WORKSHOP IN-SILICO TOXICOLOGY

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ITEM

Day 1 – afternoon session: QSAR models

Day 1, Session 13:30-18:30				
Time	**Subject**	**Content**	**Teaching and learning activity**	**Tutor**
30 min	Arrival and registration	Make sure that all computers are running		
15 min	Welcome	• Welcome training coordinator • Objective and learning outcome of this course	Tour de table – expectations and experiences Introduction to course outline and content Work in groups….	Training coordinators
30 min + 10 min discussion	Introduction to in-silico toxicology principles	• What is computational toxicology • (Q)SAR (Difference of and rule based and statistical models.), Read Across, Category approaches, TTC • Introduction to ICHM7	Lecture, demonstration of the concepts used in these models and compare them to each other.	Sylvia Escher
45 min + 15 min discussion	Introduction and demonstration of different computational toxicology tools	• Compare different models like DEREK, TopKat, ToxTree, VEGA CESAR, OECD QSAR Toolbox, Case Ultra	Demonstration of software Showing the differences in output of different models (quantitative vs. qualitative).	Emiel Rorije
30 min	**Coffee break**			
60 min	Tools and chemical structure	• Chemical representation; name, CAS No., 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
60 min + 15 min wrap up	Do your own QSAR prediction	• Work with OECD toolbox, Toxtree and VEGA • ICH M7 like assessment with Case Ultra	Learn how to do a QSAR prediction and how to judge on validity; endpoint genotoxicity	Emiel Rorije, Sylvia Escher
	End of day 1			

Day 2 – morning session: read-across

Day 2, morning session 9:00 – 13:00				
10 min	Welcome	• Objective and learning outcome of second day	Wrap up day 1 and introduction to course outline and content of days 2	Training coordinators
45 min	Lecture: grouping concept- read across	• 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?	Lecture, introducing the work flow of an read-across argument orientated to RAAF	Sylvia Escher
30 min	Work with chemical structure	• Exact match/substructure/similarity of compounds	Demonstrate looking up substance data, using different structure representations	Emiel Rorije
30	Work with MoA	• MoA	Exercise use MoA for building categories within the OECD toolbox	Emiel Rorije
30 min coffee break				
60 min	Hands on examples Read-across wiht OECD toolbox	• Example: 4-methoxycinnamaldehyde • Select analogues based on structural and pc information as well as MoA for read-across	Apply trend versus worst-case analysis	Emiel Rorije Sylvia Escher
30 min reporting	Wrap up and discuss examples	• Each group presents ist results, learnings and difficulties	Differences in approach will be worked out and discussed	All
60 min lunch break				

Day 2 – afternoon session: read-across

Day 2 afternoon session 14:00 – 18:00				
60 min Lunch break				
30 min	Introduction	• Do read-across without OECD toolbox	Demonstration of KNIME and data extraction from toxicological databases	Sylvia
60 min	Hand on example	Case studies: • one group on organophophates	A case studies will be worked out in parallel in small groups and results will be presented to each other	Sylvia Escher Emiel Rorije
20 min	Wrap up	• Groups present their approaches/learnings/difficulties		All
60 min	Read-across perspectives -1	• Introduction to other read-across tools like GenRa/US EPA	Introduction of tool and demosntration on performacne	Emiel Rorieje
30 min	Moving forward – mechanistic risk assessment	• Biological read-across • Concept of AOPs	Illustrate areas of research to improve current rea-across strategies	Sylvia Escher
18:00 break – networking				
18:10 Discussion of training content based on daily work experiences/examples from participants/networking				
19:30 Feedback on training from participants				
20:00 End of day 2				

Day 3 – morning session: TTC concept

Day 3, 9:00 to 13:00 – ends with lunch break				
Time	**Subject**	**Content**	**Teaching and learning activity**	**Tutor**
60 min including discussion	Introduction to TTC concept	• 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	• Assign the appropriate threshold for single ingredients. Compare to exposure and calculate the risk for adults/infants and less then life time exposure.	• TTC for single compound assessment	Sylvia Escher
30 min	**Coffee break**			
15 min intro + 45 min hands-on	Hands-on examples	• Use of TTC in case of complex mixtures the "Vasse Tarpits" example	• TTC for priority setting • TTC for mixtures	Emiel Rorije
30 min	Demonstration of performance of different tools	• ToxTree • OECD toolbox • Manual application of Cramer decision tree	Differences of software tools in allocation of threshold values, sensitize participants to careful use the tools	Emiel Rorije
20 min	Recent advances in the TTC concept	• Lecture introducing recent projects and results moving forward the TTC concept	Outlook and perspectives	Sylvia Escher
15 min	Wrap up and certificates			All
13:00	**Lunch**			