Interceptor ® G2

Interceptor® G2 (IG2) is a second-generation LLIN developed by BASF with a combination of chlorfenapyr and alpha-cypermethrin to control insecticide resistant mosquitoes. This novel mode of action in vector control exploits mosquito enzymatic systems against themselves and shows no cross-resistance to other insecticide classes. Unlike pyrethroids, the chlorfenapyr target site of activity is not the insect nervous system. Instead, chlorfenapyr acts, after being metabolized by P450 enzymes at the cellular level, by disrupting respiratory pathways and proton gradients through the uncoupling of oxidative phosphorylation within the mitochondria. The IG2 net has a WHO prequalification listing. Previously the net was evaluated and given an interim recommendation by the 20th WHOPES Working Group.

There have been several experimental hut trials conducted with IG2 nets. Overall, the hut trial results show that IG2 nets demonstrate improved efficacy and wash resistance compared to standard alpha-cypermethrin nets against pyrethroid resistant mosquitoes.

Royal Guard®

Royal Guard® (RG) is an ITN developed by Disease Control Technologies to provide vector control through both the personal protection of traditional mosquito knockdown and mortality, as well as a reduction in fecundity of any mosquitoes that manage to survive exposure to the products pyrethroid active ingredient. The intended benefit of the insect growth regulator, pyriproxyfen, is to reduce the fecundity of adult female mosquitoes and, therefore, yield an overall reduction in the vector population by inhibiting egg laying, larval-pupal transformation and the emergence of functioning young adult mosquitoes. The RG net has a WHO prequalification listing.

Hut trials using RG have been conducted in Tanzania and Benin, demonstrating equal or superior performance in comparison to the reference DuraNet®. RG demonstrated superiority over DuraNet® by significantly reducing the offspring of surviving wild free-flying pyrethroid resistant blood-fed mosquitoes exposed to the net.

One epidemiological trial conducted using Olyset Duo®, containing a pyrethroid and pyriproxyfen, showed additional impact over standard pyrethroid nets against clinical malaria. Separately, a randomised controlled trial conducted in Tanzania using Royal Guard showed no effect on malaria incidence, with an indication of reduced prevalence, although not statistically significant.
Ongoing/Upcoming New Net Evaluations

A cluster-randomized controlled trial including both IG2 and Royal concluded in Benin in March 2022 and has been submitted to the Lancet. Another trial is underway in Uganda comparing Royal Guard and PBO ITNs. Additional evidence is being collected through effectiveness pilot evaluations as part of the New Nets Project. Effectiveness pilots include enhanced passive case detection, cross-sectional surveys, enhanced entomology, and anthropology data collection. Below is a summary of preliminary effectiveness pilot results.

<table>
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<th>Country</th>
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| Burkina Faso*            | Observational – through 24 months | • The IG2 ITNs district saw a 25% greater reduction in malaria incidence, and PBO ITNs a 16% greater reduction, than standard ITNs two cumulative years after distribution.  
• Changes in prevalence were biased by seasonal malaria chemoprevention (SMC) implementation in 2021, and all districts saw reductions in under 5 prevalence regardless of ITN type. Modelled estimates will disentangle the effects of SMC and evaluate the effects of new nets two years post-distribution. |                         |
| Northern Mozambique*     | Observational – through 12 months | • The IG2 ITN district saw a 75% greater reduction in malaria incidence compared to standard ITN district. The RG ITN district saw a 64% greater reduction compared to the standard ITN district.  
• Reductions in prevalence were also largest in the IG2 and RG districts, 42% and 29% respectively, compared to 7% in the standard district.  
• The IG2 district also had the lowest rate of reported ITN use and ownership while demonstrating the largest gains in malaria reduction. | [July 2022](#)           |
| Western Mozambique*      | Observational – through 12 months | • The district where IG2 ITNs were distributed saw a 26% greater reduction in malaria incidence than the standard ITN district. Reductions in the PBO and standard district were similar.  
• Prevalence went down slightly in the standard ITN district (12%) but substantially (by more than 66%) in both the IG2 and PBO districts. |                         |
| Nigeria**                 | Observational – through 12 months | • SMC was implemented in the IG2 and RG ITN districts in 2021. Modelled estimates will evaluate the effect of dual-active ingredient ITNs compared to standard ITNs. |                         |
| Rwanda*                  | Observational – through 24 months | • IG2s conferred an additional 13% reduction in malaria incidence compared to standard ITNs. Standard ITNs with IRS conferred an additional 29% reduction in malaria incidence compared with standard ITNs only.  
• Prevalence was below 5.2 % at all time points in all districts in this very low burden setting, ranging from 1.2% to 0.3% two years post-distribution. |                         |
Alongside the above work, the ESSENTIALS project funded by the Bill and Melinda Gates Foundation, has also undertaken 14 experimental hut studies involving IG2 and/or RG since 2020. These trials, using a combination of new, aged, and washed nets, have taken place in Benin, Burkina Faso, and Tanzania and a final round of trials is planned for Malawi in 2022. In addition to the standard outputs of knockdown, mortality and blood feeding, mosquito longevity, fecundity and ability to re-feed have also been monitored. The results have been shared with Imperial College and have been incorporated into their meta-analyses of dual-active ingredient nets.