

A successful large-scale deployment of piperonyl butoxide long-lasting insecticidal nets (PBO LLINs) to prevent malaria in regions with high resistance is a matter of saving lives. Specifically designed to protect against pyrethroid-resistant mosquitoes, the nets continue to be a simple and yet effective tool to do so. PBO LLINs already hold a cornerstone position in the young history of the *High Burden High Impact* strategy. However, not all PBO nets are the same, as they vary in the amount of PBO contained and in their formulation. Assessing the long-term efficacy of the various products in real-life conditions of use is required if we are to reap the full benefits of this new technology and accelerate progress to end malaria as an endemic disease.

Long-lasting protection is a cost-effective investment

How PBO works

Piperonyl butoxide (PBO) is an organic compound that acts as a synergist to restore the potency of insecticides, and tackles insecticide resistance developed by *Anopheles* mosquitoes⁵. PBO does not have insecticidal activity of its own; it works by blocking certain enzymes within the mosquito that allows them to detoxify the effect of an insecticide. When an insecticide is used in combination with PBO, the pyrethroid (insecticide) on the LLINs can still have a toxic effect on the mosquito even if it has developed a resistance to the insecticide.

Despite ongoing efforts to tackle the deadly disease, malaria claimed more than 400,000 lives worldwide in 2019¹. It is widely known that malaria *can* be prevented – the most effective way of prevention is the use of LLINs which has proven to be associated with a sharp decrease in disease incidence². The increased access to these nets is a major factor behind the 60% reduction in malaria deaths since 2000 and has saved approximately 6.2

million lives since 2001^{3,4}. However, fast spreading resistance to pyrethroids has required consistent innovation and led to the initial development of PBO nets by Vestergaard. PBO LLINs are being prioritised in areas with insecticide resistance and their large-scale deployment is underway as part of the *High Burden High Impact* approach endorsed by the World Health Organization and the RBM Partnership to End Malaria^{6,7}.

As the deployment of PBO nets is expanding, it is crucial that their performance in real-life conditions is closely monitored. PBO concentration varies on different nets, and there are currently no long-term field studies confirming the efficacy of low amount PBO nets. While nets with a lower concentration of PBO might come at a lower purchase cost, there is a risk that this initial cost advantage is offset through shorter efficacy and therewith shorter replacement cycles. With financial resources being constantly under strain - even more so with the COVID-19 pandemic impeding malaria programs and threatening to redirect funding away - investing in long-term efficacy is not only the right thing to do from a human perspective, but also from a resource-management one.

Why long-term performance monitoring is required for PBO LLINs

Experimental hut studies test LLINs using 20 standard washes as a proxy for 3-year use. However, unlike for pyrethroid insecticides, washing is not the main factor for PBO loss. Instead, evaporation and daily usage affect PBO concentration significantly more than washing over time. Therefore, there is limitation in projecting the lifespan of PBO nets based on such hut studies. The ability to retain PBO in the formulation despite the various factors of loss is key in ensuring effective protection throughout the lifetime of the net - this was the ambition when PermaNet® 3.0 was developed.

PermaNet® 3.0 retains and continues to release PBO to the end of the expected product life, with a concentration of PBO of 5-10 g/kg at the end of 3 years. This was successfully demonstrated in three different long-term field studies in Ghana, India, and Kenya:

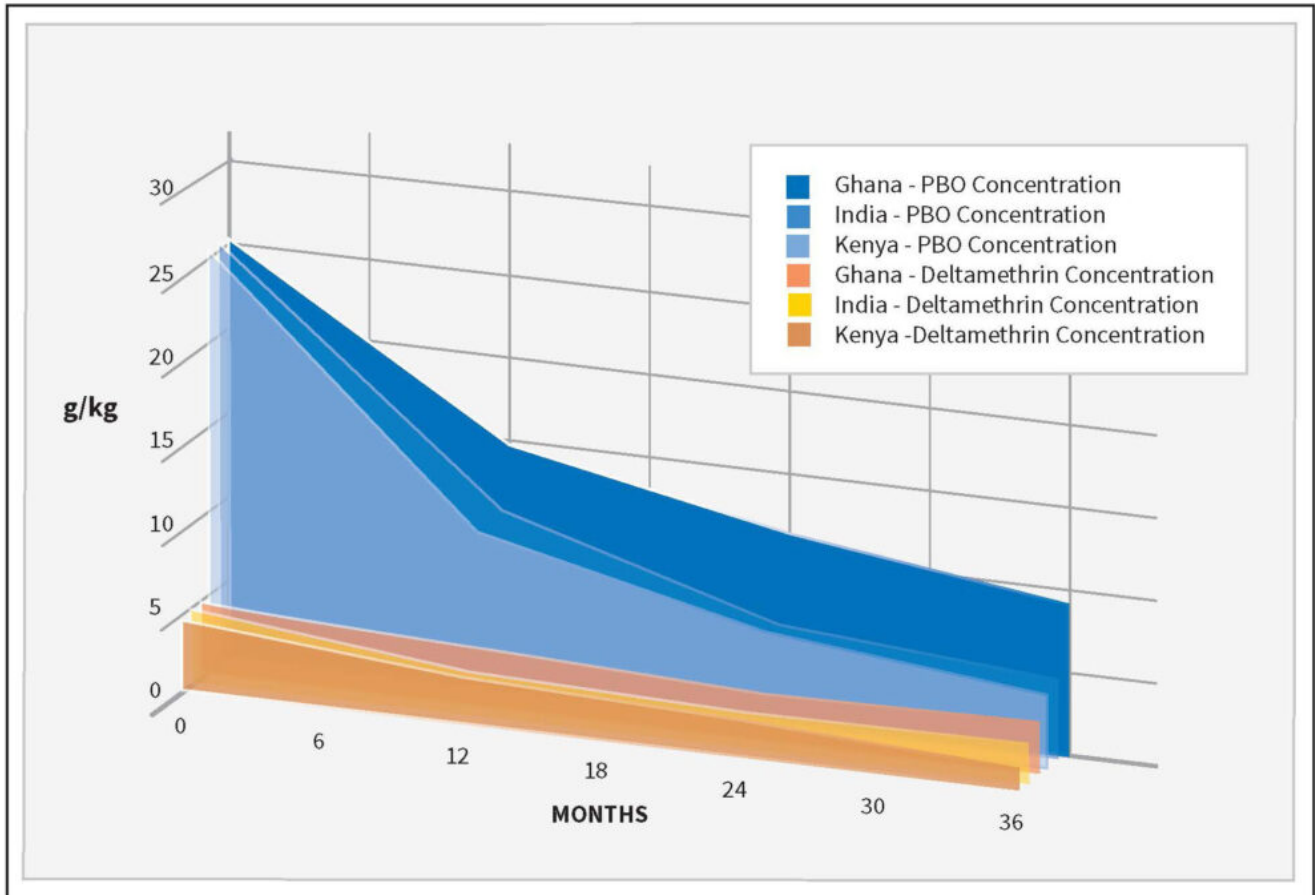


Figure 1. Deltamethrin and PBO concentrations in PermaNet® 3.0 roof at 12, 24, and 36 months in long term studies conducted in Ghana, India, and Kenya.

PBO retention is key - The Vestergaard Blue Roof Technology

PermaNet® 3.0 is the result of a long R&D process. Vestergaard designed PermaNet® 3.0 with a conscious intention to formulate an LLIN that has sustained bioavailability of both PBO and insecticide throughout the product lifetime and also has effective PBO concentration even after 3 years of use: The net has a higher concentration of PBO to begin with and relies on a unique blue roof technology to improve migration and retention control of PBO.

This patented slow-release formulation, which uses the specific characteristics of a blue

pigment, ensures that the migration of PBO and deltamethrin within the polymer is fast enough for replenishment of insecticide that is lost from the surface through use, but also slow enough to ensure presence of PBO for the expected lifetime of the LLIN.

Malaria can and must be stopped

Despite being treatable and preventable, malaria poses a serious mortality and financial burden (at least \$12 billion per year). James Snowden of GiveWell has rightly indicated, “treating malaria is very expensive, preventing malaria is very cheap.” Vestergaard is committed to doing its part to eradicate this deadly disease by developing, manufacturing, and distributing innovative and high-quality LLINs that offer effective protection from malaria for the intended product lifetime.

References

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