



VICT3R

Developing and implementing Virtual Control Groups
to reduce animal use in Toxicology Research

The role of AI-based technologies in data sharing projects supporting the drug and chemical safety assessment. The eTRANSAFE and VICT3R projects

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Application of Digital Infrastructures Leveraging AI in Human Health Risk Assessment. Brussels, 28-29 October 2025



This project is supported by the Innovative Health Initiative Joint Undertaking (IH JU) under grant agreement No 101172893. The JU receives support from the European Union's Horizon Europe research and innovation programme and COCIr, EFPIA, Europa Bio, MedTech Europe, and Vaccines Europe and Instem Scientific Limited. Funded by the European Union, the private members, and those contributing partners of the IH JU. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the aforementioned parties. Neither of the aforementioned parties can be held responsible for them.

Safety Data Sharing Saga of IMI/IHI projects

eTOX, eTRANSAFE and VICT3R

- Drug safety does not constitute the main playground for the competition between pharmaceutical companies. It is (relatively) feasible to share legacy data to improve safety assessment.
- IMI-IHI projects on this matter:
 - IMI eTOX , focused on pre-clinical toxicological data sharing, executed from 2010 to 2017.
 - IMI eTRANSAFE, addressing translational drug safety assessment through integrative knowledge management, running from 2017 to 2023.
 - IHI VICT3R to develop and implement Virtual Control Groups (VCG) (2024-2028).



Legacy data sharing to improve drug safety assessment: the eTOX project

Ferran Sanz¹, François Pognan², Thomas Steger-Hartmann³, Carlos Díaz⁴ and eTOX^{*}

NATURE REVIEWS | DRUG DISCOVERY VOLUME 16 | DECEMBER 2017 | 811

<https://doi.org/10.1038/d41573-023-00099-5>

eTRANSAFE: data science to empower translational safety assessment

Ferran Sanz, François Pognan, Thomas Steger-Hartmann, Carlos Díaz & the eTRANSAFE Consortium

Check for updates

nature reviews drug discovery

Volume 22 | August 2023 | 605–606 | 606

Food for Thought ...

Introducing the Concept of Virtual Control Groups into Preclinical Toxicology Animal Testing

Thomas Steger-Hartmann¹, Annika Kreuchwig¹, Lea Vaas¹, Jörg Wichard¹, Frank Bringezu², Alexander Amberg³, Wolfgang Muster⁴, Francois Pognan⁵ and Chris Barber⁶

Received December 4, 2019; Accepted February 19, 2020;
Epub February 25, 2020; © The Authors, 2020.

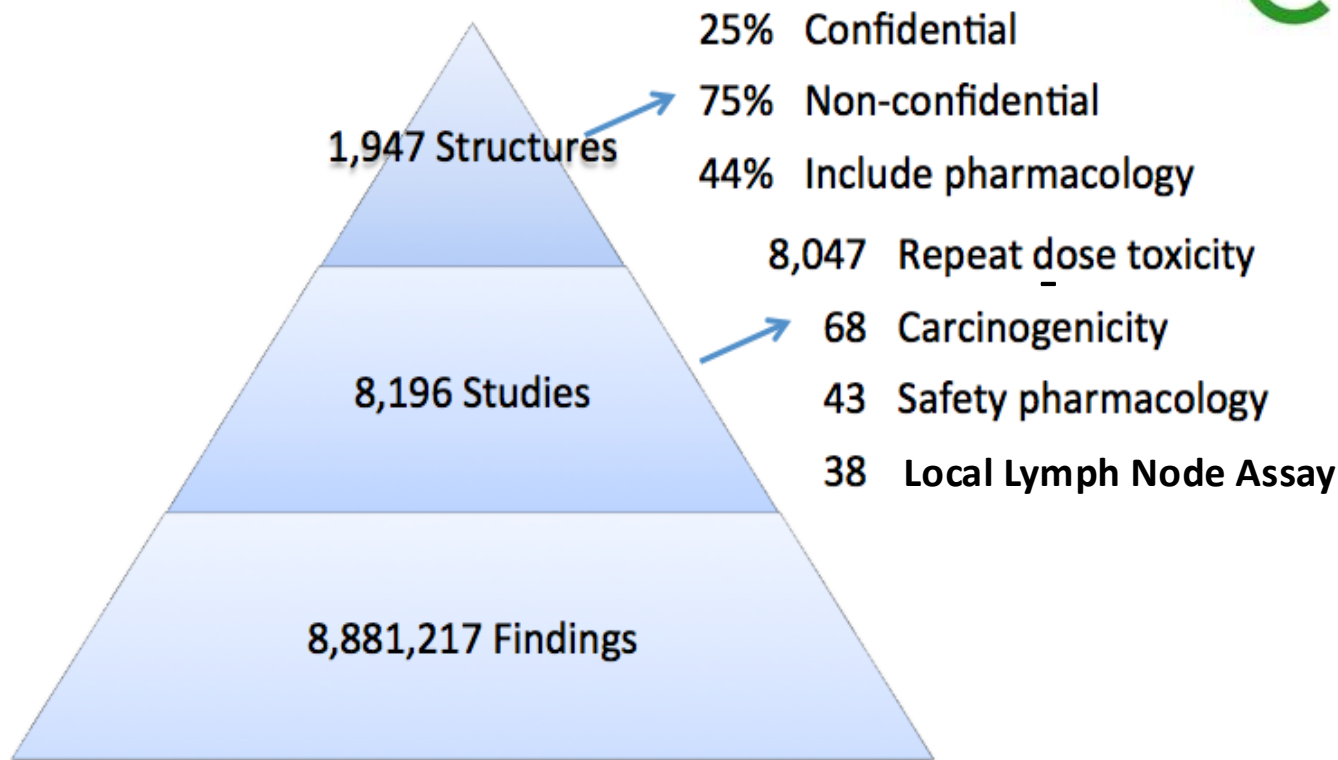
ALTEX 37(3), 343–349. doi:10.14573/altex.2001311

IHI VICT3R: Developing and Implementing Virtual Control Groups to Reduce Animal Use in Toxicology Research

Thomas Steger-Hartmann¹, Ferran Sanz², Frank Bringezu³, and Inari Soinen⁴

Toxicologic Pathology
2025, Vol. 53(2) 230–233
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The eTOX DB

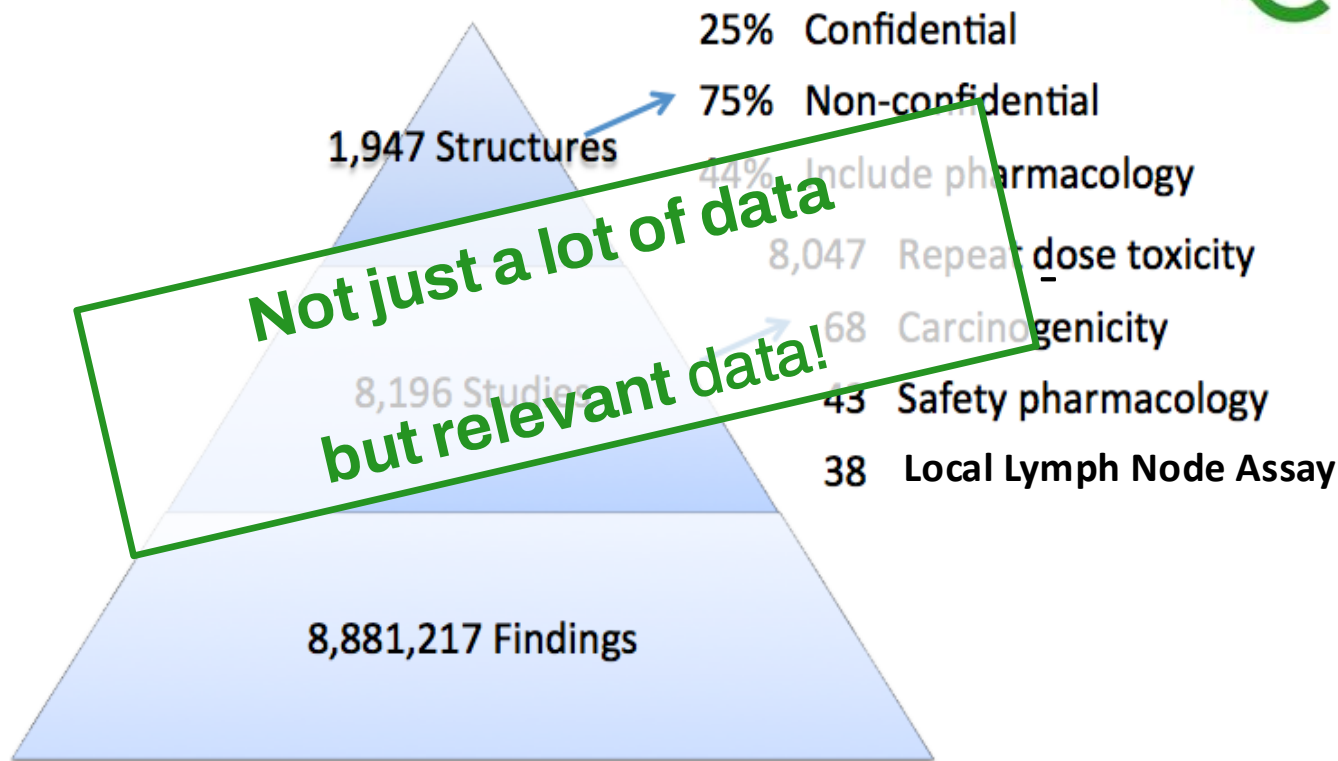


Contents of the eTOX database version 2016.3

The role of AI-based technologies in data sharing projects supporting the drug and chemical safety assessment

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Using eTOX Data in Predictive Modelling

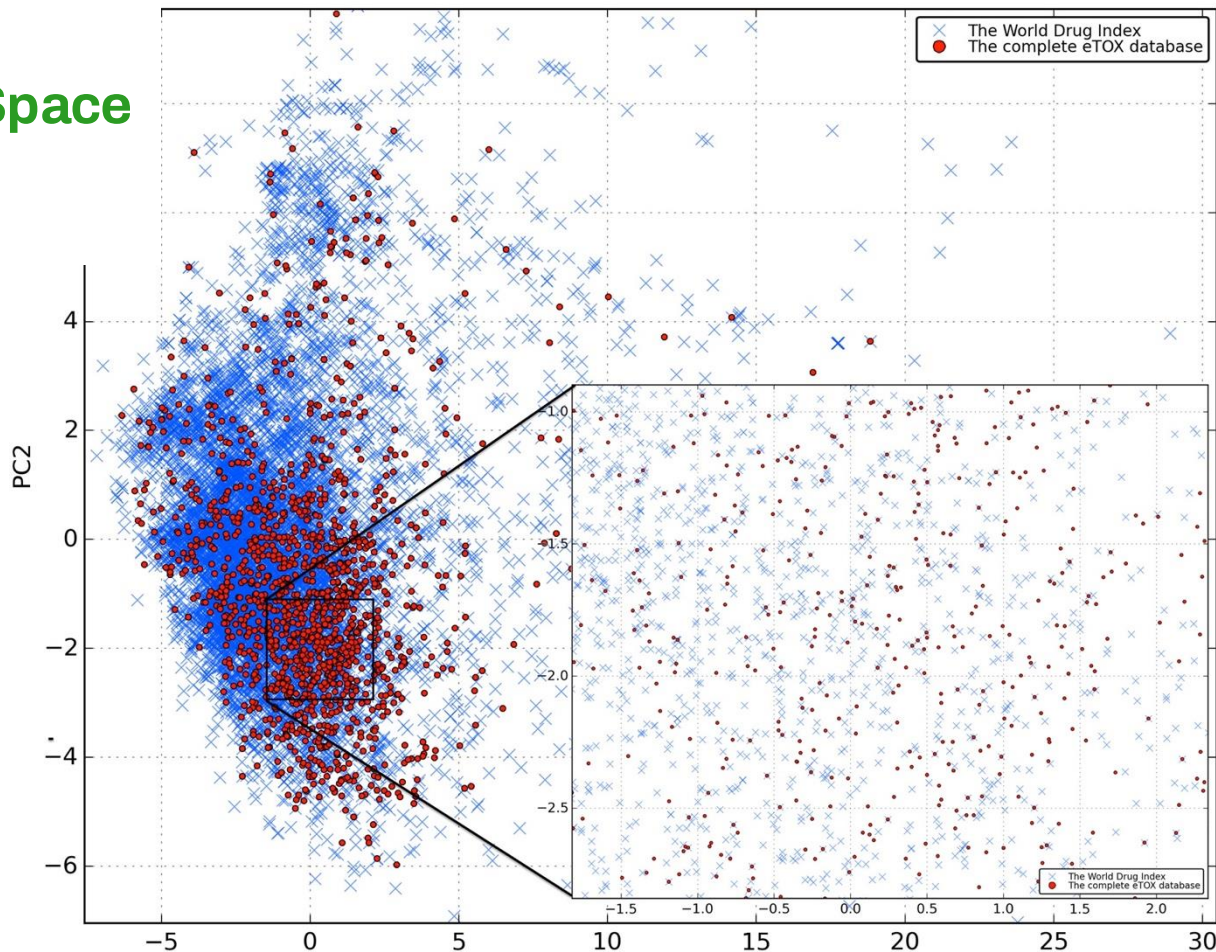


Contents of the eTOX database version 2016.3

The role of AI-based technologies in data sharing projects supporting the drug and chemical safety assessment

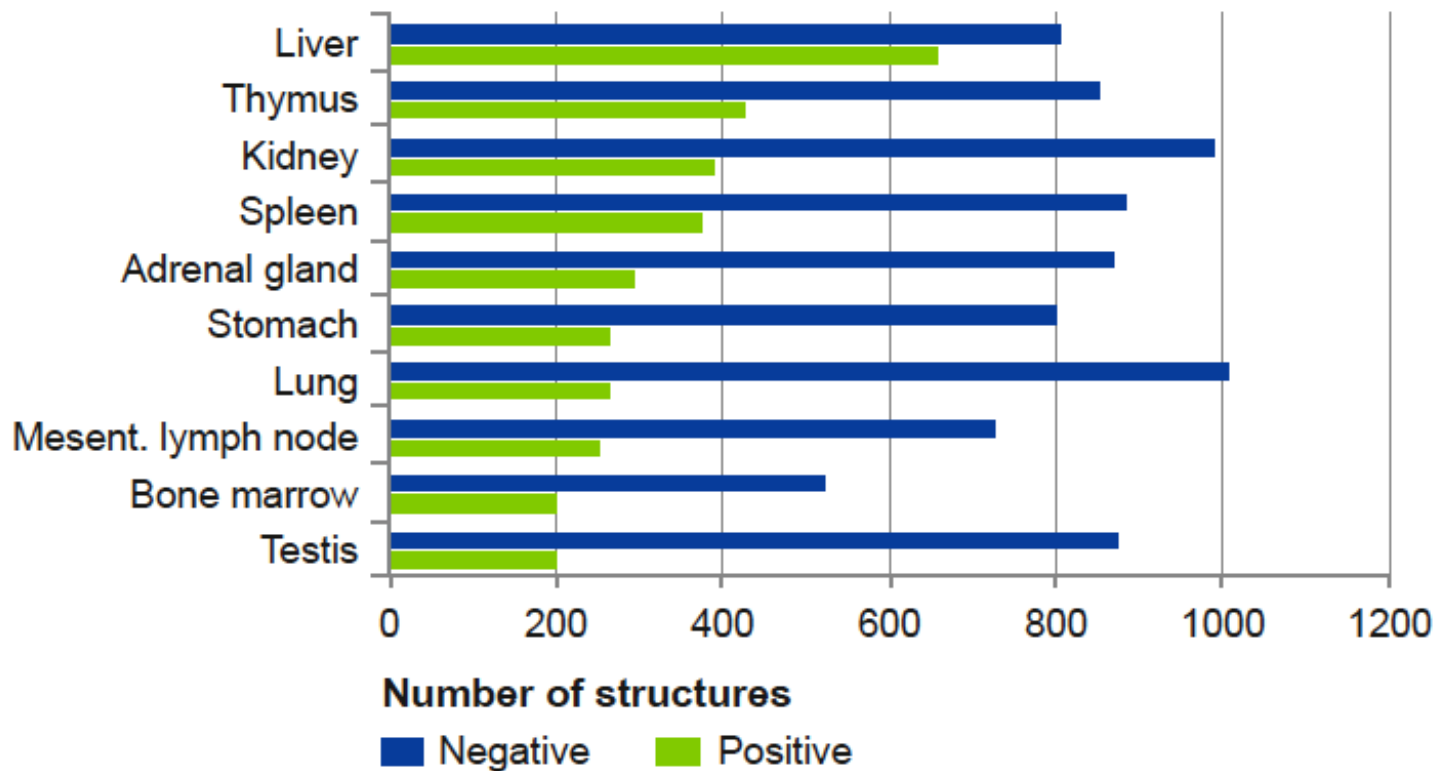
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eTOX DB: Chemical Space Coverage



Reproduced from: Pognan F.
Detection, Elimination,
Mitigation, and Prediction of
Drug-Induced Liver Injury in Drug
Discovery. In Chen M, Will Y
(eds.), Drug-Induced Liver
Toxicity, Methods in
Pharmacology and Toxicology,
Springer Science+Business
Media, 2018. pp. 21-43.

eTOX DB: Toxicological Coverage



eTRANSAFE: Data-related Achievements



- While only aggregated data were shared in eTOX, the **10,000 RDT studies shared** in eTRANSAFE have **individual animal level of detail**.
- The eTRANSAFE RDT data are **coded in the SEND standard**.
- These **data are electronically extracted from the LIMS systems** of the pharmaceutical companies, avoiding human transcription errors.
- Extraction of treatment-related findings described in the free-text RDT study reports by a **natural language processing (NLP)** using a tool developed by the project.
- The pharmaceutical companies also shared in vitro **off-target safety pharmacology data**.
- They also provided **clinical pharmacovigilance data** from periodic safety update reports (PSURs).
- Overall, eTRANSAFE **integrates information from 12 databases** containing proprietary and publicly available data generated in preclinical and clinical research, allowing preclinical vs clinical translational safety comparisons.
- The **Virtual Control Group (VCG) concept** was prototyped → VICT3R project

eTRANSAFE: AI-based Approaches



- Extraction of treatment-related findings described in the free-text RDT study reports by a **natural language processing (NLP)** using a tool developed by the project.
- Development of a machine learning (ML) platform (FLAME) for building, maintaining and using predictive models.

Corvi et al. *Journal of Cheminformatics* (2025) 17:15
<https://doi.org/10.1186/s13321-024-00925-x> Journal of Cheminformatics

SOFTWARE **Open Access**

Check for updates

PretoxTM: a text mining system for extracting treatment-related findings from preclinical toxicology reports

Javier Corvi^{1,2,14*}, Nicolás Díaz-Roussel¹, José M. Fernández¹, Francesco Ronzano³, Emilio Centeno³, Pablo Accuosto², Celine Ibrahim⁵, Shoji Asakura⁶, Frank Bringezu⁷, Mirjam Fröhlicher⁸, Annika Kreuchwig⁵, Yoko Nogami⁶, Jeong Rih⁹, Raul Rodriguez-Esteban¹⁰, Nicolas Sajot¹¹, Joerg Wichard⁵, Heng-Yi Michael Wu¹², Philip Drew⁴, Thomas Steger-Hartmann⁵, Alfonso Valencia^{1,13}, Laura I. Furlong² and Salvador Capella-Gutierrez^{1*}

Pastor et al. *J Cheminform* (2021) 13:31
<https://doi.org/10.1186/s13321-021-00509-z> Journal of Cheminformatics

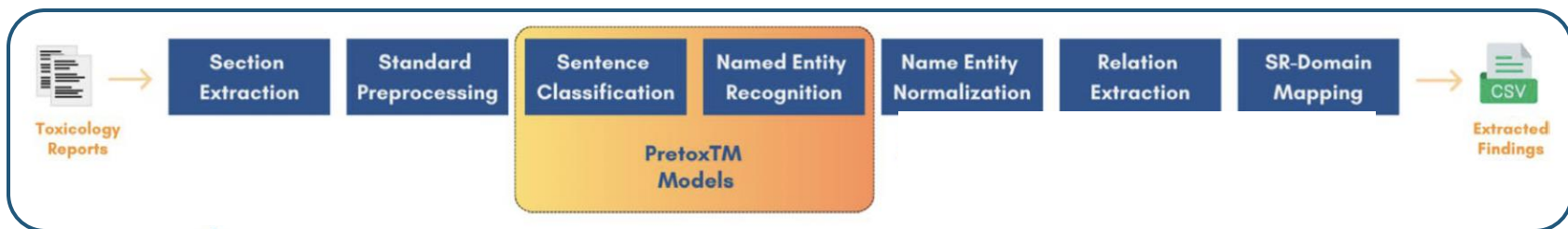
SOFTWARE **Open Access**

Check for updates

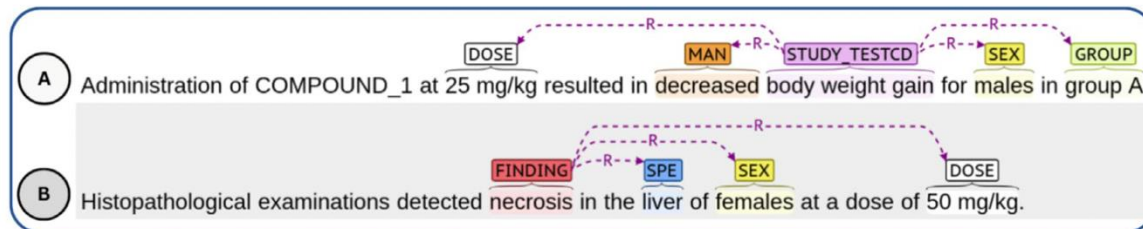
Flame: an open source framework for model development, hosting, and usage in production environments

Manuel Pastor^{*} , José Carlos Gómez-Tamayo and Ferran Sanz

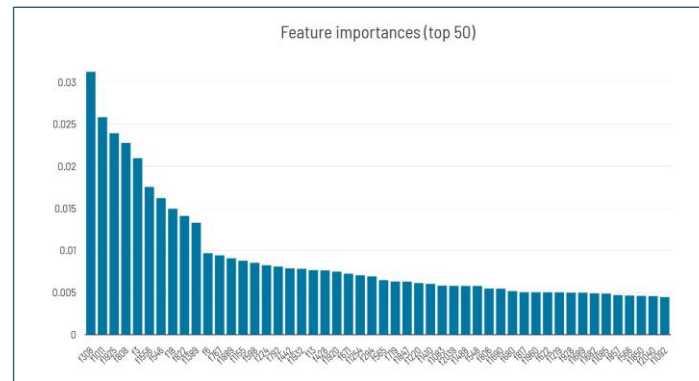
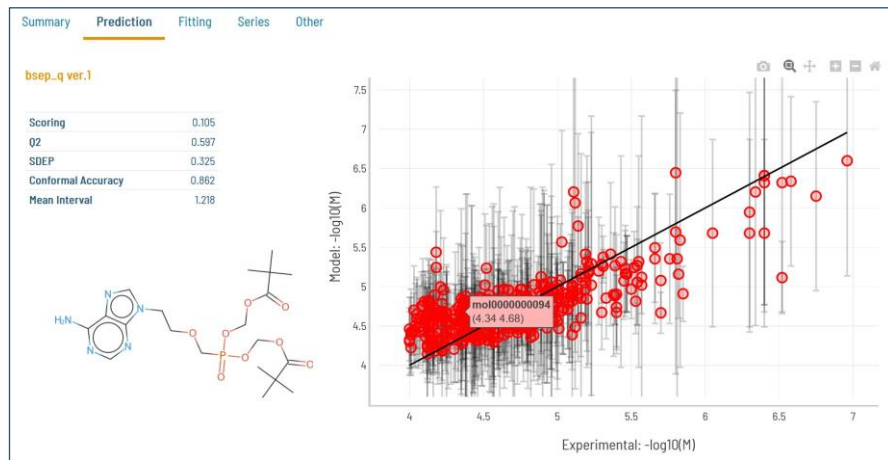
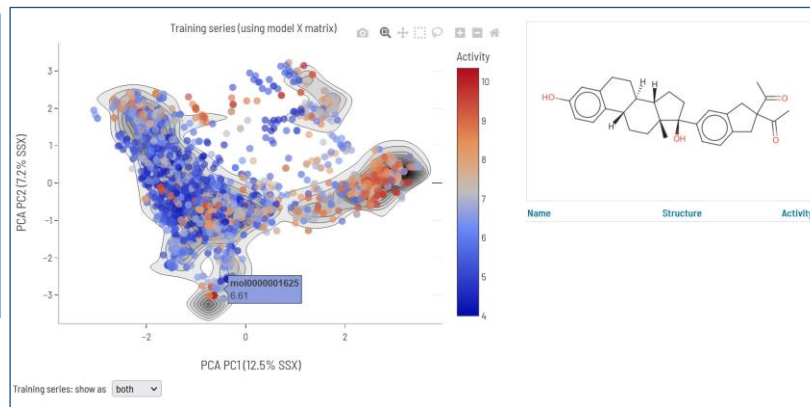
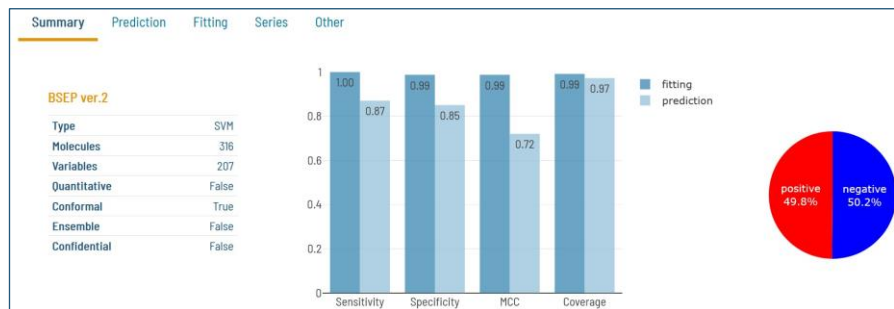
PretoxTM pipeline:



Automatic recognition of entities and relationships:



eTRANSAFE: FLAME ML Platform



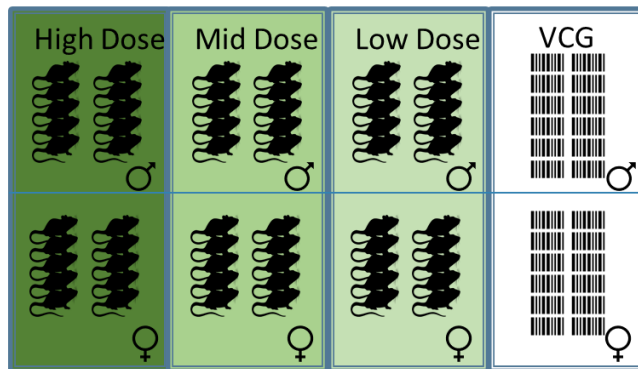
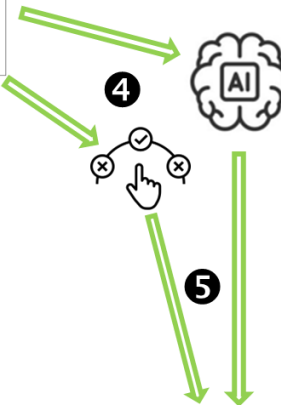
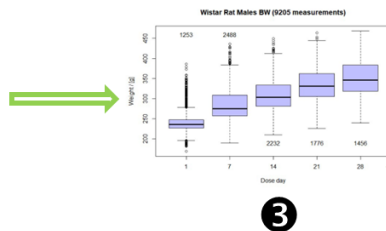
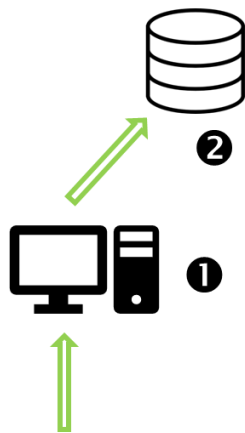
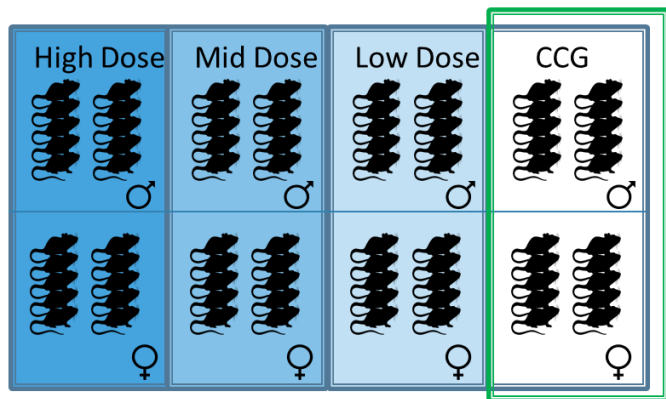
The role of AI-based technologies in data sharing projects supporting the drug and chemical safety assessment

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The VCG Concept



- ❶ Collection of historical data from CCG (concurrent control groups)
- ❷ Shared repository of data from CCG
- ❸ Data curation and characterization
- ❹ Generation of Virtual Control Groups (VCG)
- ❺ Use of VCG in new studies



Adapted from Steger-Hartmann et al. 2020, ALTEX;
<https://doi.org/10.14573/altex.2001311>

VCGs reduce animal use and increase quality

Impact on 3Rs, Quality and Costs



Animal Reduction (implementing the 3R ethical principles)

- Partial to full replacement of concurrent controls
- Reduction of satellite animals
- ...



Quality Increase

- Increase of statistical power
- Use of controls in studies usually run without controls
- Define normal ranges of in life measurements
- Detect rare spontaneous findings in histopathology



Cost Decrease

- Reduced costs associated to control animal purchase
- No experimental costs for the study of concurrent control animals
- Reduced environmental impact



Developing and Implementing Virtual Control Groups to Reduce Animal Use in Toxicology Research



This project is supported by the Innovative Health Initiative Joint Undertaking (IHI JU) under grant agreement No 1011172893. The JU receives support from the European Union's Horizon Europe research and innovation programme and COCIR, EFPIA, Europa Bio, MedTech Europe, and Vaccines Europe and Instem Scientific Limited. Funded by the European Union, the private members, and those contributing partners of the IHI JU. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the aforementioned parties. Neither of the aforementioned parties can be held responsible for them.

The IHI VICT3R Project



Project a glance:

- Kick-off: 1 September 2024
- Finalization: 29 February 2028
- Call: HORIZON-JU-IHI-2023-05-01

- Total Budget: ≈ €31M
- EU Funding: ≈ €13,5M
- Industry Contribution: ≈ €16,6M

www.vict3r.eu

www.ih.europa.eu/projects-results/project-factsheets/vict3r

 IHI-VICT3R |  @IHI-VICT3R |

The VICT3R Consortium

Academic institutions (6)



Universitat
Pompeu Fabra
Barcelona



Fraunhofer
ITEM



technische universität
dortmund



Barcelona
Supercomputing
Center
Centro Nacional de Supercomputación

Universität
Konstanz



Vrije
Universiteit
Brussel

SMEs (8)

SYNAPSE
Research Management Partners



MEDBIO
INFORMATICS



sync
work



Industry Partners (23)



MERCK

AMGEN

AstraZeneca



Boehringer
Ingelheim



Bristol Myers Squibb

instem

IPSEN

Johnson & Johnson
Innovative Medicine

NOVARTIS

Associated Network of CROs (4)



charles river



scontox

BSL Bioservice



sanofi



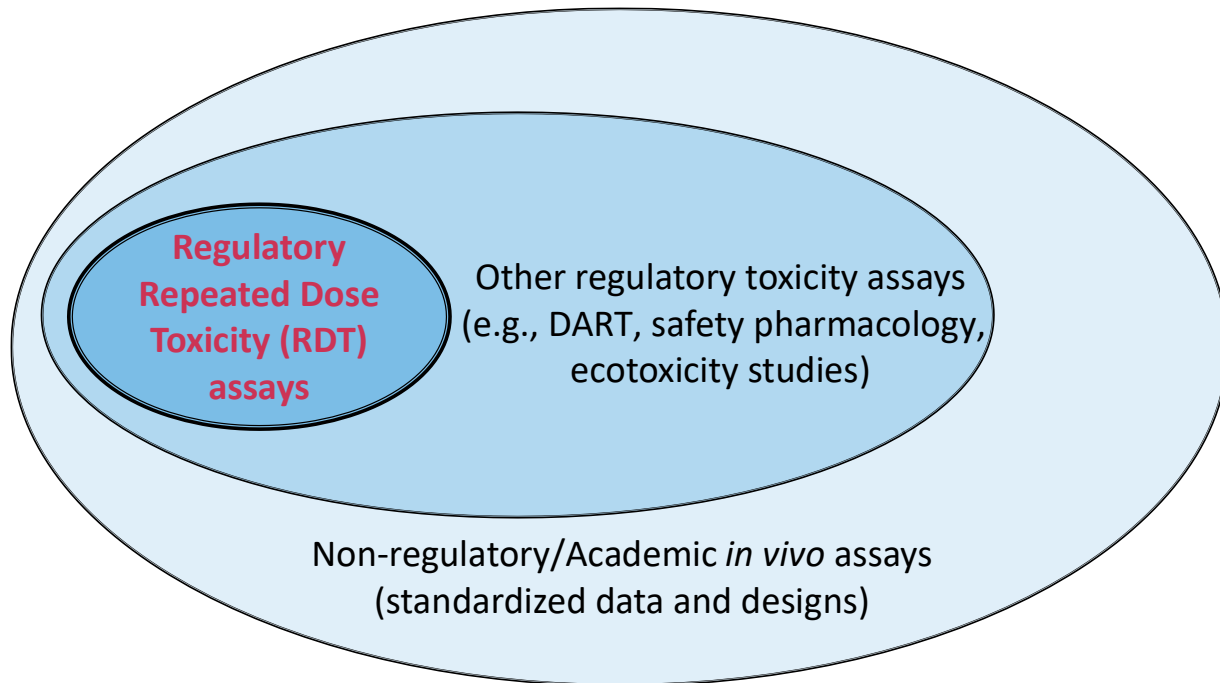
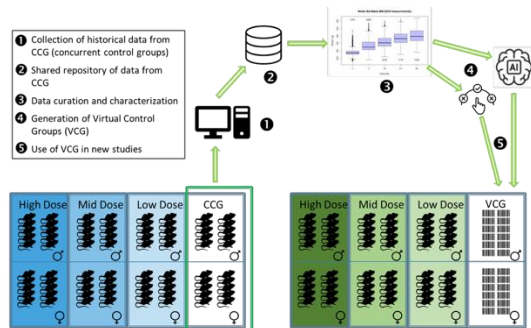
abbvie



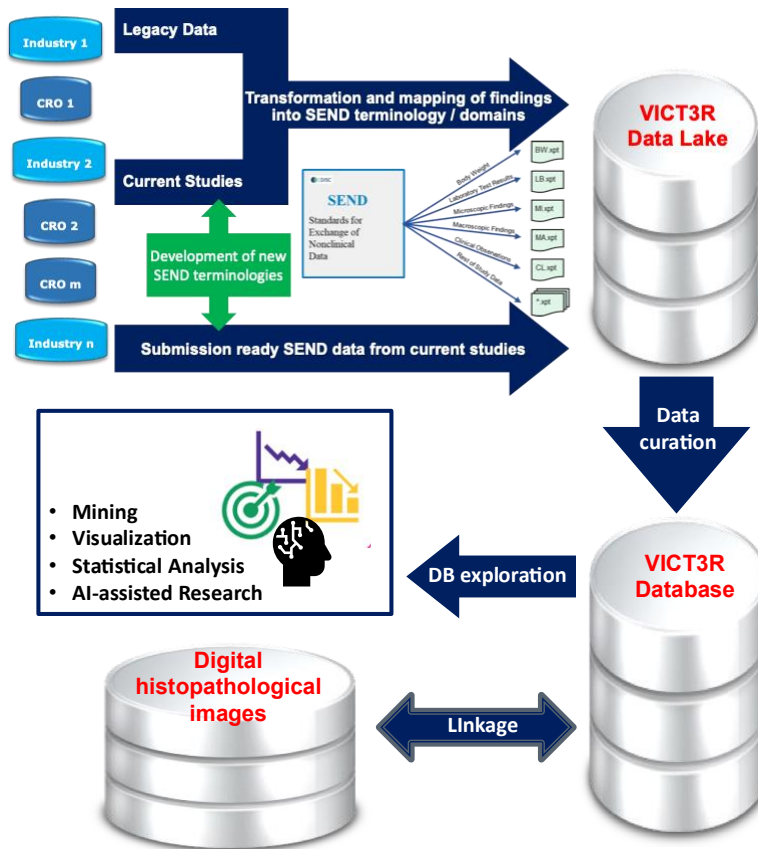
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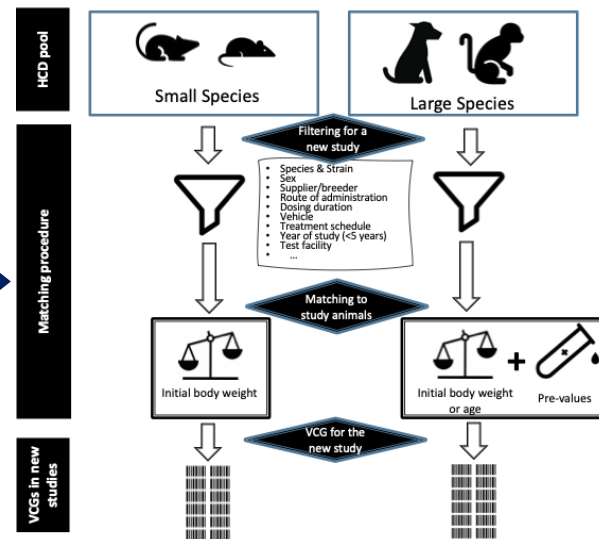
Application of the VCG concept in VICT3R



VICT3R Workflow



Reproduced from:
Sanz et al. NAM J. 2025. In press



VICT3R ongoing qualification process



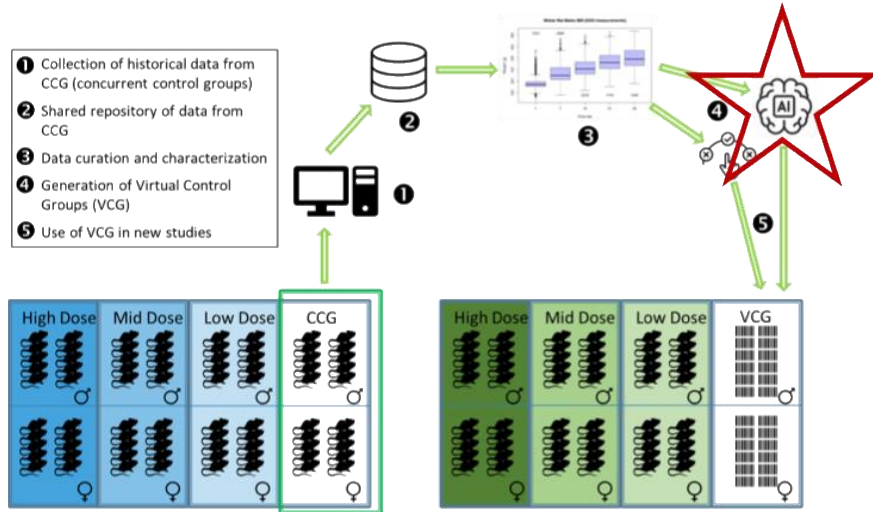
- VICT3R has initiated a request for scientific advice to the European Medicines Agency (EMA):
- CoU I: Application in dose-range finding (DRF) non-GLP studies

The Consortium submitted a series of 28 legacy studies, where the concurrent controls were replaced by adequately matched VCGs and the results were compared to those of the original study- Positive preliminary feedback from EMA.

- CoU II: Partial replacement of concurrent controls in pivotal (GLP) systemic toxicity studies
- CoU III: Full replacement of concurrent controls in pivotal (GLP) systemic toxicity studies

VICT3R: AI-based Approaches

- Generation of synthetic control animals matching the characteristics of those of the treatment group/s.
- AI-aided data imputation to overcome missing data issues.
- Extraction, analysis and display of relevant information from free-text documents and digital pathology images using foundation models (which include natural language processing, question answering, and image classification).

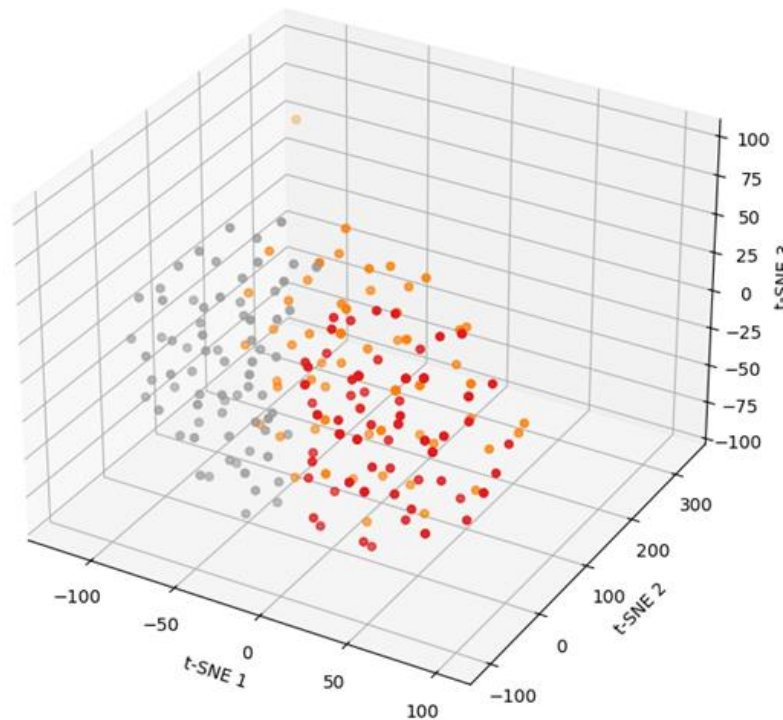


VICT3R: Generation of synthetic control animals



3D t-SNE Visualization - Using All Features from Three Studies

- A previous step for the adequate sampling of animals the generation of VCHs and for the production of synthetic control animals is the proper identification and modelling of essential covariates
- Adequate powerful visualisation tools are also required



VICT3R Data Donations (August 2025, M11)



Active beneficiaries' contributions underpin industry engagement

Control Animal Numbers per Species and VICT3R Beneficiary

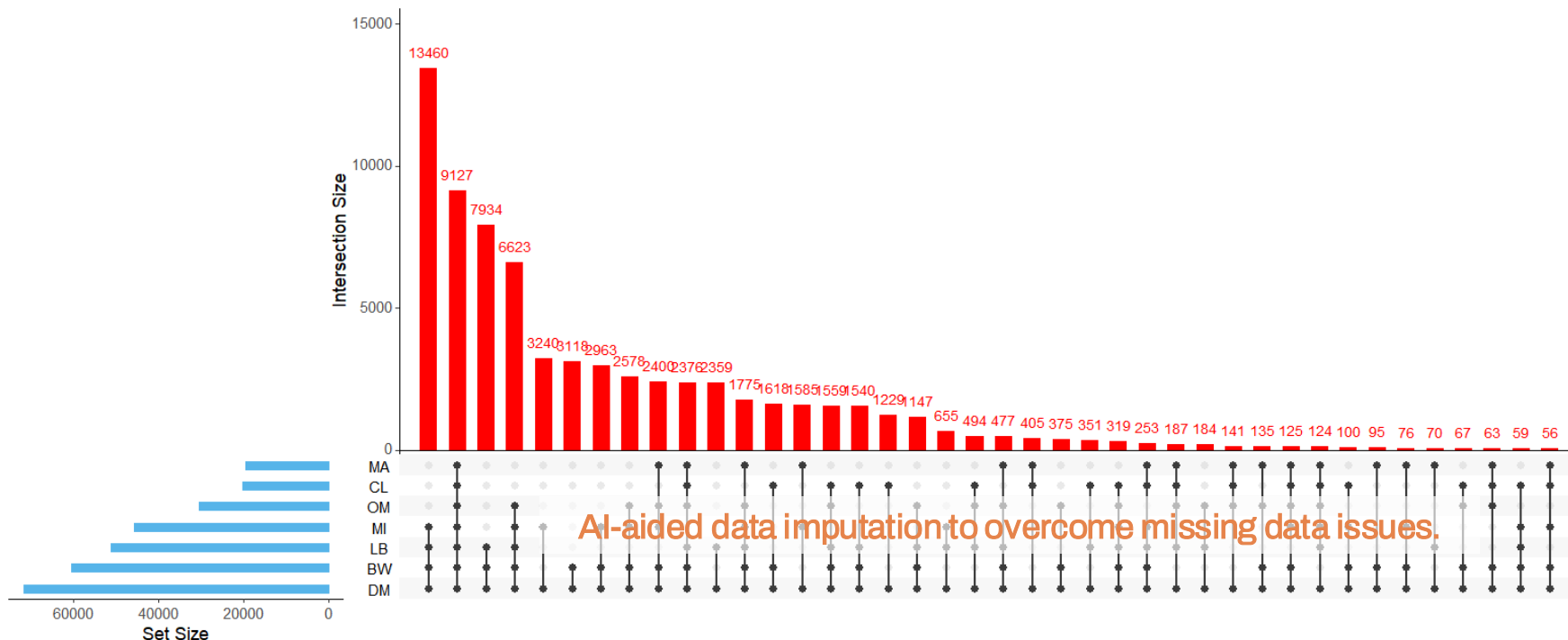
BENEFICIARY	DOG	GUINEA PIG	MINIPIG	MONKEY	MOUSE	PIG	RABBIT	RAT	Sum
1	125	0	0	0	0	0	0	846	971
2	0	0	0	160	0	0	0	0	160
3	117	0	0	82	121	9	0	490	819
4	225	0	0	533	691	0	0	2575	4024
5	180	0	0	32	227	46	0	1355	1840
6	24	0	0	0	0	0	0	134	158
7	307	0	9	377	889	44	218	2656	4500
8	12	0	18	6	0	0	0	174	210
9	2085	52	56	1442	4763	0	210	19044	27652
10	363	0	0	299	1587	0	9	6193	8451
11	0	0	0	0	0	0	0	16242	16242
12	2884	0	0	1892	0	0	0	23346	28122
13	486	0	6	231	1452	0	24	3329	5528
14	8	0	0	0	0	0	0	46	54
15	0	0	0	52	40	0	0	115	207
16	148	0	0	279	600	0	0	1076	2103
Sum	6964	52	89	5385	10370	99	461	77621	101041



VICT3R DB: Rat Data (version 2.0) Domain Coverage



Highly dimensional and sparse (for some parameters)



VICT3R: Natural Language Processing (NLP)



- Continuation of the approaches used in eTRANSAFE (PretoxTM) for the information extraction from free-text toxicological reports.
- NLP-guided analysis of the CNS-related Non-Technical Summaries (NTS) of the ALURES DB, as NTS records contain valuable details on study designs and experimental procedures, but this information is presented as free-text and written combining 22 different languages. This work has resulted on the identification of:
 - Experimental Paradigms/Frameworks (in 1135 reports)
 - Manipulations/Procedures (in 5519 reports)
 - Tests/Apparatus (in 1139 reports)
 - Data Acquisition Methods (in 4,830 reports)

Why is VICT3R relevant for other NAM Projects?



Ongoing collaboration with ASPIS

Benchmarking for in vitro tools

Data from VICT3R, especially clinical pathology values, could serve as reference for assessing the physiological/in vivo relevance of (animal-based) in vitro systems.

Optimization of physiological maps

Data from VICT3R could serve the optimization of physiological maps in ONTOX.

Interspecies comparison

Data from VICT3R could be compared with human counterparts available in ASPIS for identification of possible interspecies differences.

Characterization of background pathologies

Providing additional light onto frequency of background pathologies, interspecies differences, age-dependency, etc.

Leveraging learnings from VICT3R's regulatory qualification experience

VICT3R experience during the qualification process could be helpful for the validation of NAMs.

Take home messages



- **Biomedical research largely depends on the relevance, amount and quality of data** that is available.
- The **AI-based approaches offer new opportunities for exploiting biomedical data.**
- When planning to use AI **technologies don't forget the “garbage in, garbage out (GIGO)” principle.**



Thanks!

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Co-funded by
the European Union

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