
IN-SILICO TOXICOLOGY

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PRELIMINARY OUTLINE

of the training course scheduled for April 2-4, 2019
at Fraunhofer ITEM, Hannover, Germany

Day 1 – Afternoon: Introduction/QSAR model

Day 1, Session 1 (4 hours including 30 min break; start at 2.00 PM)				
Time	Subject	Content	Teaching and learning activity	Tutor
15 min	Welcome	<ul style="list-style-type: none"> Welcome by EFSA and training coordinator Objective and learning outcome of this course 	Tour de table – expectations and experiences Introduction to course outline and content	Training coordinators + EFSA representative
60 min including discussion	Introduction to computational toxicology	<ul style="list-style-type: none"> What is computational toxicology Statistical models Mechanistic models (Q)SAR, read-across, category approaches 	Lecture, demonstration of possibilities of some available software and models, explain the concepts used in these models and compare them to each other. Discuss the issue of chemical structure representation.	Emiel Rorije
45 min + 45 min hands-on	Introduction and demonstration of different computational toxicology tools	<ul style="list-style-type: none"> DEREK TopKat ToxTree VEGA CESAR OECD QSAR Toolbox 	Demonstration of software Showing the differences in output of different models (quantitative vs. qualitative).	Emiel Rorije, Sylvia Escher
30 min	Coffee break			
45 min	Chemical representation	<ul style="list-style-type: none"> Chemical representation; name, CAS nr, structure, SMILES, MOL-file, 2D vs. 3D. Expert systems / databases Software tools for structure representation and recognition 	Show some sources of chemical structure/identity information	Emiel Rorije
45 min	Work with chemical structure	<ul style="list-style-type: none"> Exact match/ Substructure/Similarity of compounds 	Hands-on example of looking up substance data, using different structure representations,	Emiel Rorije, Sylvia Escher
60 min	End of day 1			

Day 2 – morning: QSAR modeling

Day 2, Session 2 (4 hours including 30 min break)				
Time	Subject	Content	Teaching and learning activity	Tutor
15 min	Welcome	Objective and learning outcome of second day	Wrap-up day 1 and introduction to course outline and content of day 2	Training coordinators
60 min	Application of QSAR models, including validation	<ul style="list-style-type: none"> • What is model validation? • Statistical/qualitative • OECD QSAR Toolbox • Generating predictions • Applicability domain 	Lecture, introducing statistical indicators for validation (general model performance), introducing the idea of specific (local) validation.	Emiel Rorije
60 min	QSAR prediction – discussion on validity	<ul style="list-style-type: none"> • Work with OECD toolbox, Toxtree and VEGA • Hands-on e.g. quinone; anilines, triazene compounds 	Learn how to judge on model differences and relevance of predictions. Compare different tools and prediction on genotoxicity.	Emiel Rorije Sylvia Escher
15 min	QSAR models – perspectives?	Application of QSAR models in regulatory risk assessment, e.g. under REACH or ICHM7	Putting QSAR models into context and give perspectives.	Emiel Rorije
30 min	Wrap-up and feedback	<ul style="list-style-type: none"> • Feedback on QSAR models and tools 	Compare expectations and experiences of participants.	Emiel Rorije
Lunch break (60 min)				

Day 2 – afternoon: TTC concept

Day 2, Session 3 (4 hours including 20 min break)				
Time	Subject	Content	Teaching and learning activity	Tutor
60 min including discussion	Introduction to TTC concept	<ul style="list-style-type: none"> • Applicability of the TTC concept - refer to EFSA guidance • How were thresholds for genotoxic and non-genotoxic compounds derived? Based on which data? • TTC values overview – oral exposure, inhalation exposure, cancer, reprotoxicity 	Lecture, introduction to the TTC concept, learn about the underlying databases to better understand the applicability domain of the model. Introduce EFSA TTC guidance to participants and the use of Cramer class 2.	Sylvia Escher
45 min + 15 min discussion	Hands on examples	<ul style="list-style-type: none"> • Assign the appropriate threshold for single ingredients. Compare to exposure and calculate the risk for adults/infants and less than life time exposure. 	<ul style="list-style-type: none"> • TTC for single compound assessment 	Sylvia Escher Emiel Rorije
20 min	Coffee break			
15 min intro + 45 min hands-on	Hands on examples	<ul style="list-style-type: none"> • Use of TTC in case of complex mixtures the “Vasse Tarpits” example 	<ul style="list-style-type: none"> • TTC for priority setting • TTC for mixtures 	Emiel Rorije Sylvia Escher
30 min	Demonstration of performance of different tools	<ul style="list-style-type: none"> • ToxTree • OECD toolbox • Manual application of Cramer decision tree 	Differences of software tools in allocation of threshold values, sensilize participants to use the tools carefully	Emiel Rorije
10 min	Wrap-up/end of Day 2			

Day 3 – morning: Read-Across

Day 3, Session 4 (4.45 hours including 30 min break)				
Time	Subject	Content	Teaching and learning activity	Tutor
50 min	Grouping concept – read-across	<ul style="list-style-type: none"> • What is read-across and when do we use it? • What are the main assessment elements? • Context dependency of similarity assessment • Which databases are available? • Include an example 	Lecture, introducing the work flow of a read-across argument orientated to RAAF	Sylvia Escher
30 min +15 min reporting	Hands-on examples	<ul style="list-style-type: none"> • Select analogues based on structural and pc information as well as MoA for read-across, e.g. address repeated.dose toxicity of phthalates, organophosphates or glycoether 	Impact of MoA Trend versus worst-case analysis	Sylvia Escher Emiel Rorije,
30 min	Coffee break			
90 min	Example: prepare a TTC and read-across assessment for an unknown target compound	<ul style="list-style-type: none"> • Apply the OECD toolbox 	Hands-on with participants using the OECD toolbox. Two case studies will be worked out in parallel in small groups and results will be presented. Differences in approaches will be worked out and discussed.	Emiel Rorije, Sylvia Escher
30 min	Moving forward – read-across perspectives	<ul style="list-style-type: none"> • Biological read-across • Concept of AOPs 	Illustrate areas of research to improve current read-across strategies	Sylvia Escher
30 min	Wrap up and feedback	<ul style="list-style-type: none"> • Feedback from participant 	Did the training meet your expectations? Collection of questionnaires from participants.	Emiel Rorije, Sylvia Escher
End of training, distribution of certificates				