

## 21<sup>st</sup> Meeting of the WHO Expert Committee on the Selection and Use of Essential Medicines

27 March 2017

I am making a statement on behalf of the Global Antibiotic Research and Development Partnership (GARDP). GARDP was launched in May 2016. It is incubated by the Drugs for Neglected Diseases *initiative* (DND*i*) in collaboration with the World Health Organization (WHO) in support of the Global Action Plan for Antimicrobial Resistance. Our mission is to develop new treatments for bacterial infections where drug resistance is present or emerging, or for which only inadequate treatment exists. We aim to ensure the treatments are affordable and accessible to all in need, and in a manner which minimizes the risk of inducing resistance. Importantly, we will develop our priorities not just based on priority pathogens, but also based on populations as well as syndromes and diseases for which current treatments are inadequate.

We strongly welcome this rigorous and comprehensive review. As a potentially valuable tool in helping to guide antibiotic use, there are a few issues that GARDP would like to draw attention to, as follows.

### **Scope of syndromes**

Regarding the syndromes listed, there are certain syndromes that would be important to consider for inclusion, such as undifferentiated fever in children, persistent fevers of unknown origin, and ophthalmic infections among others. Management of certain syndromes in malnourished and co-infected paediatric populations would also be important to consider.

### **Methodology**

The methodology of the review relies on systematic reviews and on largely European and US Clinical Practice Guidelines. While rigorous in approach, this risks poor representation of data and information from L&MICs and for certain syndromes. In order to address this gap, we suggest considering the use of relevant observational data, as well as how AMR surveillance data, including from GLASS, could be integrated in such work in the future.

We would also like to draw attention to understanding safety and tolerability when reviewing published evidence. The review acknowledges that a non-inferiority trial design is not useful for detecting safety outcomes. Systematic reviews and meta-analyses of safety data are also much less common than they are for efficacy data. It may therefore be useful to also consider the use of post-marketing pharmacovigilance and analyse the content of safety databases, such as Vigiflow. This is also relevant for new antibiotics coming out of the pipeline.

We also think a narrative discussion on how to consider the use of certain antibiotics more carefully would be useful. We would welcome more advice on the use of certain classes of drugs such as carbapenems.

## Paediatrics

We would like to highlight paediatrics as an area with major gaps. Here we also suggest more observational data and other studies as supplemented evidence. We would like to point out that there is little guidance on optimal dosing in children (let alone issues around drug formulations, though this requires a different type of exercise going forward). We strongly emphasize the urgent need for more robust studies and trials for children.

## Sexually-Transmitted Infections (STIs)

Regarding STIs, GARDP would like to question the focus on urethritis, which is not part of the syndromes listed by the WHO guideline on syndromic management of STIs. The two most common syndromes are urethral discharge – which is not synonymous to urethritis – and genital ulcer. We suggest that the definitions be harmonized with those used by the WHO Department of Reproductive Health and Research.

Further, we suggest clarity in the comparative analysis of azithromycin and doxycycline. The STI section starts by mentioning their efficacy on Chlamydia, but then states that azithromycin resistance may be a problem. We would like to draw attention to the recently released WHO guidelines on management of Chlamydia that recommends azithromycin or doxycycline for urogenital Chlamydia. We also note that the review neglects to mention gonorrhea in the systematic review analysis. We would like to draw attention to the fact that the most concerning issue with azithromycin resistance is with Neisseria and not Chlamydia.

## Conclusion

Finally, we strongly support the review being used in alignment with other key WHO activities, specifically the Global Development and Stewardship Framework, the Priority Pathogens List, and the antibiotic pipeline review; specifically to help determine gaps and priorities for R&D in the areas where GARDP will be working.

Based on this existing work, GARDP will be embarking on R&D programmes to develop new treatments for neonates, children, and for STIs. We believe this review to be therefore an important step in helping us better understand how we need to prioritize development of antibiotics and how to use antibiotics in the future.

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