Written responses to open questions of the webinar 'Drug discovery strategies: Focusing on synthetic compounds and natural products' by Heike Brötz-Oesterhelt and Scott J. Hecker, originally broadcast on 11 October 2022. See webinar recording here: https://revive.gardp.org/drug-discovery-strategies-focusing-on-synthetic-compounds-and-natural-products/

Question asked	Response from the speakers
I would like to know if discovering new drugs can be a long-term alternative to reduce or prevent antimicrobial resistance.	To my opinion the answer is a clear NO. We have to take measures to extend the span of usefulness of our available antibiotic drugs. Handle antibiotics with care!!
Question for Heike: what how far are we about using spice-based molecules to fight multidrug resistant bacteria	Antibacterial spices could be one adjunct, supportive approach to classical antibiotic therapy. (Like a range of others). Food preservation is an obvious indication for use.
Please may we know whether or not, there have been toxicity studies on the natural antimicrobial products discussed in this webinar? This is due to the fact that one major property of antibiotics is their selective toxicity.	ADEP is currently evaluated in preclinical toxicology studies. Tox studies with negamycin have been published (very low acute tox). Lugdunin is currently evaluated for application on skin.
What is the potency of your beta lactamase inhibitor in comparison to existing BLI such as clavunic acid? In your opinion, are their potencies at the same level?	The "old" BLIs including clavulanic acid, sulbactam and tazobactam are generally only useful against Class A enzymes (often referred to as penicillinases) and not including Class A carbapenemases such as KPC. Our new agent QPX7728 (xeruborbactam) has equal or greater potency against Class A enzymes (and inhibits serine carbapenemases such as KPC), and also covers Class B (metalloenzymes), Class C (cephalosporinases) and Class D (oxacillinases) including the hard-to-inhibit ones from Acinetobacter.

Remaining audience questions from the webinar 'Drug discovery strategies: Focusing on synthetic compounds and natural products' by Heike Brötz-Oesterhelt and Scott J. Hecker, originally broadcast on 11 October 2022

Question asked	Response from the speakers
With the activity reporters, how do the hits distribute across these different targets? Is one reporter activated more often than others? The streptomycin abundance would make me think translation inhibition would be most common.	It depends on the group of producer organisms. For streptomycetes, the type of stress we encounter most often is cell envelope damage. (But the first set of bioreporters we have, does not detect miscoding, thus streptomycin does not show up). On the contrary, with extracts from myxobacteria, we most often encountered RNA stress.
When using antifungal with antibiotics, do they affect response on cell membrane?	Only if they have an activity against the bacterial membrane, too.