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## PROJECT NEWS

### eTOX Final Meeting

On the 28<sup>th</sup> and 29<sup>th</sup> of November 2016, eTOX celebrated the successful completion of the project with a conference on Project achievements and future perspectives. Over 70 attendees representing all eTOX partners as well as external invitees, all covering a broad cross-section of backgrounds, gathered to discuss the lessons learned from the success of eTOX and initiate the steps towards a promising sustainability phase.

Looking back there have been some challenges along the 7 years of the project. But overall the development of the system and the future plans for sustainability are quite promising, as well as other important achievements of the project. All of them demonstrating the need to jointly work private and public sectors together.

The **IMI Officer, Hugh Laverty**, congratulated all eTOX partners and its management team; there has been an outstanding learning curve, as stemming from Call 1 in IMI1. The challenge of getting the data was initially underestimated but an important DB with over 7,000 reports from all EFPIA companies participating in the project has been achieved. The Honest Broker model created in eTOX has been repeated in other projects.

The **IMI Executive Director, Pierre Meulien**, gave a keynote entitled *Current strategies and implementation of the IMI-2 programme*, available at [www.etoxproject.eu](http://www.etoxproject.eu).

## FINAL KEYNOTE

*François Pognan, Ferran Sanz, Thomas Steger-Hartmann, Carlos Díaz*  
eTOX Executive Committee

It all started about nine years ago from a wish to dig in the past of preclinical toxicology to foresee its future. Realising this was not possibly achievable by a single company, we set up the **eTOX** consortium. The task was even more challenging and enormous than we imagined in the beginning. The encountered obstacles and hurdles were numerous: company legal services had to be convinced that there is no danger in sharing data, but only benefit; data standards and controlled vocabularies for the different toxicological endpoints were still in its infancy; a common framework for modelling had to be established; a new software system unifying access to data and predictive models had to be set up ex nihilo; cross-discipline dialogue and team dynamics had to be created to generate a virtuous circle. And, on top of it all, we had to learn how to use the powerful IMI framework for public-private collaboration – **eTOX** was one of the very first IMI projects ever.

But to cut a 7-year long project story short, we did it! For the first time in safety sciences, **eTOX** achieved an effective synergic sharing of the historical toxicological data within the pharmaceutical industry. Moreover, **eTOX** has created an incredibly rich set of ontologies that enables data sharing. We are still amazed rummaging into the database and seeing so much invaluable information. There is yet a substantial analysis and exploitation work to be done, but now it is possible thanks to the user platform developed in the project, the **eTOXsys**, which is a user friendly and powerful system for accessing the **eTOX** data and predictive models. The **eTOX** shared data offer unique opportunities for predictive read-across and modelling. And then, there is the predictive algorithm part; this is like a toy chest to play with. The **eTOX** modellers have developed more than 100 models that are fully verified and documented.



The influence of **eTOXsys** on early safety assessment and on the interaction with other involved disciplines (medical chemists, pharmacologists, DMPK experts) just begins to emerge, but it is already evident that the system outcompetes the collective memories of toxicologists in the various companies ("where have I seen this finding before?"), simply because the data sets extends beyond the walls of a single company. As such, it is probably not unduly to state that the **eTOX** project has set a new paradigm for preclinical data sharing and exploitation.

What will remain after the end of the project? First of all, a sustainable product, which will live on - not only as a software platform, but also as a continued data sharing initiative, potentially reaching out to other customers and industries (regulators, agrochemical industry or cosmetics) and inspiring other future projects in the field. Secondly, a sound basis for developing further research, with a focus on how the wealth of preclinical data can help us better to predict (and minimize) toxicity in human. Thirdly, the continuity of the core team in a framework of a growing community of developers and users of the **eTOX** products. All of us had so much excitement being part of the **eTOX** adventure. The amazing team spirit and great environment allowed us to obtain the impressive set of results described above. It is only fair to say that **eTOX** has been one of the very best IMI projects we have witnessed.

Many thanks to all of the **eTOX** participants and contributors as well as IMI.

**Long live eTOXsys!**



With the final version of the **eTOXsys** Business Plans duly completed in early January of this year the next phase of this highly successful project is now underway, with **eTOXsys** becoming available to a broader user forum beyond the 13 EFPIA companies involved in the consortium, in March 2017.

Lhasa Limited has been chosen as the Business Broker, supported by Molecular Networks, to make available the **eTOXsys** database of shared EFPIA data together with the models generated during the project. Following elections, a User Board has been created that will provide the governance of the project in this new phase and whose representatives are:

**EFPIA:**

Alexander Amberg (Sanofi)  
Francois Pognan (Novartis)  
Thomas Steger Hartmann (Bayer)  
Wolfgang Muster (Roche)

**Academia:**

Ferran Sanz (IMIM)

**Models developers:**

Gerhard Eckert (UNVIE)

**Business Broker:**

Dave Watson (Lhasa Limited)  
Chihae Yang (Molecular Networks)

**Project Management:**

Eva Molero (Synapse)

The User Board will work with the users of **eTOXsys**, Lhasa Limited and Molecular Networks to ensure the continued development of the software and data sharing. It will also act as an oversight group to ensure that access for new users is provided under fair, reasonable and non-discriminatory terms with the emphasis on growing the breadth and scope of the data and promoting its use in life science research. The first meeting took place on February 27<sup>th</sup> 2017 at which there was a formal handover from the ExCom that drove the **eTOX** project for the last 7 years, to this User Board whose first task will be to elect Officers that will lead the group in these exciting early years.

Following extensive Market Research by Synapse during the **eTOX** project, and subsequent discussion within the consortium users, a clear market proposition has been created upon which Lhasa Limited and Molecular Networks have built a detailed Sales and Marketing plan. The **eTOXsys** main competitive advantage lies in the database, built from proprietary pharmaceutical industry data that is otherwise not retrievable (i.e. not in the public domain). This is complemented with the integrated ontology and the data mining platform which has been built specifically for this type of data. Also included is a series of prediction models for various human health-related endpoints in preclinical research and development. The **eTOXsys** is a valuable tool for an improved early drug candidate safety assessment, but other industries (consumer chemical, agrochemical, cosmetics) as well as regulatory agencies will find interest for read-across or safety prediction purposes.

Promotion of the software and models has already begun, with Lhasa Limited hosting a webinar on the utility of **eTOXsys** on 16<sup>th</sup> November 2016 and a further ToxExpo presentation is planned at the 56<sup>th</sup> Society of Toxicology Meeting in Baltimore (9.00am on Tuesday 14<sup>th</sup> March 2017, in the conference room 339). In addition, the Sales teams of both Lhasa and Molecular Networks will be promoting the use cases of **eTOXsys** within their Member and client base, offering live demonstrations of the utility of the software through a webinar.



The **eTOXsys** will go 'live' on the 14<sup>th</sup> March 2017; the models developed throughout the **eTOX** project will be accessible via the **eTOXsys** website as soon as the modeler's agreement is finalized. Molecular Networks' team are keen to talk through those Models most applicable to users' needs. In addition, the **eTOXsys** team is planning a final webinar for the use of **eTOXsys** (database and models) for the **eTOX** consortium members on the 21<sup>st</sup> of March 2017.

For more information, or to arrange a demonstration of **eTOXsys** for your team, please contact [info@lhasalimited.org](mailto:info@lhasalimited.org).  
For information accessing models please contact [etox@mn-am.com](mailto:etox@mn-am.com).



## eTOX SAMPLER

A sampler of the **eTOX database** has been prepared with a subset of data corresponding to 95 compounds studies, and will be accessible upon request on a free registration basis. An announcement will be launched soon through the **eTOXsys** website (<https://etoxsys.eu>) when it is ready for requests.

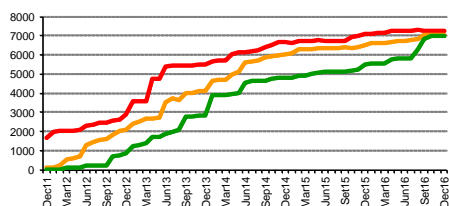
## eTOX FACTS and FIGURES

- 7 years of collaboration between 13 pharma companies, 11 academia institutions and 6 SMEs.
- 15 Consortium meetings, 1 Mid-term Review, 7 **eTOXsys** user meetings, 1 modelling workshop and 2 Hackathons were celebrated.
- 15 releases of the **Vitic Nexus eTOX database** were delivered. The final version contains **1,947 substances** (483 labelled as confidential) and **8,047 study design records** from **6,971 legacy reports**; and **265,502 substances** and **1,088,007 records** from public sources like ChEMBL, DrugMatrix and Open TG-GATES.
- Technical synchronization between **OntoBrowser**, **Vitic Nexus eTOX database** and **eTOXsys** regarding the Terminology harmonization allowed the mapping of around **20 Million of verbatim terms** to **7,262 preferred terms**, which highly improve the quality of the read across analysis and modelling challenges. Remarkably, the development of the **eTOX** common Ontology followed the standards guided by SEND codelists and INHAND controlled vocabularies, and specific efforts were devoted to harmonize the Pharmacological Action and Toxicokinetics related information.
- Several tools were developed and are freely accessible for the scientific community benefit (<http://www.etoxproject.eu/results.html>).
- 5 releases of the **eTOXsys** were launched. The final version includes the **2016.3 Vitic** release, a bunch of **99 predictive models** (all fully documented and 66 fully validated following the consortium Verification protocol), and the **Human Outcomes Module** integrated, which was designed to support and open a door for translational research from preclinical to clinical research.

## REPORT-O-METER

# 7244

The 15<sup>th</sup> and final release of the **Vitic Nexus eTOX database** contains a total of 6,971 from the 7,244 cleared reports.



**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

## UPCOMING EVENTS

**10-13.09.2017** | 53<sup>rd</sup> Congress of the European Societies of Toxicology, EuroTox. Bratislava, Slovakia.

eTOX will organize a Symposium entitled "Beyond data sharing - towards data transparency, management, mining and application to predictive safety assessment".

Info: <http://www.eurotox2017.com/>

## PUBLICATIONS

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

- ARTICLE (FIMIM): [Hepatotoxicity prediction by systems biology modeling of disturbed metabolic pathways using gene expression data](#). Carbonell P, Lopez O, Amberg A, Pastor M, Sanz F. *ALTEX 2016; In press*.
- ARTICLE (GSK): [Management of organic impurities in small molecule medicinal products: Deriving safe limits for use in early development](#). Harvey J, Fleetwood A, Ogilvie R, Teasdale A, Wilcox P, Spanhaak S *Regul Toxicol Pharmacol 2017; 84:116-123*.
- ARTICLE (UNIVIE): [Virtual screening of DrugBank reveals two drugs as new BCRP inhibitors](#). Montanari F, Cseke A, Wlcek K, Ecker GF. *J Biomol Screen 2016; In press*.

Totals of Publications:

81 articles, 74 posters, and 162 oral communications

*Thanks for the 7 years of eTOX!*