September 13, 2022

Dear Editor,

Attached is the submission of our manuscript entitled ‘Viral inactivation by quaternary ammonium compounds: A systematic review’ for consideration for publication in mSphere.

The emergence and spread of novel viral pathogens poses a constant threat against humanity, as shown dramatically with the SARS-CoV-2 pandemic, and reaffirmed with concern over the growing monkeypox and Marburg virus outbreaks. With emergence of new pathogens, uncertainties in effective infection control practices emerge. A clear example made evident with the ongoing SARS-CoV-2 pandemic is understanding how disinfectants will work against emerging viruses of concern. Therefore, there is a need to understand which viral attributes contribute the most to different modes of inactivation to inform proper surrogate selection and to predict how a virus will behave in the environment when policy decisions need to be implemented quickly.

Here, we provide a systematic review of the efficacy of quaternary ammonium compounds (QACs) against viruses to identify characteristics of viruses informative for dosing. Through the work, we show conclusively that QACs are effective against all viruses, including those lacking the enveloped virus disrupted by the primary mechanism of QAC action (disruption of lipid membranes). We also show capsid size and nucleic acid type influence inactivation, providing rapid insights into necessary dosing based on known viral properties.

In addition to providing insights into what conditions contribute to effective inactivation of viruses using QACs, the study also identifies problems with comparisons across studies, specifically lack of standard testing and reporting conditions. The recommendations of this study for testing and reporting have important implications for future study designs, including choice of study surrogates and standardization across testing labs, in addition to informing disinfectant recommendations to use with emerging viral pathogens.

We believe the enclosed study to be appropriate for mSphere. We believe this manuscript represents a

significant contribution to the field, expanding on knowledge of viral and environmental factors that broadly affect viral inactivation by QACs and can be useful in making future recommendations for sanitation protocols. In addition, our work aligns with the work previously published in mSphere, as evidenced by studies referenced in our manuscript which focus on viral inactivation such as Rockey et al, “Humidity and Deposition Solution Play a Critical Role in Virus Inactivation by Heat Treatment of N95 Respirators” and Biryukov et al, “Increasing Temperature and Relative Humidity Accelerates Inactivation of SARS-CoV-2 on Surfaces”.

This is the first submission of an original work, which is not under consideration elsewhere and will not

be submitted elsewhere while under consideration by mSphere. All authors are aware of and accept

responsibility for the manuscript. Suggested reviewers have been included during the submission of the

manuscript.

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Description automatically generatedWe look forward to your evaluation of our manuscript. Please notify me if I may be of assistance.

Best regards,

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