Summary of CompTox Data
Quaternary Ammonium Compounds

The US EPA CompTox Chemical Dashboard[1] provides access to multiple datasets, including the merged Tox21/ToxCast datasets in which >7000 chemicals have been tested in hundreds of in-vitro systems. The data can inform us about molecular pathways that may be important for further investigation. The data can also be useful to explore some endpoints that have been identified based on in-vivo analyses. It is important to recognize that there are limitations with some of the assays, the concentrations of chemicals where activity is observed. However, the composite data are useful for screening and informing – not for use as final, decision-making data.

Of the Quaternary Ammonium Compounds (QACs) in commerce, a subset are High Production Volume chemicals[2] and of these, a subset has been tested and reported in the EPA's CompTox Chemical Dashboard. The CompTox data include results of testing for activity associated with nuclear receptors, a subset of which are known to be involved in the regulation of lipid and cholesterol homeostasis. We include these assay results because of the research showing/suggesting the effects of QACs on lipid and cholesterol homeostasis[3,4,5]. Presented in Table 1, are the biological activity data reported for QACs with interaction with nuclear receptors that are well known to be involved in regulation of lipid and cholesterol homeostasis. These include the androgen receptor (AR), estrogen receptor α (ERα) and thyroid hormone receptor β (THRβ) are most common across the tested QACs. Also included are data from interactions with glucocorticoid receptor (GR) and liver X receptor (LXR). The biological activity data reported in CompTox provide additional evidence to suggest that multiple QACs could impact the ability of cells to synthesize/metabolize/transport lipids and cholesterol.

[1] USEPA. CompTox Chemicals Dashboard. Accessed February 8, 2021. https://comptox.epa.gov/dashboard/

[2] USEPA. High Production Volume Information System (HPVIS) | OPPT | US EPA. Accessed February 9, 2021. https://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report?doctype=2

[3] Herron J, Reese RC, Tallman KA, Narayanaswamy R, Porter NA, Xu L. Identification of Environmental Quaternary Ammonium Compounds as Direct Inhibitors of Cholesterol Biosynthesis. Toxicol Sci. 2016;151(2):261-270. doi:10.1093/toxsci/kfw041

[4] Hrubec TC, Melin VE, Shea CS, et al. Ambient and Dosed Exposure to Quaternary Ammonium Disinfectants Causes Neural Tube Defects in Rodents. Birth Defects Res. 2017;109(14):1166-1178. doi:10.1002/bdr2.1064

[5] Hines KM, Herron J, Xu L. Assessment of altered lipid homeostasis by HILIC-ion mobility-mass spectrometry-based lipidomics. J Lipid Res. 2017;58(4):809-819. doi:10.1194/jlr.D074724

Table 1: QACs where the Tox21/CompTox-reported active concentration (AC) 50s were below the cytotoxicity limit.

	Abbr	HPVC*	CAS Number	Androgen Receptor	Estrogen Receptor α	THRβ	Gluc. Receptor	LXR	Cytotox Limit (μM)
Didecyldimethylammonium chloride (C12, C14, C16)	DDAC/ DDMAC-10	Yes	7173-51-5	Partial agonist/ Antag.	Partial agonist/ Antag.	Antagonist	Partial agonist/ Antag.	Partial agonist/ Antag.	10.0
Dimethyldioctadecylammonium chloride	DADMAC-18	Yes	107-64-2						
Decyltrimethylammonium bromide	TAB-C10		2082-84-0						
Dodecyltrimethylammonium bromide	TAB-C12		1119-94-4	Antagonist	Agonist	Antagonist			10.4
Dodecylpyridinium bromide	PB-C12		104-73-4						
Benzyldodecyldimethylammonium bromide	BZK-C12		7281-04-1			Antagonist	Antagonist		7.3
Hexadecyl trimethyl ammonium bromide	CTAB/HTA		57-09-0		Agonist	Antagonist			8.6
Dimethyl dioctadecyl ammonium bromide	DDA		3700-67-2						
Benzalkonium chloride (C12-C16)	ADBAC	Yes	63449-41-2	Antagonist	Agonist	Antagonist			13.6
Benzyldodecyldimethylammonium chloride	BAC-C12	Yes	139-07-1	Antagonist	Agonist	Antagonist		Partial agonist/ Antag.	10.6
Benzyldimethyltetradecylammonium chloride	BAC-C14	Yes	139-08-2						
Benzyldimethyloctadecylammonium chloride	BAC-C18	Yes	122-19-0		Partial agonist/ Antagonist				9.6
Methylbenzethonium chloride	MBC		25155-18-4						
Benzethonium chloride	BTC		121-54-0	Antagonist					7.5
Cetylpyridinium chloride	CPC		6004-24-6						

*High production volume chemical