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VRIJE UNIVERSITEIT BRUSSEL

PhD in Pharmaceutical Sciences
2021-2022

INVITATION to the Public defence of

Emma ARNESDOTTER

To obtain the academic degree of

'DOCTOR OF PHARMACEUTICAL SCIENCES'

TOWARDS NEXT GENERATION RISK ASSESSMENT OF CHEMICALS
Liver toxicity as a case study

The defence will take place on

Thursday, 19 May 2022 at 5 p.m.

In Auditorium Piet Brouwer
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

and will be organised online, accessible through the following link:

https://gf.vub.ac.be/redirects/PhD_defense_Emma_Arnesdotter.php

Summary of the dissertation

Animal testing has historically been used to evaluate the human safety of chemical compounds, including cosmetic ingredients. Since 2013, the European Cosmetics Regulation prohibits animal testing for all aspects of cosmetic ingredients. However, alternative methods capable of addressing the most complex human endpoints, such as systemic toxicity, are still lacking. This doctoral thesis project supports the development of such alternative methods by focussing on key cellular events in toxicity pathways that could be suitable for inclusion in a testing strategy for the specific case of hepatotoxicity. The first study included in this doctoral thesis screened safety evaluation reports of cosmetic ingredients to identify potential target organ(s). It was found that the liver is the most commonly affected organ following repeated oral administration of cosmetic ingredients to experimental animals. In the second study, an adverse outcome pathway (AOP) network was derived and analysed to determine key events relevant for the prediction of hepatotoxicity *in vitro*. This work identified cell injury/death, increased production of reactive oxygen species, mitochondrial dysfunction and fatty acid accumulation as the most important key events. In the third study, human-relevant liver-based cell models were exposed to compounds known to induce general and liver-specific toxicities, to explore the use of toxicogenomics to derive an *in vitro* point of departure (POD) for risk assessment purposes. The results indicated that benchmark dose (BMD) modelling of gene co-expression networks recapitulate BMD modelling of genes and may be a good approach for the derivation of *in vitro* transcriptomics PODs. Overall, this doctoral thesis project has provided a considerable contribution to the development of animal-free methods for risk assessment of chemicals.

Curriculum Vitae

Emma Maria Viktoria Arnesdotter was born on 4 May 1990 in Stockholm, Sweden. She studied agricultural science in secondary school before she decided to pursue an academic career in the context of human health. She obtained a bachelor's degree in Biomedical Sciences, followed by a master's degree in Toxicology, at Karolinska Institutet, Sweden, without ever failing a single exam (not even the one in organic chemistry). Emma found her love for research during her bachelor's thesis work at the department of Oncology and Pathology while working on a project investigating the turnover dynamics of human brain tissue using retrospective ^{14}C birth dating. After completing her master's degree, Emma moved to Belgium and joined the research group of *In Vitro* Toxicology and Dermato-Cosmetology at the Faculty of Medicine and Pharmacy at the VUB, to pursue a PhD under the principal supervisors Professor Mathieu Vinken and Professor Tamara Vanhaecke. Her PhD aimed to support the development of non-animal methods for risk assessment of chemicals. During the course of her PhD, she attended a number of national and international courses on the subject of (*in vitro*) toxicology and risk assessment. Emma has contributed to seven peer-reviewed publications, of which four as first author (and a fifth soon to be submitted), as well as two conference papers. Further, she has presented her work in form of several poster presentations, of which one was awarded and selected for oral presentation at the JRC Summer School in Ispra, Italy. Finally, she has supervised one master dissertation in the biomedical sciences.