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CORRESPONDENCE

Response to the letter to the editor

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Dear Editor,

Thank you for the opportunity to respond to Dr. Braun's letter.

We recognize that biocides, including antiseptics such as octenidine dihydrochloride, generally elicit broad spectrum antibacterial activity, while decreased biocide susceptibility seems much less pervasive relative to the global rise of antibiotic resistance [1]. It should be acknowledged however, that in contrast to the established threat of antibiotic resistance, reduced susceptibility to antiseptics and disinfectants generally has received little attention and therefore still may be of concern [2, 3]. A major impediment to this matter involves the pronounced lack of standardized methods in determining biocide susceptibility, as well as the absence of a standard definition of insusceptibility to antiseptics and disinfectants [2–4].

Even when this would not be the case, in vitro assessment of biocide susceptibility might not predict accurately antimicrobial effectiveness in host-dwelling bacterial communities, due to the emergent properties arising from complex, adaptive community assemblies [5]. A particular example to this matter, is the organisation of bacterial communities as polymicrobial biofilms, which show a number of synergies to their advantage, also in resisting antimicrobial agents [6, 7]. By recognizing so, novel pharmacodynamic parameters, including minimal biofilm inhibitory concentration, minimal biofilm-eradication concentration, and biofilm bactericidal concentration, have been adopted in recent years to quantify antibiotic activity in biofilms [7]. Such biofilm-specific pharmacodynamic indices for predicting therapeutic effectiveness have been obtained through biofilm models for antimicrobial susceptibility testing, as recently comprehensively reviewed by Macià et al. [7], though it will take substantial additional effort to standardize these approaches.

Current in vitro models of biofilms might be of limited value, however to the study of in vivo biofilms [8], as we have previously indicated for bacterial vaginosis in particular [9]. Accordingly, in vivo assessment as we have applied in this [10] and previous studies [11, 12] likely is the most valid approach at present in evaluating antimicrobial effectiveness for bacterial vaginosis, though we agree with Dr. Braun that in a non-randomized study setup, this approach is also susceptible to several biases. As evidenced by these studies, treatment of biofilm-associated conditions and bacterial vaginosis in particular, is definitely warranted and likely will involve novel drug types with molecular targets and mechanisms of action beyond conventional antimicrobial strategies [13].

In conclusion, we want to emphasize that, in view of the above, the concept of antimicrobial 'resistance' or 'insusceptibility' should not be misconstrued in this context, as it refers to the collective antimicrobial tolerance of the bacterial community, rather than to the 'resistance' or 'insusceptibility' of any particular individual microbe. As indicated in the title and elsewhere in our paper [10] we therefore consistently refer to the 'resistance' of the bacterial vaginosis or polymicrobial *Gardnerella* biofilm.

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Compliance with ethical standards

Conflict of interest We certify that no actual or potential conflict of interest in relation to this article exists.

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