Newsletter

Issue Num. 16 – September 2015

In This Issue

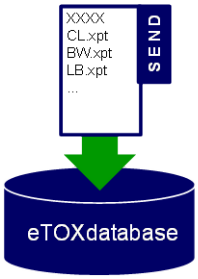
eTOX works to read SEND data

Standard for Exchange of Nonclinical Data

On December 17th 2014, the FDA made its long-awaited announcement that future submissions will be required in standardized format for those studies starting on or after December 18th 2016.

Recently, in addition to the eTOX terminologies alignment with standards, a first toxicity report based on individual animal data was provided in SEND format to the eTOXdabase in order to develop a SEND data convertor.

See Achievements section



PROJECT NEWS

Collaboration with MIP-DILI

The eTOX ExCom has been in contact with the coordinators of the MIP-DILI IMI project "Mechanism-Based Integrated Systems for the Prediction of Drug-Induced Liver Injury" in the past months to negotiate a Memorandum of Understanding (MoU) between the two projects. The MoU is in its final stage and the collaboration will be initiated soon.

eTOX Data Sharing

In the context of the Data Access Strategy established by eTOX, data has been shared with EPA (Tox21) and the DETECTIVE project. In the latter project, the data will be used to evaluate prediction models which extrapolate *in vivo* toxicity effects from *in vitro* studies.

Regulatory perspective

After the last consortium meeting, our three Scientific Advisory Board (EPA, EMA) members have been granted access to the online version of eTOXsys to provide their feedback on the usability of the system, particularly from a regulatory perspective.

KEYNOTE

Linkage to human safety information

Message from Prof. Johan van der Lei, Head of the Department of Medical Informatics, Erasmus Universitair Medisch Centrum, Rotterdam

During the **eTOX** extension phase (ENSO) a new task entitled "Linkage to human safety information" has been included. This task centres on providing linkage to systems exploiting human endpoint data sources for drug safety. The ultimate objective is to aid the toxicologist´s task by allowing a form of cross-comparison of pre-clinical and clinical outcomes during the drug discovery and development process.

Work is progressing. A number of web-services related to different data sources have been identified, responding to the need to access the literature, the need to retrieve information from drug labels, spontaneous reports from the US or Europe, or information from observational databases. A deliverable was produced that outlines our plans.

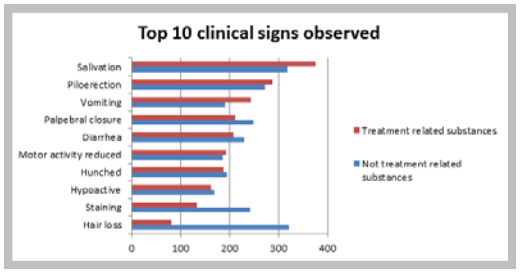
These efforts represent a fundamental challenge that we face in scientific research. Knowledge is increasingly generated in distinct silos. As the depth of the knowledge in a given silo increases, the hurdle to cross the boundaries and move into other domains becomes more and more difficult. Each silo of expertise comes with its own methodology, topics of interest, and a specific language to handle results. Many of us agree that ***breakthroughs will require interdisciplinary collaborations***, but how to achieve these collaborations often remains elusive.

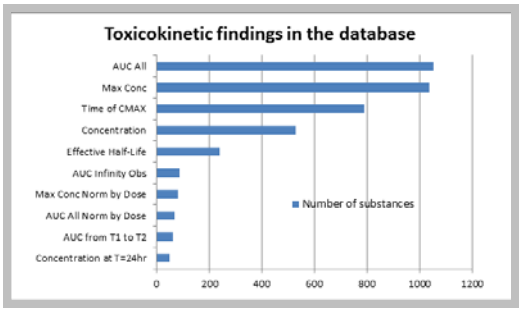
In our efforts to link to human safety information we are on the one hand trying to develop useful web-services for the **eTOX** community. In that sense, it is all about developing software, modules, and user-friendly interfaces. On the other hand, and on a more fundamental level, we are addressing the issue of bridging communities. Although, we work in different communities, the task is to discover where we do share a common research topic. We have to ask ourselves how our own research can contribute to the research questions that others face. It is in fact at the intersection, where we all move away from our own comfort zone that breakthroughs typically happen. I am very hopeful that our joint work in **eTOX** on human outcomes will represent a significant advance for this critical field.

ACHIEVEMENTS

- In August, Lhasa launched **the eleventh release of the Vitic eTOXdatabase** (2015.2) containing 1,757 substances (394 labeled as confidential, over 200 substances changed their status from confidential to nonconfidential from the previous release) associated with 6,309 preclinical studies. ChOX part has been updated and includes 230,192 substances with 1,033,498 records from ChEMBL20. In this release, the 27-Mar-15 CDISC SEND version was applied for terminology standardisation (codelists considered: laboratory test name, pk parameters, route of administration, sex of participants, species, and strain/substrain); and we have advanced standardisation of toxicokinetic parameters and clinical signs.

Vitic Nexus eTOX database 2015.2

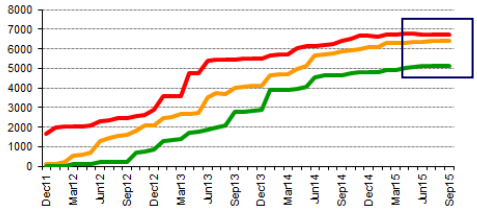




- In August, Bayer transferred **the first study record in SEND format** to Lhasa under confidential agreement. The study data were provided in different files split by data domains defined by the FDA SEND implementation guidelines (SENDIGv3.0). Precise mapping between SEND variables and **eTOXdatabase** fields should allow the integration of these other type of data.
- The terminology curation team is following the guidelines published by the **International Harmonization of Nomenclature and Diagnostic Criteria** (INHAND). Up to date, the team has aligned the **eTOX** common ontology with 6 of 9 final published manuscripts.

REPORT-O-METER 6742

Necessary transitions of contracts from GGA to EPAM took longer than expected resulting in a transient delay in the extraction process. Currently, new deliveries are ongoing.



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-MN-UNIVIE-VUA): Integrative modeling strategies for predicting drug toxicities at the eTOX project. Sanz F, Carrió P, López O, Capoferri L, Kooi D, Vermeulen NP, Geerke DP, Montanari F, Ecker GE, Schwab C H, Kleinöder T, Magdziarz T, Pastor M. *Mol Inf* 2015; 34: 477–84.
- ARTICLE (CT): Garcia-Serna R, Vidal D, Remez N, Mestres J. Large Scale Predictive Drug Safety: From Structural Alerts to Biological Mechanisms. *Chem Res Toxicol* 2015. *In press*.

The IMI Bibliometric analysis of ongoing projects was published in June 2015. The **eTOX** project was highlighted in the top position in terms of citation indicators.

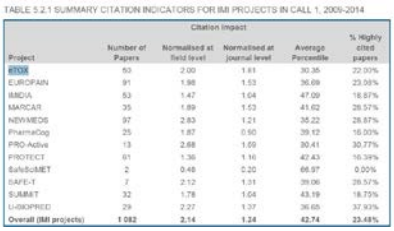


TABLE 5.2.1 SUMMARY CITATION INDICATORS FOR IMI PROJECTS IN CALL 1, 2009-2014

Project	Number of Papers	Citation Impact: Normalised at field level	Citation Impact: Normalised at journal level	Citation Impact: Average Percentile	% Highly cited papers
eTOX	60	2.00	1.61	30.35	22.00%
EUROPAIN	91	1.98	1.53	36.69	23.08%
INDIA	53	1.47	1.04	47.09	16.67%
MARCAR	35	1.89	1.53	41.62	28.57%
NEWMEDS	97	2.83	1.21	35.22	28.87%
PharmaCog	25	1.87	0.50	39.12	16.00%
PRO-Active	13	2.68	1.59	30.41	30.77%
PROTECT	61	1.36	1.16	42.43	16.39%
SafeBaMET	2	0.48	0.20	66.97	0.00%
SAFE-T	7	2.12	1.01	39.06	28.57%
SUMMIT	32	1.78	1.04	43.19	18.75%
U-BIOPRED	29	2.27	1.07	36.65	37.93%
Overall (IMI projects)	1 082	2.14	1.24	42.74	23.48%

UPCOMING EVENTS

- **05-06.10. 2015 |** Stratified medicine and prevention of adverse drug reactions. Edinburg, UK. Info: http://www.bps.ac.uk/meetings/BTS_BPS
- **08-11.11. 2015 |** American College of Toxicology 36th Annual Meeting. Summerlin, Nevada (USA). Info: http://www.actox.org/am/am2015
- **19-20.11. 2015 |** FutureTox III: Bridges for Translation. Arlington, Virginia (USA). Info: http://goo.gl/HScLC4