WORKSHOP IN SILICO TOXICOLOGY

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and the Environment
Ministry of Health, Welfare and Sport

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ITEM

Day 1 – 13:30-18:00 CET

Day 1, pre-meeting 13:30-14:00				
Arrival and technical check				
Day 1, start of training course 14:00				
Time	**Subject**	**Content**	**Teaching and learning activity**	**Tutor**
15 min	Welcome	• Welcome • Explain outline of the course – booklet/exercises/lectures	Round of introduction Experience and expectations	Training coordinators
45 min	Introduction to in silico toxicology principles	• What is computational toxicology? • (Q)SAR (differences of and rule-based and statistical models), read-across, category approaches, TTC • Introduction to ICHM7/EFSA guidance	Lecture, of concepts	Sylvia Escher
45 min	Tools and chemical structure	• Chemical representation; name, CAS No., structure, SMILES, MOL file, 2D vs. 3D • Expert systems/databases	Show some sources of chemical structure/identity information; Exercise 1 – work with different inputs	Emiel Rorije
Coffee break (15 min)				
15 min	Wrap-up exercise	• Plenary discussion on exercise/questions and difficulties		Sylvia Escher; Emiel Rorije
45 min + 10 min discussion	Introduction and demonstration of different computational toxicology tools	• Compare different models such as 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
60 min	QSAR prediction – endpoint mutagenicity	• Short intro to genotoxicity assessment • EFSA/ICH M7 like assessment with Vega and MultiCase • Principles of QSAR assessment and expert review	Learn how to do a QSAR prediction and how to judge on validity for the endpoint genotoxicity	Sylvia Escher
End of training day one				

Day 2 morning session – genotoxicity assessment/read-across

Day 2, pre-meeting 8:30-9:00				
Welcome and technical questions				
Day 2 morning session 9:00-13:00				
Time	**Subject**	**Content**	**Teaching and learning activity**	**Tutor**
20 min	Welcome	• Wrap-up of genotoxicity assessment to prepare for first exercise	Wrap up day 1 and introduction to course outline and content of days 2	Training coordinators
30 min	Exercise on QSAR predictions	• Genotoxicity assessment	Discuss your results/approach in break-out groups	Emiel Rorije Sylvia Escher
30 min	Discussion of exercise in plenary	Each group presents its results and outlines its rationale to come to a conclusion		
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 workflow of a read-across argument orientated to RAAF	Sylvia Escher
Coffee break (15 min)				
30 min	Work with chemical structure	• Exact match/substructure/similarity of compounds	Use the QSAR toolbox for category definition and read-across based on structural descriptors	Emiel Rorije
15 min	Discussion of exercise in plenary	Show results, time for questions		
30 min	Work with MoA	• MoA demo, use one profiler	Use the QSAR toolbox for category definition and read-across based on MoA	Emiel Rorije
30 min	Hands-on examples Read-across with OECD toolbox	• Select analogues based on structural and pc information as well as MoA for read-across	Apply trend vs. worst-case analysis	Emiel Rorije Sylvia Escher
Lunch break (60 min)				

Day 2 afternoon session

Day 2 afternoon session 14:00-17:30				
Time	**Subject**	**Content**	**Teaching and learning activity**	**Tutor**
Wrap-up example – presentation per group (30 min)				
30 min	Read-across with OECD toolbox – more advanced exercise	• Combine different grouping approaches using subcategorization	Demo on how to combine different read-across and search techniques using the OECD QSAR toolbox	Emiel Rorije
15 min	Hands-on example	• Exercise on similarity combined with MoA to define source compounds in a read-across assessment	A case study will be worked out in parallel in small groups	Sylvia Escher Emiel Rorije
30 min	Wrap-up	• Groups present their approaches/learnings/difficulties	Presentation in plenary	All
15 min	Demonstration	• Introduction to other read-across tools such as ToxRead, Derek, GenRA	Introduction of tool and demonstration of performance	Emiel Rorije
Coffee break (15 min)				
30 min + 15 min questions	Read-across with other tools and approaches	• Read-across using repeated dose information guided by the OECD QSAR toolbox and other tools	Introduction to difficulties with read-across using an example that is not OECD QSAR toolbox-driven	Sylvia Escher
45 min		• Use NAM data to support read-across, EUTOXRISK/GENRA • Concept of AOPs	Illustrate areas of research to improve current read-across strategies	Sylvia Escher

Day 3 – 9:00-14:00 CET – TTC concept

Day 3, 9:00-13:00				
Time	**Subject**	**Content**	**Teaching and learning activity**	**Tutor**
45 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	• Lecture, introduction to the TTC concept, learn about the underlying databases to better understand the applicability domain of the model. Introduce participants to EFSA TTC guidance and the use of Cramer class 2.	Sylvia Escher
45 min	Hands-on examples	• Assign the appropriate threshold for single ingredients. Compare to exposure and calculate the risk for adults/infants and less than life-time exposure.	• TTC for single-compound assessment	Sylvia Escher
15 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
ca. 30 min	The EUROMIX project	• Mixture assessment – broadening the scope	• Use in silico tools for mixture assessment	Emiel Rorije
ca. 20 min	Perspectives – inhalation TTC	• TTC is established for oral exposure – what about other routes such as inhalation exposure?	• Overview of recent advances	Sylvia Escher
12:45-13:45	**Lunch break**			
15 min	Wrap-up and certificates			All
14:00	**End of training**			