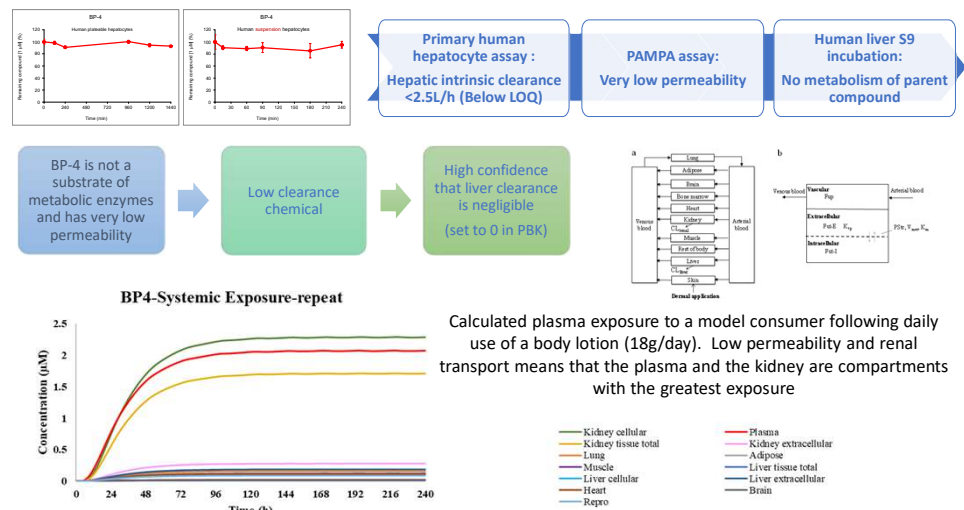


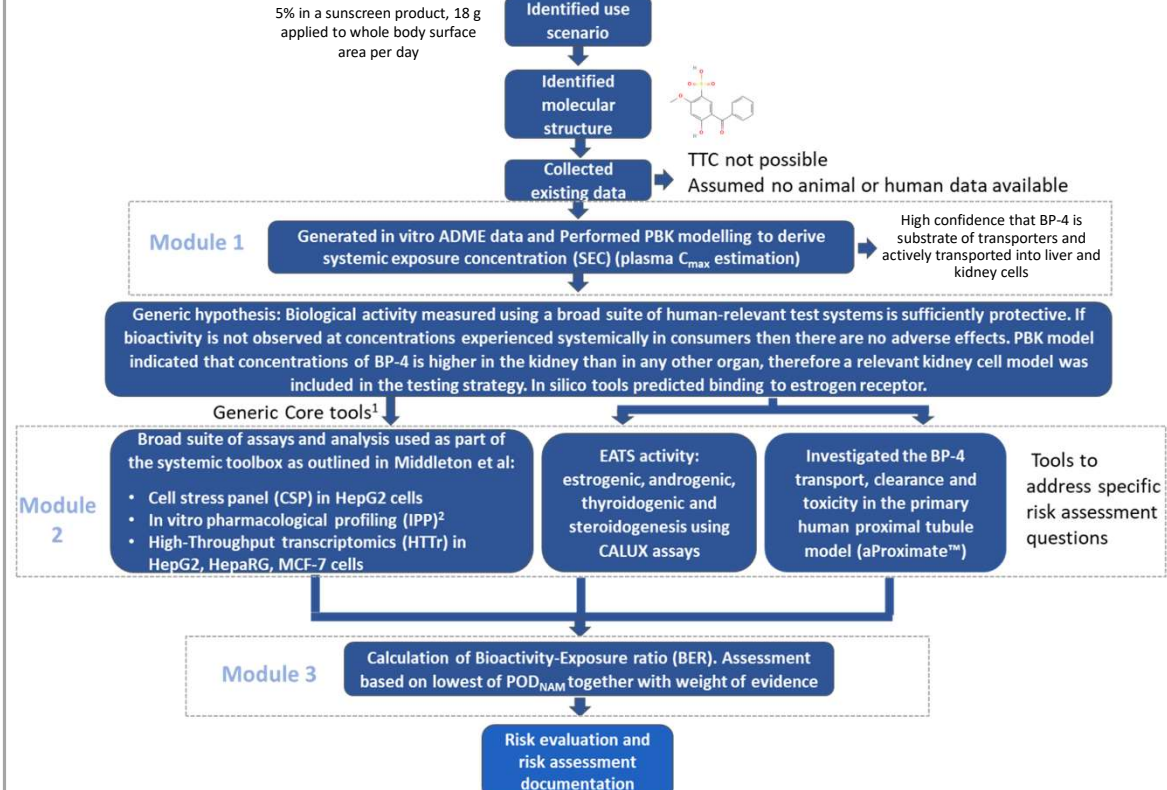
Introduction

The purpose of this work was to see if new approach methodologies (NAMs) could be used to evaluate the systemic safety of a UV filter present at a high level (up to 5%) in a sunscreen lotion. The exposure-led and hypothesis driven safety assessment was based on the International Cooperation on Cosmetics Regulation principles of Next Generation Risk Assessment and the Safety Evaluation Ultimately Replacing Animal Testing (SEURAT-1) *ab initio* safety assessment workflow. The overall hypothesis was that if biological activity measured using a broad suite of human-relevant test systems is not observed at concentrations experienced systemically by sunscreen users, there can be no adverse effects associated with product use. Different assays assessing bioactivity and exposure were used to test this hypothesis.

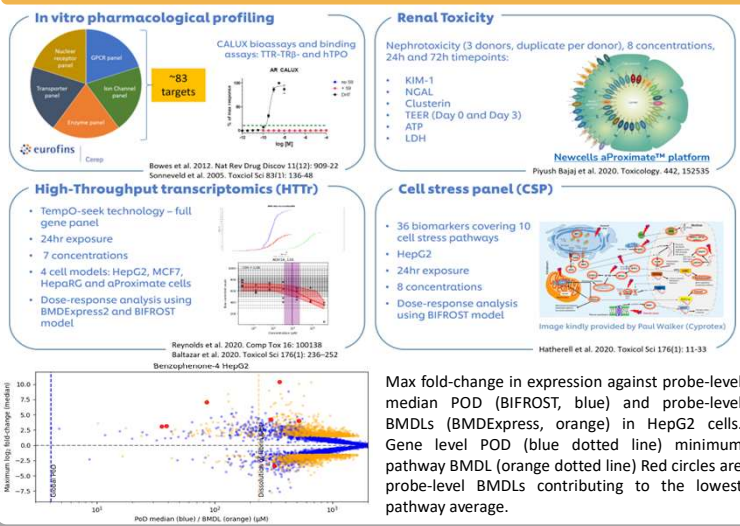
MODULE 1: Exposure NAMs



Methods



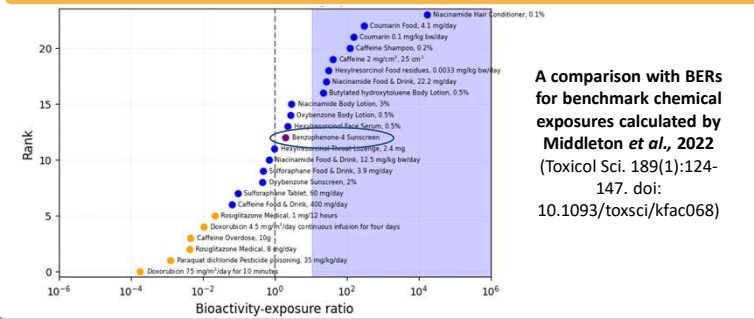
MODULE 2: Bioactivity NAMs and dose-response modelling



MODULE 3: Bioactivity:Exposure Ratios (BERs)

NAM	Cell type	POD_{NAM} Type	POD_{NAM} Value (μM)	BER (using C_{max} of 2.1 μM)	BER from individual C_{max} (μM)	Prob. BER>1
Cell stress panel	HepG2	Global PoD	140	67	110 (11, 1200)	1.0
HTTr	HepG2	Global PoD	4.2	2	3.4 (0.32, 35)	0.85
HTTr	HepaRG	Global PoD	52	25	42 (4, 430)	1.0
HTTr	MCF7	Global PoD	5.5	2.6	4.4 (0.42, 45)	0.90
HTTr	HepG2	Pathway BMDL	240	114	190 (18, 2000)	1.0
HTTr	HepaRG	Pathway BMDL	530	252	430 (41, 4400)	1.0
HTTr	MCF7	Pathway BMDL	330	157	260 (25, 2700)	1.0
hTPO-inhibition	-	LOEC	300	143	240 (23, 2500)	1.0
T4 binding to TTR	-	LOEC	630	300	510 (48, 5200)	1.0
Renal biomarkers	PTC	Global PoD	>1000	NA	NA	NA
HTTr (renal cells) (24 h)	PTC	Global PoD	320	152	260 (25, 2600)	1.0

Is the assessment protective?



Conclusion
 Using highly conservative approaches in the calculation of BERs, the systemic exposure concentration is not likely to lead to perturbations in bioactivity that could lead to an adverse outcome in the human body when benzophenone-4 is used at 5% in a sunscreen body lotion product.

Acknowledgements
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