PREMIER

PRIORITISATION AND RISK EVALUATION OF MEDICINES IN THE ENVIRONMENT

The PREMIER project:

Managing Big Data for Environmental Risk Assessment of Human Pharmaceuticals

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 875508.
The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

PREMIER General Information

Period: 01/09/2020 to 30/08/2026

Duration: 6 years

EFPIA companies: 10

Academic & SMEs: 15

Budget: € 9 Million

IMI: € 4.5 Million (in cash)
EFPIA: € 4.5 Million (in kind)

Project Coordinator:

Ad Ragas

Radboud University Nijmegen

Project Leader:

Jason Snape

AstraZeneca AB

PREMIER: Addressing Unmet Needs

Current strategy to assess the environmental impact of pharmaceuticals is impracticable for assessing the 1000+ untested legacy pharmaceuticals, because it:

Is time consuming

Is very costly

Requires intensive animal testing

Additionally, the current strategy is inappropriate for addressing legacy pharmaceuticals because it:

Is market application driven

Does not identify and focus on medicines of potential concern

Requires an identified owner to conduct and pay for the studies

PREMIER Aims

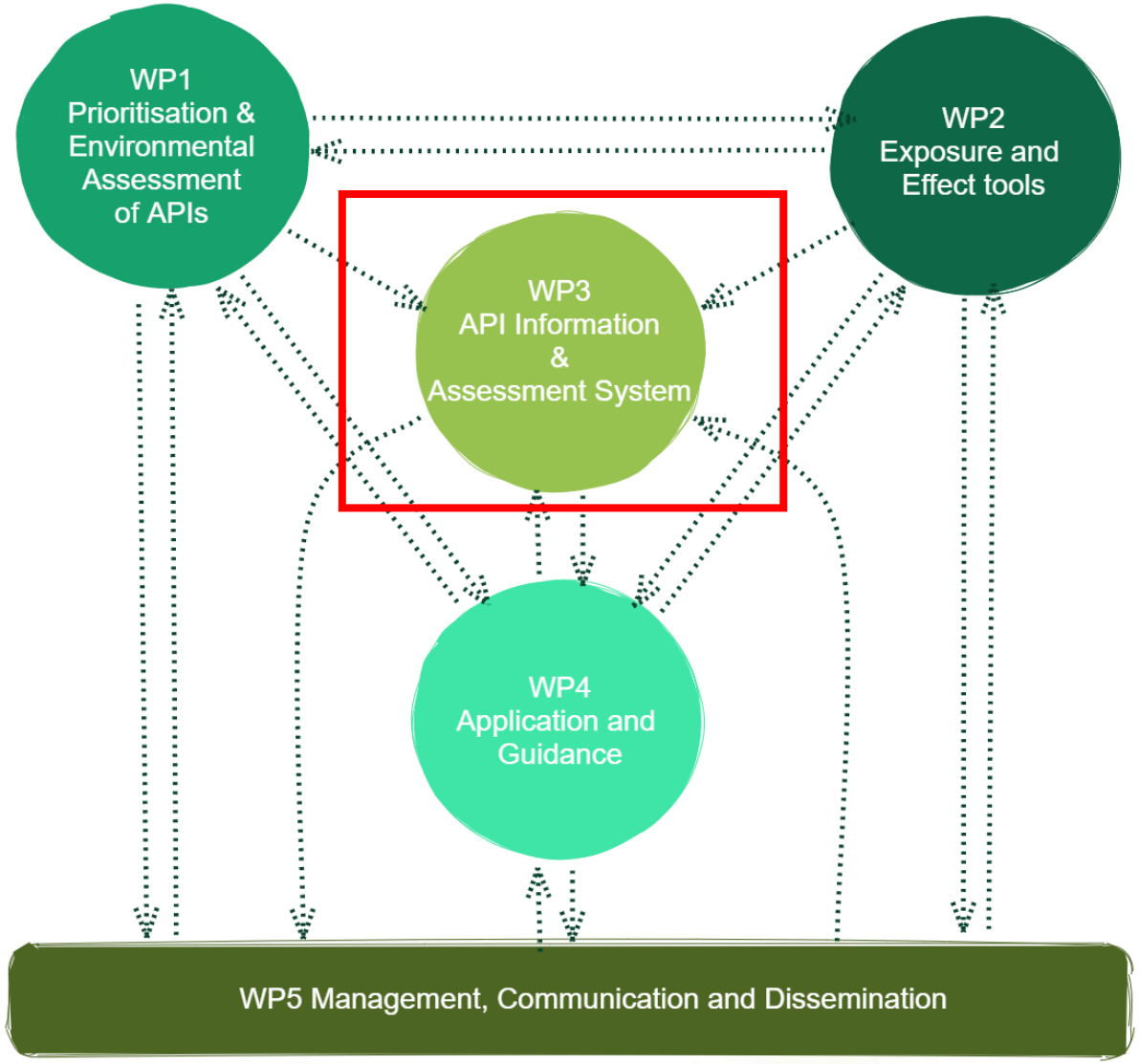
1. Create a **public database** on the *universe of APIs* used in the EU and containing all available *data relevant for environmental risk assessment*

2. Develop novel **predictive tools** for assessing the *exposure and effects* of APIs and explore *feasibility of green design*

3. Develop **decision trees** and **guidance** for *prioritization* of APIs, *regulatory assessments* and *stakeholder questions*

4. Integrate database, tools and decision trees into a **digital assessment system**

How Will We Achieve Our Aims?



PARTICIPANTS – CONSORTIUM

Research Institutions

Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

Fraunhofer ITEM

eawag aquatic research

LEUPHANA UNIVERSITÄT LÜNEBURG

Radboud University

UNIVERSITY of York

GÖTEBORGS UNIVERSITET

UNIVERSITY OF HELSINKI

UNIVERSITY OF EXETER

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS

Regulatory Institutions

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

SMEs

teamit RESEARCH

eco logic

E·C·T Oekotoxikologie GmbH

Industry

Lilly

Roche

BAYER

Bristol Myers Squibb

MSD

AstraZeneca

SANOFI

NOVARTIS

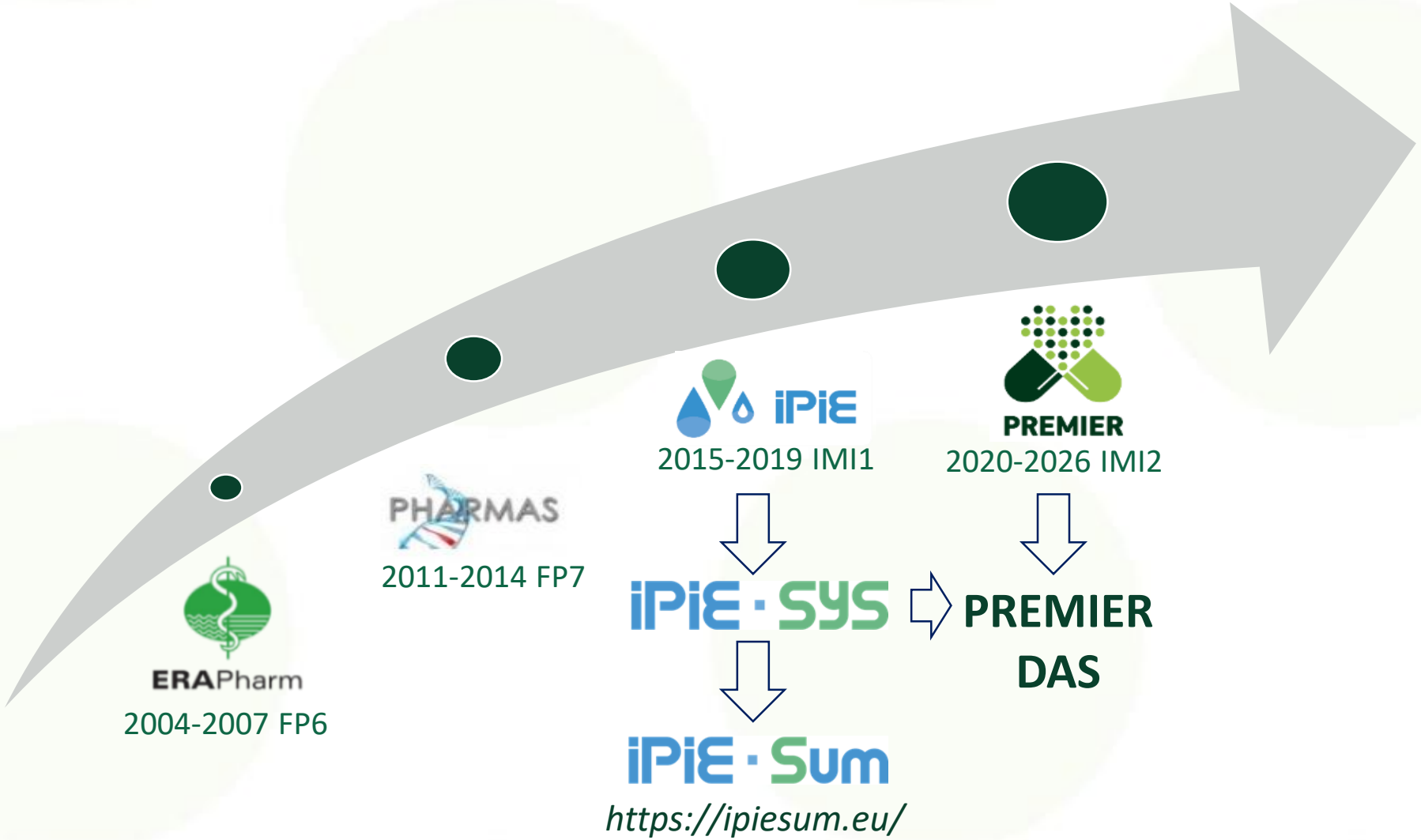
SERVIER

gsk

The DAS: Digital Assessment System

Database:	substance properties (APIs) for ERA
QSAR/QSPR tools:	predict substance properties
Models:	predict exposure, effects & risks
Decision trees:	to support regulatory decisions (e.g. EMA guideline)

PREMIER History



Database Contents

Identity & structure:	CAS, Smiles, InChI, MW, structure, etc.
Exposure/Fate:	partition coefficients, degradation
Bioaccumulation:	BCFs, BAFs
Effects:	acute & chronic ecotoxicity data
***MECs**:*	*UBA database, EMPO database*
***Consumption**:*	*IQVIA (?), DDDs, products*
***Other**:*	*excretion, MoA (?), ATC, etc.*

Where do our data come from?

Universe APIs: Art. 57 (EMA), DrugBank

Industry: iPiEsys (200-300), newly extracted

Testing: 25 case study APIs (industry & public)

Databases: Drugbank, Pubchem, USEPA's ecotox, UBA, etc.

Literature: Web of Science, Scopus, Google Scholar, etc.

EPARs: EU, national, FDA, etc.

Proprietary: IQVIA?

What will the data be used for?

Purpose	Who?
Development of predictive tools	Scientists (PREMIER partners)
Prioritization and environmental risk assessment of APIs at various levels of detail	All stakeholders (industry, regulators, water boards, water companies, scientists, NGOs)
Support formal regulatory decisions (e.g. EMA guideline)	EMA & national agencies
Data access (Letter of Access) ?	Generic companies

Database Issues....

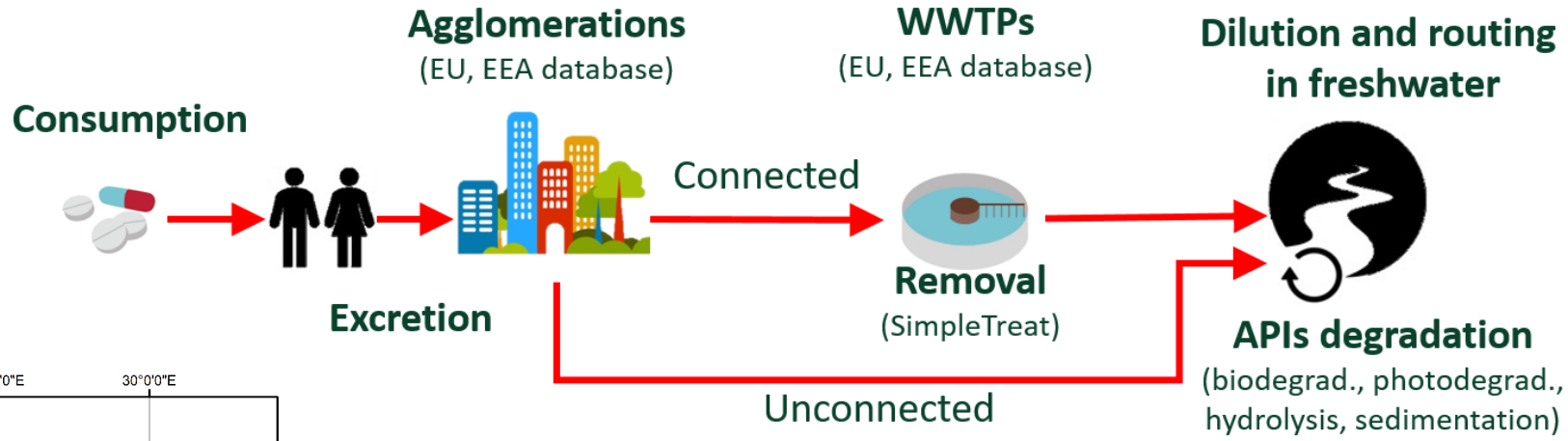
Identification: CAS?, Products?, Salts?

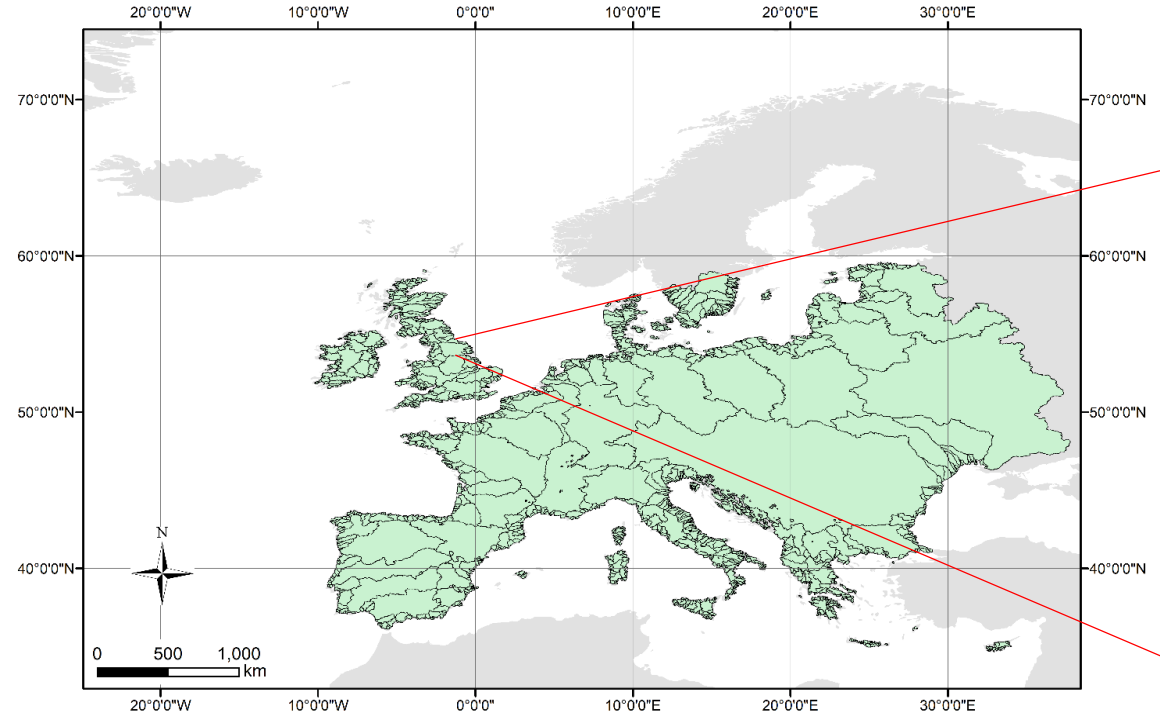
Confidentiality: How to deal with proprietary data?

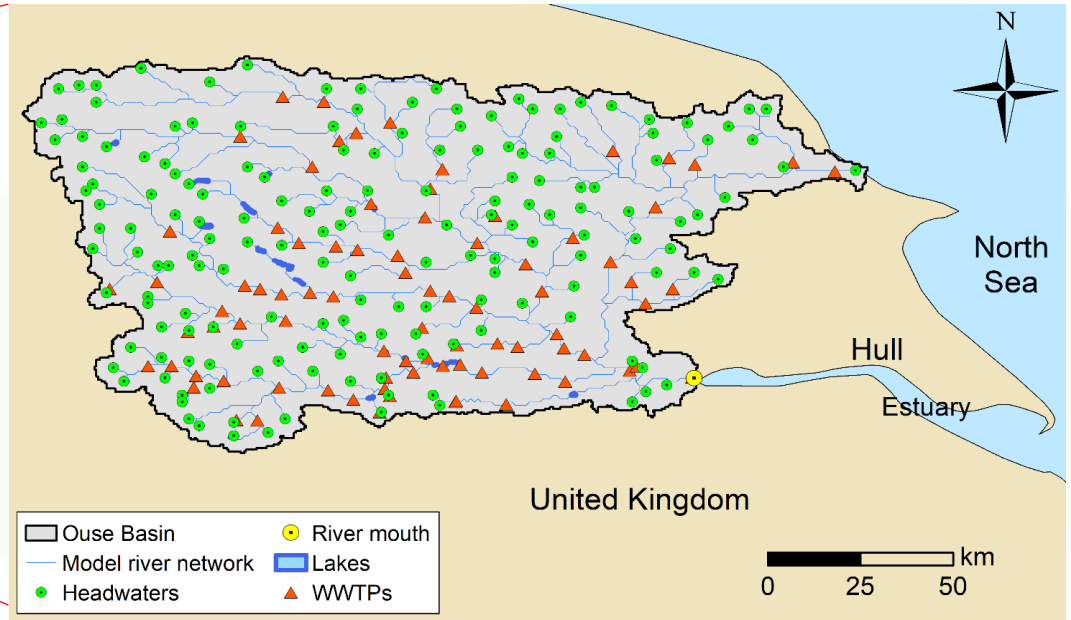
Data quality: How to assess? By whom? For whom?

Provenance: Each data entry will be tracked..., but is this feasible for all industry, database and EPAR data?

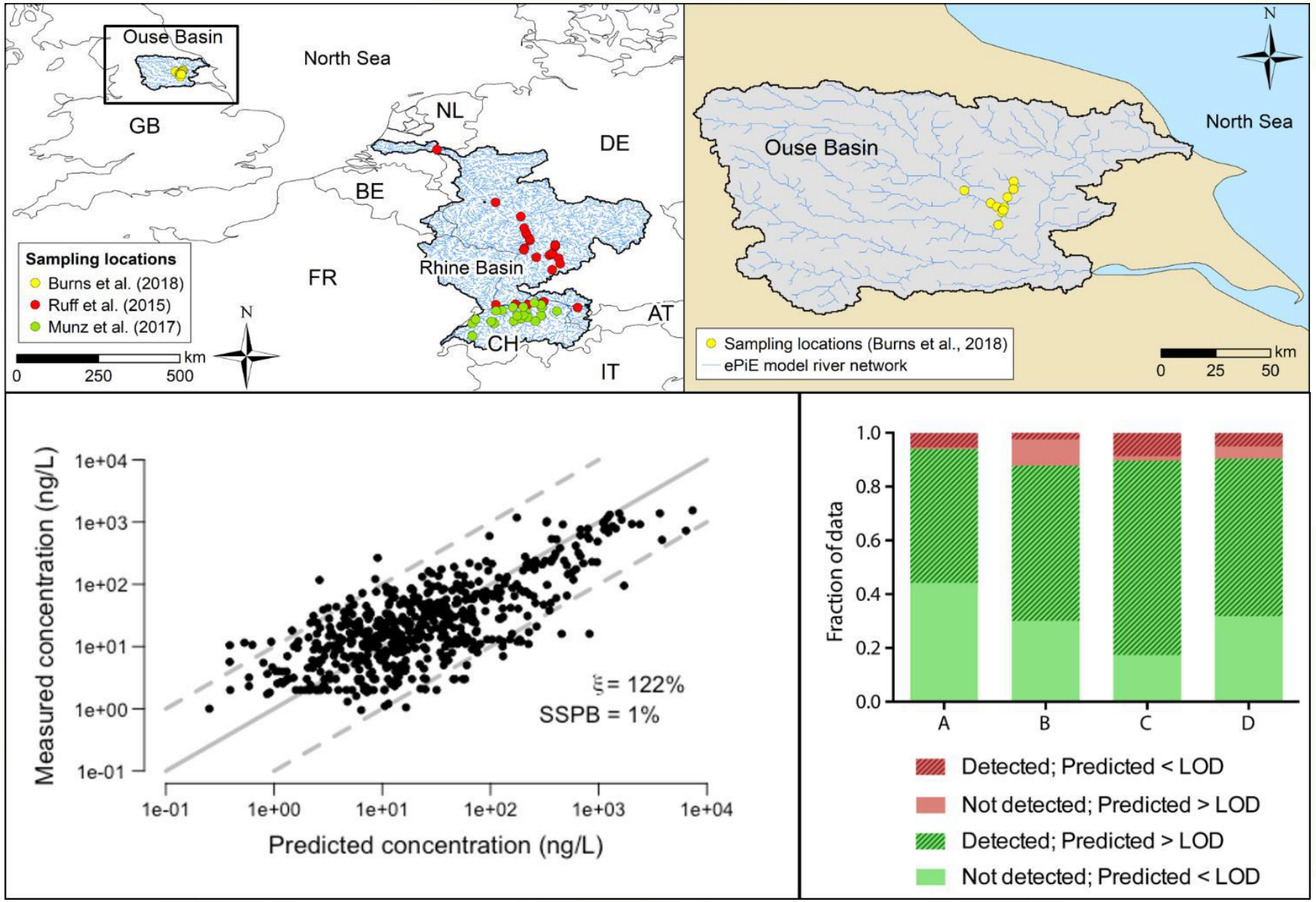
The ePiE model



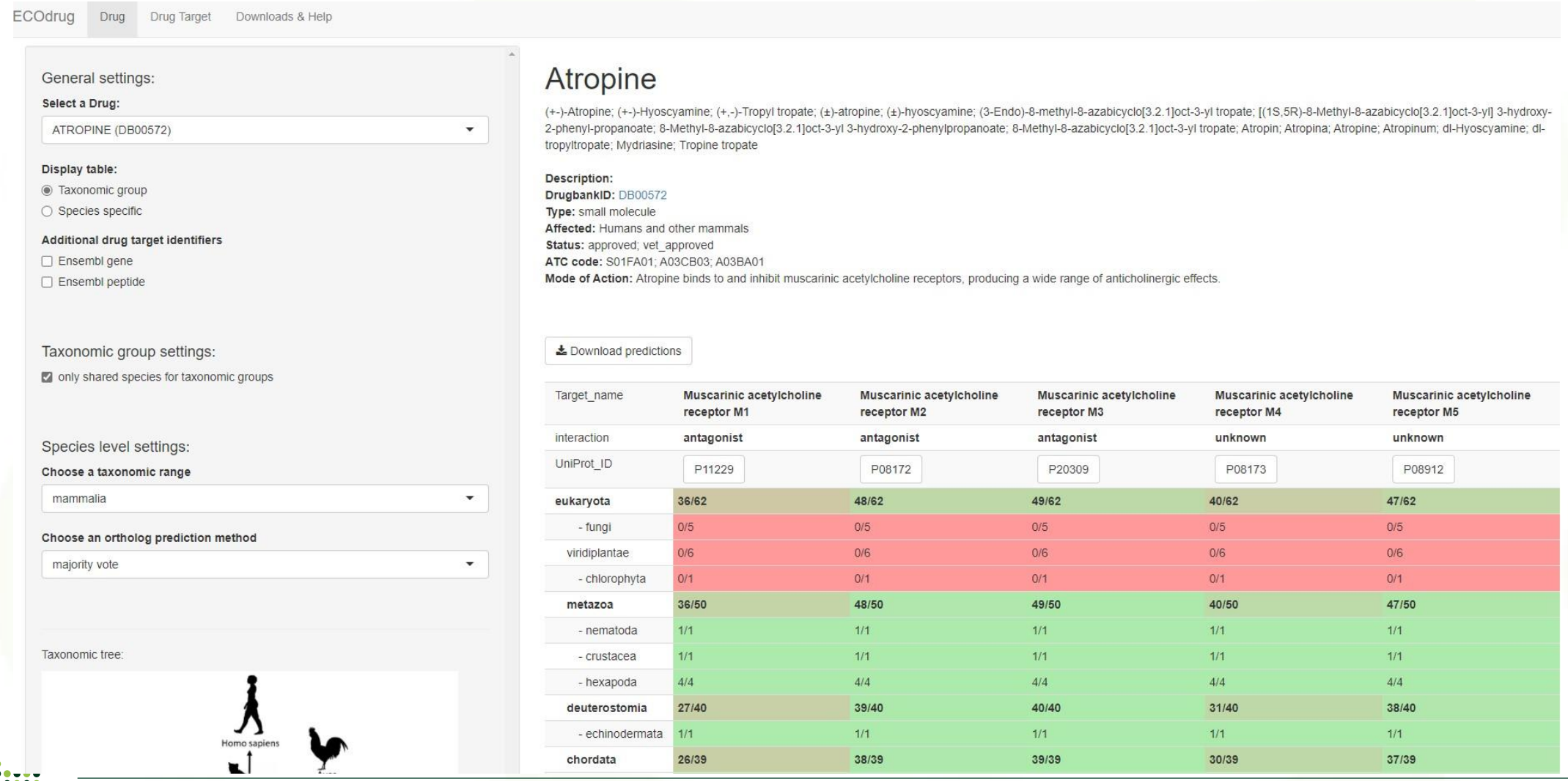




ePiE validation



EcoDrug: are drug receptors convserved in non-human species?



Target_name	Muscarinic acetylcholine receptor M1	Muscarinic acetylcholine receptor M2	Muscarinic acetylcholine receptor M3	Muscarinic acetylcholine receptor M4	Muscarinic acetylcholine receptor M5
interaction	antagonist	antagonist	antagonist	unknown	unknown
UniProt_ID	P11229	P08172	P20309	P08173	P08912
eukaryota	**36/62**	**48/62**	**49/62**	**40/62**	**47/62**
- fungi	0/5	0/5	0/5	0/5	0/5
viridiplantae	0/6	0/6	0/6	0/6	0/6
- chlorophyta	0/1	0/1	0/1	0/1	0/1
metazoa	**36/50**	**48/50**	**49/50**	**40/50**	**47/50**
- nematoda	1/1	1/1	1/1	1/1	1/1
- crustacea	1/1	1/1	1/1	1/1	1/1
- hexapoda	4/4	4/4	4/4	4/4	4/4
deuterostomia	**27/40**	**39/40**	**40/40**	**31/40**	**38/40**
- echinodermata	1/1	1/1	1/1	1/1	1/1
chordata	**26/39**	**38/39**	**39/39**	**30/39**	**37/39**

http://ecodrug.org/

PREMIER: The Sustainability Challenge

Confidentiality: How to deal with confidential data?

Ownership: data, IT infrastructure, models, DAS

Hosting: Simomics, EMA, third party?

Maintenance: Who will update? Who will pay?

Sustainability: How to guarantee long-term access?

Thank you!

Questions?

https://imi-premier.eu/

a.ragas@fnwi.ru.nl

PREMIER

PRIORITISATION AND RISK EVALUATION OF MEDICINES IN THE ENVIRONMENT

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 875508. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.