BACKGROUND

The Malaria Policy Advisory Group of the World Health Organization (WHO) has recommended that WHO explores the use of non-inferiority studies as part of the evaluation process for vector control products (1). The aim of this study design is to generate evidence to support extension of a policy recommendation based on epidemiological evidence demonstrating the public health value of a ‘first-in-class’ product to ‘second-in-class’ products. ‘Second-in-class’ products are not required to demonstrate epidemiological impact but will require solid and directly comparable entomological data.

The case of such data requirement is exemplified by mosquito nets treated with a pyrethroid insecticide and the synergist piperonyl butoxide (PBO). Pyrethroid-PBO nets were given an interim endorsement as a new product class in 2017 (2) based on epidemiological data demonstrating the efficacy of one product, generated through one cluster randomized trial conducted with Olyset®Plus (manufactured by Sumitomo Chemicals Co. Ltd) (3). At the time, four other net products containing PBO had been assessed and recommended by the WHO Pesticide Evaluation Scheme (WHOPES) as pyrethroid nets. In the transition from WHOPES to the new WHO evaluation system, these recommendations were converted to a prequalification listing. However, the four nets differ from Olyset®Plus in terms of their design/specifications. Key differences include: the location of the PBO (i.e., all net panels or just the top panel); the PBO loading dose; the type and content of pyrethroid; and the regeneration time, wash resistance and bioavailability of the PBO. Therefore, it remains unclear whether these second-in-class products should be covered by the policy recommendation that was developed based on the epidemiological data generated by the first-in-class product (in this case Olyset®Plus).

Similar considerations apply to extension of policy recommendations to second-in-class vector control tools within other intervention classes.
PROPOSAL

WHO is planning to introduce non-inferiority determination using data on entomological endpoints as a standard requirement of the evaluation process for vector control tools.

NEXT STEPS

A study protocol for non-inferiority studies focused on insecticide treated nets and indoor residual spraying has been developed by WHO and been posted for public consultation until 31 December 2018 (http://www.who.int/malaria/publications/atoz/non-inferiority-protocol/en/). Non-inferiority studies on four second-in-class mosquito nets treated with a pyrethroid-PBO nets are planned for 2019. These studies are designed to allow assessment of whether non-inferiority studies generate the desired evidence-base to support an extension of policy to second-in-class products. Once available, data will be assessed by a WHO Evidence Review Group, and the findings will be presented to the Malaria Policy Advisory Group.

Meanwhile, WHO would like to alert all manufacturers of vector control tools to this development. Manufacturers of pyrethroid-PBO nets that are not currently prequalified are encouraged to include Olyset®Plus as an active comparator in their experimental hut studies, and to power the studies as outlined in the WHO study protocol for non-inferiority studies. This is to avoid manufacturers being required to re-run experimental hut studies, if/when non-inferiority studies become a standard WHO requirement.

COMMENTS

Interested parties may, by 31 December 2018, provide their comments on this Notice of Intent and/or the non-inferiority study protocol in writing to the WHO Global Malaria Programme, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland. Comments can also be sent by email to: vc-noninferiority@who.int.

References

