

ADBAC Issues Steering Committee (ISC) comments to the Scientific Guidance Panel regarding the use of analytical methodology for measuring of antimicrobial quaternary ammonium compounds (QACs) in environmental and biomonitoring samples

For the *Biomonitoring California Scientific Guidance Panel* meeting scheduled March 8, 2021

The ADBAC Issues Steering Committee (ISC) is a consortium of companies supporting the United States EPA and European Biocidal Product Regulation (BPR) registration of antimicrobial quaternary ammonium compounds (QACs) administered by Ignite Solutions, which is part of Household and Commercial Products Association (HCPA) trade association. Its members include companies that make sanitizing and disinfecting products and manufacture antimicrobial QACs.

Executive Summary

The quaternary ammonium compounds represent a diverse group of compounds which account for the wide toxicological properties' compounds demonstrated within the class. An analytical method used to detect quaternary ammonium compounds needs to utilize methodology that has been validated for specificity of the identified quaternary ammonium compound and sensitivity in the matrices in which measurement are made.

Comment 1. Quaternary Compounds Structurally Diverse Class of Compounds

The class of compounds generically referred to as Quaternary Ammonium compounds, as a class, include a wide variety of chemical structures. This diversity has been noted in OEHHA documents prepared for the SGP. It is well recognized that the chemical structure of a compound is a key factor for a compound's properties including its toxicological properties. The antimicrobial quaternary ammonium compounds supported by the ADBAC ISC and for which supporting documentation has been submitted to OEHHA by the ADBAC ISC and Quat Residue Group (QRG) fall within the sub-class of compounds identified in the EPA Registration Final Work Plans for ADBAC and DDAC.

Comment 2. Validated Analytical Methodology

Analytical methodologies used to identify, and report levels of quaternary ammonium compounds need to possess sufficient specificity to differentiate between the various classes of quaternary ammonium compounds. A method that reports all or most quaternary ammonium compounds into an aggregated measurement can have limited utility.

A number of published papers reference the use of mass spectroscopy as a method to identify and report levels of quaternary ammonium compounds in various matrices. While liquid chromatography combined with mass spectroscopy (LC-MS) methodology has the potential to produce sensitive and specific analytical methods there are disadvantages of LC-MS that need to be addressed as part of the validation of the method.

- a. Complexity: Both LC and MS methods can be difficult to optimize. Combining the two leads to a complex co-dependent synergy. Care must be taken to choose conditions for optimum sensitivity and reproducibility.
- b. Limited dynamic range: Compared to other quantitative techniques LC-MS can have a limited range where the response is linear with respect to concentration.
- c. Excessive selectivity: In quantitative analysis it is usual that the MS is set to only detect specific analytes. This results in a very 'clean' looking chromatogram and it is easy to forget that there can be a lot of components still present, but not seen. These components can cause problems with reproducible quantitation and can be difficult to trace if they are not being looked for e.g. matrix effects found in environmental samples.
- d. Expense: Mass spectrometers that can couple to LC systems are expensive to buy and run. Regular servicing and appropriate and stable laboratory environmental conditions are needed to ensure system stability and reproducible results.

Numerous publications discuss the requirements to validate that the LC-MS method developed can reproducibly with the required selectivity and sensitivity measure the target analyte or analytes. Studies submitted for governmental review that contain quaternary ammonium compound concentrations utilize validated measurement methodology, for example radiolabeling or use in simple aqueous mixtures, to ensure compound levels reported are valid. The identity or level of a quaternary ammonium compound found in an environmental or biological system using LC-MS or other analytical methods should only be reported from methods that have documented method validation.

References

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