

## **Will the sides of the net be depleted before the roof of the net?**

PermaNet® 3.0 has been designed to last for a minimum of 3 years in the field, when used as recommended.

## **Have you done any research into how the conical form of PermaNet® 3.0 will be constructed?**

Yes, studies have been conducted in the laboratory using a sticky net to investigate mosquito arrival patterns at a conical net and the results from the research will be used for the design of the conical form of PermaNet® 3.0.

## **Why not use the synergist with Deltamethrin incorporated in PE on the sides of the net?**

The sides of the nets are based on coating technology and the roof is based on incorporation technology. For technical reasons, the synergist cannot be coated along with the insecticide. Consumer surveys continue to indicate preference for a softer net. We therefore decided to keep using multifilament PET for the sides rather than monofilament PE, which would result in a stiffer fabric in the sides.

## **Is Polyethylene (PE) not a stronger material than Polyester (PET)? – why don't you just make the whole net in PE?**

The strength of a given netting material depends on several interlinked factors, such as the

knitting pattern, the thickness of the yarns, or their construction. Therefore, one cannot simply compare “PE” nets with “PET” nets. Most of the published reports show that longevity is highly variable depending on the area and user. In some areas, PE nets show considerable wear and tear in less than 3 years.

## **Why is the roof of PermaNet® 3.0 different from the sides?**

The design of PermaNet® 3.0 is based on studies on mosquitoes behaviour (Guillet et al, 2001)  
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and McCall et al (unpublished) that have shown that the majority of mosquitoes land on the roof of the net first, before making their way down the sides of the net. The sides of the net are made from multifilament polyester, which is softer and more comfortable for the user than monofilament polyethylene. The sides of the net have a specially designed knitting pattern for enhanced lifetime.

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### *References*

1. Guillet, P. et al. (2001) Combined pyrethroid and carbamate 'two-in-one' treated mosquito nets: field efficacy against pyrethroid-resistant *Anopheles gambiae* and *Culex quinquefasciatus*. *Med Vet Entomol* 15 (1): 105-12.

## **Is PBO likely to select for kdr resistance?**

PBO has been used in agriculture for 50+ years and there is no published record of PBO selecting for kdr resistance in any other insect species. The selection pressure for insecticide resistance development in mosquitoes involves many factors, for example agricultural insecticide use and exposure to oils, which also need to be taken into consideration.

## How does PermaNet® 3.0 work against kdr resistant mosquitoes?

PBO has been shown to overcome kdr resistance against alpha-cypermethrin in species of aphids and whitefly.<sup>1</sup> The baseline metabolic enzymes of kdr resistant mosquitoes (i.e. mosquitoes resistant to pyrethroids) are inhibited in the same way the susceptible mosquitoes are affected. Mosquitoes with kdr resistance are probably also affected by the enhanced penetration of deltamethrin into the insect.

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### *References*

1. Bingham, G. et al. (2007) Temporal synergism by microencapsulation of piperonyl butoxide and  $\alpha$ -cypermethrin overcomes insecticide resistance in crop pests. *Pest Manag. Sci.* 63: 276–281.

## How does PermaNet® 3.0 work against resistant *Culex* mosquitoes?

PermaNet® 3.0 may increase the mortality rate and/or the degree of blood feeding inhibition (i.e. personal protection) as observed in Vietnam and Togo<sup>1</sup>.

### References

1. WHO (2009). Report of the twelfth WHOPES Working Group meeting. World Health Organisation, Geneva, Switzerland, 120pp.

## Can PBO slow the development of resistance?

It is difficult to predict because of the many inter-related factors that contribute to the development of insecticide resistance in mosquitoes and field studies are required to investigate this. One laboratory study<sup>1</sup> has shown that the speed of development of resistance to deltamethrin in *An. stephensi* larvae and adults was slowed by 6-21 % when selected over 16 generations (~190 days) with deltamethrin and PBO.

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### References

1. Kumar, S. et al. (2004). Variations in the insecticide-resistance spectrum of *Anopheles stephensi* after selection with deltamethrin or a deltamethrin-piperonyl-butoxide combination. *Ann Trop Med Parasitol* 98(8): 861-71.

## Will resistance to PBO develop?

PBO has been used as a synergist for more than 50 years and as yet, no long term resistance has developed. The use of a synergist targets a resistance mechanism and not an active site in the nervous system. For resistance to develop to PBO it would mostly likely involve such large trade-offs in the insect that it would no longer be viable. The resistant individual would be so heavily disadvantaged it would be unable to compete with the susceptible insects in the population.

Two cases of PBO resistance have been reported: one in house flies<sup>1</sup> and one in diamond backed moths<sup>2</sup>, but this resistance was lab selected and not only was never seen in the field but the lab strains were so unfit they are no longer available – further selection to reproduce these strains has been unsuccessful to date. In addition, the mechanism by which this resistance was conferred is not known.

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### *References*

1. Sawicki, R. M. (1974) Genetics of resistance of dimethoate selected strain of house flies (*Musca domestica*) to several insecticides and MDP synergists. *J. Agri. Food Chem.* 22: 344 – 349.
- 2, Sun, C. N. et al. (1985) Insecticide resistance in diamond-backed moth. In: *Proceedings from the 1st International work shop on the DBM.* AVR DC Publ. no. 86 – 248 Ed. Taleskar, N. S. Taiwan. pp. 359 – 371.

## Does PermaNet® 3.0 have a WHOPES recommendation or

## approval?

PermaNet® 3.0 was evaluated in December 2008 at the 12th WHOPES Working Group meeting and given an [interim recommendation](#).

## Where should PermaNet® 3.0 be used?

PermaNet® 3.0 should be used in areas where reduced efficacy of ITNs / LNs (e.g. areas of West Africa) is already apparent due to resistance and also in areas where pyrethroid resistance is documented or may be emerging to ensure effective malaria protection.

## How does PermaNet® 3.0 perform with different types and combinations of resistance mechanism?

The efficacy of PermaNet® 3.0 depends on the level of resistance and type of resistance mechanisms present in an area. PermaNet® 3.0 has been tested in experimental huts against different field strains of vector species with a variety of resistance mechanisms. Results from these studies have shown that PermaNet® 3.0 has a significantly improved efficacy when compared with mono-treated long lasting nets (i.e. pyrethroid only nets) and conventionally treated nets in terms of both mortality and/or personal protection.

## What does the rise of resistance mean for all of the bed nets currently in use around the world?

It is not yet known what will happen in the face of rising resistance in malaria vectors. However, it is of great concern because reduced efficacy of bednets is likely to have an impact on transmission rates and could therefore compromise control efforts and/or elimination and eradication efforts.

## Why does PermaNet® 3.0 have an increased efficacy with pyrethroid-resistant malaria vectors?

The synergist increases the efficacy of the deltamethrin and works in two major ways: by enhancing the penetration of the deltamethrin into the insect<sup>1</sup> and by inhibiting the metabolic enzymes the mosquito uses to sequester or break down this insecticide

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### References

1. Ahmad, M. et al (2006) Delayed cuticular penetration and enhanced metabolism of deltamethrin in pyrethroid-resistant strains of *Helicoverpa armigera* from China and Pakistan. *Pest Manag. Sci.* 62: 805 – 810.
2. Moores, G. et al. (2005). Use of 'temporal synergism' to overcome insecticide resistance. *Outlooks on Pest Management* 16(1): 7-9.

## Why is resistance an important public health issue?

The development of pyrethroid resistance in *Anopheles gambiae* has been highlighted in recent years due to the increased reliance on pyrethroid treated nets for malaria prevention and control. To date, pyrethroids are the only class of chemical approved by the WHO for use on mosquito nets. In the last decade,

*kdr*

resistance has become widespread in West Africa and also been detected in East Africa.

Previously, pyrethroid treated nets have remained effective even in areas with high levels of the *kdr*

gene. However, in 2007 the first report

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of the reduced efficacy of pyrethroid treated ITNs in an area of high *kdr*

resistance was published and it is likely that if current trends continue, insecticide resistance may compromise control as it did in the last era of malaria eradication in the 1950's and 60's

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### References

1. N'Guessan, R. et al. (2007) Reduced efficacy of insecticide-treated nets and indoor residual spraying for malaria control in pyrethroid resistance area, Benin. *Emerg Infect Dis* 13(2): 199-206.
2. Kelly-Hope, L., H. et al. (2008) Lessons from the past: managing insecticide resistance in malaria control and eradication programmes. *Lancet Infect Dis* 8(6): 387-9.

## What is PermaNet® 3.0, and how is it different from other bed nets?

PermaNet® 3.0 is a new generation long-lasting insecticidal net that has improved increased efficacy against pyrethroid-resistant malaria vectors that transmit malaria. It is made from two polymers—polyester (on the sides) and polyethylene (in the roof) —with two chemicals—Deltamethrin and a synergist (PBO). Additionally, the roof and sides of the net regenerate 100% bioefficacy after just one day with susceptible *Anopheles gambiae*, unlike other polyethylene nets that can take up to 15 days for complete regeneration

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*References*

1. Itoh, T. (2005) Reference: Lindblade et al. (2005) Evaluation of longlasting insecticidal nets after 2 years household use. *Tropical Medicine & International Health* 10, 1141–1150. *Trop Med Int Health* 10(12): 1321-1326.