envu™ Mosquito Management

Improving the lives of those at risk

from vector-borne disease

Fludora® Fusion
The First Two-Way IRS Combination

Fludora® Fusion features two unrelated modes of action for a perfect fit in an insecticide resistance management strategy. This first two-way insecticide combination product enhances the reliability and cost-effectiveness of your IRS program, supporting the objectives to achieve coverage and disease impact.

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Features

- Combines two unrelated modes of actions (MoA)
- Contains two different modes of action applied at their full effective dose rates.
- PQ dossier supported by 13 studies translating to a recognition of residual performance of 6-8 months (under certain conditions even longer)
- Tested and proven effective against more than a dozen resistant mosquito strains, expressing various resistance mechanisms.
- Furthermore, in a range of other field trials, residual life up to 12 months has been observed depending on type of surface and mosquito strain.
- Packed in a small unit-dose sachet
- Proven to have 4-year storage stability in all climatic zones.

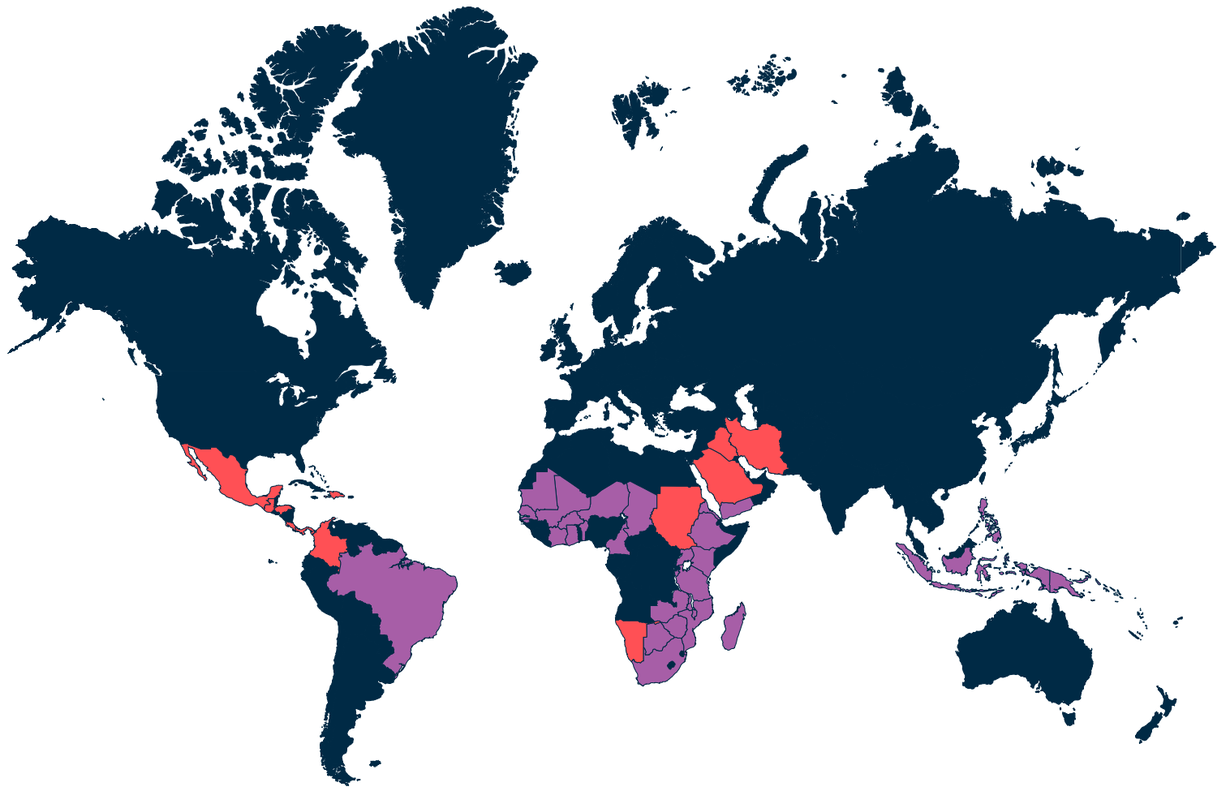
Benefits

- The complementary effect of the two MoA improves robustness of results under field conditions compared to either active ingredient applied alone at equivalent rates proven in multiple trials).
- When used in rotation with other single MoA insecticides, mosquitoes would then be exposed to three different modes of action.
- Independent recognition and support of residual life
- Fludora® Fusion gives reliable results against mixed populations of mosquitoes. It has a strong fit in resistance management strategies incorporating rotation or mosaic approach and a perfect rotation partner for bendiocarb and broflanilide and future chemistry (eg Broflanilide)
- As neither of the Fludora® Fusion active ingredients are at risk PBO negation effects, but would rather enhance Fludora® Fusion‘s effects, this makes Fludora Fusion the perfect companion IRS partner for next generation LLIN‘s.
- Well tested and proven – further reinforced by positive feedback from operational usage across more than a dozen countries. It can be applied once for season-long Control.
- Provides opportunity for reduced transport and storage costs compared to other products with bulkier packs
- Provides greater flexibility in using leftover stock in following season

Product Basics

- **Active ingredients:** Clothiandin (500 g/kg) and deltamethrin (62.5 g/kg)
- **Formulation type:** Wettable powder (WP)
- **Packaging:** 100g or 80g wettable powder in an aluminum sachet (WP) or wettable powder in soluble bag in an aluminium sachet (WP-SB)
- **Dose rate:** 200 mg/m² clothiandin and 25 mg/m² deltamethrin
- **Dilution rate:** One 100 g sachet per 10 L sprayer or 80 g sachet per 8 L sprayer
  20 structures can be sprayed with 1 kg (10 sachets) of Fludora® Fusion (assuming two structures are sprayed per 10 L sprayer)

Fludora® Fusion
Worldwide registration and approval status



WHO-PQ Status:
Fludora® Fusion achieved WHO-PQ Listing in December 2018.
WHO-PQ Reference Number: 008-006

www.who.int/pq-vector-control/prequalified-lists/FludoraFusion/en/

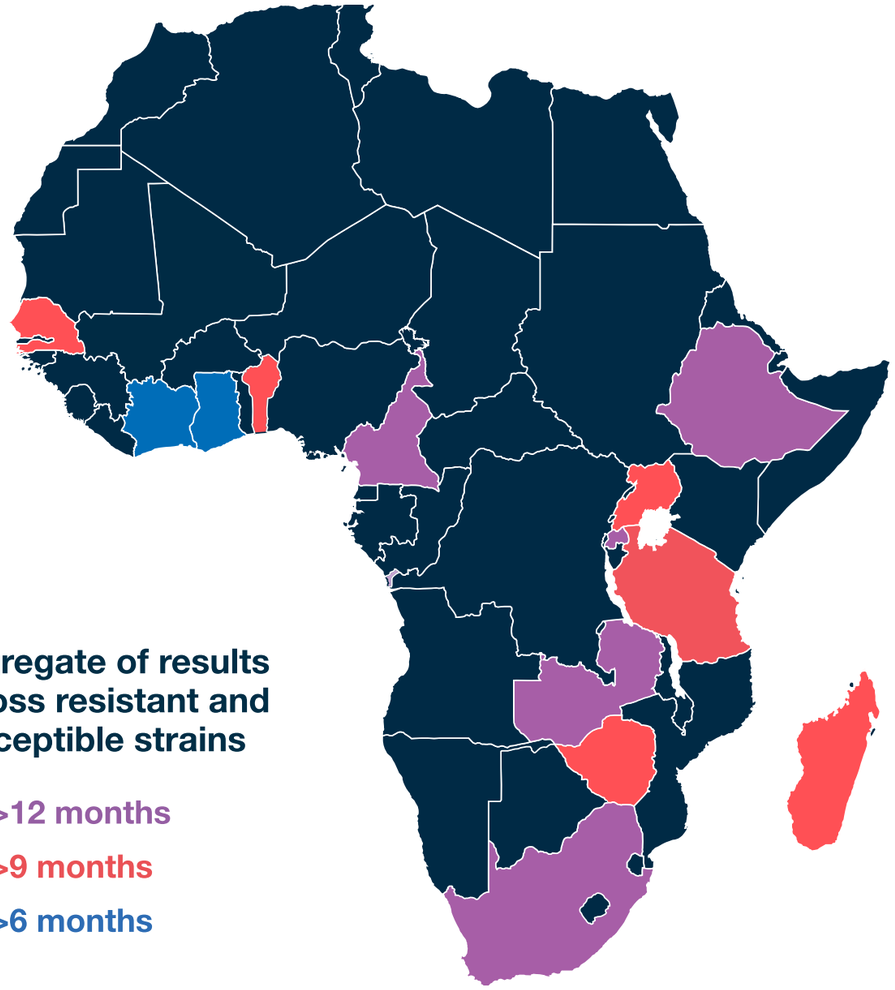
Fludora® Fusion
Trial results

Fludora® Fusion has been assessed as part of an extensive trial program across more than a dozen countries in Africa and Asia.

Knowing that variability of results can be a challenge in IRS operations, we used a broad range of settings to confirm that the combination generally gives more robust results than either active ingredient applied alone. In doing so, we were able to take into account the influence of different spray operators, spray equipment, surface types, and climatic settings. This gives greater confidence in Fludora® Fusion over similar products with minimal field testing completed.

The results of these trials are summarized on the following pages. We would like to emphasize that the experience of one trial location should not be seen as predictive for the results across an entire country. The extensive results generated across multiple countries gives confidence that Fludora® Fusion is a robustly performing product across most situations and conditions. Please note that most of these assessments reflect cone-bioassay results with mortality measured at 72-hours post exposure (unless otherwise stated).

Summary of Residual Activity observed from trials



Aggregate of results across resistant and susceptible strains

- >12 months
- >9 months
- >6 months

Countries included:
Benin, Ethiopia, Ghana, Madagascar, Rwanda, Senegal, South Africa, Tanzania, Zimbabwe, Zambia, Côte d'Ivoire, Cameroon

Trial results pending:
Mali

Overall conclusions from all trials:

These trials support a residual lifespan commonly in the range of 9 - 12 month. Where there are problematic surface types, then more limited residuality may be seen (less than 6 months). Even in these conditions, Fludora® Fusion performs as well as or better than alternatives.

The Fludora® Fusion combination can be expected to outperform the individual active ingredients applied solo at the same dose rates.

In experimental hut trials involving free-flying mosquitoes, no clear conclusion can be drawn regarding higher deterrency or induced exiting attributed to the potential effects of deltamethrin in the mixture. Higher exiting does not indicate lower mortality. Fludora® Fusion more frequently achieved higher mortality levels of free-flying mosquitoes compared to either active ingredient applied alone.

Fludora® Fusion is proven to be an effective and long-lasting IRS insecticide.

Feedback from Operational Use:

We surveyed representatives from six African countries that had used Fludora® Fusion in their malaria control programs. Here is what they have to say:

100% of respondents stated that Fludora® Fusion didn't create any additional logistics and transport challenges. The majority of respondents (86%) said that Fludora® Fusion was better than other insecticides they had used before, in terms of ease of logistics.

88% of respondents stated that Fludora® Fusion was better (ie. easier) than other insecticides in terms of mixing and spraying.

100% of respondents said that the acceptance of Fludora® Fusion by residents of sprayed houses was very high - higher than other insecticides used (mainly due to it being odourless and non-staining).

Fludora Fusion® is neither just a neonicotinoid nor a pyrethroid. It has a dual mode of action.

Further rationale for the difference of the combination vs individual insecticides

If the performance of Fludora® Fusion was mainly reliant on the pyrethroid insecticide, we would expect the following to occur:

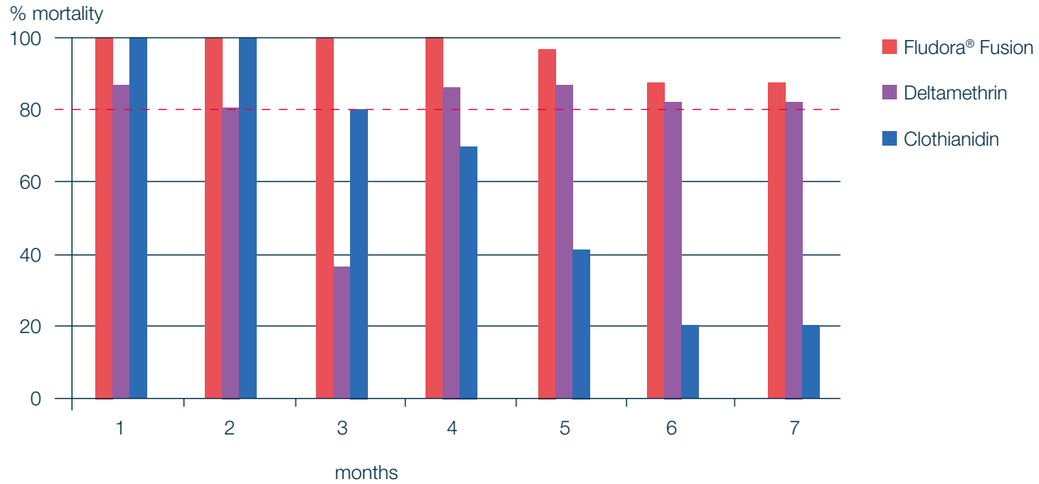
Hypothesis (if there is strong reliance on the pyrethroid, we would expect:)	**Reality**
Lack of efficacy in basic laboratory screening against characterized pyrethroid-resistant strains.	Fludora® Fusion performed very well in lab and field trials against a range of pyrethroid-resistant strains.
The same results in field trials between Fludora® Fusion and deltamethrin against pyrethroid-susceptible strains.	Fludora® Fusion performed significantly better than deltamethrin alone in trials in Tanzania (two sites), Ghana, Senegal, Côte d'Ivoire, and Benin. Furthermore, this was the case even for the 24 hr mortality assessments before clothianidin alone had exerted its full effect.

Conversely, if the results achieved with Fludora® Fusion were solely reliant on the clothianidin in the combination, we would expect no difference in efficacy between Fludora® Fusion and clothianidin alone when tested against highly pyrethroid-resistant strains.

Hypothesis (if there is strong reliance on the pyrethroid, we would expect:)	**Reality**
Lack of efficacy in basic laboratory screening against characterized pyrethroid-resistant strains.	Fludora® Fusion performed very well in lab and field trials against a range of pyrethroid-resistant strains.

This may just seem like a nice way to illustrate a theory, this is actually exactly what we have observed in some of the field trials comparing Fludora® Fusion with the individual insecticide components.

Residual activity of different insecticides on mud surface against a wild mosquito strain from Mbé in wall cone biossays - 120 hs holding time (Côte d'Ivoire)



Role of Fludora® Fusion in Resistance Management

The main objective of insecticide resistance management is to protect the integrity of novel active ingredients. This may be achieved by reducing the selection pressure on the target mosquito population to such an extent that resistance development is prevented or slowed down. This is done through ensuring that mosquito populations not only are prevented from passing resistance mechanisms from one generation to the next, but also avoiding continuous exposure to only single modes of action. This can be achieved through the varied use of techniques and modes of action to change the selection pressure.

Traditional approaches for resistance prevention or management with insecticides is to deploy different modes of action in rotations, mosaics or mixtures, and for malaria vector control that can also mean combining different types of interventions (e.g. LLINs and IRS) including different modes of action.

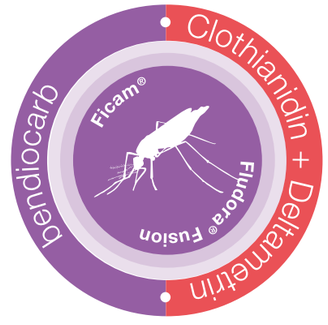
As Fludora® Fusion is a combination or mixture of two different modes of action, its use exposes target mosquitoes to two different modes of action simultaneously. This provides an advantage in terms of efficacy - with an expected higher level of control achieved.

Including Fludora® Fusion in a planned rotation with another insecticide class (e.g. a carbamate or broflanilide) opens up the opportunity of exposing that population to three different modes of action within that rotation. Adoption of mixtures in such rotations might therefore further delay resistance.

As neither of the active ingredients rely on P450's for activation, they are not at risk of PBO negation. In fact, pyrethroids work better in the presence of PBO. This makes Fludora® Fusion the ideal companion IRS product for any LLITN campaigns.

Relevance of Ficam® (bendiocarb) in a rotation with Fludora® Fusion

We recommend that Fludora® Fusion be used as part of an overall insecticide resistance management plan with the aim of exposing mosquito populations to multiple modes of action over time and reducing reliance on single modes of action. Using Fludora® Fusion in such a way helps to ensure that the effectiveness of clothianidin (and the neonicotinoid class) is maintained for as long as possible.



Bendiocarb remains the only carbamate insecticide that has been retained on the WHO-PQ list of insecticides. Bendiocarb, like organophosphates, operates on a completely different target site and mode of action to neonicotinoids and pyrethroids. As such, and with other modes of action available for rotation limited, Ficam® (bendiocarb) is still an effective and robust rotation option to consider for Fludora® Fusion.

We welcome dialogue and discussion around how Ficam® and Fludora® Fusion can be integrated into an IRS program most cost-effectively in order to achieve the objective of preventing resistance development and optimising resources.

Find out more about Envu Against Malaria at:

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