Value of Products based On the ADBAC and DDAC based Disinfectants

For the University of Massachusetts Lowell *Toxic Use Reduction (TURI) Science Advisory Board* meeting scheduled for November 18, 2020

The ADBAC and DDAC Issues Steering Committee (ADBAC/DDAC ISC) are science-based task forces administered by Ignite Solutions, which is part of Household and Commercial Products Association (HCPA) trade association. The ADBAC/DDAC ISCs were formed to conduct studies and analyses needed by US EPA for federal registration and related risk assessment activities for alkyl dimethyl benzyl ammonium chloride (ADBAC) and didecyl dimethyl ammonium chloride (DDAC) based disinfectants.

Brief:

Alkyl dimethyl benzyl ammonium chloride (ADBAC) and Didecyl dimethyl ammonium chloride (DDAC) are a class of quaternary ammonium compounds ("Quats") that are a demonstrably safe, necessary, and effective tool for combating COVID-19 and other pathogens. The products are approved for use in all settings—Including home, healthcare, retail, and restaurants—and are recognized by the United States Environmental Protection Agency (U.S. EPA) for their effectiveness in combatting bacteria and viruses. Indeed, Quats were one of the first product platforms added to the U.S. EPA "N" list of registered disinfectant products for this purpose. Furthermore, guidance for proper Quats use has been noted in the registration of these substances by US EPA and reviews in the EU by ECHA, and promulgated through the Quats Education Program.[1]

Questioning the use of Quats, may inadvertently promote the use of cleaning products that clean or sanitize (which does not kill the virus), but fail to disinfect. In fact, studies have shown that cleaning without properly disinfecting spreads viruses to more surfaces, which increases the risk of infection. As the country attempts to re-open its economy, send children back to school and protect public health, it is critical that all products that are proven to disinfect and that can be utilized in a safe manner are available and used properly.

Benefits of Disinfectant Quat Based Products:

[1] http://www.quats.org/resources/

Today, the broad class of chemicals that can be described as Quats are commonly found in a variety of consumer and commercial products from cleaning products, fabric softeners, personal hair care products. Within the broad class of Quats it is a select group that possess the structure that enables the Quat to function as a bacterial and viral killing EPA registered disinfectant.[2] The antimicrobial activity of quaternary ammonium compounds was first reported in 1916 and a Quat was the first antimicrobial product registered with the precursor to the EPA in 1947. This product, still in use today is based on the quaternization of benzyl chloride with tertiary amines that can come from natural oil such as coconut oil. The discovery of the disinfectant Quats was useful to doctors and were used to sterilize hands and instruments prior to surgery. Upon EPA registration the Disinfectant Quats were then used to disinfect utensils in restaurants and medical equipment.

The Disinfectant Quats are now the most common active ingredient used in disinfecting products and have been safely used for over 75 years. Disinfecting Quat products are widely used in hospitals, schools, commercial buildings, food service and clinics. These products are also widely available for household use. When used to disinfectant surfaces, the Disinfectant Quat active is present at very low concentrations.

The EPA has identified product containing Disinfectant Quats to be effective surface disinfectants. With the SARS-CoV-2 (COVID-19) outbreak, the use of disinfecting products are an essential and a primary tool to prevent transmission of the virus and ensure public health. In March 2020, the EPA released a list of EPA-registered disinfectant products that are qualified for use against COVID-19. Specifically, Disinfectant Quat containing products constitute about two-thirds of the products on the EPA's "N" list of effective products for COVID-19.

Products containing the disinfectant quats are critical to the safe re-opening of businesses and schools and delivery of health care services in clinics and hospitals. In combating COVID-19, workers are using these products to disinfect surfaces and equipment between use by customers, students and patients to ensure the health and safety of the community. And because of the non-specific nature of the antimicrobial mechanism of action of disinfectant Quats, it is unlikely that viruses or bacteria can develop resistance to them (Gerba, 2015).

Not only do Disinfectant Quats play an important role in disinfecting and the safe delivery of healthcare, but also data from product registrations and peer reviewed studies have amply demonstrated to federal and state regulatory agencies that these Quats have little to no unwelcome impact on physical health and the environment. Disinfectant Quats are poorly absorbed into test species bodies and do not bioaccumulate in the human body or in the environment. More importantly, the European Chemicals Agency (ECHA) recently completed its review for Disinfectant Quats as a disinfectant in veterinary and food preparation areas and recommended no changes in concentrations, use or practices.

[2] Antimicrobial quats, ADBAC and DDAC, attached as Document 1

Human Health Safety:

Disinfectant Quats are heavily regulated for human and environmental safety around the world (DeLeo, 2020). The EPA registers Quat-based disinfectants after assessing their efficacy and safety for use. There are more than 30 different Quat compounds registered for use in formulating cleaning, sanitizing and disinfecting products.

Along with masks and hand washing, hospital workers, janitors, restaurant workers and business owners are using Disinfectant Quat based products to disinfect and sanitize surfaces and equipment and to reduce risk and slow the transmission of COVID-19. Proper use of cleaning products, regardless if they are natural or chemical, are necessary both for the performance of the product and the health of the workers and those that will occupy the space later.

After years of study and multiple recent reviews by the U.S. EPA and EU ECHA, proper use of Quats is well understood to maximize their effectiveness against bacteria and viruses, and to protect the safety of consumers at home and janitorial staff and others in industrial, institutional, and commercial settings.

The Quats Education Program provides instruction on Disinfectant Quat-based products and how the product must be applied in order to assure sanitizing and disinfecting efficacy. Following the label instructions is essential to assure efficacy and effective disinfecting of any product. The surfaces should be allowed to air dry as most Quat-based product formulations are “no-rinse” products (The Quats Education Program, 2009). This feature of Quats binding quickly to other molecules is one of the features that make them such a desired and safe product. They relatively quickly perform their task and then become inactive. [3]

Occupational Asthma:

Regulatory agencies, including the U.S. EPA, guided a study monitoring the concentration of Disinfectant Quats from occupational cleaning conditions. The study established that the exposure to a Disinfectant Quat for liquid pour, mopping and ready to use products is extremely low and falls significantly below the concentration that might result in respiratory irritation. Therefore, it is unlikely Disinfectant Quats causes irritant induced asthma (Allergy Asthma Clinical Immunology, 2019).

A review that examined available studies on Disinfectant Quats and occupational asthma referencing asthma was conducted by LaKind and Goodman in 2019, *Quaternary Ammonium Compounds and Occupational Asthma*. The published review found that the up to date literature contain many “unresolved methodological issues including: poor understanding of exposure pathways considering that Disinfectant Quats

[3] Human health hazard assessment of quaternary ammonium compounds: Didecyl dimethyl ammonium chloride and alkyl (C12–C16) dimethyl benzyl ammonium chloride, attached as Document 2

are non-volatile, lack of quantitative data allowing for identification of an asthma threshold, insufficient information on whether these Quats are sensitizers or act via dose dependent irritation or some other mechanism, and inability to quantify risk of new-onset asthma attributable to Quats."

All this evidence suggests that despite Disinfectant Quats being respiratory irritants in experimental conditions (i.e. forced inhalation of aerosolized particles in animal studies), these Quats are unlikely to be the source of occupational asthma for cleaning and janitorial workers in regular occupational settings because of their low volatility and lack of sensitization potential. (LaKind and Goodman, 2019).

Developmental and Fertility:

Two recent studies by Hrubec and Herron were reviewed by both EPA and ECHA and the European Biocidal Products Committee. The EPA concluded that the Agency's datasets on developmental and reproductive effects on file, which meet the rigorous GLP guideline standards for study conduct and reporting, are complete and sufficient for human risk assessment. In contrast, EPA described the Hrubec publication as speculative. The results were not considered in EPA risk assessments of Dsinfectant Quats. Likewise, in a recent review by European authorities, open literature publications including the Hrubec 2017 paper were identified but because this paper does not meet even the most minimal criteria for quality and reporting of essential data on the test substance or study conduct, it was not deemed relevant to human risk assessment. None of the effects Hrubec reported were considered in the Biocidal Product Regulation assessment.

A paper by Herron et al, 2019 evaluated the effects of a massive dose of the active ingredients – 120 mg/kg - in pregnant mice and claimed that effects on steroid biosynthesis could be of concern. Such potential concerns can be quickly addressed applying a fundamental principle of toxicology – everything can be toxic – it is the dose that must be considered. In EPA's 2017 dietary exposure assessment for quats, they utilized well established and conservative modeling to quantify dietary exposure based on approved uses (food contact surfaces without a water rinse, for example). EPA estimates that dietary exposures in the general population for a typical food-contact use product is not more than 0.02 mg/kg/day. Thus, the Herron publication (and, incidentally, the Hrubec paper before it) describes effects in pregnant mice at doses that are 6,000-times higher than EPA's conservative dietary human exposure estimate. On this basis alone, the relevance of their work to human risk lacks any basis.

The Hrubec and Herron studies were published in peer-reviewed scientific journals, but not without significant commentary and professional criticism. As noted above, a detailed Letter to the Editor was submitted ~~published~~ addressing numerous shortcomings of the Hrubec study and the absence of relevance of the Herron study findings to human exposure was noted above. As mentioned, ECHA and the evaluating Competent Authority concluded that none of the requirements were fulfilled for the

Hrubec at al. (2017) publication and thus, this paper should not be considered in the risk assessment of the Dsinfectant Quats (ADBAC or DDAC).

We suggest that priority consideration be assigned to the robust, extensive, and quality-controlled dataset of guideline-compliant regulatory studies found in the U.S., Europe, and beyond, that have been accumulating for more than two decades. Equating screening level studies with the same reliability and utility as guidelines studies is inappropriate. It is noteworthy that screening level and in vitro evaluations are typically only considered when well-established guideline-based studies are not available as established in the statute. This is far from the existing circumstance with the Disinfectant Quats.

Environmental Fate:

Disinfectant Quats have strong affinity for sewage sludge, sediments, and soils. An assessment of Disinfectant Quats' environmental safety studies provided evidence of rapid biodegradation in conventional wastewater treatment systems, aquatic systems, and soils (DeLeo, 2020). DeLeo's assessment concluded that Quats are largely removed during waste-water treatment, and those residues discharged in treated effluent are likely to rapidly bind to suspended solids or sediments, thus mitigating their toxicity (DeLeo, 2020).[4]

Conclusion:

Given the extraordinarily long history of the safe use of the Disinfectant Quats, the on-going registration of these chemicals in Europe by ECHA and registration review by the U.S. EPA, products containing Disinfectant Quats are a poor candidate for listing or monitoring by State Programs. Additionally, dissuading the use of Disinfectant Quats during the COVID-19 pandemic is unjustified; constitutes unwise public health policy: and risks undermining consumer and institutional confidence in an effective, safe and important product that would help reduce transmission and infection rates as schools and the economy re-open. The use of Disinfectant Quats is especially important for disinfecting our food handling, hospitals and healthcare facilities. We are very pleased to answer any questions you may have or to provide additional data on subjects that you believe need more attention.

Thank you for your consideration.

[4]Assessment of ecological hazards and environmental fate of disinfectant quaternary ammonium compounds, attached as Document 3