# KILLING BY

A next-generation mosquito net for insecticide-resistant mosquitoes is being developed on our doorstep.

Researcher: Dr Mthokozisi Sibanda, University of Pretoria Institute for Sustainable Malaria Control

alaria is a devastating parasitic disease that affects almost 250 million people worldwide, with 90% of all malaria-related deaths occurring in sub-Saharan Africa.

The World Health Organization (WHO) recommends the use of long-lasting insecticidal nets (LLIN) as the main technique to suppress mosquito populations, thereby reducing malaria transmission. But, with mosquitoes becoming resistant to the pyrethroid insecticide used in LLINs, malaria cases have been increasing.

Clearly, the net needs to be more effective.

#### A challenge on two fronts

Dr Mthokozisi Sibanda, an extraordinary senior lecturer at the University of Pretoria Institute for Sustainable Malaria Control, explains the challenge.

"There are two main types of insecticide-resistance mechanisms that need to be tackled: enzymemediated resistance and knockdown resistance," he says. "With enzyme-mediated resistance, the mosquito secrets enzymes to break down a pyrethroid insecticide. With knockdown resistance, the walls of the target site are thickened, thus preventing or delaying the penetration of the insecticide." Combatting both types of resistance would be a lifesaver.

Biotechnology company African Applied Chemical (AAC) has developed and prototyped two nextgeneration LLIN products – Vikela<sup>™</sup> and Vikela<sup>™</sup> 2.0 – that hold exciting promise. Vikela<sup>™</sup> incorporates a pyrethroid and piperonyl butoxide (PBO), an oily liquid that neutralises enzymes and prevents them from breaking down the pyrethroid insecticide. PBO is completely safe for humans. For Vikela<sup>™</sup> 2.0, the LLIN incorporates a pyrethroid insecticide, PBO and nootkatone insecticide for additional effectiveness.

"Nootkatone is a natural and safe insecticide that is very effective against pyrethroid-resistant mosquitoes," Dr Sibanda says.

#### **Innovative fibre**

The most important criterion required by the WHO to register an LLIN is that it should be able to kill at least 80% of the mosquito test population after 20 washes.

"The biggest technical challenge is ensuring that the insecticide formulation incorporated into an LLIN can resist being washed off," Dr Sibanda says.

The proprietary Bi-Ko<sup>™</sup> slow-release technology has been used to manufacture the two Vikela<sup>™</sup> products. The technology is a textile fibre specially engineered to store and slowly release liquid formulations. "When washed, only the active that has been released from the internal reservoir of the fibre is washed off," he explains. "The rest of the liquid active is protected within the fibre and will be released continually, ensuring continued effectiveness even after repeated washing."

To solve the problem of both forms of insecticide resistance, AAC has devised a process of dissolving the solid insecticide into the PBO. This liquid insecticidal formulation is then released using the Bi-Ko<sup>™</sup> technology. The PBO achieves a dual purpose: it acts to deliver the insecticide in liquid form – greatly increasing effectiveness, as mosquitoes ingest more of the insecticide than when it is in solid form, thus mitigating knockdown resistance – and prevents enzymes from sequestering the pyrethroid insecticide.

"This is a unique design feature and makes our product effective against insecticide-resistant mosquitoes," Dr Sibanda says.

### Next steps

LLIN products have to be registered with the WHO before they can be sold. Registration is only possible after the product has gone through Phase I (laboratory studies), Phase II (small-scale field studies) and Phase III (large-scale field studies).

AAC has successfully completed Phase I on both mosquito net prototypes and is in the process of completing Phase II. On successful completion of Phase II, the company will be eligible for interim registration of the products.

The main buyer of registered mosquito nets is the Global Fund, which distributes them free of charge in malaria-endemic areas.

## How is this research transdisciplinary?

The Bi-Ko<sup>™</sup> slow-release technology was the result of collaboration among UP's Department of Chemical Engineering, the School of Health Systems and Public Health under the University of Pretoria Institute for Sustainable Malaria Control and the Institute for Polymer Research in Germany.



Vikela<sup>™</sup> fibre production