

New insecticide Active Ingredient - Target Product Profile

Disease Area: Malaria

Candidate: New insecticide Active Ingredient for mosquito control

Version: 2.1

Table of Contents

VERSION: 2.1 1

1 MEDICAL NEED / DIFFERENTIATION STRATEGY/USE CASE: 3

2 PROJECT CASCADE: 4

3 EXECUTIVE SUMMARY WITH ANNOTATIONS 4

4 ADDITIONAL VARIABLES OF INTEREST 7

5 CHANGE MANAGEMENT 8

1 Medical Need / Differentiation Strategy/Use Case:

Medical Need:

Vector control using insecticides is a proven method to reduce malaria transmission. The development of new insecticide AI will support the fight against resistance build up against conventional products being used in vector control in malaria endemic countries.

Intended Use Case Scenario:

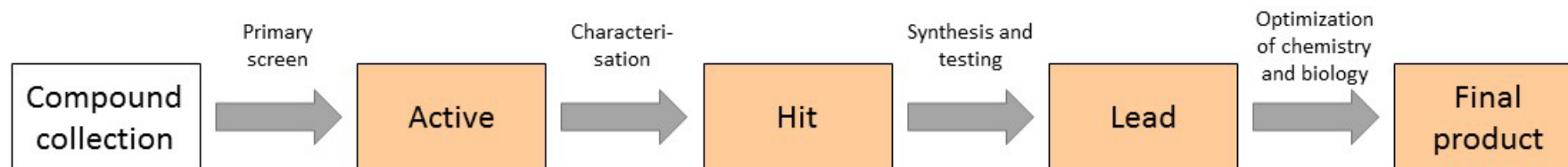
These new active ingredient will be formulated as LLITN and/or LLIRS

Critical Assumptions:

One of the main objective is to help the market introduction of new solutions helping to prevent insecticide resistance build up in mosquito population.

The target profile will evolve through time depending of the project phase (active, hit, lead then final product).

2 Project cascade:



3 Executive Summary with Annotations

	Active	Hit	Lead	Final Product
Potency *	Ca. 0.1x permethrin	Confirmed to be greater than 0.1 x permethrin on S Strain.	1. Potency confirmed to be similar to or greater than permethrin on S strain, <i>Anopheles gambiae</i> and <i>A. arabiensis</i> 2. A.I. Cost-efficacy estimated to be within 5-fold of permethrin.	Cost-efficacy at least equivalent to permethrin.
Cross-resistance	Unknown	An assessment made from all available data	No more 10 fold cross-resistance seen with the following resistant strains:Kdr, Mace, Rdl, Metabolism (oxidative; esterase;GST)	As for Lead
Spectrum	Active against adult stage of a single mosquito spp	As for Active but species used will usually be <i>Aedes aegypti</i> or an <i>Anopheles</i> spp.	1. Effective against <i>Anopheles gambiae</i> and <i>A. arabiensis</i> spp. 2. Effective against other mosquito spp	As for Lead

	Active	Hit	Lead	Final Product
Speed of Effect	Unknown	Lethal effect seen within 72h of insect exposure to a treated surface for 30 minutes (IRS) and up to 20 minutes (ITNs) exposure	As for Hit	As for Hit.
IRS and ITN Fit	Unknown	Contact kill demonstrated on an inert surface.	As for Hit. Hydrolytic and Photo stability	IRS: Six months residual efficacy of formulated AI demonstrated on IVCC standard surfaces (cement, wood, mud). ITN: Five years predicted efficacy on a net in normal use including washing.
Patent Status	Unknown	Freedom to operate issues understood, and potential paths to resolution identified if necessary	Preliminary patent scope identified; freedom to operate issues are understood, and are likely to be resolved.	Freedom to operate for the a.i. and production process must be available. Minimum requirement for end use and/or application patents. AI and process patents whilst desirable are not essential
Exploitable Chemistry	Unknown	Integrity, purity, stability of sample verified	Multiple examples of potency within series; indication of an SAR; viable synthetic routes to multiple analogs	NA
Human Safety/Toxicology	Unknown	No obvious tox alerts are apparent upon expert inspection of chemical structure.	No alerts from preliminary acute oral rodent toxicity screen at 50 mg/kg for AI Ames negative	1. Acute oral toxicity >50 mg/kg, acute dermal toxicity >50 mg/kg (no worse than WHO class II) 2. No GHS categories 1a or 1b for Carcinogenicity, Mutagenicity or Reprotoxicity. No risk of endocrine disruption. 3. Desirable: No neuropathology Low dermal penetration

	Active	Hit	Lead	Final Product
Environmental Safety	Unknown	Unknown	If Log Kow > 4 biodegradation tests required	The compound must pass the WHOPES environmental risk assessment. Hazard criteria which may trigger higher tier assessment include: 96 hour LC 50 (fish, algae) & 48 EC50 (daphnia) >1 mg/l Non bio-accumulating: log Kow <3, Bio-concentration Factor <2000, unless chronic NOEL > 1 mg/l
Cost of Goods	Unknown	No obvious CoG issues based upon complexity of chemical structure.	As for hit	Length of synthesis deemed to be commercially viable; no prohibitively expensive raw materials. Cost-efficacy calculated to be at least equivalent to permethrin
Crop Value	Unknown	Existing information regarding non vector pest activity has been reviewed.	Spectrum of activity against non-vector pests has been investigated.	Spectrum of commercially useful activity against non-vector pests established as part of the development case
User Acceptability	Unknown	Unknown	Unknown	1. No classification for irritancy or skin sensitisation 2. No unacceptable odour 1 day after treatment 3.No staining

* Table of relative potency

Insecticide	Relative Potency
DDT	1
Bendiocarb	1
Permethrin	10
Cypermethrin	20
Bifenthrin	20
Lambda-cyhalothrin	100
Deltamethrin	200

4 Additional Variables of Interest

Variable	Minimum <i>The minimal target should be considered as a potential go/no go decision point.</i>	Optimistic <i>The optimistic target should reflect what is needed to achieve broader, deeper, quicker global health impact.</i>	Annotations <i>For all parameters, include here the rationale for why this feature is important and/or for the target value.</i>

5 Change Management

Version	Key Changes from previous version	Change Made By
2.0	Re-formatting according to BMGF template	Mathias Mondy
2.1	Revision of the “medical need” section	Robert Sloss