14 November 2019

Open Source Models and Tools For Chemical Risk Assessment in Humans, Animals and the environment

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Senior Scientific Officer
Scientific Committee and Emerging Risks Unit

Trusted science for safe food

efsa
European Food Safety Authority

41st Focal Point Meeting

Open Source Tools and Transparency

EDITORIAL

EFSA Journal

APPROVED: 26 March 2015 PUBLISHED: 27 March 2015

doi:10.2903/j.efsa.2015.e13031

Increasing robustness, transparency and openness of scientific assessments

Hardy A, Dorne JLCM, Aiassa E, Alexander J, Bottex B, Chaudhry Q, Germini A, Nørrung B, Schlatter J, Verloo D, Robinson T

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 12 July 2017

doi: 10.2903/j.efsa.2017.4971

Guidance on the use of the weight of evidence approach in scientific assessments

EFSA Scientific Committee,
Anthony Hardy, Diane Benford, Thorhallur Halldorsson, Michael John Jeger, Helle Katrine Knutsen, Simon More, Hanspeter Naegeli, Hubert Noteborn, Colin Ockleford, Antonia Ricci, Guido Rychen, Josef R Schlatter, Vittorio Silano, Roland Solecki, Dominique Turck, Emilio Benfenati, Qasim Mohammad Chaudhry, Peter Craig, Geoff Frampton, Matthias Greiner, Andrew Hart, Christer Hogstrand, Claude Lambre, Robert Luttik, David Makowski, Alfonso Siani, Helene Wahlstroem, Jaime Aguilera, Jean-Lou Dorne, Antonio Fernandez Dumont, Michaela Hempen, Silvia Valtueña Martínez, Laura Martino, Camilla Smeraldi, Andrea Terron, Nikolaos Georgiadis and Maged Younes

Abstract

Organisations should not aim at '*increase trust*' rather aim to demonstrate *Trustworthiness*

Information should be

- Accessible
- Intelligible
- Useable
- Assessable

Professor David Spiegelhalter
EFSA 3rd scientific Conference
September 2018

Four Pillars of Chemical Risk Assessment

Risk assessment

- **Fit for purpose**
- **Uses tiered approaches depending on data available, time and resources**

Step 1
Hazard Identification

Identify toxic effects

Step 2
Hazard Characterisation

Quantify toxic effects:
- **Dose response**
- **Reference Point**
- **Reference value**

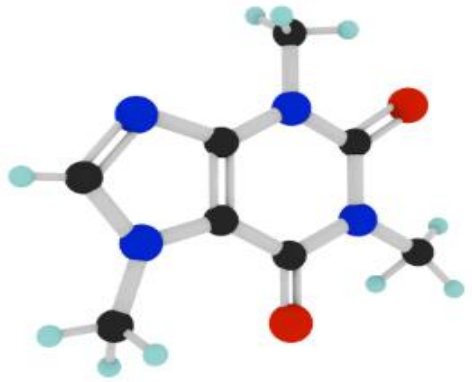
Step 3
Exposure Assessment

Occurrence x Consumption

Step 4
Risk Characterisation

Hazard vs Exposure: Risk

What does OpenFoodTox Contain?



4,750 Substances

1,800 Scientific outputs

Inventory of EFSA's chemical RA since its creation in 2002

Easy Reference and Crisis

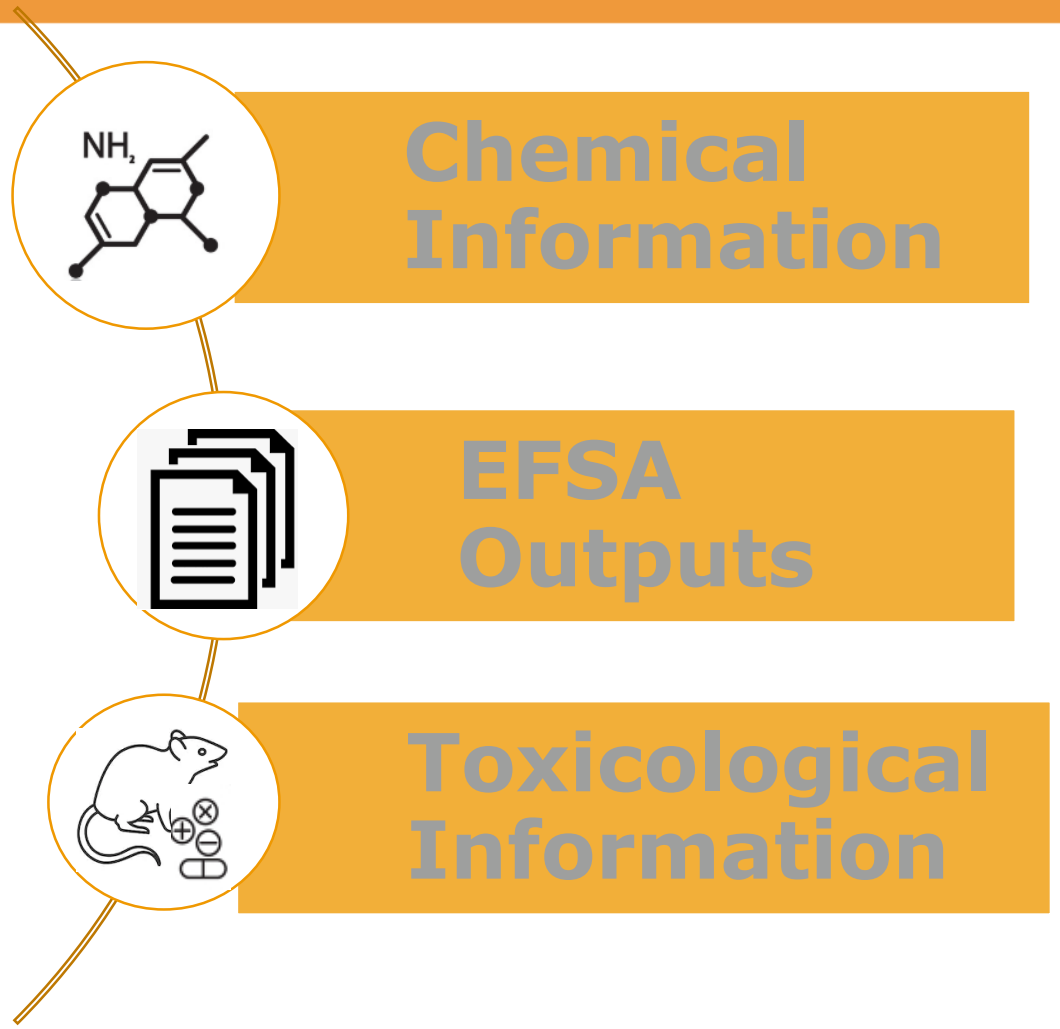
- Crisis: Free, Quick, Easy access to EFSA's Chemical Hazards Data
- Tool for stakeholders

Avoid duplication of efforts

International Harmonisation and Data Sharing

- OECD Harmonised Templates
- Data sharing

What does OpenFoodTox Contain? (2)



Substance Identity : CAS, IUPAC, SMILES etc.

- Single Substances (e.g. flavourings)
- Group of Substances (e.g. mixture/formulation)

- **Opinions**
- **Conclusions on Pesticides**
- **Statements**

Title, Publication date, link etc.

Genotoxicity

Reference Points

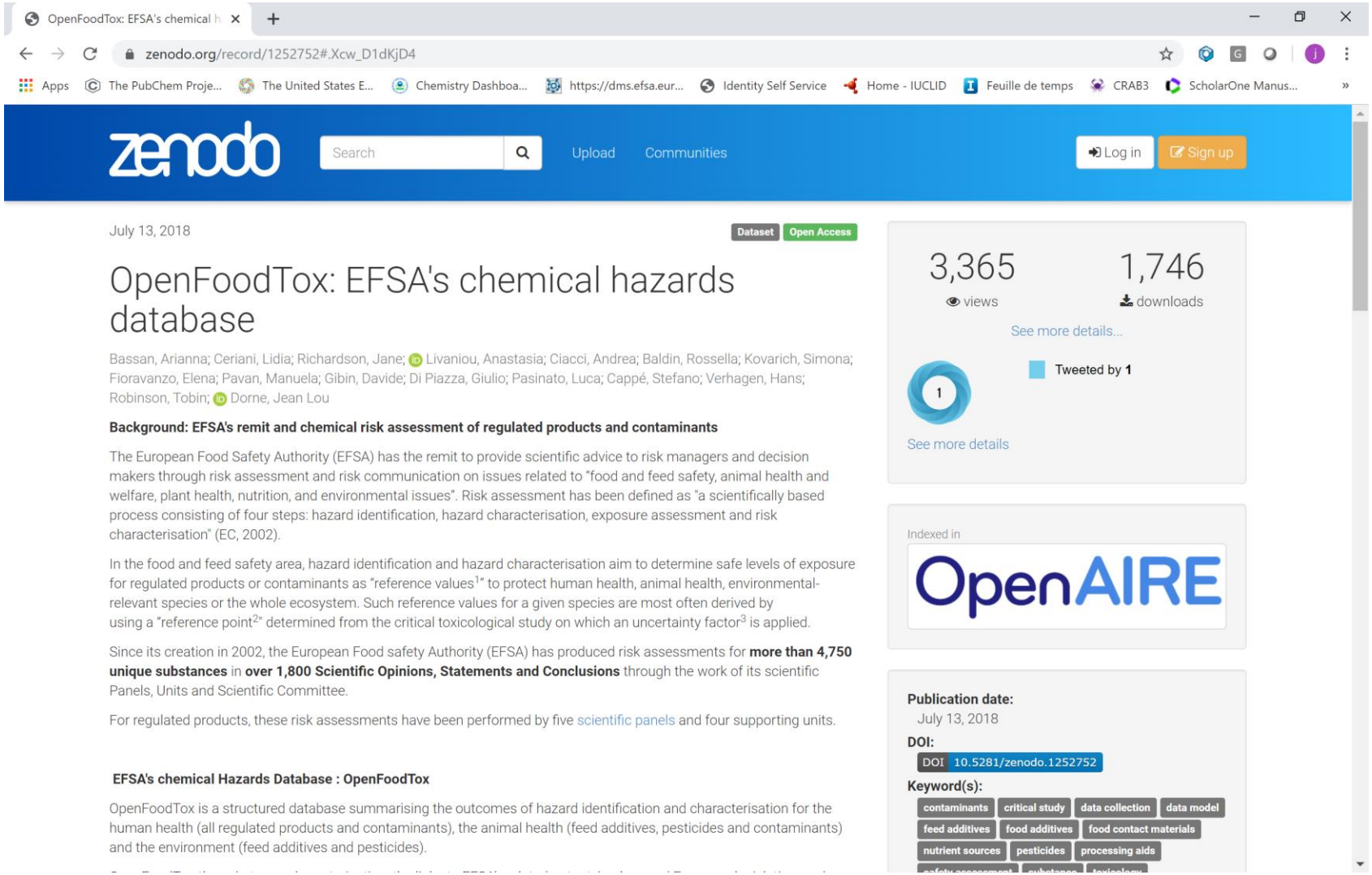
- Human and Animal health and Ecological RA

Reference Values

- Regulated products: e.g. ADI for pesticides
- Nutrients: e.g DRV for vitamins and minerals
- Contaminants: TDI for acrylamide

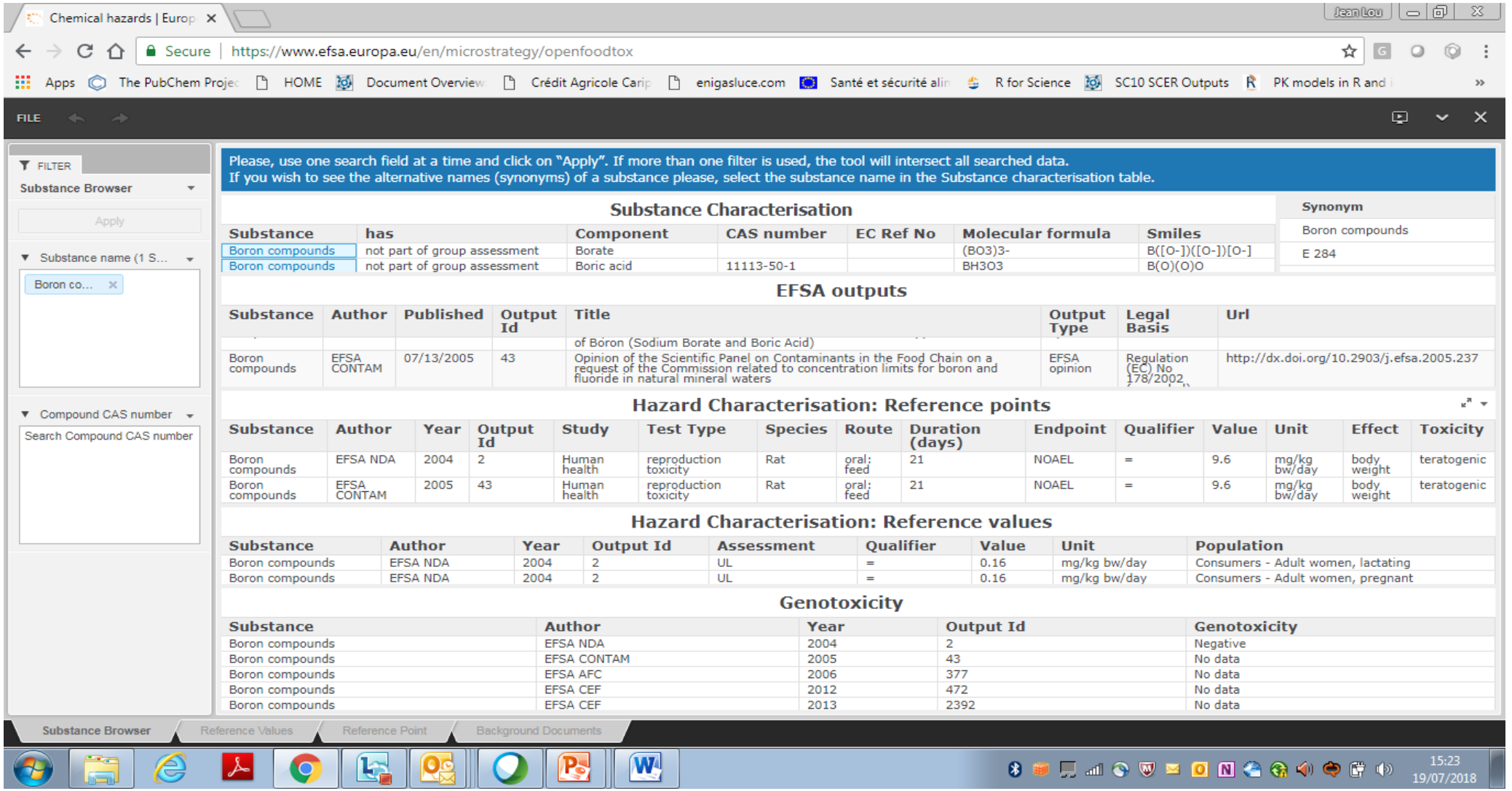
Downloading All Data From OpenFoodTox

https://doi.org/10.5281/zenodo.780543

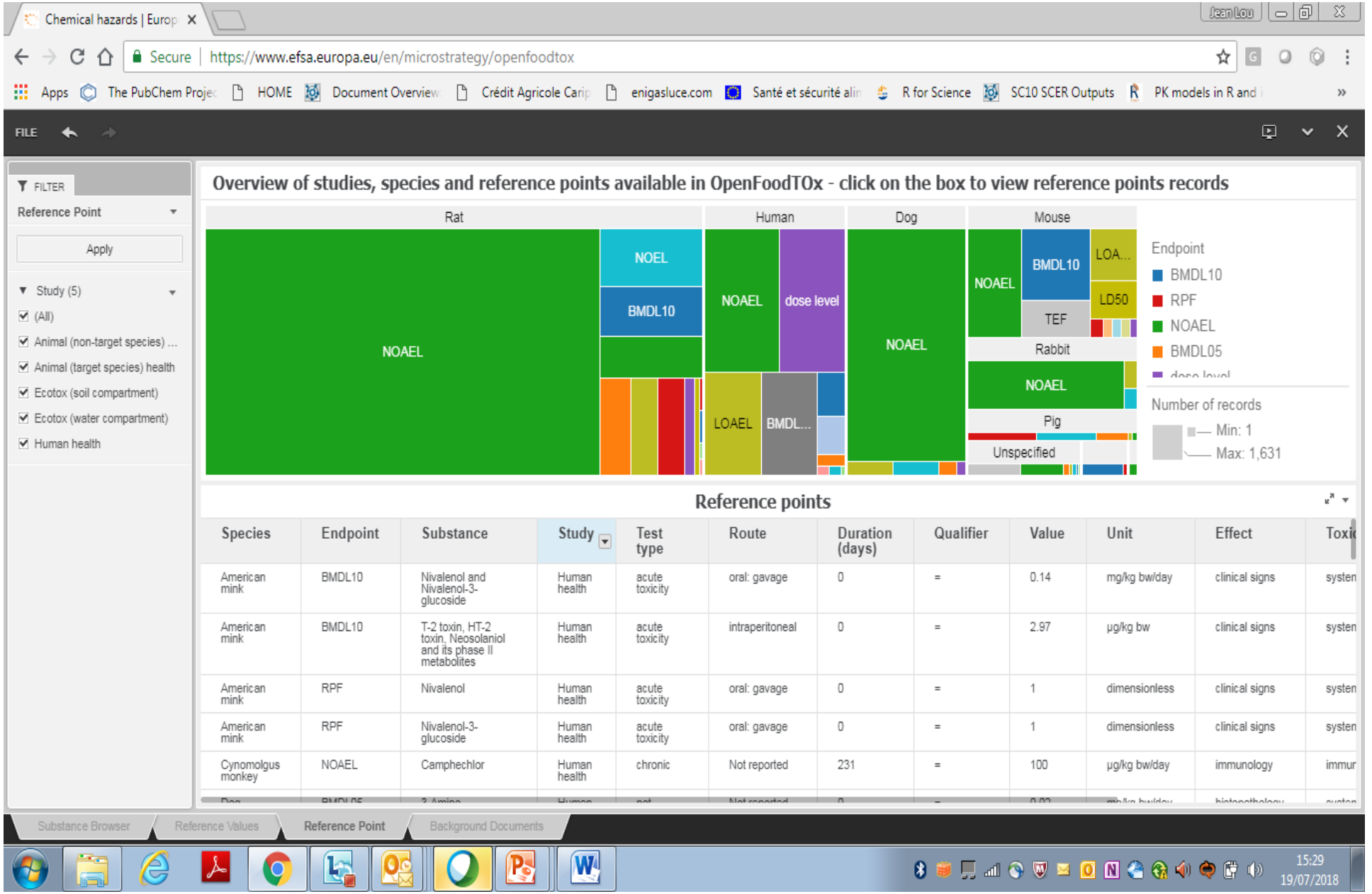


Microstrategy Tool (1)

https://www.efsa.europa.eu/en/microstrategy/openfoodtox



Microstrategy Tool (2)



The Future of OpenFoodTox 2.0 2018-2022

Collect new properties

- Physico-chemical properties, TK data, bioaccumulation etc
- Summary exposure estimates
- Intermediate effects (mechanistic data)

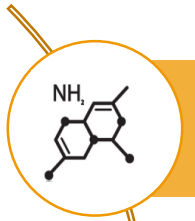
New and updated OECD harmonised Templates

- Design template for Weight of evidence, biological relevance and uncertainty
- Update mechanistic (OHT 201) and TK template

Link OpenFoodTox with modelling platforms

- QSAR models e.g VEGA
- Published EFSA values and Predicted values

OpenFoodTox 2.0



Chemical Information
Exposure

→ Structure
→ Physico-chemical properties
→ Summary Exposure

EFSA Outputs

Toxicological Information

→ Genotoxicity
→ Toxicokinetics *vitro vivo*
→ Toxicodynamics *vitro vivo*

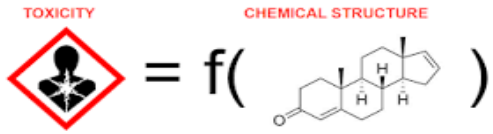
Modelling Platform

EXTERNAL SCIENTIFIC REPORT

APPROVED: 31 March 2017 AMENDED 14 July 2017

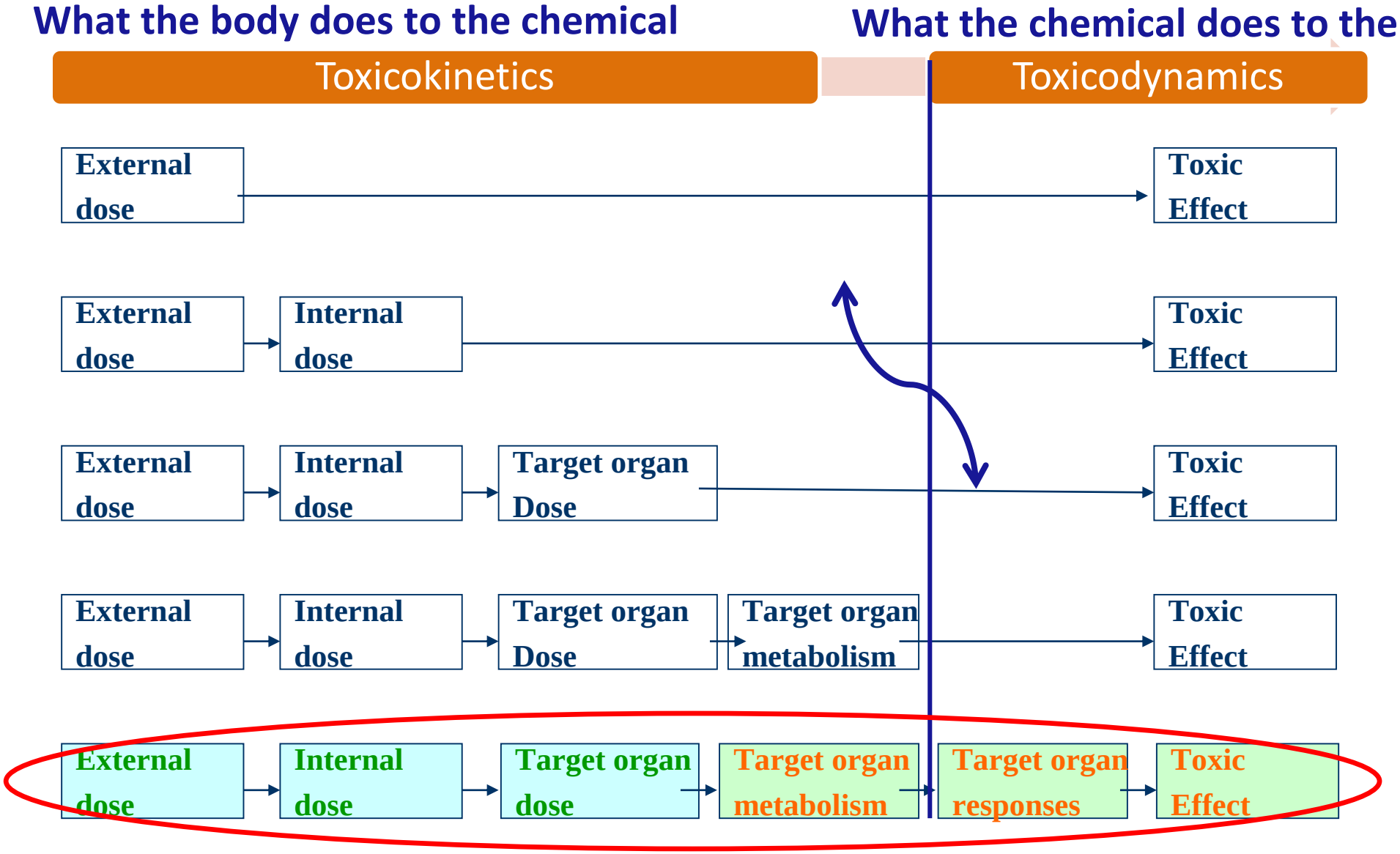
doi:10.2903/sp.efsa.2017.EN-1206

Developing innovative *in silico* models with EFSA's OpenFoodTox database

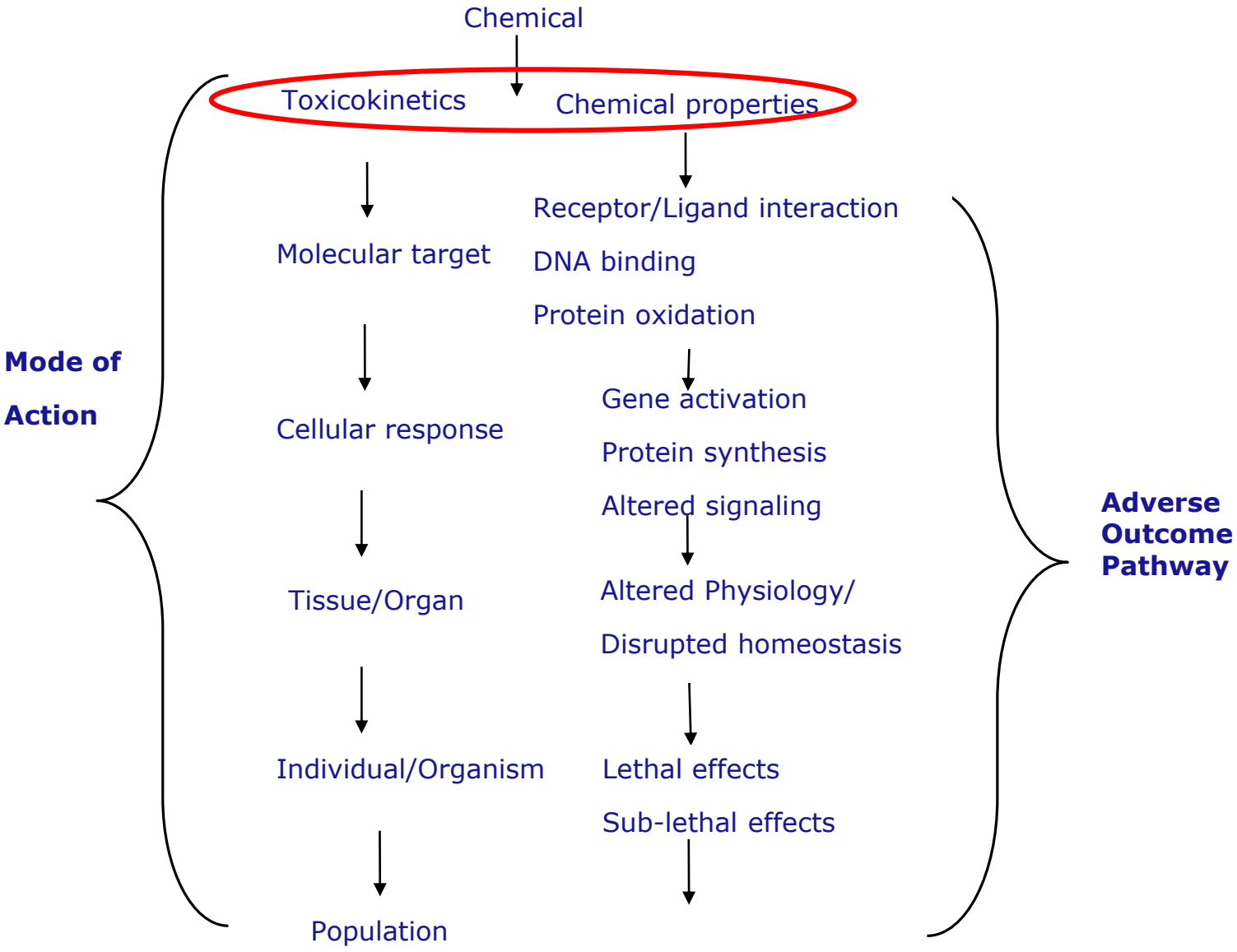


New Approach Methodologies (NAMs)

Connecting Exposure, Dosimetry and Effects



Mode of Action and Adverse Outcome Pathways



State of play in EFSA

- **Alternatives to animal testing are key for EFSA:**

➢ Development of new tools for chemical risk assessment (RA): Fit for purpose for regulatory contexts (data poor, data rich)

➢178 REFIT exercise of the EU Food Law requires publications of all available data used in EFSA : Open data and *in silico* models

➢EFSA's upcoming Chemical Risk Assessment strategy

- **EFSA active in this area:**

➢Open source toxicological databases (OpenFoodTox)

➢Development of physiologically-based kinetic (PB-K) models for humans (incl. TK and IVIVE), farm animals and fish

➢International cooperation: OECD PBK guidance for RA applications

➢Platform for generic TK and IVIVE modelling

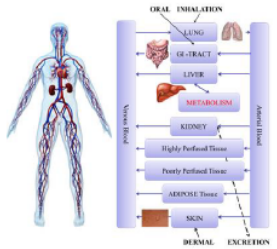
Toxicokinetic-Toxicodynamic collaboration

- International Cooperation (2016-2020)
  - State of the art Workshop at JRC with national and international bodies (US-EPA, FDA, EFSA, RIVM,HSE, etc)
  - OECD Guidance document: Use of TK/PB-K models in RA (2020)

JRC CONFERENCE AND WORKSHOP REPORTS

EURL ECVAM WORKSHOP ON NEW GENERATION OF PHYSIOLOGICALLY-BASED KINETIC MODELS IN RISK ASSESSMENT

Paini A, Joossens E, Bessems J, Desalegn A, Dorne JL, Gosling JP, Heringa MB, Klaric M, Kramer N, Loizou G, Louisse J, Lumen A, Madden JC, Patterson EA, Proença S, Punt A, Setzer RW, Suciu N, Troutman J, Yoon M, Worth A, Tan YM.



2017

Computational Toxicology 9 (2019) 61–72

Contents lists available at ScienceDirect

Computational Toxicology

journal homepage: www.elsevier.com/locate/comtox

Next generation physiologically based kinetic (NG-PBK) models in support of regulatory decision making

A. Paini[a,*], J.A. Leonard[b], E. Joossens[a], J.G.M. Bessems[a,r], A. Desalegn[a], J.L. Dome[c], J.P. Gosling[d], M.B. Heringa[e], M. Klaric[f], T. Kliment[a], N.I. Kramer[g], G. Loizou[h], J. Louisse[i,m], A. Lumen[j], J.C. Madden[k], E.A. Patterson[l], S. Proença[a,g], A. Punt[m], R.W. Setzer[n], N. Suciu[o], J. Troutman[p], M. Yoon[q,s], A. Worth[a], Y.M. Tan[l]

[a] European Commission Joint Research Centre, Ispra, Italy
[b] Oak Ridge Institute for Science and Education, 100 ORAU Way, Oak Ridge, TN 37830, USA
[c] European Food Safety Authority, 1a, Via Carlo Magno, 1A, 43126 Parma PR, Italy
[d] School of Mathematics, University of Leeds, Leeds, UK
[e] RIVM - The National Institute for Public Health and the Environment, Bilthoven, The Netherlands
[f] Cosmetics Europe, Brussels, Belgium
[g] Institute for Risk Assessment Sciences, Utrecht University, P.O. Box 80177, 3508TD Utrecht, The Netherlands
[h] Health and Safety Executive, Buxton, UK
[i] Division of Toxicology, Wageningen University, Tuinlaan 5, 6703 HE Wageningen, The Netherlands
[j] Division of Biochemical Toxicology, National Center for Toxicological Research, US Food and Drug Administration, Jefferson, AR 72079, USA
[k] School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Byrom Street, Liverpool L3 3AF, UK
[l] School of Engineering, University of Liverpool, Liverpool L69 3GH, UK
[m] RIKILT Wageningen University and Research, Akkermaalsbos 2, 6708 WB Wageningen, The Netherlands
[n] U.S. Environmental Protection Agency, National Exposure Research Laboratory, 109 TW Alexander Drive, Research Triangle Park, NC 27709, USA
[o] DISTAS, Università Cattolica del Sacro Cuore, Piacenza, Italy
[p] Central Product Safety, The Procter & Gamble Company, Cincinnati, OH, USA
[q] SciToVation, 6 Davis Drive, PO Box 110566, Research Triangle Park, NC 27709, USA
[r] Flemish Institute for Technological Research (VITO), Mol, Belgium
[s] ToxStrategies, Research Triangle Park Office, 1249 Kildaire Farm Road 134, Cary, NC 27511, USA

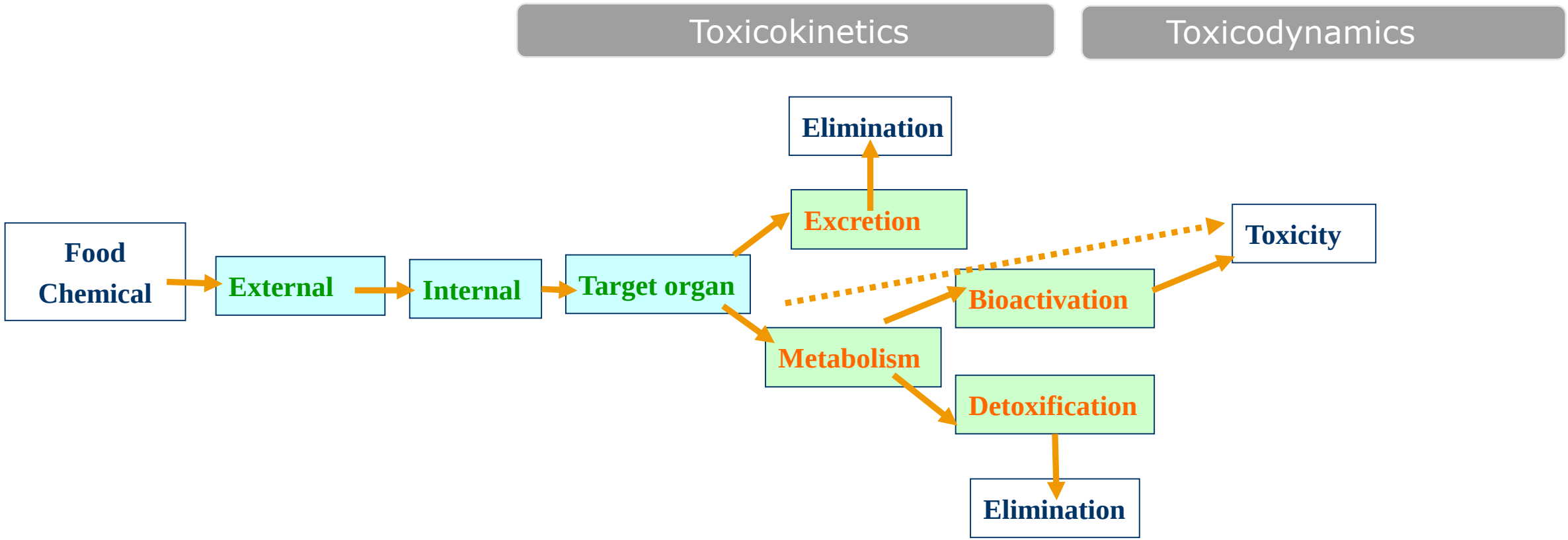
Toxicokinetics and Toxicity

✓ **Main evolutionary goal of biotransformation: DETOX (TOXIFY ?)**

Metabolism (liver + other tissues):

From Lipophilic (+ absorption) to hydrophilic (+ excretion in urine or bile).

✓ **Can we predict Kinetics quantitatively for humans, animals and other species ?**



Models for Farm animals and the environment

Toxicology in Vitro 60 (2019) 61–70

Contents lists available at ScienceDirect

Toxicology in Vitro

journal homepage: www.elsevier.com/locate/toxinvit

Review

Physiologically based kinetic models for farm animals: Critical review of published models and future perspectives for their use in chemical risk assessment

L.S. Lautz[a,*], R. Oldenkamp[a], J.L. Dorne[b], A.M.J. Ragas[a,c]

[a] Department of Environmental Science, Institute for Water and Wetland Research, Radboud University Nijmegen, Houtlaan 4, 6525 XP Nijmegen, The Netherlands
[b] European Food Safety Authority, Via Carlo Magno, 1A, 43126 Parma, Italy
[c] Department of Science, Faculty of Management, Science & Technology, Open University, 6419 AT Heerlen, The Netherlands

Contents lists available at ScienceDirect

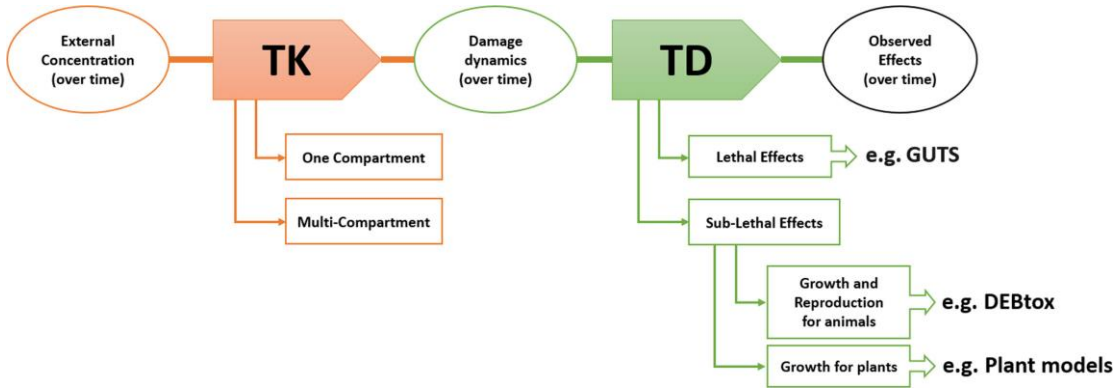
Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

Dynamic energy budget models in ecological risk assessment: From principles to applications

Jan Baas [a,*], Starrlight Augustine [b], Gonçalo M. Marques [c], Jean-Lou Dorne [d]



Science of the Total Environment 651 (2019) 516–531

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Generic physiologically-based toxicokinetic modelling for fish: Integration of environmental factors and species variability

Audrey Grech [a,b,c], Cleo Tebby [a], Céline Brochot [a], Frédéric Y. Bois [a], Anne Bado-Nilles [c], Jean-Lou Dorne [d], Nadia Quignot [b], Rémy Beaudouin [a,c,*]

[a] Institut National de l'Environnement Industriel et des Risques (INERIS), Models for Ecotoxicology and Toxicology Unit, Parc ALATA, BP2, 60550 Verneuil-en-Halatte, France
[b] Analytica Laser, 3 rue de l'arrivée, 75015 Paris, France
[c] Institut National de l'Environnement Industriel et des Risques (INERIS), UMR-I 02 SEBIO, Parc ALATA, BP2, 60550 Verneuil-en-Halatte, France
[d] European Food Safety Authority (EFSA), Scientific Committee and Emerging Risks Unit, Via Carlo Magno 1A, 43126 Parma, Italy

EFSA Journal

SCIENTIFIC OPINION

ADOPTED: 27 June 2018

doi: 10.2903/j.efsa.2018.5377

Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms

EFSA Panel on Plant Protection Products and their Residues (PPR), Colin Ockleford, Paulien Adriaanse, Philippe Berny, Theodorus Brock, Sabine Duquesne, Sandro Grilli, Antonio F Hernandez-Jerez, Susanne Hougaard Bennekou, Michael Klein, Thomas Kuhl, Ryszard Laskowski, Kyriaki Machera, Olavi Pelkonen, Silvia Pieper, Robert H Smith, Michael Stemmer, Ingvar Sundh, Aaldrik Tiktak, Christopher J. Topping, Gerrit Wolterink, Nina Cedergreen, Sandrine Charles, Andreas Focks, Melissa Reed, Maria Arena, Alessio Ippolito, Harry Byers and Ivana Teodorovic

Stepwise approach to develop physiologically-based Kinetic models

1.Data Collection

- Physiological and biochemical parameters for each species
- Chemical specific parameters including phys-chem, TK etc.

2.Integrate the data into an algorithm

- Physiologically-based model
- Harmonise sensitivity, variability and uncertainty analysis

3. Develop case studies and guidance document

- Compare published and predicted values
- Guidance : TK data/models in RA (OECD in prep, EFSA 2020+)

4. Develop an Open source platform for users

- All Data and models integrated into a user-friendly platform
- Predict TK ad TD properties and accelerate the RA process

Open source PBK models in 4 Fish species@EFSA

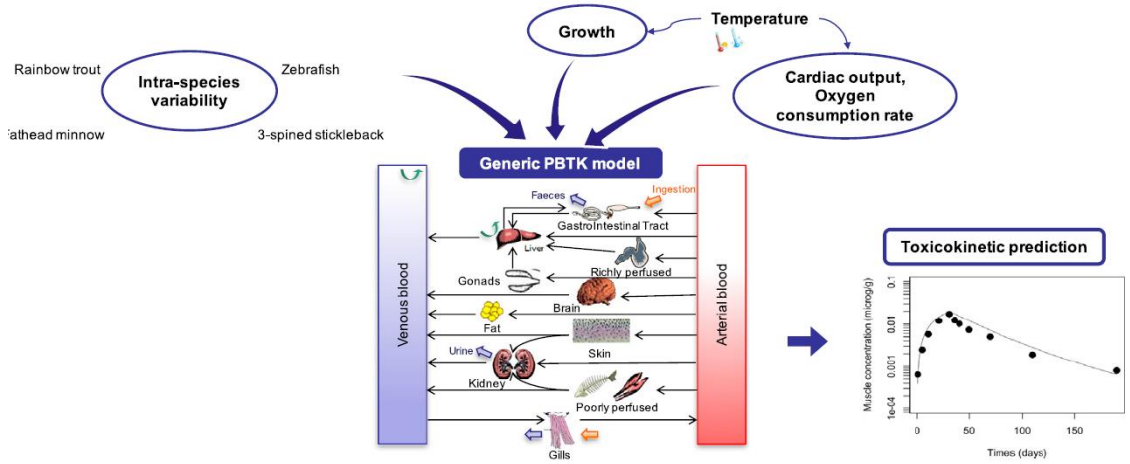
Contents lists available at ScienceDirect

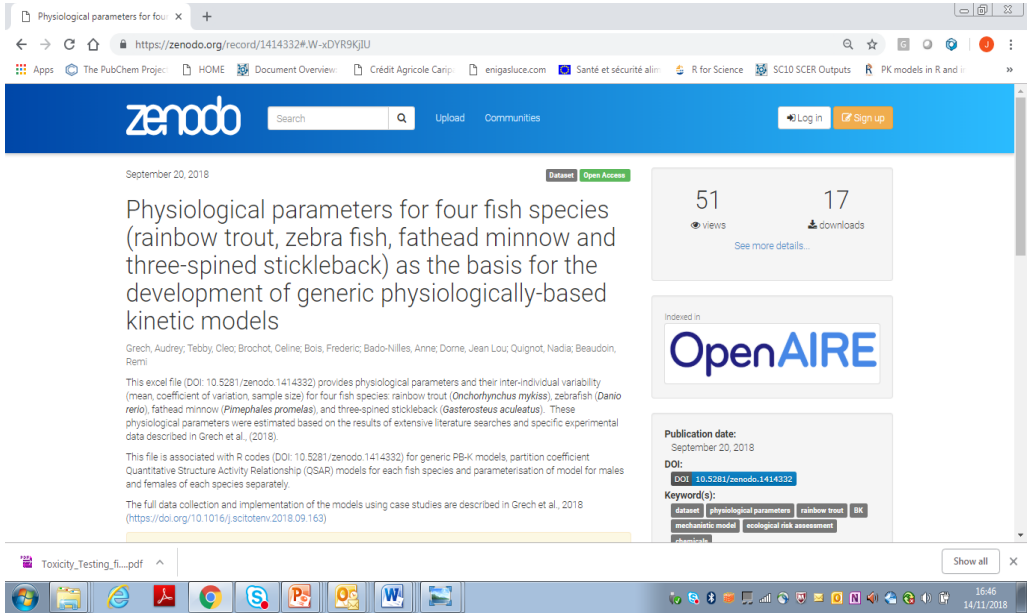
Science of the Total Environment

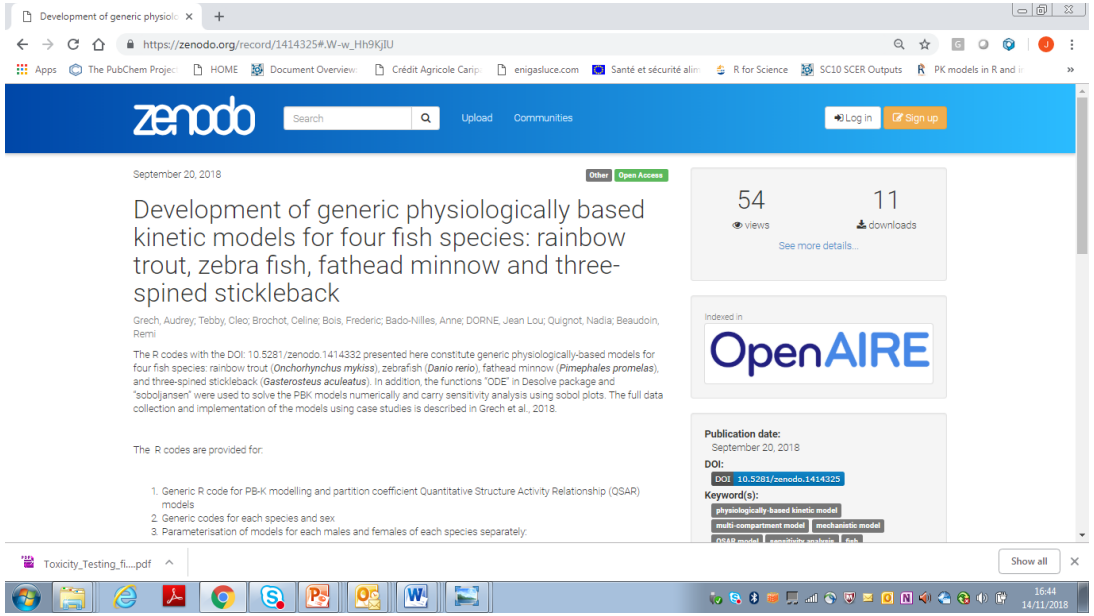
journal homepage: www.elsevier.com/locate/scitotenv

Generic physiologically-based toxicokinetic modelling for fish: Integration of environmental factors and species variability

Audrey Grech [a,b,c], Cleo Tebby [a], Céline Brochot [a], Frédéric Y. Bois [a], Anne Bado-Nilles [c], Jean-Lou Dorne [d], Nadia Quignot [b], Rémy Beaudouin [a,c,*]







Physiologically-based kinetic models for Farm Animals

Contents lists available at ScienceDirect

Toxicology Letters

journal homepage: www.elsevier.com/locate/toxlet

Generic physiologically based kinetic modelling for farm animals: Part II. Predicting tissue concentrations of chemicals in swine, cattle, and sheep

L.S. Lautz[a,*], S. Hoeks[a], R. Oldenkamp[a], A.J. Hendriks[a], J.L.C.M. Dorne[b], A.M.J. Ragas[a,c]

[a] Department of Environmental Science, Radboud University Nijmegen, Houtlaan 4, 6525 XZ, Nijmegen, the Netherlands
[b] European Food Safety Authority, Via Carlo Magno 1A, 43126, Parma, Italy
[c] Department of Science, Faculty of Management, Science &Technology, Open University, 6419 AT, Heerlen, the Netherlands

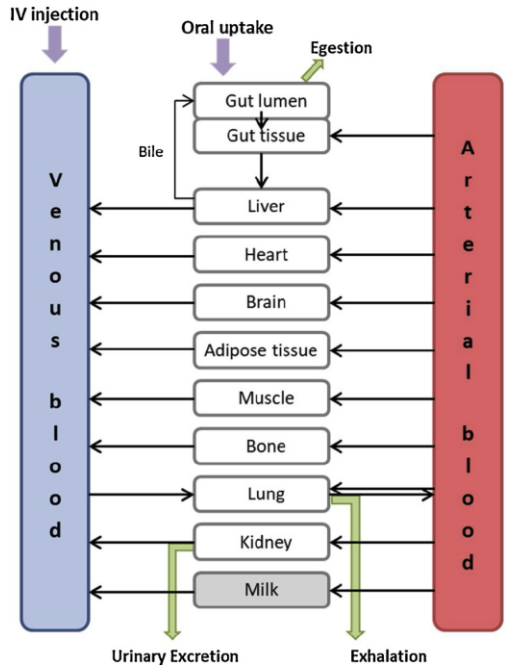
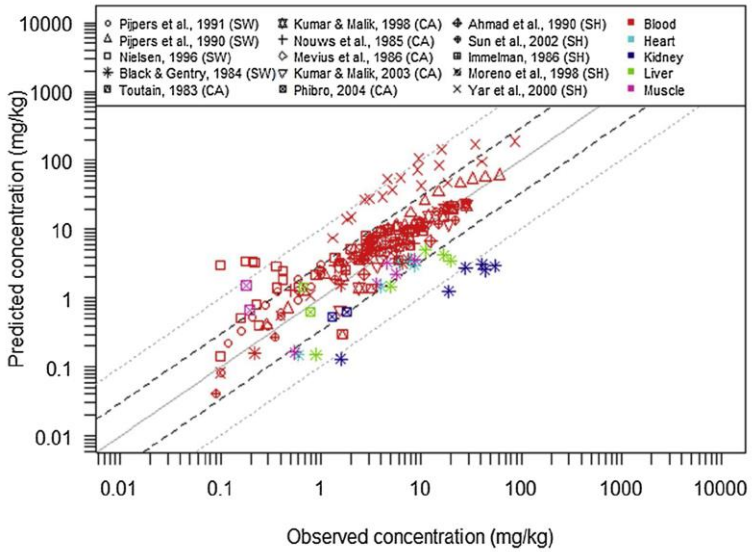


Fig. 1. Schematic description of the PBK model developed for cattle, sheep, and swine. Uptake and excretion sites are presented in the purple and green, respectively.



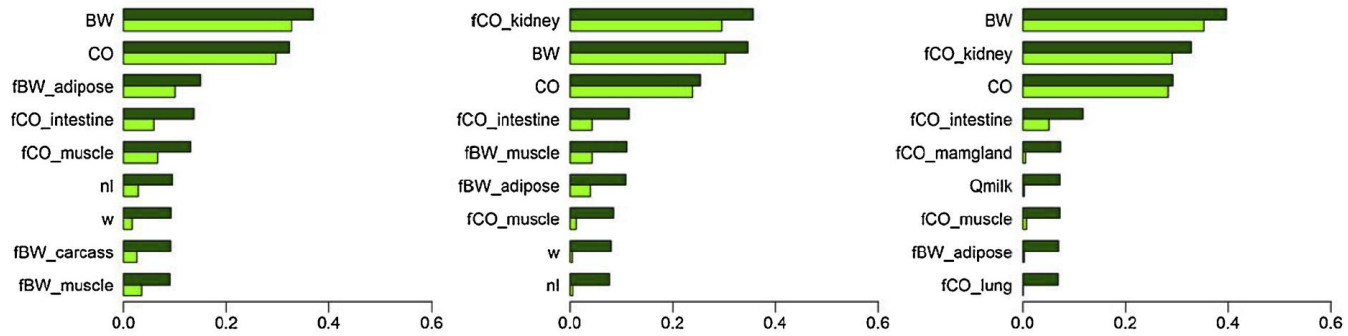


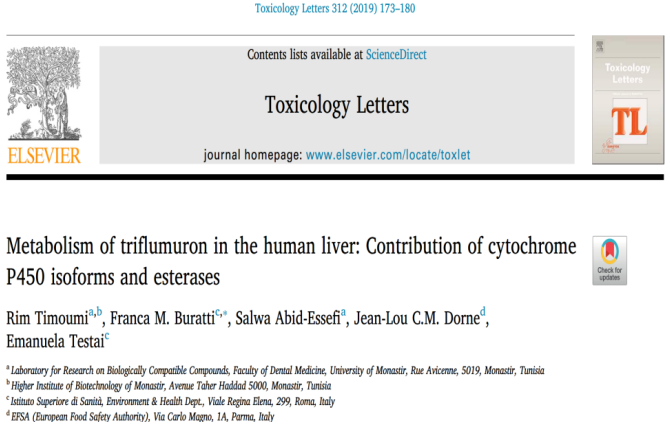
Fig. 5. Sensitivity analysis of the cattle (upper panels), sheep (middle panels) and swine (lower panels) PBK model applied to oxytetracycline.

Quantitative In vitro In Vivo Extrapolation for Humans

- New data requirements for pesticides (283/284 2013) : Compare in vitro metabolism rat/human

➢ Collaborative case studies with national/international (2016-2020):

1. Use of human *in vitro* metabolism data and QIVIVE models in RA
2. Prediction of human kinetics for compounds relevant to EFSA panels (e.g. pesticides, contaminants, food additives, botanicals)


Toxicology Letters 312 (2019) 173–180

Contents lists available at ScienceDirect

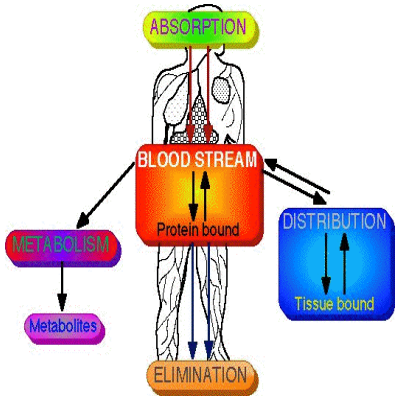
Toxicology Letters

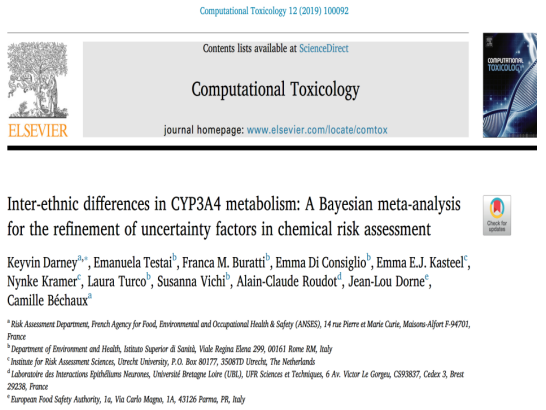
journal homepage: www.elsevier.com/locate/toxlet

Metabolism of triflumuron in the human liver: Contribution of cytochrome P450 isoforms and esterases

Rim Timoumi[a,b], Franca M. Buratti[c,*], Salwa Abid-Essefi[a], Jean-Lou C.M. Dorne[d], Emanuela Testai[c]

[a] Laboratory for Research on Biologically Compatible Compounds, Faculty of Dental Medicine, University of Monastir, Rue Avicenne, 5019, Monastir, Tunisia
[b] Higher Institute of Biotechnology of Monastir, Avenue Taher Haddad 5000, Monastir, Tunisia
[c] Istituto Superiore di Sanità, Environment & Health Dept., Viale Regina Elena, 299, Roma, Italy
[d] EFSA (European Food Safety Authority), Via Carlo Magno, 1A, Parma, Italy




Computational Toxicology 12 (2019) 100092

Contents lists available at ScienceDirect

Computational Toxicology

journal homepage: www.elsevier.com/locate/comtox

Inter-ethnic differences in CYP3A4 metabolism: A Bayesian meta-analysis for the refinement of uncertainty factors in chemical risk assessment

Keyvin Darney[a,*], Emanuela Testai[b], Franca M. Buratti[b], Emma Di Consiglio[b], Emma E.J. Kasteel[c], Nynke Kramer[c], Laura Turco[b], Susanna Vichi[b], Alain-Claude Roudot[d], Jean-Lou Dorne[e], Camille Béchaux[a]

[a] Risk Assessment Department, French Agency for Food, Environmental and Occupational Health & Safety (ANSES), 14 rue Pierre et Marie Curie, Maisons-Alfort F-94701, France
[b] Department of Environment and Health, Istituto Superior di Sanità, Viale Regina Elena 299, 00161 Rome RM, Italy
[c] Institute for Risk Assessment Sciences, Utrecht University, P.O. Box 80177, 3508TD Utrecht, The Netherlands
[d] Laboratoire des Interactions Epithéliums Neurones, Université Bretagne Loire (UBL), UFR Sciences et Techniques, 6 Av. Victor Le Gorgeu, CS93837, Cedex 3, Brest 29238, France
[e] European Food Safety Authority, 1a, Via Carlo Magno, 1A, 43126 Parma, PR, Italy

➢ Guidance on use of human *in vitro* metabolism studies to be developed by Pesticide panel (Nov 2019-2021)

➢ Take into account difference in metabolism for human risk assessment

Opensource Source Tools

- **TK plate :** Generic PBK and QIVIVE models for single compounds and mixtures in humans, farm animals and fish (**Prototype in 2020**)
- **OpenFoodTox 2.0**: Integrating Tox data and QSAR models (**2019-2022**)
- **Case studies** for interactions (humans, fish, bees etc)

Toxicology and Applied Pharmacology 370 (2019) 184–195

Contents lists available at ScienceDirect

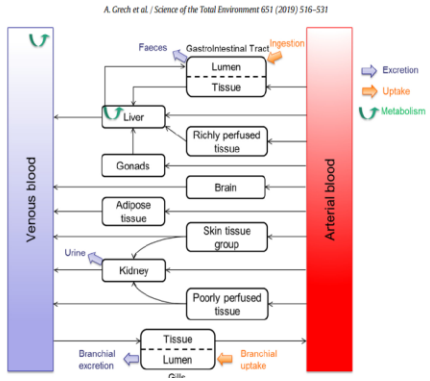
Toxicology and Applied Pharmacology

journal homepage: www.elsevier.com/locate/taap

Investigating the interaction between melamine and cyanuric acid using a Physiologically-Based Toxicokinetic model in rainbow trout

Cleo Tebby[a], Céline Brochot[a], Jean-Lou Dorne[b], Rémy Beaudouin[a,c,*]

[a] Institut National de l'Environnement Industriel et des Risques (INERIS), Models for Ecotoxicology and Toxicology Unit, Parc ALATA, BP2, 60550 Verneuil-en-Halatte, France
[b] European Food Safety Authority (EFSA), Scientific Committee and Emerging Risks Unit, Via Carlo Magno 1A, 43126 Parma, Italy
[c] Institut National de l'Environnement Industriel et des Risques (INERIS), UMR-I 02 SEBIO, Parc ALATA, BP2, 60550 Verneuil-en-Halatte, France



Archives of Toxicology
https://doi.org/10.1007/s00204-018-2325-6

TOXICOGENOMICS

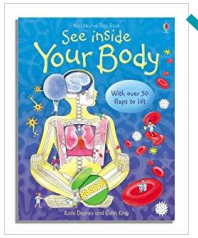
The Yin–Yang of CYP3A4: a Bayesian meta-analysis to quantify inhibition and induction of CYP3A4 metabolism in humans and refine uncertainty factors for mixture risk assessment

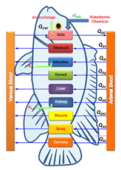
Nadia Quignot[1] · Witold Wiecek[2] · Billy Amzal[1] · Jean-Lou Dorne[3]

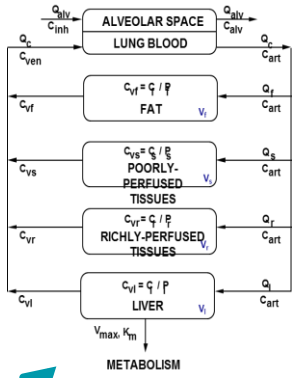
Building a TK platform for species of relevance

External dose → Internal dose → Target organ dose → Target organ metabolism

Physiological Data







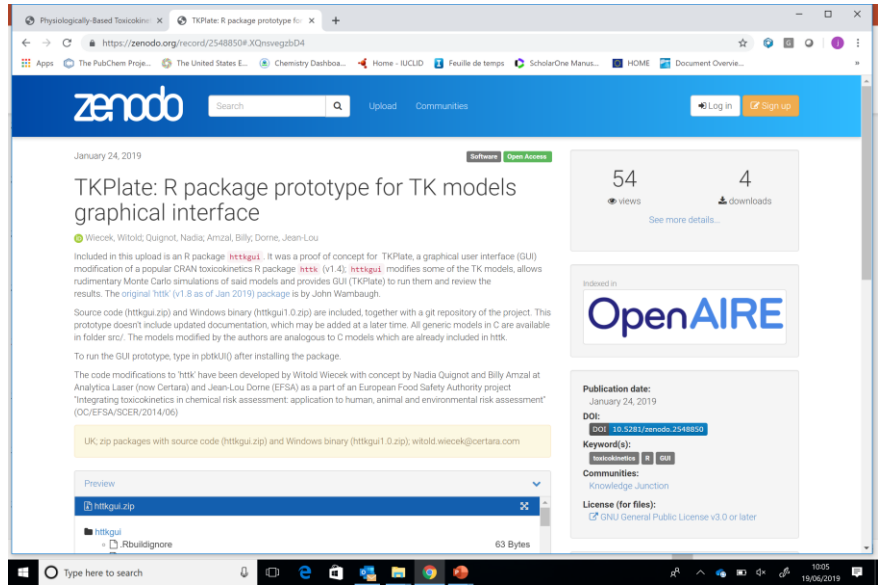
Chemical Specific –Data

Exposure
Physico-chemical
Metabolism

Internal Dose
TK parameters
Tissue residues
Reverse dosimetry

Species-specific TK
Interspecies
Differences
Human Variability
TKTD modelling

Sensitivity
Uncertainty



Connecting metabolism and variability in humans

In vitro metabolism

Toxicology Letters 312 (2019) 173–180

Contents lists available at ScienceDirect

Toxicology Letters

journal homepage: www.elsevier.com/locate/toxlet

Metabolism of triflumuron in the human liver: Contribution of cytochrome P450 isoforms and esterases

Rim Timoumi[a,b], Franca M. Buratti[c,*], Salwa Abid-Essefi[a], Jean-Lou C.M. Dorne[d], Emanuela Testai[c]

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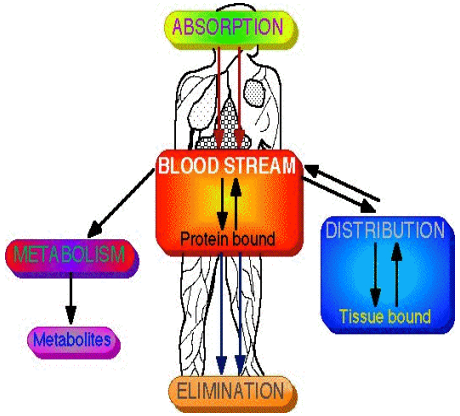
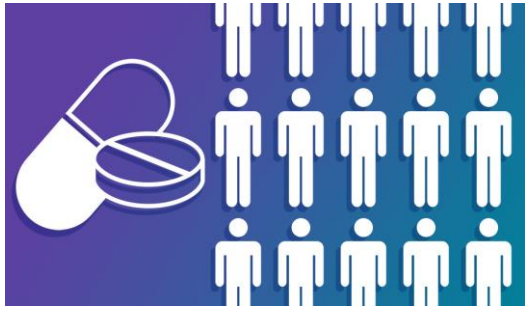
[d] EFSA (European Food Safety Authority), Via Carlo Magno, 1A, Parma, Italy





In vivo variability/ uncertainty

Computational Toxicology 12 (2019) 100092

Contents lists available at ScienceDirect

Computational Toxicology

journal homepage: www.elsevier.com/locate/comtox

Inter-ethnic differences in CYP3A4 metabolism: A Bayesian meta-analysis for the refinement of uncertainty factors in chemical risk assessment

Keyvin Darney[a,*], Emanuela Testai[b], Franca M. Buratti[b], Emma Di Consiglio[b], Emma E.J. Kasteel[c], Nynke Kramer[c], Laura Turco[b], Susanna Vichi[b], Alain-Claude Roudot[d], Jean-Lou Dorne[e], Camille Béchaux[a]

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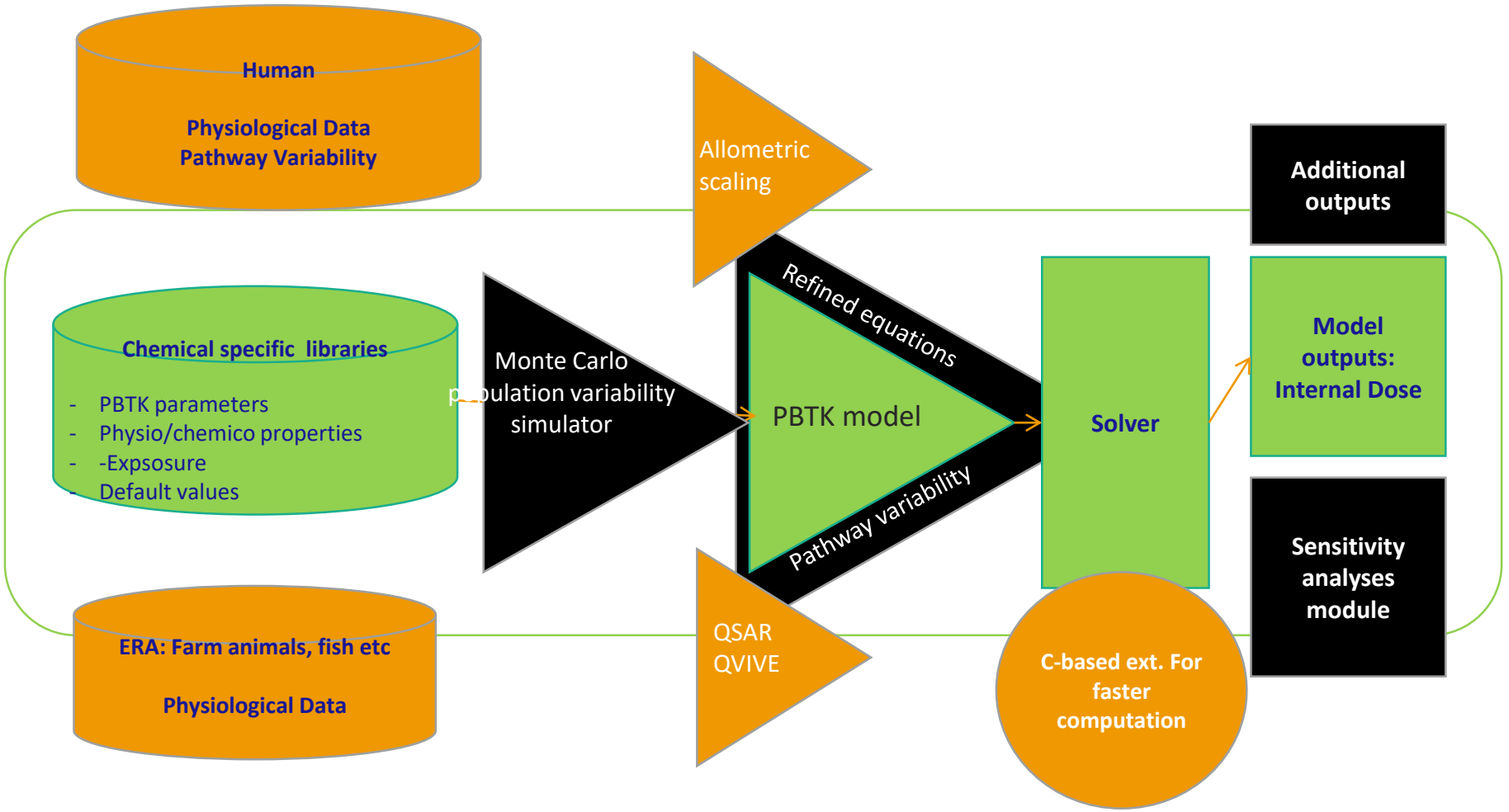
[e] European Food Safety Authority, 1a, Via Carlo Magno, 1A, 43126 Parma, PR, Italy

TK Plate: Open Source Models

MODELLING WORKFLOW



The Benefit of Cooperation

- APCRA "Accelerating the Pace of Chemical Risk Assessment"

➢Created under the lead of US-EPA together with EFSA, ECHA, Health Canada, NTP and other agencies (Japan, Singapore etc.).

➢Aims to provide 1. Common understanding of NAMs (regulatory contexts and examples), 2. Master list of common chemicals of interest for ongoing and future NAM applications, 3. Potential sources of NAM information for sharing and use. 4.Develop and share case studies of mutual interest.

➢Desired outcomes 1. Address data gaps in existing evaluations, 2.Evaluate data poor chemicals, 3.screening and prioritisation 4.Acceleration of the pace of assessments and risk-based evaluations.

➢Yearly meetings in the US, Europe, Canada with the next meeting planned for October 2019 in Research Triangle Park US-EPA

The Benefit of cooperation II

- Successful collaborations within ACPRA

➢US-EPA led Case study (2017): How conservative are *in vitro* predictions compared with *in vivo* point of departures (PODs) ?

➢Cooperation with Health Canada, ECHA, ECHA and others.

➢EFSA's support

1. Regular conference calls,
2. Curated *in vivo* Tox data for relevant compounds from OpenFoodTox,
3. Description OpenFoodTox

Utility of In Vitro Bioactivity as a Lower Bound Estimate of In Vivo Adverse Effect Levels and in Risk-Based Prioritization

Katie Paul Friedman*, Matthew Gagne[†], Lit-Hsin Loo[‡], Panagiotis Karamertzanis[§], Tatiana Netzeva[§], Tomasz Sobanski[§], Jill Franzosa[¶], Ann Richard*, Ryan Lougee*, Andrea Gissi[§], Jia-Ying Joey Lee[‡], Michelle Angrish[||], Jean-Lou Dorne[III], Stiven Foster[IIII], Kathleen Raffaele[IIII], Tina Bahadori[||], Maureen Gwinn*, Jason Lambert*, Maurice Whelan[IV], Mike Rasenberg[§], Tara Barton-Maclaren[†], Russell S. Thomas*

Possible joint activities with MS and Focal Point ?

- Sharing opensource databases + relevant models

- Joint case studies and training. Illustrate NAM applications (human, animals, ecology) incl. *in vitro* data, metabolism and TK modelling, OMICs, biomonitoring and risk-based evaluations.

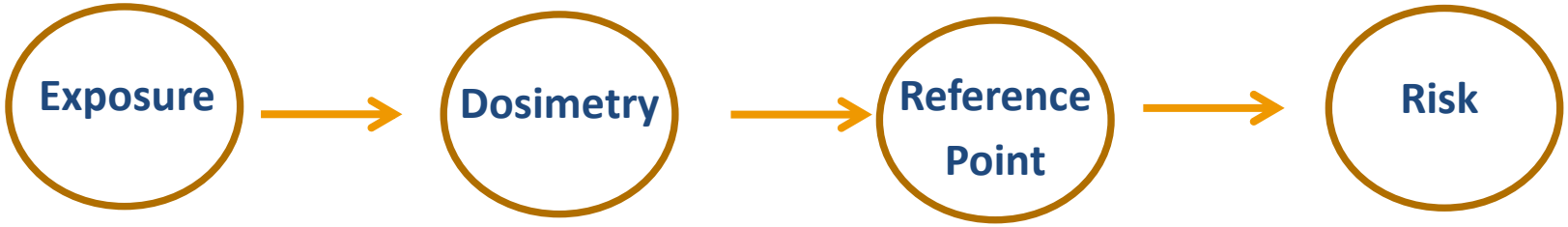
- Identify common mid-term and long-term priority areas for collaboration for new tools and case studies

1. TK models for all test species in regulatory area,
2. Tools integrating state of the art information (in vitro, AOP, OMICs etc.) ?,
3. Common guidance documents

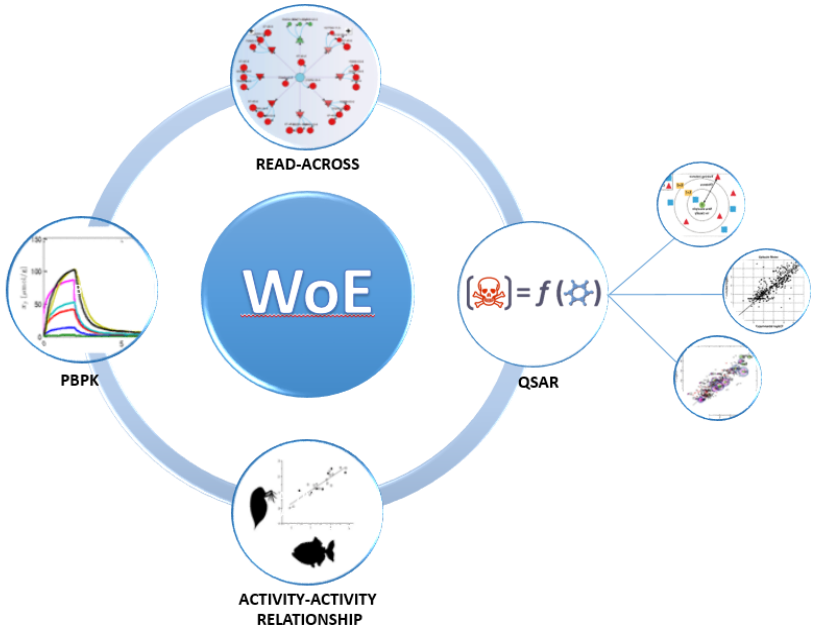
- PhD Programmes ?

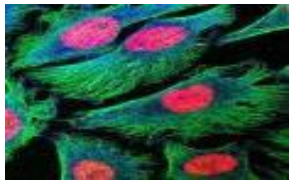
- Feedback proposal from focal point ?

Integrating State Of The Art Methods And Data Streams

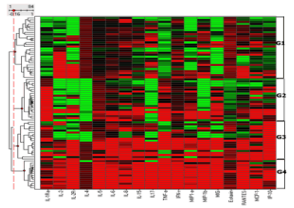


OpenFoodTox and MATRIX



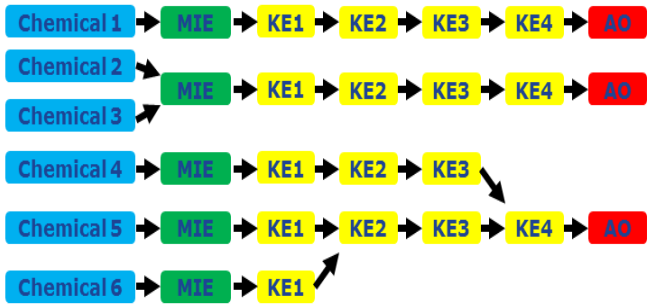


In vitro

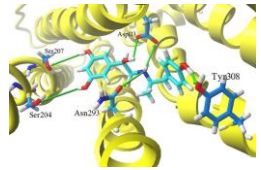


OMICs

Epidemiological Data



AOP/MoA



In Silico

Conclusions and Future Perspectives

- **Open source Tools support risk assessment**

-Reduce animal testing

-Train current and next generation of Risk Assessors

- **TKPlate**

➢Support Open source models for RA community

➢Open source models on EFSA knowledge junction (Zenodo)

➢Further development: Range of test species + case studies

➢Training staff and RA community

- **Future Collaboration with Member States**

Sharing data, models, developing common case studies ?

- **New speciality section in EUROTOX: IN²TOX (*In vitro in silico*)**

Kick off 9 Sep 2019 Helsinki

Acknowledgements: Cooperation is key

➢ **Data collection, Modelling, TK platform**

- CERTARA Paris, London;
- INERIS, Paris, France;
- Radboud University, Niemigen, The Netherlands;
- ISS, Rome, Italy;
- University of Utrecht, The Netherlkands,
- ANSES, Paris;
- Open Analytics, Antwerp, Belgium
- EFSA: Jose Cortinas-Abrahantes

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