A strategy was developed together with valuable input from clinicians and experts from pharmacovigilance area.

eTOX contacted by EFPIA data sharing initiative

An EFPIA working group who developed a data sharing concept for preclinical studies of marketed compounds contacted eTOX to discuss the feasibility of our database for this approach. The Ex-Com expressed its high interest in a collaboration which would significantly expand eTOX's scope.

KEYNOTE

Systems Pharmacology applied to prediction and understanding of drug toxicity at the FDA

Message from Associate Director for Drug Safety/OTS/CDER, Food and Drug Administration: Darrell R. Abernethy, MD, PhD

The evolution of eTOX from the initial vision to its current very tangible capabilities to assemble toxicity data provided by eTOX partners into functional common datasets that can be used to develop predictive toxicity models is a tribute to both the leadership and membership of eTOX. It should not come as a surprise that similar efforts are underway in other regions of the world that are active in the identification and development of new molecular entities as drugs.

In the United States, the development of a pharmacological mechanism-based drug safety prediction program is underway at the FDA[1]. The elements have recently been described in some detail[2], and not surprisingly, many of the challenges that have confronted eTOX are being identified and worked through. Drug discovery, development, and regulatory science are moving forward in their ability to understand and leverage the evolving tools of systems toxicology and pharmacology.

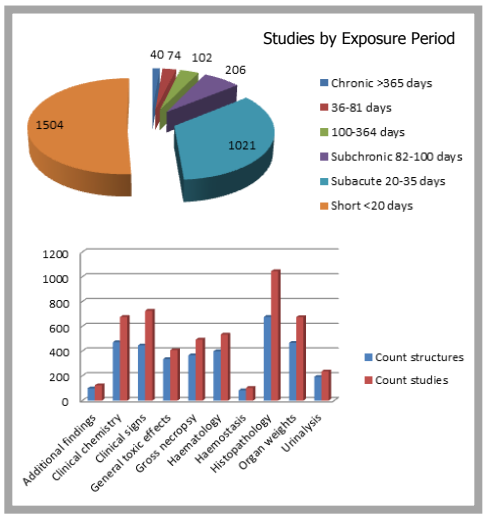
It seems appropriate that this effort and eTOX be in good communication. To that end *we look forward to continued and increased dialogue and interchange of information with our eTOX colleagues. Development of reliable predictive systems models for drug toxicity is a very big task and we can learn much from each other with a goal of preventing duplication of effort wherever possible.* Discussions have begun around development of ontology structures that are compatible and built in a manner that optimizes integration across a broad array of structured databases. We believe there are a number of other opportunities for similar dialogue and interchange, and look forward to identifying them and participating actively.

1. Abernethy DR, Woodcock J, Lesko LJ. Pharmacological mechanism-based drug safety assessment and prediction. *Clin Pharmacol Ther.* 2011; 89: 793-797.
2. Bai JP, Abernethy DR. Systems pharmacology to predict drug toxicity: integration across levels of biological organization. *Annu Rev Pharmacol Toxicol.* 2013; 53: 451-473.

ACHIEVEMENTS

- Mid November 2013, Lhasa Limited launched the **seventh release of the Vitic Nexus eTOX database**, with 1,137 structures (616 confidential) linked to 2,953 study records contributed by **all** EFPIA partners of the eTOX consortium. It is intended that the EcoRisk Prediction project from the 11th IMI call uses the **eTOX database** platform for the extension to ecotoxicological data and endpoints.
- EMBL has developed a **Standardizer tool** for input/output structures standardization among the predictive system steps, which will be deployed to the scientific community in the near future.
- A **Predictive Module Developer Declaration** has been defined to be signed by all modeling partners wishing to release their Predictive Modules with **eTOX**. The aim of this Declaration is to provide reassurance to end users that they can freely use any predictive model developed in the project without infringing third party rights. Up to date, 4 partners (DTU, IL, LJMU and MN) have signed PMDDs for a total of 41 models.

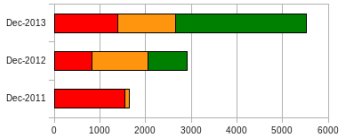
Vitic Nexus **eTOX** database 2013.4



- This month, the **version 2 beta** of the predictive system, **eTOXsys,** was deployed by MN as a boxed version to be installed at EFPIA partners premises. This release contains 5 virtual machines: Server (MN), DB-proxy (LL), 3 prediction modules with 41 models (31 IL, 7 MN, 2 LJMU and 1 DTU). On site, visits at the EFPIA partners by LL and MN will follow to study use cases and thereby improve system usability and performance.

REPORT-O-METER 5519

After 2 years of reports processing, over 50% of the 5519 cleared reports are part of the Vitic **eTOX**dabase, and another 25% is already under Quality Checks process to be included in the near future.



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-(UNIVIE): Ligand and structure-based classification models for Prediction of P-glycoprotein inhibitors. Klepsh F, Poongavanam V, Ecker GF. *J Chem Inf Model* 2013 Sep 19. [Epub ahead of print]
- ARTICLE-(CNIO): Overview of the chemical compound and drug name recognition (CHEMDNER) task. Krallinger et al. Proceedings of the 4th BioCreative Challenge Evaluation Workshop vol. 2, 2-33.

UPCOMING EVENTS

- **28-30.01.14 |** Clinical Genomics 2014. Boston (USA). Info: http://clinicalgenomics-usa.com/
- **31.01.14 |** Translational Research Knowledge Management in Action, eTRIKS. Barcelona (Spain). Info: http://goo.gl/bGHFTh /
- **16-20.03.14 |** CINF-RSC CICAG Symposium: Chemical Schemas, Taxonomies and Ontologies at the 247th ACS National Meeting & Exposition. Dallas (USA). Info: http://goo.gl/hzDq9q
- **23-27.03.14 |** 53rd Annual Meeting of Society of Toxicology – SOT 2014. Phoenix (USA). Info: http://toxicology.org/AI/MEET/AM2014/#