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**Boosting the battle
against malaria**



Bringing forward new tools to combat malaria

Although great progress has been made in the fight against malaria, it continues to be responsible for hundreds of thousands of deaths every year – and recently, progress appears to have stalled. Regaining momentum requires persistence, partnership and innovation. The New Nets Project is a groundbreaking initiative to push forward promising new tools to eradicate the disease. BASF's innovative new Interceptor® G2 mosquito net is part of the project.

By Janet Anderson

Every two minutes, a child dies of malaria. Worldwide, the disease killed an estimated 435,000 people in 2017 – the latest year for which figures from the World Health Organization (WHO) are available. Nowhere is the problem more severe than in Africa, where a disproportionate number of these deaths occur, but it affects many other regions, too. According to the WHO, half the world’s population is at risk of contracting malaria. With climate change, the number of regions threatened by malaria is growing.

Over the past two decades, through a concerted global effort by public health bodies, NGOs and many other organizations, huge progress in fighting the disease has been made and cases of malaria had been falling year on year. A range of tools has contributed to this success, in particular impregnated mosquito nets. However, according to the latest World Malaria Report, in 2017 the number of cases increased from 217 million to 219 million. In Africa, there were an estimated 3.5 million more malaria cases in 2017 compared with the previous year. The increase can partly be attributed to population growth. However, another important reason is that some of the key tools we have used in the fight against malaria are becoming less effective.

Vector control and the rise of resistance

Tackling malaria requires a toolbox that includes both drugs to treat it and methods for controlling the mosquitoes – the vectors – that transmit it. Among these, long-lasting insecticide-treated mosquito nets (LLINs) have played a vital role. They protect the individual and, crucially, the community by killing mosquitoes and stopping them from spreading the disease further. According to the WHO, vector control is one of the few methods that can reduce malaria transmission from a very high level to close to zero.

It is estimated that since 2000, thanks to various interventions some 663 million cases of malaria have been averted, and that 69 percent of this total is due to nets. Achim Reddig, BASF’s global business manager for public health, has seen for himself the impact nets can have. He worked for ten years in South America, where he was responsible for the launch of BASF’s first-generation Interceptor bed net. “In some villages the incidence of malaria was nearly 100 percent. Children were sick and could not attend school, so literacy was very low. Bed nets not only reduced the incidence of malaria,

they also improved lives by enabling people to go to work and children to attend school. It looks simple, but the mosquito net is a very effective tool,” he says.

Over the past two decades, almost two billion nets have been distributed to people in regions across the world where the malaria burden is high. However, the success of this intervention has given rise to a new problem. Until recently there was only one class of insecticide recommended by the WHO for LLINs – pyrethroids. Heavy reliance on this insecticide for both public health and pest control purposes has led to mosquito populations becoming resistant. This is rendering conventional LLINs less effective over time. “The same technology has been used for decades,” says Reddig. “Resistance has now been reported in 68 countries. If the fight against malaria is to regain momentum, there is an urgent need to develop and test new tools.”

Fresh momentum in the fight

The New Nets Project aims to accelerate this process by building evidence around a new generation of nets treated with different types of insecticides. The project is being co-financed by the Global Fund and Unitaid, who are each investing US\$33 million, along with other financial partners including ▶



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Achim Reddig
Director of Global Public Health at BASF

Proven to prevent malaria

According to the WHO, mosquito control is one of the best ways to combat malaria. Since 2000, almost 2 billion long lasting insecticide-treated mosquito nets have been distributed, preventing more than 450 million cases of malaria.

Young families receive BASF mosquito nets in the northern border regions of Namibia



Kate Kolaczinski

Manager of the Global Fund’s involvement in the New Nets Project

“Progress on fighting malaria is stalling and insecticide resistance is likely one of the reasons for this. Finding nets that work even where mosquitoes are resistant to the currently used insecticides is a priority for us.”

the U.S. President’s Malaria Initiative and the Bill & Melinda Gates Foundation. A consortium of experts led by the Innovative Vector Control Consortium (IVCC) has been appointed to implement it. The group includes PATH, Population Services International (PSI) the Alliance for Malaria Prevention, the London School of Hygiene and Tropical Medicine, with support from Imperial College London, Liverpool School of Tropical Medicine, and Tulane University. Initiated in 2018, the project will run until 2022.

BASF’s Interceptor® G2 mosquito net is one of the nets involved. Unlike other bed nets, Interceptor® G2 is treated with two active ingredients – the current standard pyrethroid, and a new class of insecticide, chlorfenapyr. In contrast to pyrethroids, which work by impeding nerve transmission, chlorfenapyr, which belongs to the pyrrole class of chemistry, disables an insect’s ability to produce energy. Chlorfenapyr has been

used in agriculture and urban pest control worldwide since 1995 and has been repurposed by BASF for public health use. As its mode of action is so different from pyrethroids, it is effective on mosquitoes that are resistant. Although it works more slowly, this has an additional beneficial effect, as it allows the mosquitoes to continue reproducing for a short while, passing on susceptible genes to the next generation. The effect of this is to slow down the growth of resistance in the overall mosquito population.

BASF has invested eleven years developing Interceptor® G2, working closely with leading experts in the field including the IVCC and the London School of Hygiene and Tropical Medicine. In 2017, the WHO awarded the new nets an interim recommendation following extensive testing to prove that they are effective against resistant mosquitoes and cause no undue hazard to people.

However, before the WHO can issue normative guidance to countries to buy the new nets, it requires that epidemiology trials be undertaken. The Interceptor® G2 LLIN has a higher price than pyrethroid-only nets, reflecting the fact that it has two active ingredients rather than just one. Before health ministries can invest public monies, it must be demonstrated that the net brings additional public health value by reducing more cases of malaria than conventional nets.

Epidemiological trials under the usual WHO procedures are complex, costly and can take many years. In the meantime, resistance in the mosquito population is growing. There is therefore a sense of urgency in the malaria fighting community. That is why the New Nets consortium has come together to drive forward testing and piloting.

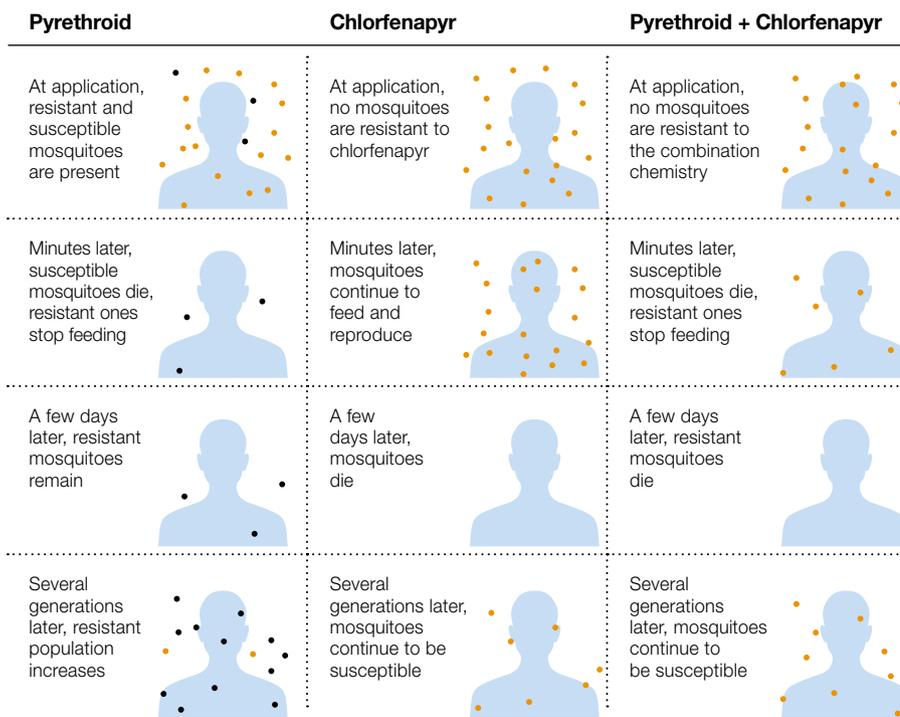
Distribution and testing

“Interceptor® G2 is the only net with a new active ingredient to combat adult mosquitoes. The New Nets Project will get it out to those regions where it is most needed, where resistance is growing. At the same time, it will help push through the last mile of the WHO process,” says Reddig. “The objective is to make much-needed innovation available to the malaria community faster.”

Last year, 40,000 Interceptor® G2 nets were distributed to villages in Tanzania, East Africa, for randomized control trials funded by the UK government and the Wellcome Trust. Under the New Nets Project, a second trial will begin in Benin, West Africa, next year. The data gathered will be compared with data from conventional nets. The hopes are this will show that the new tools can

Interceptor G2®: Dual ingredients to combat resistance

Pyrethroids control susceptible mosquitoes fast, but resistant mosquitoes survive and reproduce, eventually becoming more numerous. Interceptor G2® bed nets contain both a pyrethroid and chlorfenapyr, a new insecticide for public health. Chlorfenapyr works more slowly, allowing susceptible mosquitoes to reproduce, passing on their genes and maintaining the level of susceptibility in the population.



• Susceptible mosquitoes



• Resistant mosquitoes

help with the fight against malaria in regions where resistance is growing.

In parallel, a further two million Interceptor® G2 nets are being delivered to Burkina Faso for an operational pilot distribution. With a population of around 19 million, Burkina Faso accounted for 6% of malaria deaths worldwide in 2017. Malaria is responsible for over 60 percent of hospitalizations and over 30 percent of deaths in the country. Small children under five are particularly vulnerable.

This first national campaign will be followed by campaigns in Rwanda, Mali and Mozambique. The pilot distribution will provide an assessment of impact in a real-life setting. As part of the national malaria control campaign, the nets are to be distributed to whole regions over two weeks. Data will be gathered from health facilities and entomological surveys, while net use rates are monitored, and the prevalence of the disease is measured through rapid diagnostic tests.

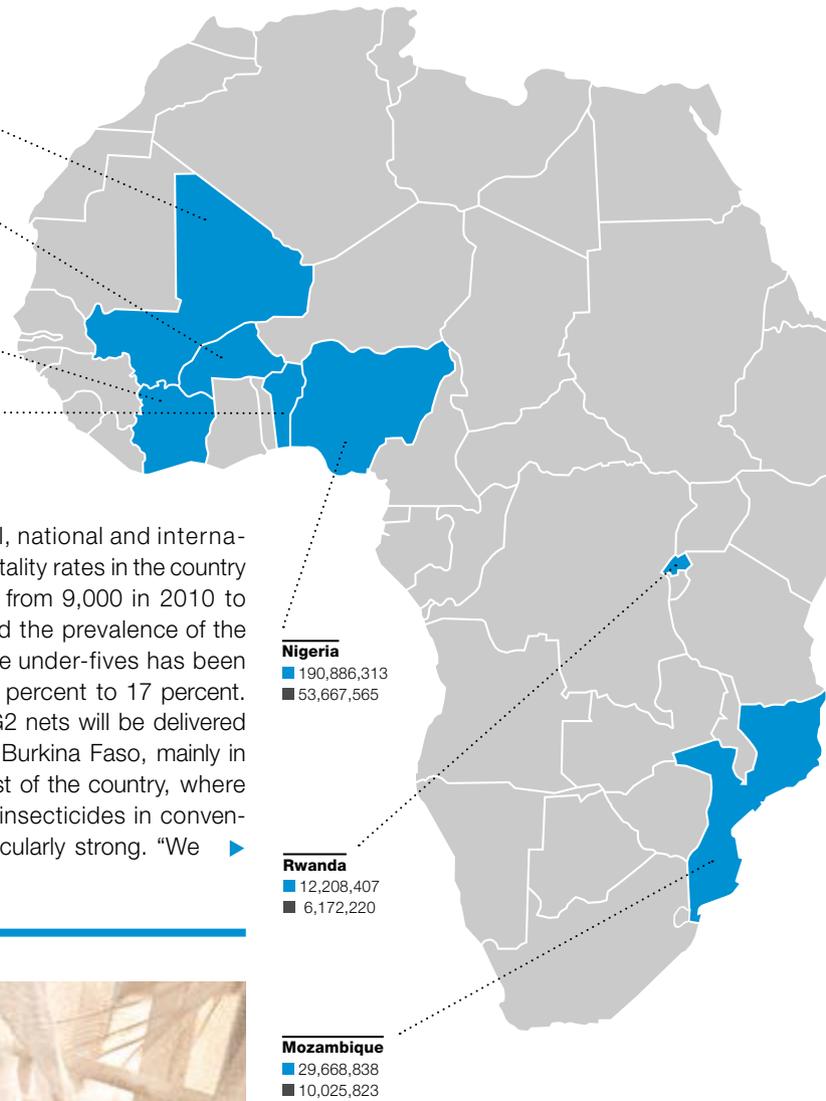
Dr. Yacouba Savadogo has worked for many years fighting malaria in Burkina Faso and is national coordinator for the Programme National de Lutte contre le Paludisme (PNLP). He has seen the progress that can be made through concerted

As part of the New Nets Project, the efficacy and cost-effectiveness of Interceptor® G2 mosquito nets will be trialed in at least seven African countries.

Figures for 2017

| | |
|----------------------|--------------|
| Mali | ■ 18,541,977 |
| ■ 7,160,192 | |
| Burkina Faso | ■ 19,193,381 |
| ■ 7,907,562 | |
| Côte d'Ivoire | ■ 24,294,747 |
| ■ 3,373,486 | |
| Benin | ■ 11,175,693 |
| ■ 4,111,699 | |

efforts by regional, national and international bodies. Mortality rates in the country have been halved from 9,000 in 2010 to 4,294 in 2018 and the prevalence of the parasite among the under-fives has been reduced from 65 percent to 17 percent. The Interceptor® G2 nets will be delivered to ten districts of Burkina Faso, mainly in the south and west of the country, where resistance to the insecticides in conventional nets is particularly strong. "We ▶



■ Population at risk
 ■ Estimated malaria cases
 Source: WHO World Malaria Report 2018

6%

Burkina Faso
 accounted for 6% of malaria deaths worldwide in 2017.

Pregnant women and children under five are particularly vulnerable to malaria



ZERO by 40

In 2018, the Bill & Melinda Gates Foundation, IVCC, and leading agriculture companies, including BASF, established ZERO by 40, an initiative to share ideas, develop new mosquito-control tools and help eradicate malaria by 2040.

Research commissioned by ZERO by 40 estimates that 841 million cases of malaria could be prevented between now and 2040. Beyond that, the benefits would be seen in children's education with fewer school days missed, and in the wider economy as farmers are able to tend to the harvest and fewer people miss work. Together this could lift up to 84 million people in agricultural households out of poverty.

will be monitoring the results and looking to see if there is acceptance of the nets," says Dr. Savadogo, who has coordinated many campaigns in the country.

Targeting tools and funding, supporting innovation

"Progress on fighting malaria is stalling and insecticide resistance is likely one of the reasons for this. Finding nets that work even where mosquitoes are resistant to the currently used insecticides is a priority for us," says Kate Kolaczinski, Manager of the Global Fund's involvement in the New Nets Project. "The project will contribute to the evidence base around some of these new nets – helping us understand what role they may have in improving malaria control. Doing pilots in a range of countries will give national governments a clearer picture of how these nets may perform in their setting; armed with that information, they will be better able to plan and push for scale-up once a WHO policy is in place."

Accelerating early adoption and supporting onward scale-up of the new nets are key to the project. Thinking ahead about the scale-up if the nets do have added value is crucial. "We need to intensify efforts in the highest burden countries and learn how best to target new malaria tools – that means understanding which tools to use where and which will yield the most value for money and impact," says Alexandra Cameron, Senior Technical Manager, Unitaid. "We are priming the market so that if and when the new nets are recommended by the WHO, we are that much further ahead – the countries will be ready with their policies and procurement practices so there will be less time lag in adoption."



Dr. Nick Hamon
CEO of the Innovative Vector
Control Consortium (IVCC)

"Not many others have the know-how to develop new chemicals from scratch. With insecticide resistance on the rise, BASF's efforts to innovate should be supported and commended. We are doing pioneering work together."



Dr. Yacouba Savadogo
National coordinator,
Programme National de Lutte
contre le Paludisme (PNLP),
Burkina Faso

"We have to combine many strategies and put our forces together to fight malaria across whole regions, because mosquitoes do not respect borders."



Interceptor® G2 mosquito
nets are manufactured to
ISO 9001:2015 standards



Interceptor® G2 mosquito
nets ready to be shipped
to Burkina Faso



Testing in BASF's laboratories in Germany

Photos: Xiao Nan/BASF, (top) Yan Andres/BASF



Alexandra Cameron
Senior Technical Manager,
Unitaid

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The production volumes procured for the pilots will also help the project to negotiate significant price reductions. “These reductions are needed to make the new nets a sustainable choice for countries looking for the best value for money in controlling malaria,” says Dr. Nick Hamon, CEO of IVCC.

The Interceptor® G2 net is not intended to replace conventional nets, but introducing it in a targeted way will help contain the growth of resistance and keep the cheaper conventional nets effective for longer. “Our net is complementary to the universe of tools to keep people protected. In the long term, it will help keep the overall cost down of the fight against malaria,” says Reddig. “If we allow the cheaper pyrethroid-only nets to become ineffective due to resistance, then we will need to replace them entirely with a new tool that might be twice as expensive.”

By guaranteeing price levels and volumes, the New Nets Project also makes investment in future research more sustainable. “We are very pleased to be able to contribute toward this next phase of the fight against malaria,” says Reddig. “The generous support of the Global Fund and Unitaid and the expertise provided by IVCC and other partners means we can get the nets into the countries in the quantities required to save lives, but it also enables us to fuel the next cycle of innovation.”

Getting back on track toward elimination

In 2018, BASF joined IVCC, the Bill & Melinda Gates Foundation, and other leaders in the agricultural industry in ZERO by 40, an unprecedented initiative to share ideas, collaborate in developing new mosquito control tools, and ultimately to help eradicate malaria by 2040.

“Chemical companies’ efforts in this area can be transformational,” says Hamon. “Not many others have the know-how to discover, develop and deliver new public health insecticides and formulations from scratch. With insecticide resistance a threat in malaria endemic countries, BASF’s efforts to innovate and bring to market novel vector control tools and solutions should be supported and commended. We are doing pioneering work together.”

In spite of the recent global figures, Dr. Savadogo is optimistic about the chances of eradicating malaria entirely. “With combined and continuous efforts, we can do it,” he says. “But we have to combine many strategies and put our forces together to fight malaria across whole regions, because mosquitoes do not respect borders.”



For further information on BASF's Public Health business and range of solutions, please visit:
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September 2019

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