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## **Advancing environmental risk assessment: investigating the relevance of non-conventional endpoints for effect prediction**

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## Curriculum vitae

Sofie Rasmussen was born on 30<sup>th</sup> of July 1995 in Frederiksberg, Denmark. She attended Søgerskolen in Smørum and graduated high school from Herlev Gymnasium in 2015, with classes in biology, mathematics and psychology. In June 2018, she completed her BSc in Environmental Engineering from Technical University of Denmark (DTU), which included a semester abroad at Monash University in Australia. The bachelor's degree was concluded with a thesis under supervision of Dr. Steffen F. Hansen focusing on environmental risk assessment of biopharmaceuticals.

Immediately following, she started a Master of Science (MSc) in Environmental Engineering at DTU in September 2018. During this time, she worked as a teaching assistant and in 2019 she was awarded Teaching Assistant of the Year by the student organisation (Polyteknisk Forening) at DTU for her assistance in the bachelor course 12102: “Environmental processes”. Furthermore, she worked with Prof. Anders Baun on ecotoxicity of nanopesticides and their conventional counterpart on freshwater algae. For her master thesis, she evaluated toxicity of produced water discharge from offshore oil and gas activities under supervision of Prof. Anders Baun, Prof. Simon I. Andersen and Dr. Lars M. Skjolding, before completing her MSc degree in January 2021.

In April 2021, Sofie started working as an environmental consultant at Rambøll in Denmark, where she was involved in several projects including chemical content of produced water, air emissions and environmental permits involved in construction projects. In July the same year, she moved to the Netherlands and started her PhD at the Institute of Environmental Sciences (CML) under the supervision of Prof.dr.ing Martina Vijver, Dr.ir Thijs Bosker and Dr. Henrik Barmantlo. Her PhD project aimed to explore how nonconventional testing schemes can aid in the evaluation of freshwater toxicity, and her research contributed to the European Union’s Horizon 2020

research and innovation program CHRONIC (<https://chronic-mc.eu/>) granted Martina Vijver and fellow researchers.

Within CML, Sofie was lead instructor on the laboratory part of the master course: “Ecotoxicity” in January 2022 at Leiden University and presented her work at multiple times internal meetings. Furthermore, she (co-) supervised the internships of two BSc. students and two MSc. students and was a member of the PhD Committee. As part of Sofie’s project, she visited as a guest researcher Roskilde University (Denmark, 2022), Syngenta (UK, 2023) and Lund University (Sweden, 2023) adding experimental and communication skills to her portfolio in both academic settings and industry. Her work was presented at the CHRONIC training events in Wageningen (the Netherlands, 2022), Aveiro (Portugal, 2022), Aarhus (Denmark, 2023) and Roskilde (Denmark, 2024).

## List of publications for this thesis

**Rasmussen, S. B.**, Bosker, T., Barmantlo, S. H., Berglund, O., & Vijver, M. G. (2024). Non-conventional endpoints show higher sulfoxaflor toxicity to *Chironomus riparius* than conventional endpoints in a multistress environment. *Aquatic Toxicology*, 275, 107074. <https://doi.org/10.1016/j.aquatox.2024.107074>

**Rasmussen, S. B.**, Bosker, T., Ramanand, G. G., & Vijver, M. G. (2024). Participatory hackathon to determine ecological relevant endpoints for a neurotoxin to aquatic and benthic invertebrates. *Environmental Science and Pollution Research*, 31, 22885–22899 <https://doi.org/10.1007/s11356-024-32566-w>

## Other publications

**Rasmussen, A. S. B.**, Hammou, A., Poulsen, T. F., Laursen, M. C., & Hansen, S. F. (2021). Definition, Categorization, and Environmental Risk Assessment of Biopharmaceuticals. *Science of the Total Environment*, 789, Article 147884. <https://doi.org/10.1016/j.scitotenv.2021.147884>

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All the thanks in the world cannot cover the gratitude I have for my parents, for their help and their constant support even when they have no clue what I am doing. Thank you to my friends and family in Denmark for still standing by my side even when calls were few and long between.

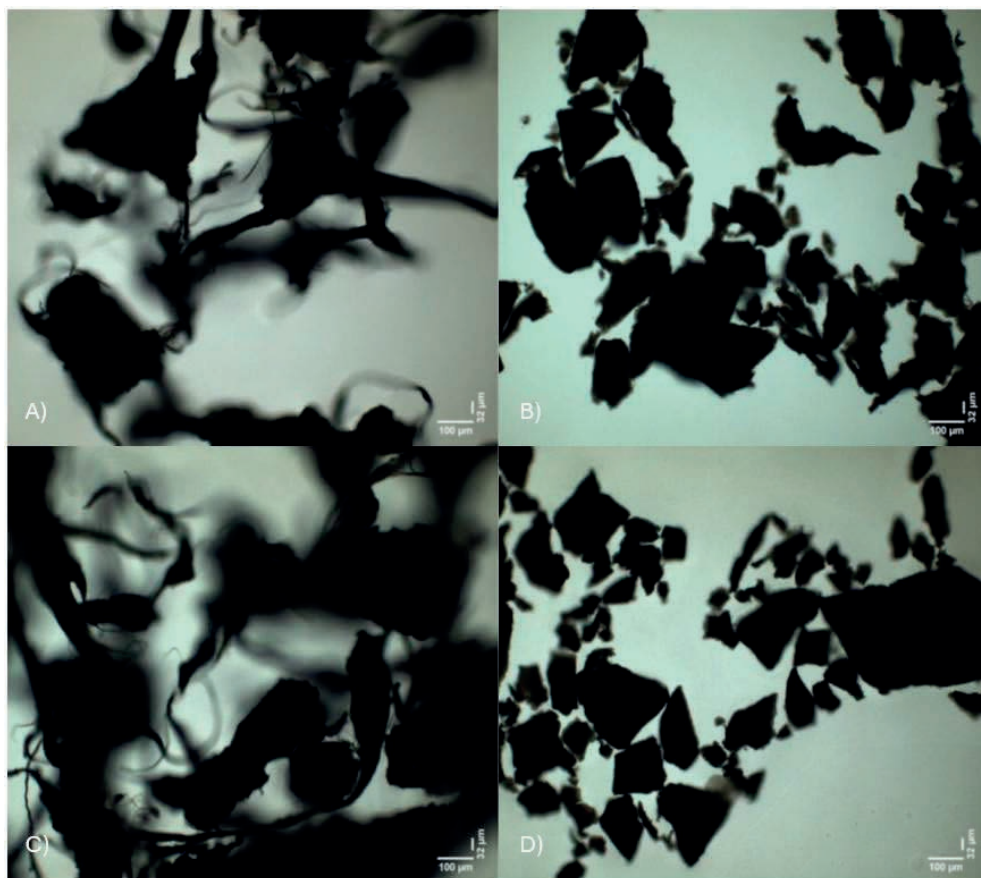
But my deepest gratitude goes to my partner Tor, this project could not have been done without your support. I am forever grateful for your love throughout this personal project of mine. Every hard step and every time I wanted to quit, you helped me overcome my fear and struggles. Tor, thank you for standing by me and supporting me throughout this project. Thank you for letting me move to another country to pursue a dream and for committing to a long-distance relationship and being my steady rock. Thank you, a trillion times, for giving me Manaia and for being the best parent for her, I could ever wish for. Jeg elsker dig uendelig meget.

## 7 Appendix

### Appendix A

#### Appendix to Chapter 4

#### 7.1 Microscopy pictures of PE and PBAT plastic particles



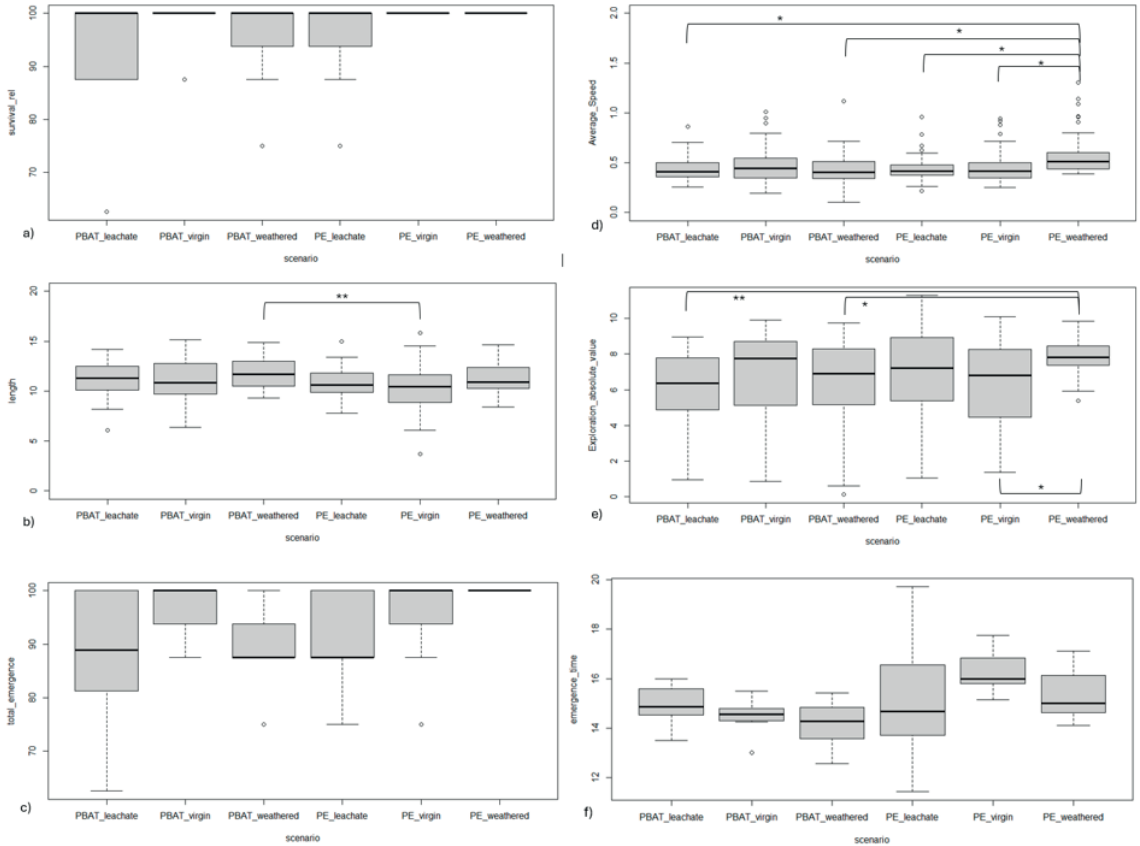
**Figure A.1** Microscopy pictures confirming size of the plastic particles larger than  $32\ \mu\text{m}$ . Pictures were taken using a Zeiss Imager M2 microscope after rinsing and drying. A) PE unleached particles. B) PBAT unleached particles. C) PE leached particles. D) PBAT leached particles.

## 7.2 Tracking settings

*Table A.1 Settings used for tracking and analysis in AnimalTA.*

<b>Tracking settings</b>	
Video cropping	600 seconds
Scale	41.42 px/cm
Tracking threshold	31
Distance threshold	2.5
<b>Analysis settings</b>	
Exploration	Modern
Area of interest	0.05 cm <sup>2</sup>
Swimming threshold	0.75 cm/s
Crawling threshold	0.25 cm/s

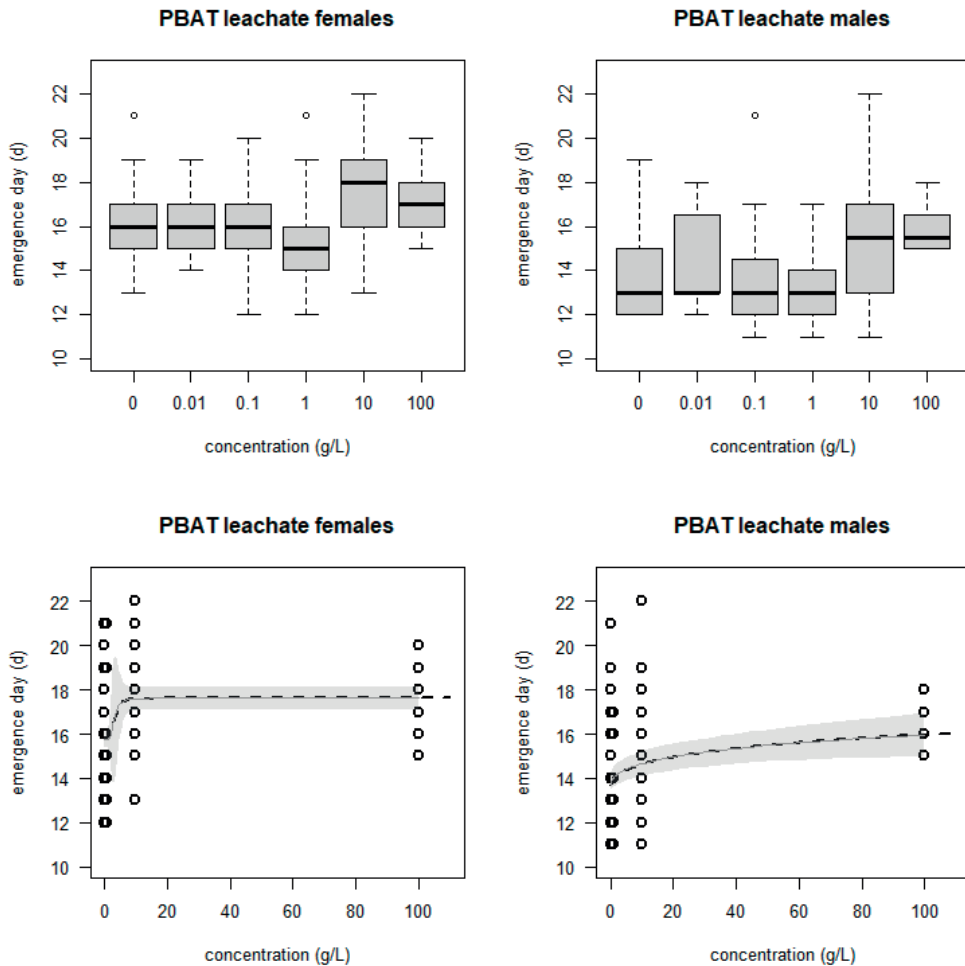
### 7.3 Controls



**Figure A.2** Experimental outcomes of control *C. riparius* larvae depending on their corresponding scenario, a) shows survival in % at day 10, b) the raw length of the *C. riparius* larvae at day 10, c) shows total emergence in % after 23 days of experimentation, d) shows mean velocity at day 10, e) the exploration value in absolute terms at day 10, and f) the average day of emergence. Significant differences is indicated on the figure,  $p < 0.05 = *$ ,  $p < 0.01 = **$

### 7.4 Gender differences

Only high concentrations of PBAT leachate were found to cause some developmental effects. Therefore, the data analysis of endpoints related to development were repeated for PBAT leachate taken gender differences into account, to see if gender impact the effects.



**Figure A.3** Emergence day of *C. riparius* after exposure to PBAT leachate. A) and B) shows the raw data of emergence day depending on exposure concentration of the plastic leachate in g/L added plastic for females and males, respectively. C) and D) shows the corresponding dose-response curves for females and males. EC50 values were determined based on the dose-response curves: EC50, female = 3.20 (0-8) g/L and EC50, male = 594 (0-5,212) g/L. No significant differences between the curves were found ( $p > 0.05$ )



8	2,2	239,1	Pentaethylene glycol	C10H22O	-0,9	14	837	3	<b>X</b>
	5	487		6					
9	1,1	262,1	Tris(2-hydroxyethyl) isocyanurate	C9H15N3	-0,8	21	861	3	<b>X</b>
	9	032		O6					
<b>Negative</b>									
<b>mode</b>									
1	2,9	145,0	Adipic Acid	C6H10O4	0,5	10	851	3	<b>X</b>
0	8	507							

## 7.6 Burrowing data

### Aim of this endpoint

As part of the experiment, the burrowing behaviour of chironomids larvae were checked on day 10. This endpoints were aimed at assessing the ability of chironomids to fully burrow into the sediment after being taken out. *C. riparius* being detritus feeders requires them to move out of their u-shaped burrows to feed. This leaves them vulnerable to predators, being able to burrow is essential for their survival (Hölker & Stief, 2005; Langer-Jaesrich et al., 2010). Plastic leachate have been found to cause reduced locomotion of other aquatic organisms (Lin et al., 2022; Reyes & Medina, 2024). It was hence assessed whether either the plastic particles or the leachate of either PBAT or PE plastic would decrease *C. riparius* burrowing abilities.

### Method

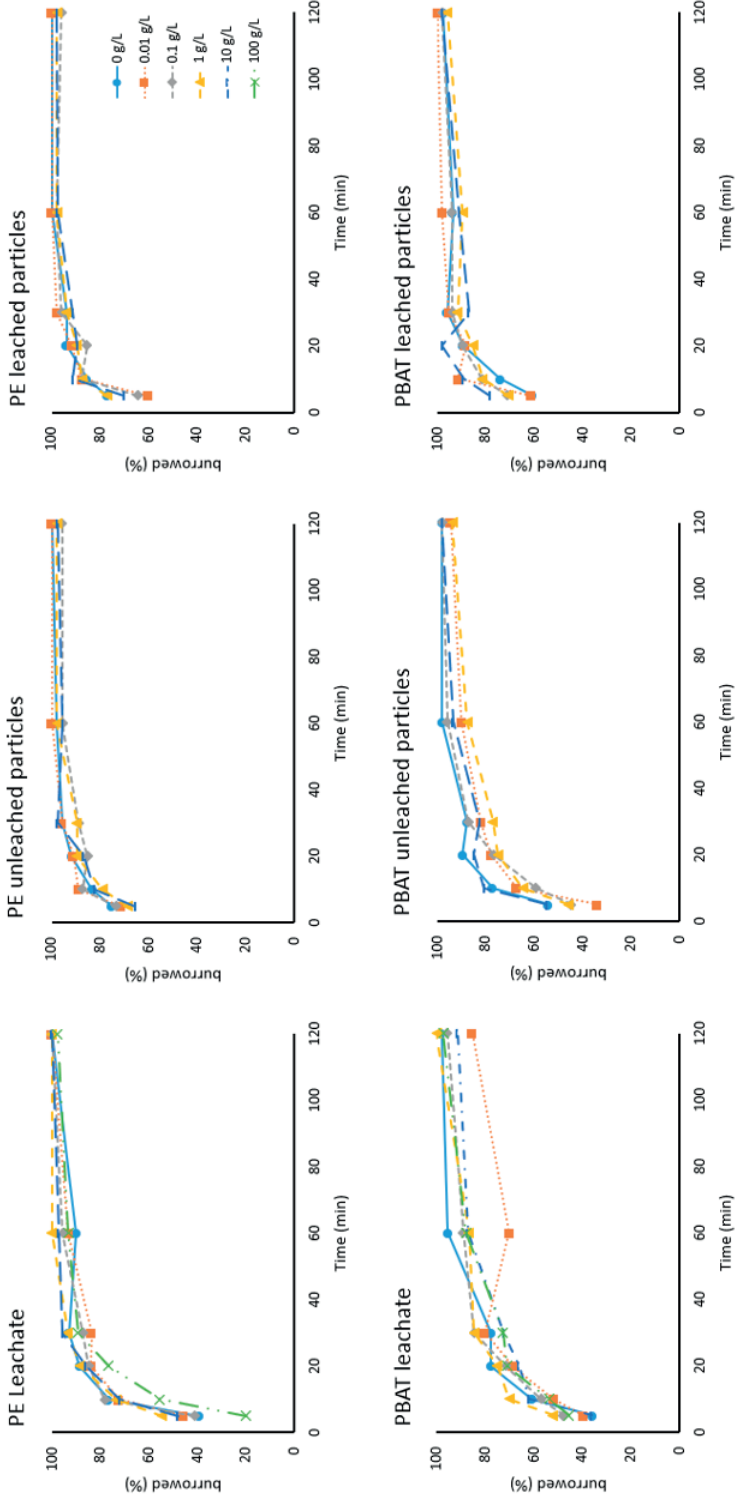
At day 10 of exposure to the plastics, the larvae were removed from test beakers to assess their survival, growth and swimming. Burrowing behaviour was tested once the larvae were placed back in their respective test beakers (n=6). This was done by counting how many individuals were visible at different time intervals. Measurements were done at 0, 5, 10, 20, 30, 60, and 120 minutes after the larvae were returned to the test beakers. These time intervals were chosen based on the previous literature and after observing larval behaviour in a controlled environment (Hölker & Stief, 2005). All larvae were counted as visible on time 0. The data for the burrowing includes several time points per replicate. To avoid losing any variance, generalised linear mixed models were applied in R to test for differences.

## Results

*Table A.3 Results of generalized linear mixed models (p values).*

Plastic		PE			PBAT		
Treatment	variable	leachate	unleached particles	leached particles	leachate	unleached particles	leached particles
	<b>Concentration</b>	0.225	0.918	0.764	0.756	0.735	0.507
	<b>Time</b>	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

As seen in Table C.3 concentration of either of the plastic types were not found to impact the burrowing abilities. None of the added plastic types were found to differ significantly from the corresponding controls. Time was found to significantly impact the number of visible larvae in the burrowing test under all scenarios. Under all scenarios, the number of burrowed larvae increased over the 2 hour period (See *Figure A.4*).



**Figure A.4** observed visual larvae in test beakers over a two-hour period at day 10. Averages per treatment are plotted ( $n=6$ )

## Appendix B

Appendix to Chapter 5

### 7.7 Heatmap of prediction tendency

		No effect							
Type of chemical									
	pesticide	3	4	7	0	3	1	3	
	metal	6	2	1	0	2	8	1	
	pharmaceutical	12	5	8	1	6	0	0	
	nanoparticle	5	1	3	0	1	7	0	
	radiation	2	1	2	0	0	0	0	
	plastic	1	2	1	0	2	2	0	
	mixture	2	0	0	0	0	0	0	
	PFAS	2	3	1	0	0	0	0	
	additive	3	4	5	0	5	0	0	
	food	2	1	2	0	0	1	0	
	arsenic	0	0	1	0	0	4	0	
	particle	1	1	1	0	1	0	0	
	parafilm	1	0	1	0	0	0	0	
	Organobromine	1	1	0	0	0	0	0	
	alcohol	0	0	0	0	0	0	0	
	PAH	0	2	2	0	2	0	0	
	salt	0	0	0	0	0	0	0	
	oil	0	0	0	0	0	0	0	
Type of endpoint	mortality				behavioural	physiological	molecular	epigenetics	
	growth								
	reproductive								
		conventional			non-conventional				

*Figure B.1 Heatmap of observations showing 'No effect' based on type of chemical and endpoint*

Linear effect							
Type of chemical	conventional			non-conventional			
	mortality	growth	reproductive	behavioural	physiological	molecular	epigenetics
pesticide	4	2	3	3	2	2	0
metal	3	6	2	0	0	3	5
pharmaceutical	2	5	4	0	4	4	0
nanoparticle	1	5	6	0	1	0	3
radiation	1	0	3	1	0	0	0
plastic	0	3	2	0	1	2	0
mixture	0	1	1	0	1	0	1
PFAS	0	0	2	0	1	0	1
additive	0	1	0	1	2	5	0
food	0	0	1	1	0	0	0
arsenic	0	0	1	0	0	3	0
particle	0	0	0	0	0	0	0
parafilm	0	0	0	0	0	0	0
Organobromine	0	0	1	0	0	0	0
alcohol	0	0	0	0	0	0	0
PAH	0	0	0	0	0	0	0
salt	1	1	1	1	0	0	0
oil	0	0	0	0	1	0	0
Type of endpoint	conventional			non-conventional			

*Figure B.2 Heatmap of observations showing 'Linear effect' based on type of chemical and endpoint*

Acclimation							
Type of chemical							
pesticide	6	3	13	5	3	4	5
metal	7	7	9	1	3	5	2
pharmaceutical	0	1	5	0	2	9	1
nanoparticle	2	2	2	2	0	5	0
radiation	3	2	2	0	1	0	0
plastic	3	0	2	1	1	5	1
mixture	2	3	1	0	1	1	2
PFAS	2	1	2	0	0	1	1
additive	1	1	2	1	1	1	1
food	0	0	0	1	0	0	0
arsenic	0	0	2	0	0	8	0
particle	0	0	0	0	0	0	0
parafilm	0	0	0	0	0	0	0
Organobromine	0	0	0	0	0	0	0
alcohol	0	0	0	0	0	0	0
PAH	1	0	0	0	1	0	0
salt	0	0	0	0	0	0	0
oil	0	0	0	0	0	0	0
Type of endpoint	mortality	growth	reproductive	behavioural	physiological	molecular	epigenetics
	conventional			non-conventional			

*Figure B.3 Heatmap of observations showing 'Acclimation' based on type of chemical and endpoint*

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Sensitisation							
Type of chemical							
pesticide	6	4	2	6	0	6	6
metal	6	4	17	0	2	6	2
pharmaceutical	5	5	23	1	4	7	1
nanoparticle	9	5	15	1	3	10	2
radiation	2	3	8	2	4	0	1
plastic	5	2	9	0	1	3	0
mixture	2	0	3	3	0	0	2
PFAS	3	0	4	0	0	2	2
additive	4	3	8	0	2	1	0
food	0	0	1	0	0	0	2
arsenic	1	4	2	0	0	8	0
particle	1	2	1	0	1	0	0
parafilm	0	2	1	0	0	0	0
Organobromine	0	0	0	0	2	0	0
alcohol	1	0	1	0	1	0	0
PAH	1	0	1	0	0	0	0
salt	0	0	0	0	0	0	0
oil	0	0	1	0	0	0	0
Type of endpoint	mortality	growth	reproductive	behavioural	physiological	molecular	epigenetics
	conventional			non-conventional			

Figure B.4 Heatmap of observations showing ‘Sensitisation’ based on type of chemical and endpoint

Sensitisation							
Type of chemical							
pesticide	6	4	2	6	0	6	6
metal	6	4	17	0	2	6	2
pharmaceutical	5	5	23	1	4	7	1
nanoparticle	9	5	15	1	3	10	2
radiation	2	3	8	2	4	0	1
plastic	5	2	9	0	1	3	0
mixture	2	0	3	3	0	0	2
PFAS	3	0	4	0	0	2	2
additive	4	3	8	0	2	1	0
food	0	0	1	0	0	0	2
arsenic	1	4	2	0	0	8	0
particle	1	2	1	0	1	0	0
parafilm	0	2	1	0	0	0	0
Organobromine	0	0	0	0	2	0	0
alcohol	1	0	1	0	1	0	0
PAH	1	0	1	0	0	0	0
salt	0	0	0	0	0	0	0
oil	0	0	1	0	0	0	0
Type of endpoint	mortality	growth	reproductive	behavioural	physiological	molecular	epigenetics
	conventional			non-conventional			

Figure B.4 Heatmap of observations showing ‘Sensitisation’ based on type of chemical and endpoint