



Evidence Base for New Dual-AI Nets

Interceptor® G2

Interceptor® G2 is a second-generation insecticide-treated net (ITN) 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 Interceptor® G2 net has a [WHO prequalification listing](#) and as of March 2023 an official [WHO policy recommendation](#):

- A *strong recommendation* for the deployment of pyrethroid-chlorfenapyr ITNs vs pyrethroid-only nets for prevention of malaria in adults and children in areas with pyrethroid resistance.
- A *conditional recommendation* for the deployment of pyrethroid-chlorfenapyr ITNs instead of pyrethroid-PBO nets to prevent malaria in adults and children in areas with pyrethroid resistance.

There have been several experimental hut trials conducted with Interceptor® G2 nets. Overall, the hut trial results show that Interceptor® G2 nets demonstrate improved efficacy and wash resistance compared to standard alpha-cypermethrin nets against pyrethroid resistant mosquitoes.

[A Chlorfenapyr Mixture Net Interceptor® G2 Shows High Efficacy and Wash Durability against Resistant Mosquitoes in West Africa.](#)

[Efficacy of Interceptor® G2, a new long-lasting insecticidal net against wild pyrethroid-resistant *Anopheles gambiae* s.s. from Côte d'Ivoire: a semi-field trial.](#)

[Which intervention is better for malaria vector control: insecticide mixture long-lasting insecticidal nets or standard pyrethroid nets combined with indoor residual spraying?](#)

[Evaluation of efficacy of Interceptor® G2, a long-lasting insecticide net coated with a mixture of chlorfenapyr and alpha-cypermethrin, against pyrethroid resistant *Anopheles gambiae* s.l. in Burkina Faso.](#)

[Efficacy of interceptor® G2, a long-lasting insecticide mixture net treated with chlorfenapyr and alpha-cypermethrin against *Anopheles funestus*: experimental hut trials in north-eastern Tanzania.](#)

Furthermore, a [randomised controlled trial](#) was conducted in Tanzania showing that after two years, Interceptor® G2 ITNs provided significantly better protection than standard ITNs (44% lower incidence and 55% lower odds of infection compared to standard ITNs). Trial results indicate that Interceptor® G2 nets would be more cost-effective over a 2-year period, in an area with highly pyrethroid-resistant mosquitoes, than standard, pyrethroid-only nets.

A cluster randomised controlled trial in [Benin](#) demonstrated that children in clusters that received Interceptor® G2 nets had a 46% lower incidence of malaria at 24 months; participants of any age had 53% lower odds of malaria infection at 6 months and 40% lower odds at 18 months after ITN distribution and were exposed to a 66% reduction in entomological inoculation rate compared with those living in clusters that received pyrethroid-only nets.

Royal Guard®

Royal Guard® 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 mosquitos.

The Royal Guard® net has a [WHO prequalification listing](#), and as of March 2023 an official [WHO policy recommendation](#):

- A *conditional recommendation* for the deployment of pyrethroid-pyriproxyfen nets instead of pyrethroid-only nets to prevent malaria in adults and children in areas with pyrethroid resistance

Hut trials using Royal Guard® have been conducted in Tanzania and [Benin](#), demonstrating equal or superior performance in comparison to the reference DuraNet®. Royal Guard® 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. A cluster randomised controlled trial in [Benin](#), Royal Guard® net showed a small reduction in malaria incidence in the first year of the study that was attenuated in year 2, and no effect on malaria infection prevalence in either year. However, a 58% reduction in indoor entomological inoculation rate was seen. Lower net usage in the Royal Guard® arm, as well as potential physical and bio-efficacy durability issues, may have contributed to the lack of effect.

New Nets Project Evaluations

Additional evidence of the impact of dual-active ingredient nets was 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. Results from the effectiveness pilots have shown that while mass ITN distributions are associated with decreases in malaria transmission regardless of net type:

- Distribution of Interceptor® G2, PBO, or Royal Guard® ITNs are more effective at controlling malaria than distribution of standard, pyrethroid-only ITNs (through 1 year).
- This improved control is more sustained with Interceptor® G2, leading to greater numbers of malaria cases averted.

The average cost per additional case of malaria averted using an Interceptor® G2 net as compared to a standard net in the pilot evaluations using end of project pricing is \$0.66 – \$3.56.

Overleaf, is a summary of effectiveness pilot results by country.

Country	Type of study	Main findings on differential ITN performance	Reference
Burkina Faso	Observational – through 36 months	<ul style="list-style-type: none"> The Interceptor® G2 district saw a 19% greater reduction in malaria incidence, and PBO ITNs a 25% greater reduction than standard ITNs three cumulative years after distribution. An estimated 3,350 (1,000 – 6,100) cases of malaria were averted per 10,000 residents by distributing Interceptor® G2 instead of standard ITNs in Banfora District, and an estimated 4,350 (2,500 – 6,500) cases were averted per 10,000 residents by distributing PBO instead of standard ITNs Orodara District. In the Interceptor® G2 pilot evaluation district of Banfora, 145,343 malaria cases were averted over 3 years; in Orodara District, the PBO pilot evaluation district, 124,606 malaria cases were averted. 	New Nets Project Final Report (2023)
Northern Mozambique	Observational – through 24 months	<ul style="list-style-type: none"> The Interceptor® G2 district saw a 35% greater reduction in malaria incidence compared to standard ITN district. The Royal Guard® district saw a 28.5% greater reduction compared to the standard ITN district. An estimated 3,200 (1,150 – 5,900) cases of malaria were averted per 10,000 residents by distributing Interceptor® G2 instead of standard ITNs in Cuamba District. An estimated 3,000 (1,300 – 5,050) cases were averted per 10,000 residents by distributing Royal Guard® nets instead of standard ITNs in Mandimba District. In the Interceptor® G2 pilot evaluation district (Cuamba), 85,055 malaria cases were averted over 2 years; in the Royal Guard® pilot evaluation district (Mandimba), 59,369 malaria cases were averted. 	
Western Mozambique	Observational – through 24 months	<ul style="list-style-type: none"> The district where Interceptor® G2 ITNs were distributed saw a 35% greater reduction in malaria incidence than the standard ITN district. Reductions in the PBO and standard district were similar. An estimated 6,950 (3,150 – 12,400) cases of malaria per 10,000 residents were averted by distributing Interceptor® G2 instead of standard ITNs in Guro District. In the Interceptor® G2 pilot evaluation district (Guro), 76,971 malaria cases were averted over 2 years. 	
Nigeria ^A	Observational – through 24 months	<ul style="list-style-type: none"> Incidence data analysis in Nigeria was confounded by migration, suboptimal reporting, inconsistent data quality, and inconsistent use of the public health sector. Largest cumulative decreases in prevalence from baseline to Year 2 were observed in the Interceptor® G2 (62%) and Royal Guard® districts (41%), but these decreases reflect the combined impact of the new net distribution and newly implemented SMC campaigns with four rounds of MDA. 	

Country	Type of study	Main findings on differential ITN performance	Reference
Rwanda*	Observational – through 24 months	<ul style="list-style-type: none"> • Interceptor® G2s conferred an additional 58% reduction in malaria incidence compared to standard ITNs. Standard ITNs with IRS conferred an additional 71% reduction in malaria incidence compared with standard ITNs only. • An estimated 2,100 (1,000 – 3,650) cases of malaria were averted per 10,000 residents by distributing Interceptor® G2 instead of standard ITNs in Karongi District, and an estimated 5,700 (3,500 – 8,800) cases per 10,000 residents were averted by utilizing IRS in addition to standard ITNs in Ruhango District. • In the Interceptor® G2 pilot evaluation district (Karongi), 85,364 malaria cases were averted over 2 years; in the IRS plus standard ITN pilot evaluation district (Ruhango), 223,377 malaria cases were averted. • The standard ITN plus IRS district was the only New Nets Project pilot district to record zero prevalence at any point during the project (zero positive RDTs out of 289 tested in year 2). 	New Nets Project Final Report, 2023

*Funding for Nigeria pilot split between New Nets Project and Global Fund

Modelling Estimates

Over the course of the New Nets Project (NNP), when combining NNP with Global Fund's Net Transition Initiative and President's Malaria Initiative procurements, Interceptor®G2 nets averted an estimated 13 million malaria cases (and approximately 24,600 deaths). Over the next five years it is estimated that Interceptor®G2 nets will avert an additional 38 million malaria cases (and approximately 73,000 deaths) compared with standard pyrethroid nets.

Additional Studies

Alongside the above work, the [ESSENTIALS](#) project funded by the Bill and Melinda Gates Foundation, have undertaken experimental hut studies involving Interceptor® G2 and/or Royal Guard®. These trials, using a combination of new, aged, and washed nets, have taken place in Benin, Burkina Faso, Tanzania, and Malawi. 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.

In addition, a cluster-randomized controlled trial is underway in [Uganda](#) comparing Royal Guard® and pyrethroid-piperonyl butoxide (PBO) ITNs.