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African leadership in vector control product evaluation: the case of CREC/LSHTM/PAMVERC Facility, GLP-certified Facility in Benin, West Africa

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Associate Professor, LSHTM
Facility Manager and Lead Scientist
CREC/LSHTM Collaborative Research Programme

IVCC stakeholder Forum, October 2023

Malaria Vector Control

Two core interventions:



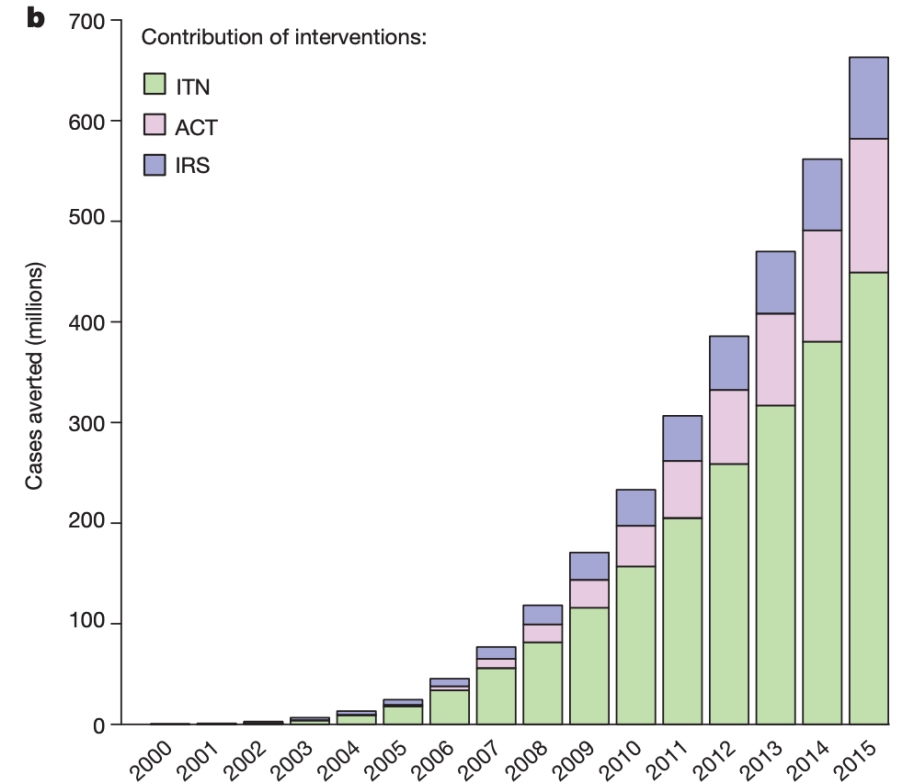
Long-lasting insecticidal nets

Insecticide: Pyrethroids



Indoor Residual Spraying

Insecticides: Pyrethroids, carbamates, organophosphates and DDT



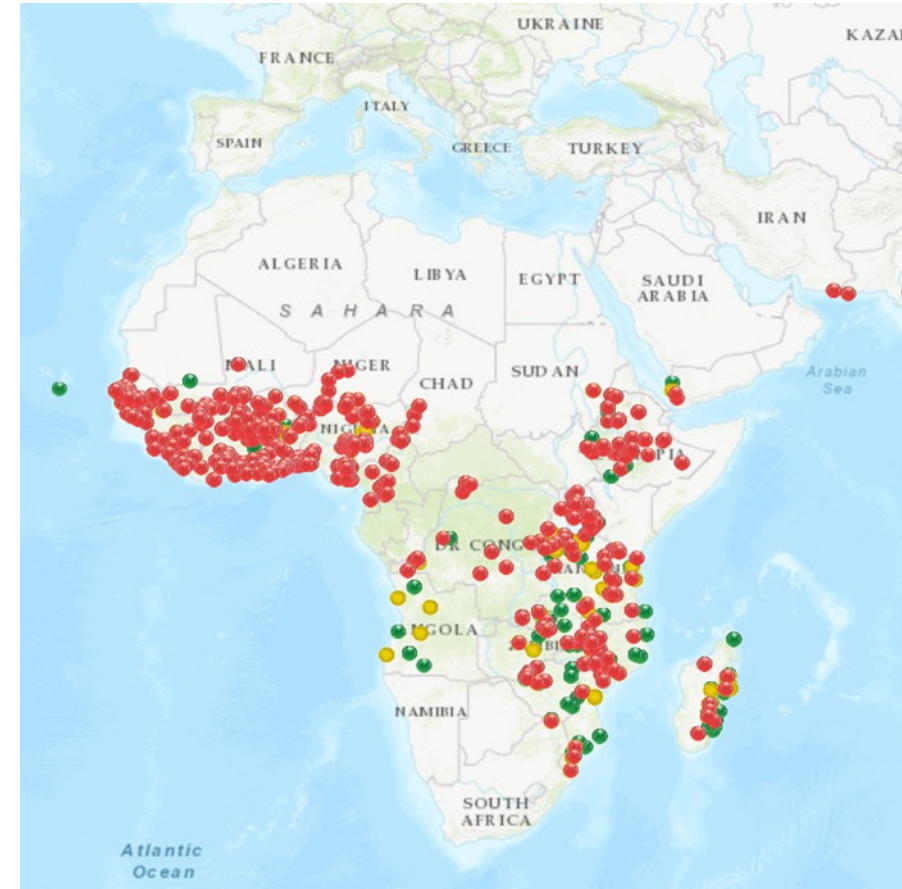
ITNs and IRS contributed nearly 80% reduction in malaria

Source: Bhatt et al, 2015

Insecticide resistance in malaria vectors



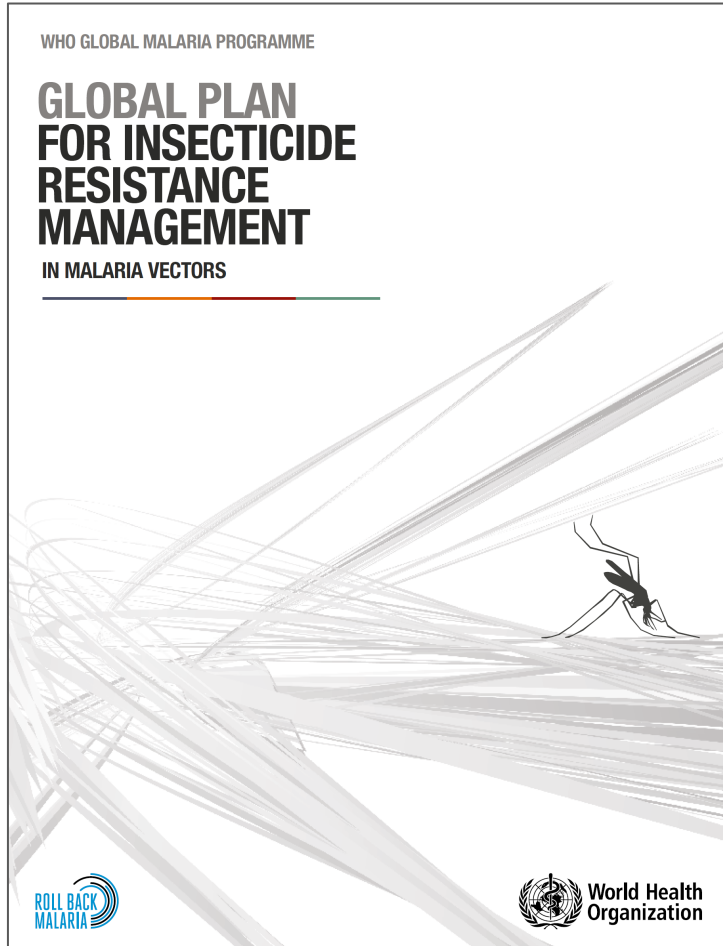
Insecticide resistance: 1990 to 2000



Insecticide resistance: 2015 to 2020

Resistance is widespread and increasing in intensity across Africa

Mitigating insecticide resistance in malaria vectors



WHO Call to action - 2012

Five pillars of strategy

- I Plan and implement insecticide resistance management strategies in malaria-endemic countries.
- II Ensure proper, timely entomological and resistance monitoring and effective data management.
- III Develop new, innovative vector control tools.
- IV Fill gaps in knowledge on mechanisms of insecticide resistance and the impact of current insecticide resistance management strategies.
- V Ensure that enabling mechanisms (advocacy, human and financial resources) are in place.

IR, insecticide resistance

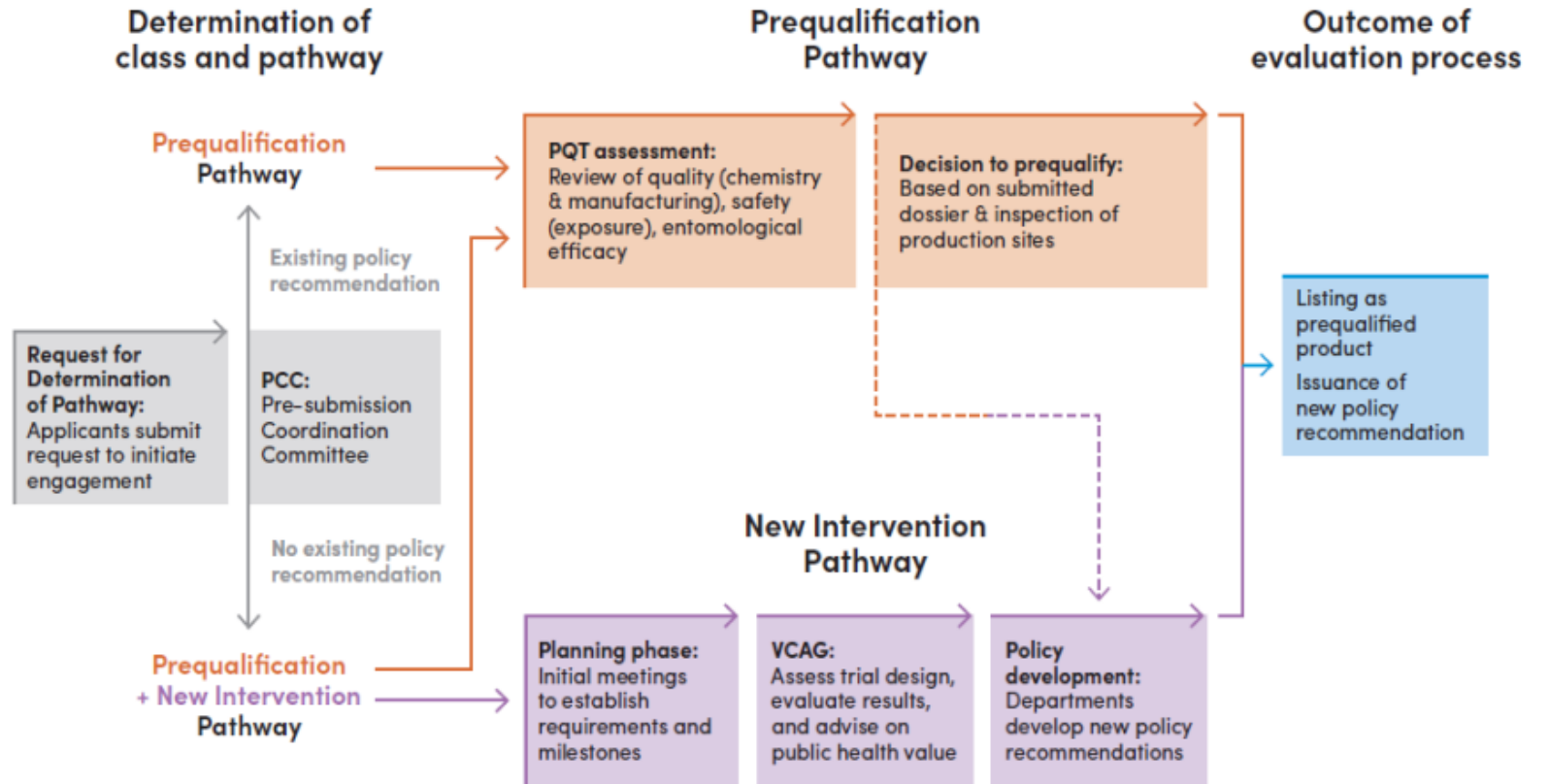
Pillar I: Application of insecticide resistance management (IRM) strategies in malaria vector control programmes.

- Rotations
- Mixtures
- Mosaics
- Combinations

Pillar III: Identification of new chemical products (for IRS and LLINs) with new modes of action

Norms, standards and processes underpinning WHO vector control policy development

Evaluation pathway for vector Control Interventions



VCP **Vector Control Products**

Vector Control Product List

Displaying: 1 - 25 of 87

[Download list as CSV file](#)

Product Type: PQT/VC Ref Number: Title:

Applicant: Active Ingredient/Synergist:

PQT/VC Ref Number	Product Name	Applicant	Product Type	Active Ingredient/Synergist	Date of Prequalification
004-018	2GARD	Tagros Chemicals India Pvt. Ltd	IRS	Clothianidin, Deltamethrin	18 Nov, 2021
002-004	Abate 1 SG	BASF AGRO B.V.	Larvicide	Temephos	18 Apr, 2018

[+ About Vector Control Products Prequalification](#)

[+ What We Do Documents A-Z](#)

List of Prequalified Vector Control Products







Prequalification Pipeline

[+ Prequalification Procedures & Fees](#)


Post-prequalification Procedures & Fees

[+ Prequalification reports](#)

WHO Prequalification assessment (PQT/VCP)

- [Module 1: Administrative information and labelling](#) 
- [Module 2: Discipline summaries](#) 
- [Module 3: Quality](#) 
- [Module 4: Safety](#) 
- [Module 5: Efficacy](#) 
- [Module 6: Inspections](#) 

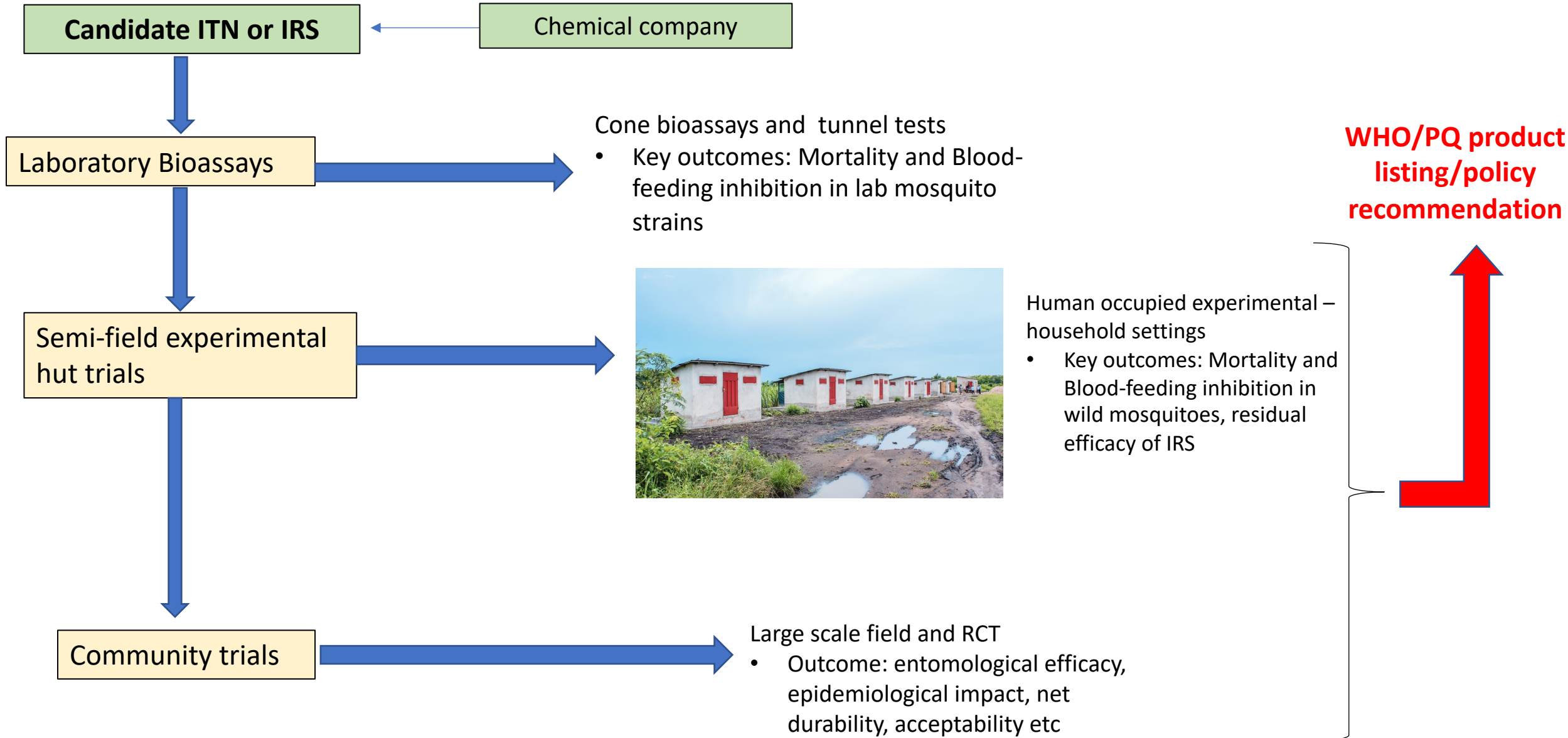


[Module 5: Efficacy](#) 

- Supporting lab, semi-field and field studies
- Current data requirements are specified in the WHO Testing Guidelines
 - [Guidelines for laboratory and field testing of long-lasting insecticidal nets](#)
 - [Guidelines for efficacy testing of spatial repellents](#)
 - [Guidelines for testing the efficacy of insecticide products used in aircraft](#)
 - [Guidelines for testing mosquito adulticides for indoor residual spraying and treatment of mosquito nets](#)
 - [Guidelines for laboratory and field testing of mosquito larvicides](#)
 - [Guidelines for efficacy testing of insecticides for indoor and outdoor ground-applied space spray applications](#)
 - [Guidelines for efficacy testing of mosquito repellents for human skin](#)
- For products claiming equivalence to an existing prequalified product, please review the following information to understand the data requirements per product type:
 - [Determination of equivalence for public health pesticides and pesticide products](#)

Following applicable WHO testing guidelines

Identifying new vector control products – what is involved?



Good laboratory practice for generation of efficacy data for vector control product prequalification



World Health Organization

WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

Contact us ▾ | Glossary & Acronyms | FAQ



PRODUCT STREAMS ▾

EVENTS

NEWS

ABOUT



VCP

Vector
Control
Products

+ About Vector Control Products
Prequalification

Assessment overview

WHO undertakes a comprehensive evaluation of the safety, efficacy, and quality of vector control products, based on information submitted by the applicants, and an [inspection](#) of the relevant manufacturing site including any contract research organization sites as necessary.

The assessment framework of VCP Prequalification is built on science and policy and includes:

Information for

Manufacturers

Regulatory agencies

Quality control laboratories

Procurement agencies

3. For prequalification - Applicant **develops** and **submits** a product dossier which includes data and information to support the safety, efficacy, and quality requirements appropriate to the product type and generated according to good laboratory practices (GLP) and appropriate quality management system.

The CREC/LSHTM/PAMVERC GLP-certified research facility



- Performs laboratory, semi field, community trials of vector control products since 2005.

Established OECD
GLP System
(2015-2018)

Inspection by
Accreditation
Body (SANAS)
(December 2018)

OECD GLP
Certification
(January 2019)



**What did we do to achieve GLP
certification?**

Infrastructural Improvements and equipment management

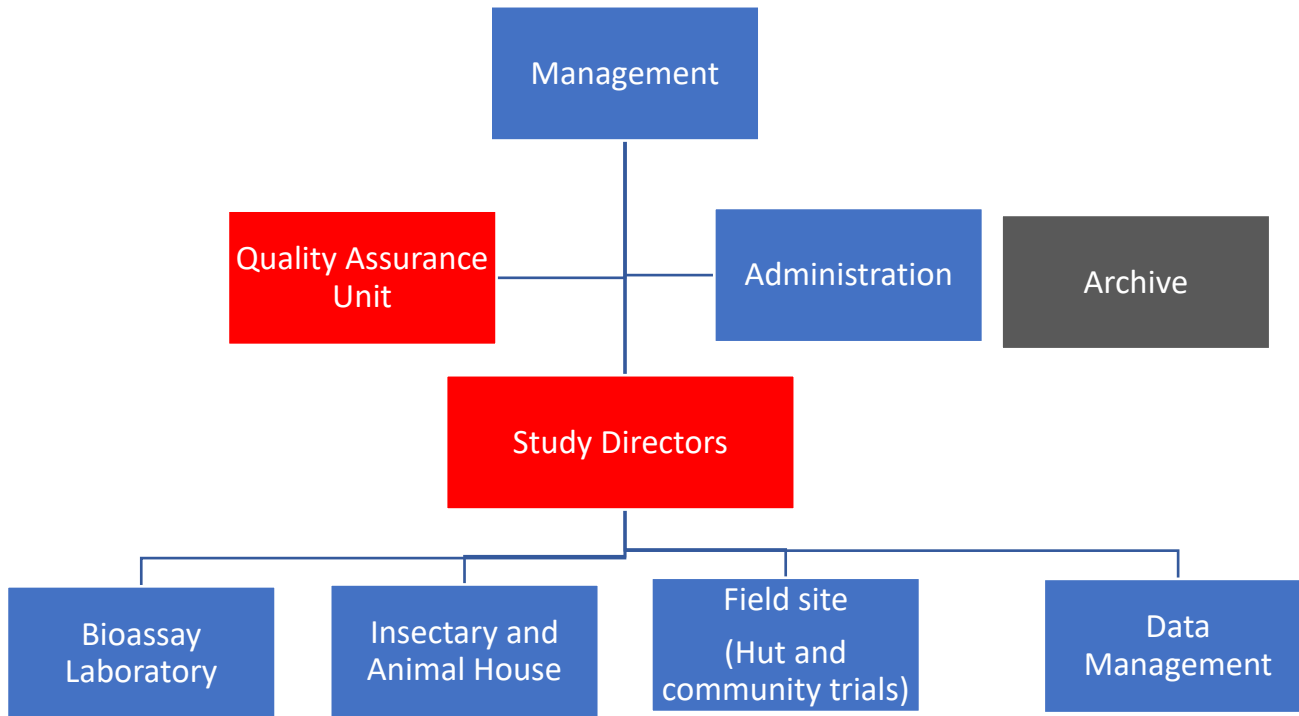


- Improved quality of infrastructure - ensure separation of processes and environmental control.
- Established equipment management system (inventory, calibration, maintenance, retirement etc).

- Balances
- Potter tower
- Shaker bath
- Incubators
- Fume hoods
- Data loggers
- Refrigerators
- Etc



Personnel structure and training



Staff are trained and assessed for competence every 1-2 years

SN	TRAINING CODE	TITLE	TRAINING FREQUENCY
1	101-BL	Phase 1 laboratory techniques in the evaluation of Long-lasting insecticidal nets (LLINs)	24 months
2	102-BL	Phase 1 laboratory techniques in the evaluation of insecticides for Indoor Residual Spraying (IRS)	24 months
3	103-BL	Resistance Bioassay techniques	24 months
4	104-BL	Safety and waste management	12 months
5	105-FS	Phase 2 experimental hut evaluation of LLINs and IRS	24 months
6	106-IA	Insectary and Animal House Techniques	24 months
7	107-QA	Good Laboratory practice	24 months
8	108-QA	Study Director and Quality assurance training	12 months
9	109-GS	Administrative and financial procedures	24 months
10	110-GS	General support and housekeeping	24 months
11	111-DM	Archiving procedures	24 months
12	112-DM	Data management procedures	12 months

Management of test items (insecticidal products)



- Reception, registration, storage and usage of all test items received by the Facility
- Avoid contamination between products
- Ensure staff safety



Data management and archiving

- Developed system for double data entry, computer validation systems, physical and electronic archives for long-term storage of project data



Quality Assurance Unit

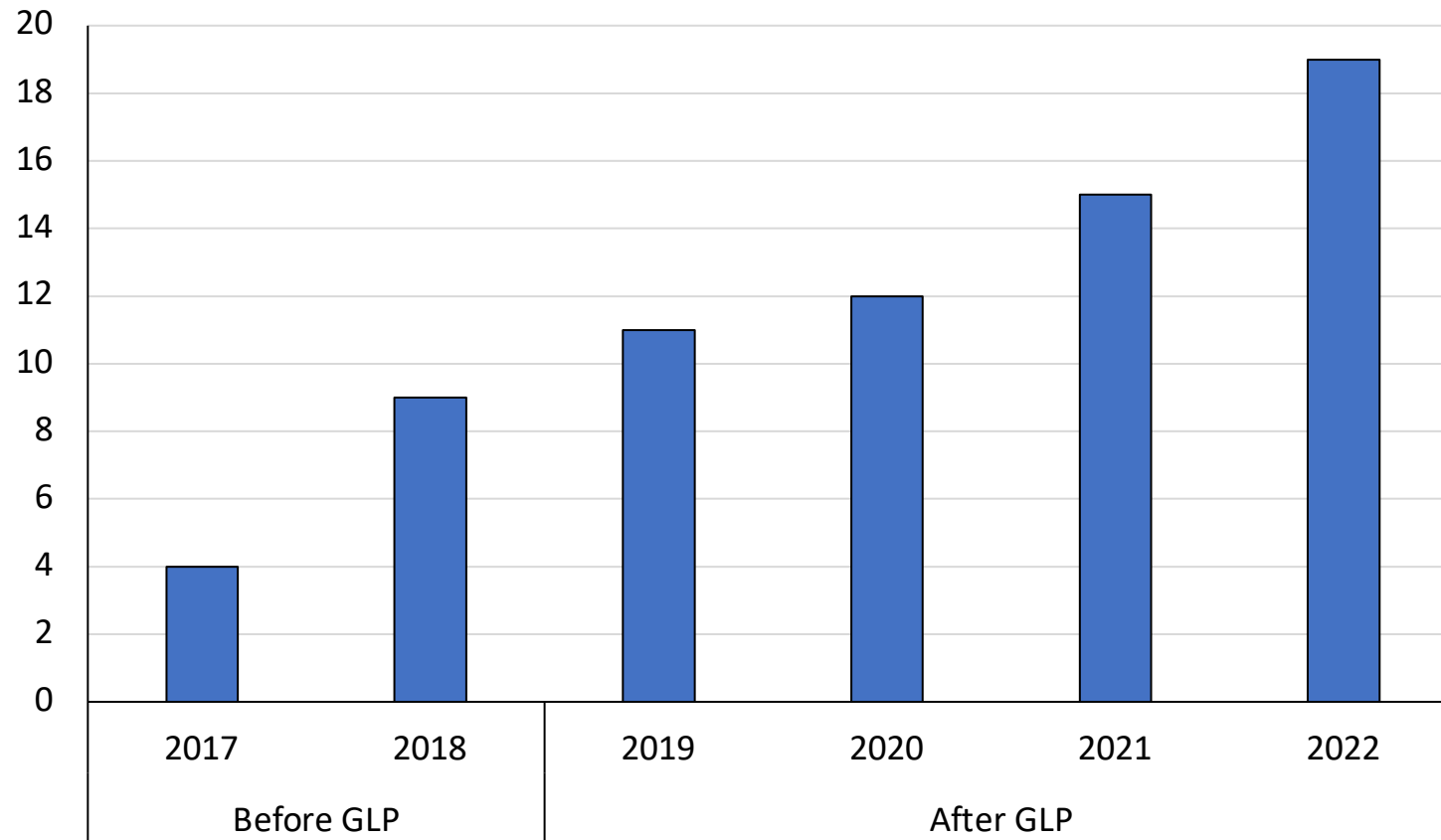
- Quality assurance unit set up and trained.
- Ensure continuous compliance through inspections and follow-up
- Assess performance through quality indicators



Unit	Quality Indicators (annual)	Limits
Insectary	Total number of adult mosquito cages produced:	
	• Kisumu strain	250 min
	• Vkper strain	150 min
	• Cove strain	150 min
Animal house	Percentage of animal deaths in a year on total animals maintained at the animal house	30% max
	Proportion of in-house animal births to total animals each year	20% min
Bioassay laboratory	Percentage of laboratory assays performed with control mortality >10%	
	• Cone tests	10% max
	• Cube tests	10% max
	• Cylinder tests	10% max
	• CDC Bottle tests	10% max
	Tunnel tests with control mortality > 10% and blood feeding < 50%	20%
	Overall percentage of block substrates rejected during spray applications using potter tower	25% max
	Proportion of tests conducted outside required temperature range.	10% max
Proportion of raw data sheets with hand errors	30% max	
Field site	Overall level of mortality in control huts for all hut trials performed during the year	20% max
	Proportion of raw data sheets with hand errors	30% max
	Proportion of IRS hut applications performed outside +/-20% target dose	10% max
Data Management	Number of computer breakdown/major faults in a year.	3 max
Administration	Proportion of Cove-Cotonou trips in which a project vehicle broke down	5% max
	Proportion of procurements with extreme delays between demand and delivery (>14days for local items and >3 months for international items)	3 days
	Number of unexplained absences and lateness to work	5%
Archive	Time lap between official end of study and archiving	3 months max
Whole Facility	Number of days with complete power failures lasting >6hours	0 days
	Staff satisfaction	

Increase in number of projects and vector control product brands tested

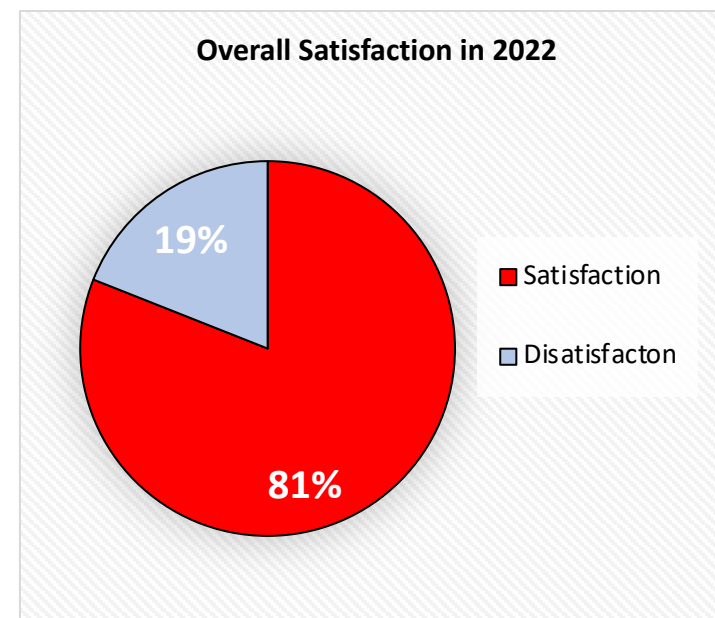
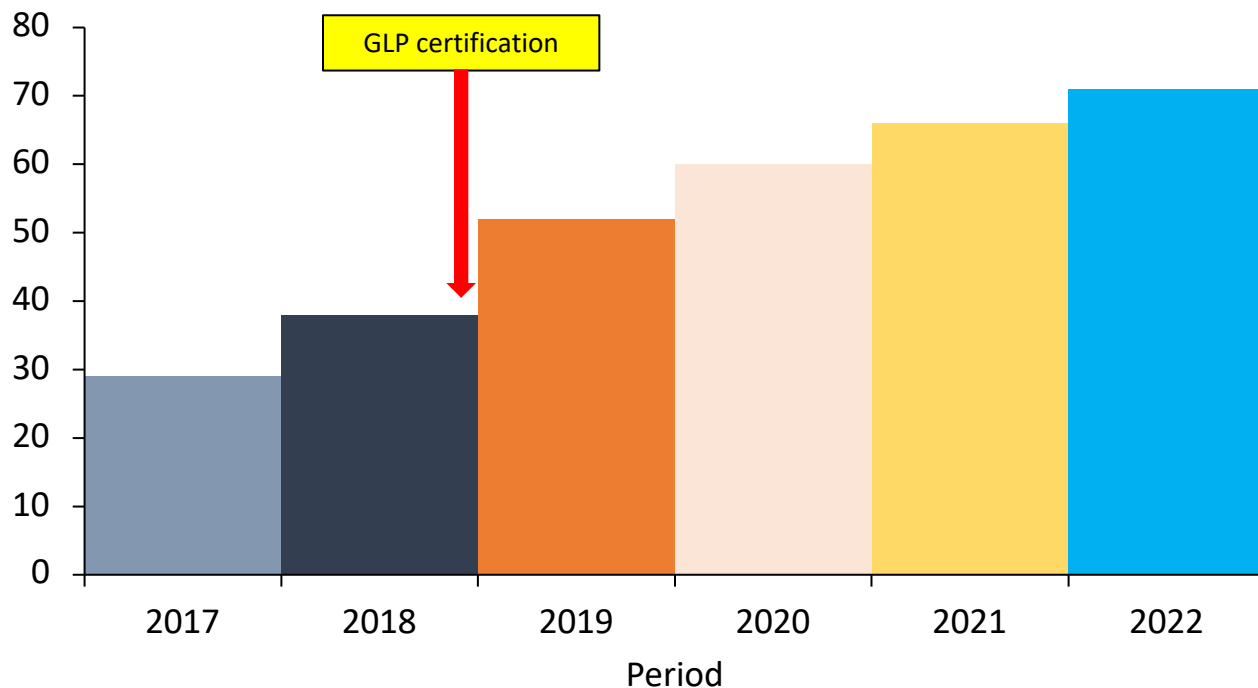
Number of new projects



- *57 vector control product testing projects after GLP*
- *29 new brands of vector control products (IRS, ITNs, SR, personal repellent) tested since GLP accreditation up to 2022*

Increase in employee participation and satisfaction

No. of full time CREC/LSHTM/PAMVERC staff



- 'I feel proud working in a GLP laboratory with high standards'
- 'I am more confident that my work is actively contributing to fighting malaria'
- 'I have learned so many new skills since we acquired GLP and my professionalism has improved substantially.'

Vector Control Product Testing (for WHO/PQ listing and country registration)

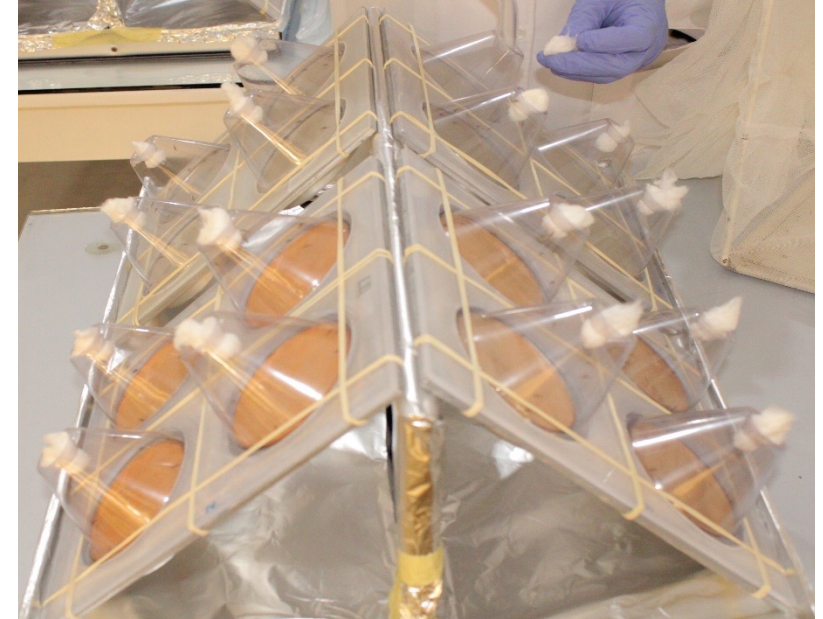
CREC/LSHTM/PAMVERC – Phase I GLP laboratory testing of **IRS products**



Potter spray tower



Different types of substrates
(concrete, mud, tile, wood, etc...)



WHO cone bioassays (1 week and
monthly intervals) for residual activity
assessment

CREC/LSHTM/PAMVERC – Phase I GLP laboratory testing of **ITN products**



Regeneration time



Efficacy and wash resistance (cone and tunnel tests)

CREC/LSHTM/PAMVERC – Phase II GLP experimental hut evaluation of insecticide products



- 74 experimental huts in Cove, Benin
- Vector population resistant to pyrethroids but susceptible to carbamates and OPs

Used for testing indoor vector control tools such as IRS insecticides, ITNs, spatial repellents etc

- **LN: Non-inferiority (mortality and blood-feeding inhibition)** to reference LN
- **IRS: Non-inferiority (mortality)** to reference IRS product

CREC/LSHTM/PAMVERC – Community trials



- Epidemiological impact
- Durability evaluation of nets
- Bioefficacy testing
- Chemical activity
- E.g New Nets Project RCT



- IRS campaign
- Efficacy evaluation
- Residual activity
- Operational feasibility
- Community acceptance
- E.g VECTRON T500 community trial



Management of test systems (insectary mosquitoes)

- Separation of insectary strains to control contamination
- Development of insectary management manuals and SOPs
- Characterisation and assessment of fitness every 3-4 months



	Strains	Colony name	Species	Phenotypic characterization	Source of collection	genotypic characterization
1	Kisumu	An. gambiae Kisumu	An. gambiae	susceptible to all insect.	BEI resources (Kenya)	None
2	VKPer	An. gambiae Vkper	An. gambiae	pyrethroid and DDT resistant	Burkina Faso	Kdr (L1014F)
3	Covè	An. gambiae sl Covè	An. coluzzii	pyrethroid and DDT resistant	Covè; Benin	Kdr (L1014F); Overexpressed P450s (CYP6P3)
4	Akron	An. coluzzi Akron	An. coluzzii	Resistant to pyrethroids, DDT, OPs and carbamates	BEI resources (Benin)	Ace-1 mutation; Kdr (L1014F); over-expressed oxidases
5	FUMOZ	An. FUMOZ	An. funestus	pyrethroid and DDT resistant	BEI resources (Mozambique)	CYP6P9a and CYP6P9b
6	Aedes ROCK	Aedes ROCK	Aedes aegypti	susceptible to all insecticide	BEI resources	None
7	Aedes Dandji	Aedes Dandji	Aedes aegypti	pyrethroid and DDT resistant	Dandji; Benin	Not characterized
8	Culex Dandji	Culex Dandji	Cx. quinquefasciatus	pyrethroid and DDT resistant	Dandji; Benin	Not characterized
9	Culex Covè	Culex Covè	Cx. quinquefasciatus	pyrethroid and DDT resistant	Covè; Benin	Not characterized
10	Culex TPRI	Culex TPRI	Cx. quinquefasciatus	susceptible to all insecticide	Tanzania	Not characterized

Development of next generation ITN Products



RESEARCH ARTICLE

A Chlorfenapyr Mixture Net Interceptor[®] G2 Shows High Efficacy and Wash Durability against Resistant Mosquitoes in West Africa

Raphael N'Guessan^{1,2,3}, Abibatou Odjo², Corine Ngufor^{1,2,3}, David Malone⁴, Mark Rowland^{1,3*}

**SCIENTIFIC
REPORTS**

nature research



OPEN

Efficacy of Royal Guard, a new alpha-cypermethrin and pyriproxyfen treated mosquito net, against pyrethroid-resistant malaria vectors

Corine Ngufor^{1,2,3}, Abel Agbevo^{2,3}, Josias Fagbohoun^{2,3}, Augustin Fongnikin^{2,3} & Mark Rowland^{1,3}

Science Translational Medicine

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RESEARCH ARTICLE

VECTOR CONTROL

Efficacy of the Olyset Duo net against insecticide-resistant mosquito vectors of malaria

Corine Ngufor,^{1,2,3*} Raphael N'Guessan,^{1,2,3} Josias Fagbohoun,² Damien Todjinou,² Abibath Odjo,² David Malone,⁴ Hanafy Ismail,⁵ Martin Akogbeto,² Mark Rowland^{1,3}

- Perform non-inferiority testing of second in class ITN products

Development of new IRS Products

RESEARCH ARTICLE

Indoor residual spraying with a mixture of clothianidin (a neonicotinoid insecticide) and deltamethrin provides improved control and long residual activity against pyrethroid resistant *Anopheles gambiae* sl in Southern Benin

Corine Ngufor^{1,2,*}, Augustin Fongnikin², Mark Rowland¹, Raphael N'Guessan^{1,2}



Ngufor et al. *Malar J* (2020) 19:249
https://doi.org/10.1186/s12936-020-03325-2

Malaria Journal

RESEARCH

Open Access

Indoor spraying with chlorfenapyr (a pyrrole insecticide) provides residual control of pyrethroid-resistant malaria vectors in southern Benin

Corine Ngufor^{1,2,3*}, Augustin Fongnikin^{2,3}, Neil Hobbs^{1,2}, Martial Gbegbo^{2,3}, Laurette Kiki^{2,3}, Abibath Odjo^{2,3}, Martin Akogbeto^{2,3} and Mark Rowland^{1,3}



Fongnikin et al. *Parasites Vectors* (2020) 13:466
https://doi.org/10.1186/s13071-020-04341-6

Parasites & Vectors

RESEARCH

Open Access

Efficacy of Fludora[®] Fusion (a mixture of deltamethrin and clothianidin) for indoor residual spraying against pyrethroid-resistant malaria vectors: laboratory and experimental hut evaluation

Augustin Fongnikin^{2,3}, Nadia Houeto^{2,3}, Abel Agbevo^{2,3}, Abibath Odjo^{2,3}, Thomas Syme^{1,2,3}, Raphael N'Guessan¹ and Corine Ngufor^{1,2,3*}



scientific reports

OPEN

Efficacy of broflanilide (VECTRON T500), a new meta-diamide insecticide, for indoor residual spraying against pyrethroid-resistant malaria vectors

Corine Ngufor^{1,2,3*}, Renaud Govoetchan^{1,2,3}, Augustin Fongnikin^{2,3}, Estelle Vigninou², Thomas Syme^{1,2,3}, Martin Akogbeto² & Mark Rowland^{1,3}



Epidemiological trials of next generation ITNs

Tanzania trial - published

Effectiveness and cost-effectiveness against malaria of three types of dual-active-ingredient long-lasting insecticidal nets (LLINs) compared with pyrethroid-only LLINs in Tanzania: a four-arm, cluster-randomised trial



Jacklin F Masha*, Manisha A Kulkarni*, Eliud Lukole, Nancy S Matowo, Catherine Pitt, Louisa A Messenger, Elizabeth Mallya, Mohamed Jumanne, Tatu Aziz, Robert Kaaya, Boniface A Shirima, Gladness Isaya, Monica Taljaard, Jacklin Martin, Ramadhan Hashim, Charles Thickstun, Alphaxard Manjurano, Immo Kleinschmidt, Franklin W Masha, Mark Rowland, Natacha Protopopoff



1. Interceptor (pyrethroid-only)
2. Olyset Plus (pyrethroid-PBO)
3. Royal Guard (pyrethroid + pyriproxyfen)
4. **Interceptor G2 (pyrethroid-CFP)**



- Interceptor G2 induced 44% reduction in malaria incidence compared to standard pyrethroid LLIN over 2 years

Benin trial - NNP -published

Efficacy of pyriproxyfen-pyrethroid long-lasting insecticidal nets (LLINs) and chlorfenapyr-pyrethroid LLINs compared with pyrethroid-only LLINs for malaria control in Benin: a cluster-randomised, superiority trial



Manfred Accrombessi*, Jackie Cook*, Edouard Dangbenon, Boulais Yovogan, Hilaire Akpovi, Arthur Sovi, Constantin Adoha, Landry Assongba, Aboubacar Sidick, Bruno Akinro, Razaki Ossè, Filémon Tokponnon, Rock Aikpon, Aurore Ogouyemi-Hounto, Germain Gil Padanou, Immo Kleinschmidt, Louisa A Messenger, Mark Rowland, Corine Ngufor, Natacha Protopopoff, Martin C Akogbetot



1. Interceptor (pyrethroid-only)
2. Royal Guard (pyrethroid + pyriproxyfen)
3. **Interceptor G2 (pyrethroid-CFP)**



- Interceptor G2 induced 46% reduction in malaria incidence compared to standard pyrethroid LLIN over 2 years

Other types of studies

- Spatial repellents
- Personal repellents
- Larvicides
- Household spray products
- Durability testing of novel ITNs distributed in other African countries e.g Mozambique (PATH), Liberia (PMI/ABT)

Operational research to support NMCP:

- Chemoprevention of malaria – UNITAID Funded PSI/LSHTM/CREC – IPTI+ project
- Evaluation of malaria RDTs – PATH/PMI INSIGHTS

CREC/LSHTM – Capacity building



© CREC/LSHTM

- MSc and PhD students from LSHTM and local Universities in Benin.
- Internships in vector control
- Training of vector control experts: IR testing, conduct of bioefficacy testing (cone, tunnel, bottle bioassay), etc..

Challenges

- **Sustainability – funding challenges**

- transforming to a hybrid contract research organization (CRO) and academic research unit.
- expanding beyond vector control product evaluation e.g analytical chemistry, diagnostics, genomics, consultancies etc

- **Ensuring equitable partnerships**

- building partnerships based on mutual benefit and respect
- building south-south/regional collaborations to foster research

- **Advanced training**

- Soft skills
- Business development/management
- Data analysis and modelling
- Artificial intelligence

Strategic Focus 2022-2027

Vector control product testing

- Expand product testing range e.g ATSBs, Aedes control etc
- **Expand testing capacity – more laboratory space, repellents**

Molecular characterisation

- **Establish molecular laboratory**
- Mosquito infection studies

Chemical analysis of insecticide products

- Establish an analytical chemistry laboratory (HPLC and GC) to GLP
- Become a reference centre for ITN quality assessment.

Operational research

- Expand capacity for operational research in vector control to support decision making at national and regional levels.
- Pilot evaluations of new vector control tools
- Modelling of vector control data for decision making

Training and capacity building

- Establish online training courses in entomology and VC product testing

Vector control product testing south-south partnerships



Tanzania, Moshi



Tanzania, Muheza



Cameroon



Ethiopia (TDRC)



Cote D'Ivoire



Burkina Faso



ACKNOWLEDGEMENTS

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BORNE DISEASE

PATH


INDUSTRY PARTNERS



www.crec-lshtm.org



CREC/LSHTM/PAMVERC team