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Novel insecticides are vital to malaria elimination, but so are the ways we use them, asserts Director of Market Development & Access, Public Health Melinda Hadi.

Vector resistance, an evolutionary phenomenon, will eventually emerge to any widely and repeatedly used insecticide. Mosquito resistance to pyrethroid is widespread and a significant hurdle in malaria elimination efforts.

According to the [WHO's World Malaria Report 2023](#), global malaria cases reached 249 million in 2022 - well above the estimated number of cases before the COVID-19 pandemic and an increase of five million over 2021.

New long-lasting insecticidal nets (LLINs) combining pyrethroid and chlorfenapyr, such as Interceptor G2 and PermaNet® Dual, have shown enhanced efficacy in pyrethroid-resistant areas. While pyrethroids disrupt the mosquito's nervous system, chlorfenapyr, a new class of insecticide, impairs the insect's energy production.

"Having two insecticides in one product hopefully somewhat mitigates that resistance, but it's not a true, comprehensive solution because of the existing high levels of resistance to pyrethroids including deltamethrin [the pyrethroid in PermaNet® Dual]," says Hadi.

And how long until mosquitoes develop resistance to chlorfenapyr as well?

"No one knows for sure," says Hadi. "But repeated use will likely yield resistance, just as with pyrethroids.

"To preserve the mosquito killing power of chlorfenapyr, we need something else; another tool or a different mode of action."

## Implementing insecticide resistance management strategies

Insecticide Resistance Management (IRM) aims to preserve or prolong the susceptibility of mosquitoes to insecticides, in order to maintain the effectiveness of insecticide-based vector control.

Strategies include rotating between different insecticides with varied modes of action, such as deploying one insecticide at a time, deploying different insecticides in neighbouring geographical areas or adjacent homes, or bundling two insecticides in one product.

Melinda Hadi explains, “The probability of a mosquito developing resistance is reduced if it’s not consistently exposed to a single insecticide. The principle is that A would protect B and vice versa.”

“However, this approach requires multiple effective insecticides. The severe existing resistance to pyrethroids means we risk missing the chance to rotate chlorfenapyr unless a net treated with another mode of action becomes available. And if we lose the value of protection that comes from those insecticides, the efficacy of tools like bed nets may be compromised.”

Another option is indoor residual spraying (IRS), the application of a residual insecticide to internal walls and ceilings of housing structures. [The World Health Organization \(WHO\) endorses IRS](#) as “a core vector control intervention that can rapidly reduce malaria transmission”.

But while IRS is effective, it’s also expensive and laborious to implement. Bed nets are much more cost-effective and designed to last three years.

## **An innovation pipeline**

Vestergaard is currently developing the next generation of LLINs using non-pyrethroid insecticides to offer a robust IRM strategy that can be bundled or rotated with chlorfenapyr.

“We’re making a push in our innovation pipeline because we’re in the game now of wanting to protect chlorfenapyr. We’re working on a portfolio of LLINs with new ingredients,” says Hadi.

However, challenges remain. Delivering these new tools could take years. Will chlorfenapyr still be as effective by then? And will next-generation LLINs be implemented at scale to match the number of PermaNet® Dual nets in communities? Will these new nets be affordable enough for that even to be possible?

“We’re scaling up PermaNet® Dual substantially, so if we want to implement a rotation strategy, we’d have to be prepared to launch several million of these new nets,” Hadi notes.

“Given the higher costs of these novel chemistries, it’s very likely this net is going to be more expensive than PermaNet® Dual. So the question is, who will be willing to purchase them?”

## **What do we do in the meantime?**

“We shouldn’t be pessimistic,” says Hadi.

She says understanding and monitoring are key, using tools like IR Mapper, a collaboration between Vestergaard and the Kenya Medical Research Institute’s Centre for Global Health Research, which aggregates peer-reviewed data to create user-friendly visualisations of the spread and intensity of resistance.

Vestergaard is also working with partners to investigate how best to test for resistance to

chlorfenapyr and how to generate and interpret the data.

“We must monitor the susceptibility of mosquitoes to chlorfenapyr,” Hadi says.

She adds that Vestergaard has a responsibility to support National Malaria Control Programmes in tracking chlorfenapyr susceptibility in areas where PermaNet® Dual has been deployed.

“We have a duty to invest in research to better understand the mechanisms involved in resistance development.”

But monitoring can only get us so far, Hadi admits.

“It’s a bit of a conundrum when you can’t actually make any decisions with the data that you collect, because we can’t actually offer a LLIN rotation strategy yet.”

“We still need our next product.”