Newsletter

In This Issue

eTOX at SOT 2014

53rd Annual Meeting of Society of Toxicology (23rd-27th March 2014, Phoenix, Arizona)
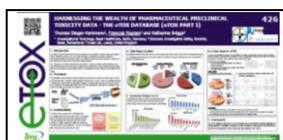
Harnessing the Wealth of Pharmaceutical Preclinical Toxicity Data — The eTOX Database

eTOX Ontologies: Enhancing Standards for Better Knowledge Management of Animal Study Data

New Frontiers in the *in silico* Prediction of *in vivo* Drug Toxicity: The IMI eTOX Project

eTOX consortium presented these posters that display the content of the database, the development of the ontologies and the modeling activities.

PROJECT NEWS

eTOX presented at the Annual Meeting of the Netherlands Society for Toxicology (NVT), Leiden

On February 12th, eTOX was presented at the Pharmaceutical Toxicology section meeting of the NVT with the title "Novel approaches for Drug Safety Testing". The audience expressed a high interest in the achievements of the eTOX project. An ad hoc on-line demo of the database and eTOXsys was organized in parallel to the conference reception.

5th eTOXsys user meeting, Barcelona

The meeting was held at SYNAPSE premises on February, 17-18th 2014. Two main topics dominated the meeting: on the first day the strategic alignment of eTOX to the needs of FDA's Standardization for Exchange for Nonclinical Data (SEND) initiative was discussed; and the day 2 discussions focused on the necessary improvements of eTOXsys for query and result display. Furthermore first real world use cases of eTOX and the first model validation results were presented.

Planning Scientific Advice with EMA

eTOX is currently exploring possibilities to strengthen the alignment of the database and the predictive systems with regulatory authorities. For that purpose a preparatory teleconference will be held with EMA's Innovation Task Force on April 2nd, 2014.

## KEYNOTE

Knowledge is power
Message from Joseph Jimenez, CEO Novartis

In the healthcare world, sharing knowledge improves our ability to tackle some of today's most pressing health issues. The benefits of transparency touch researchers, payors and patients themselves. *Data sharing, in particular, can help shed light on unanswered questions in medicine*. Pharma companies, governments and academics alike are sharing decades of research data and forging collaborative partnerships to discover new and innovative treatments.
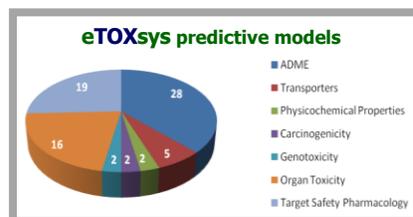
Many of the recent collaborative projects around data transparency focus on sharing clinical trial data, but we have taken the lead for transparency and collaboration in preclinical data with the **eTOX** initiative. Sharing data at the early stages of research gives us the ability to improve the safety of new medicines and reduce the use of animals in medical research – both potential game changers. I commend the **eTOX** team, which in short timeframe has created a comprehensive database, combining public data and legacy pre-clinical reports collected from 13 top pharma companies. *This database has allowed our teams to break new ground in the use of computer simulation modeling to better predict the toxicology profiles for new molecular entities*. The team has also developed a harmonized set of preclinical data terminology by mapping synonyms for research terms that have evolved over time and differ between companies. This will be an integral component of the **eTOXsys** platform, as it has the potential to make data mining and development of predictive models much quicker and simpler.

On many levels, we have made great progress, but there is more work to be done. We have already collected more than 4,000 systemic toxicologyrecords, but in order to fulfill the potential of the **eTOX** program, we need to continually build our inventory of shared data to uncover new approaches to research and engage in more effective drug development.
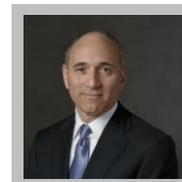
- In preparation of the next release of the **Vitic Nexus eTOX database** (2014.1), the following **SEND controlled vocabularies** have been applied through the OntoBrowser tool in order to harmonize part of the verbatim terms: laboratory test name, pk parameters, route of administration, sex of participants, species, and strain/substrain.

CDISC SHARE
Standard for the Exchange of Nonclinical Data

- EMBL has published their open source **Standardizer tool** for input/output chemical structures standardization at https://github.com/flatkinson/standardiser (documentation: https://wwwdev.ebi.ac.uk/chembl/extra/francis/standardiser/).

- MN has released the API 2.0 of the **eTOXsys**. In consequence, the flexible modeling framework **eTOX**lab has been revised to fit with the new requirements. From now on, predictions computed will provide Applicability Domain and Reliability Indexes information to accompany the prediction results.

- LL, accompanied by MN where possible, have conducted 3 user centred design studies (GSK, AZ and Bayer) in order to better understand how people work with **eTOXsys** and the data it contains. This has resulted in a set of clear use cases (i.e., search for compounds that exhibit a particular combination of effects that are treatment-related and share a common substructure). In addition testing protocols are being defined and harmonized and a wiki has been set up for transparent communication between LL and MN.

- Modelers team has already contributed 74 models for diverse endpoints, based on public data, which are currently implemented in the online **eTOXsys** version.

- An interdisciplinary **team formed by Toxicologists, Pathologists and Models developers** (TPM) has been defined to guide and pilot the model building of *in vivo* endpoints predictions, based on data recorded in the **eTOX**database.

eTOXsys predictive models
- ADME
- Transporters
- Physicochemical Properties
- Carcinogenicity
- Genotoxicity
- Organ Toxicity
- Target Safety Pharmacology

REPORT-O-METER   5717

The next **Vitic Nexus eTOX database** release (April 2014) will include data from 52% of the 5,717 cleared reports, contributing with over 4,000 study records to the project database.
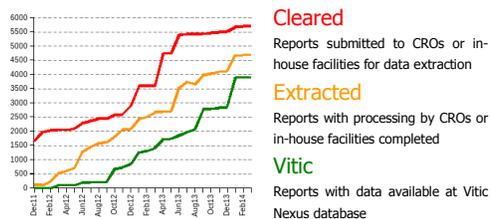
Cleared
Reports submitted to CROs or in-house facilities for data extraction

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-(VUA): Towards Automated Binding Affinity Prediction Using An Iterative Linear Interaction Energy Approach. Vosmeer CR, Pool R, van Stee MF, Peric-Hassler L, Vermeulen NPE, Geerke DP. *Int J Mol Sci* 2014;15(1):798-816.

- ARTICLE-(FIMIM): A knowledge-driven approach to extract disease-related biomarkers from the literature. Bravo A, Cases M, Queralt-Rosinach N, Sanz F, Furlong LI. *BioMed Res Int*. 2014, *in press*.

UPCOMING EVENTS

- **06-09.04.14 |** 7th International Biocuration Conference Biocuration 2014. Toronto (Canada). Info: http://goo.gl/LC3HPr

- **23-25.04.14 |** 7th Noordwijkerhout Symposium on Pharmacokinetics, Pharmacodynamics and Systems Pharmacology. Noordwijkerhout (The Netherlands). Info: http://goo.gl/w3JMsB

- **02-04.07.14 |** RICT 2014 - Interfacing Chemical Biology and Drug Discovery 50th International Conference on Medicinal Chemistry. Rouen, Normandy (France). Info: http://www.rict2014.org

- **01-05.05.14 |** 10th International Conference on Chemical Structures. Noordwijkerhout (The Netherlands). Info: http://www.int-conf-chem-structures.org/general-information.html

---