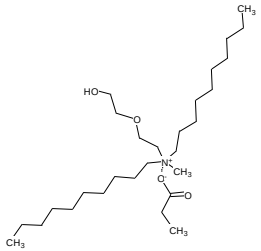
PBT modelling for the Bardap 26 metabolites M1a, M1b and M1c

Structures considered:

Parent compound **Didecylmethylpoly(oxyethyl)ammonium propionate**	[redacted]
 Representative structure CAS No. 94667-33-1 EC No. 619-057-3 SMILES: CCC([O-])=O.CCCCCCCCCC[N+](C)(CCCCCCCCCC)CCOCCO	

[redacted]

Biodegradation:

[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Conclusion: Although the VEGA predictions are not within domain for M1b and M1c, they are in line with predictions of EPI Suite, which are within domain. Therefore, the three metabolites can be considered not persistent, also considering that according to Annex XIII screen criteria: substances are classified as potentially P or vP if: BioWin 2 (non-linear model prediction): Does not biodegrade fast and Biowin 3 (ultimate biodegradation time): timeframe prediction: ≥ months OR Biowin 6 (MITI non-linear model prediction): Does not biodegrade fast and Biowin 3 (ultimate biodegradation time): timeframe prediction: ≥ months.

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Conclusion: VEGA and T.E.S.T. are not powered enough to perform BCF prediction of quaternary ammonium substances and therefore the predictions are considered out of domain. In the case of T.E.S.T, no value is provided when the prediction is out of domain for 4 out of 5 models i.e., FDA, Group contribution, Hierarchical clustering and single model. Although, the predictions of VEGA are out of domain, they are in line with the ones generated by Epi Suite™. For the three metabolites, the predicted values are well below the BCF threshold of 2000 L/kg.

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[redacted]

[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]

* ECOSAR v.2.00. https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model
** https://www.vegahub.eu/about-qsar/
*** T.E.S.T. version 4.2. https://www.epa.gov/chemical-research/users-guide-test-version-42-toxicity-estimation-software-tool-program-estimate.
$The counterion has not been taken into account.

Conclusion: VEGA and T.E.S.T. are not powered enough to perform ecotoxicity predictions of quaternary ammonium substances and therefore the fish and Daphnia LC50 predictions are considered out of domain. In the case of T.E.S.T, no consensus prediction is provided, as 3 out of 4 models are out of domain i.e., FDA, Group contribution and Hierarchical clustering model. Although, the predictions of VEGA are out of domain, they are in line with the ones generated by ECOSAR. For the ECOSAR modelling, the three metabolites have been classified under the cationic surfactant special class. Accordingly, their predicted LC50 values are at least 10-fold higher than the LC50 values of the parent compound. Therefore, they do not fulfil the T criterion and are not expected to present higher toxicity as compared to the parent compound.

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