28 February 2020

Evidence Base for New Dual-AI Nets

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.

Published Experimental Hut Trials with IG2 nets:
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.

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® 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.

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. Neither of those trials are currently published. However, there is one epidemiological trial that has been conducted using an ITN containing a pyrethroid and pyriproxyfen. Although done with the Olyset Duo net, it showed in principle that a net containing pyriproxyfen could have additional impact over standard pyrethroid nets against clinical malaria.

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Ongoing/Upcoming New Net Evaluations

A cluster-randomized control trail including both IG2 and Royal Guard nets started in Tanzania in early 2019, and a cluster-randomized control trial as part of the New Nets Project in Benin will start in 2020. Additional evidence is being collected through effectiveness pilot evaluations as part of NNP. Below is a summary of current RCT and effectiveness pilot evidence generation and when results will be available.

	2018	2019	2020	2021	2022
RCT in Tanzania^	Nets distributed Dec			mid yr RCT results comparing IG2 to standard, RG to standard, and PBO to standard	
RCT in Benin			Nets distributed March		mid yr RCT results comparing IG2 to standard, RG to standard, and PBO to standard
Burkina Faso effectiveness pilot*		Nets distributed Oct	Q4 results comparing IG2 to standard and PBO to standard yr 1	Q4 results comparing IG2 to standard and PBO to standard yr 2	Q4 results comparing IG2 to standard and PBO to standard yr 3
Rwanda effectiveness pilot*			Nets distributed March	Q1 results comparing IG2 to standard and IG2 to standard plus IRS yr1	Q1 results comparing IG2 to standard and IG2 to standard plus IRS yr2
Mali pilot (operational evidence with evaluation of routine health center data)			Nets distributed June	Q1 results comparing IG2 to standard yr 1	Q1 results comparing IG2 to standard yr 2
Mozambique effectiveness pilots*			Nets distributed June/July Manica (West)	Q2 results comparing IG2 vs standard vs PBO yr 1	Q2 results comparing IG2 vs standard vs PBO yr 2
			Nets distributed June/July Niassa (North)	Q2 results comparing IG2 vs standard vs Royal Guard yr 1	Q2 results comparing IG2 vs standard vs Royal Guard yr 2
Nigeria effectiveness pilot**			Nets distributed Oct	Q4 results comparing IG2 vs PBO; and Royal Guard vs standard yr1	Q4 results comparing IG2 vs PBO; and Royal Guard vs standard yr2

^Funded by MRC, Wellcome and BMGF
**Effectiveness pilot includes enhanced passive case detection, cross-sectional surveys, enhanced entomology, anthropology*
***Funding for Nigeria pilot split between NNP and Global Fund*

Alongside the above work, additional hut trials in Tanzania, Burkina Faso, and Mozambique using IG2 and Royal Guard will be conducted as part of the ESSENTIALS project funded by BMGF. Those trials began in late 2019 and will initially test new nets but will go on to test artificially- or field-aged nets. Lastly, there is a plan by LSTM to conduct a hut trial using IG2 in Malawi beginning in March 2020 as part of the PIIVeC project.