Pan-African Registration Landscape for Vector Control Tools

Fact-base – July 2019

Executive summary | Contents of this document

Context of this document

- Innovation to Impact (i2i) – in partnership with AU, AUDA-NEPAD, WHO, BMGF, IVCC, ALMA, industry, RECS,[1] and country regulators – has conducted an extensive study of Vector Control (VC) registration across Africa to establish a comprehensive fact-base
- This document provides an overview of the pan-African landscape for VC tools
- For detailed materials on country-level processes, please see "Selected African Country Registration Processes for Vector Control Tools" fact-base

Section title	Summary
Project context	• Project context and objectives • Country selection and criteria • Interviews conducted • Country assessment framework
Pan-African registration landscape for VC tools	• Categorization of registration processes of various African countries • Key challenges and themes that emerged from the research
Summary table of selected country processes	• Summary of detailed information on country-level processes

1. African Union; African Union Development Agency – New Partnership for African Development; World Health Organization; Bill and Melinda Gates Foundation; Innovative Vector Control Consortium; African Leaders Malaria Alliance, Regional Economic Communities

Disclaimer on methods of information gathering

- Information was gathered in the following ways:
  - Interviews (over the phone and in-person) with various stakeholders[1]
  - Desktop research leveraging reports and officially published documentation
- Research was conducted from December 2018–August 2019, and all information presented represents the state of registration process at the time of data collection—changes may have occurred since
- Given the recent implementation of WHO PQT-VC, there is a possibility that country regulators did not have WHO PQT-VC in mind when making comments or comparisons to the WHO process
  - We expect some country regulators may have been referring to WHOPES requirements – we attempted to standardize by comparing the list of dossier requirements given to us with PQT-VC requirements
  - We interpreted imprecise comments such as "WHO approval is needed," as a requirement for a WHO PQT-VC listing
- We have collected factual information to the best of our ability. However, we acknowledge that the registration processes described are complex, that stakeholders sometimes have varied information, and that we can not always capture all of the details or nuance

1. List of stakeholder types and number of interviews can be viewed in the Project Context section

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Project context

Malaria continues to be a significant burden, and vector control (VC) is instrumental to reducing it

A more robust WHO evaluation system (PQT-VC) for VC products is now largely in place

Crucial need to begin optimizing registration practices in endemic Sub-Saharan Africa (SSA), where processes and requirements vary significantly

i2i is collaborating with key stakeholders incl. AU, AUDA-NEPAD, WHO, BMGF, IVCC, ALMA, and industry as well as RECs[1] and SSA countries to address this issue

1. African Union; African Union Development Agency – New Partnership for African Development; World Health Organization; Bill and Melinda Gates Foundation; Innovative Vector Control Consortium; African Leaders Malaria Alliance, Regional Economic Communities

Project objectives

Focus of these materials

Build a comprehensive fact base around registering VC products in sub-Saharan Africa

Deepen the understanding of existing challenges through selected country reach out

Co-create opportunities to optimize access to VC tools through engagement with broader African stakeholders

Understanding of landscape is based on interviews with over 130 stakeholders

To shape high level view of African process landscape, interviewed …

- **18** African and global partners[1]
- **9** RECs[2] and pan-African leadership
- **20** Industry players

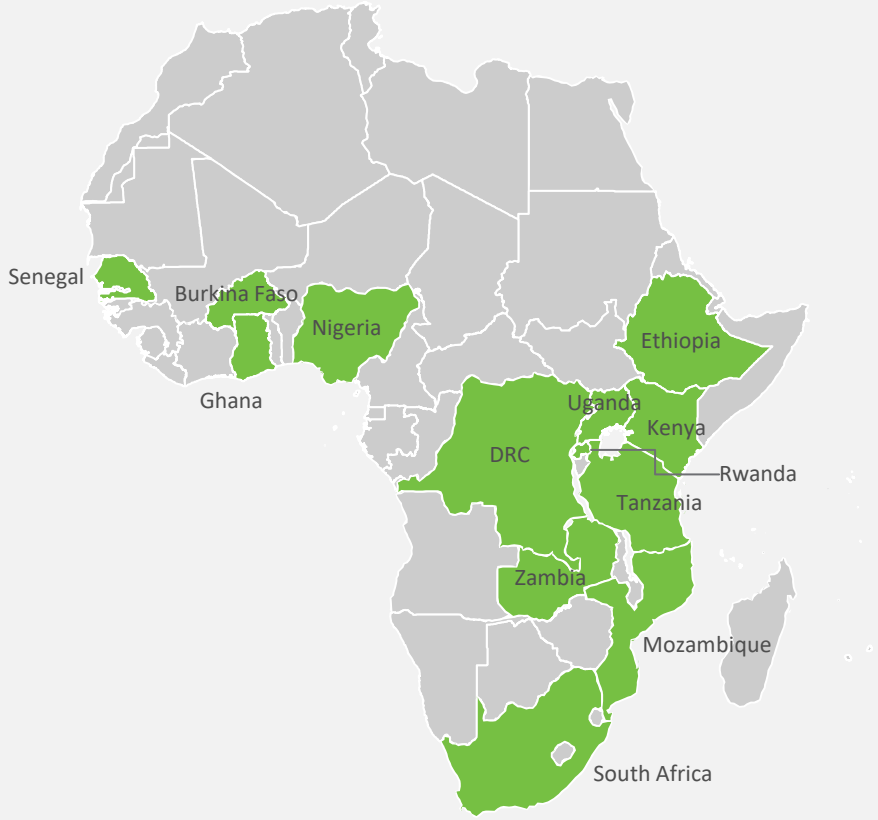
To build country-specific knowledge, interviewed …

- **26** Regulatory authorities[3]
- **29** National Malaria Control Programs and relevant Ministries
- **7** National research institutes
- **6** Country-level representatives from global partners
- **17** Country-level representatives from industry players

1. Includes Global Fund, PMI, Unicef; 2. Regional Economic Communities; 3. Includes CILSS

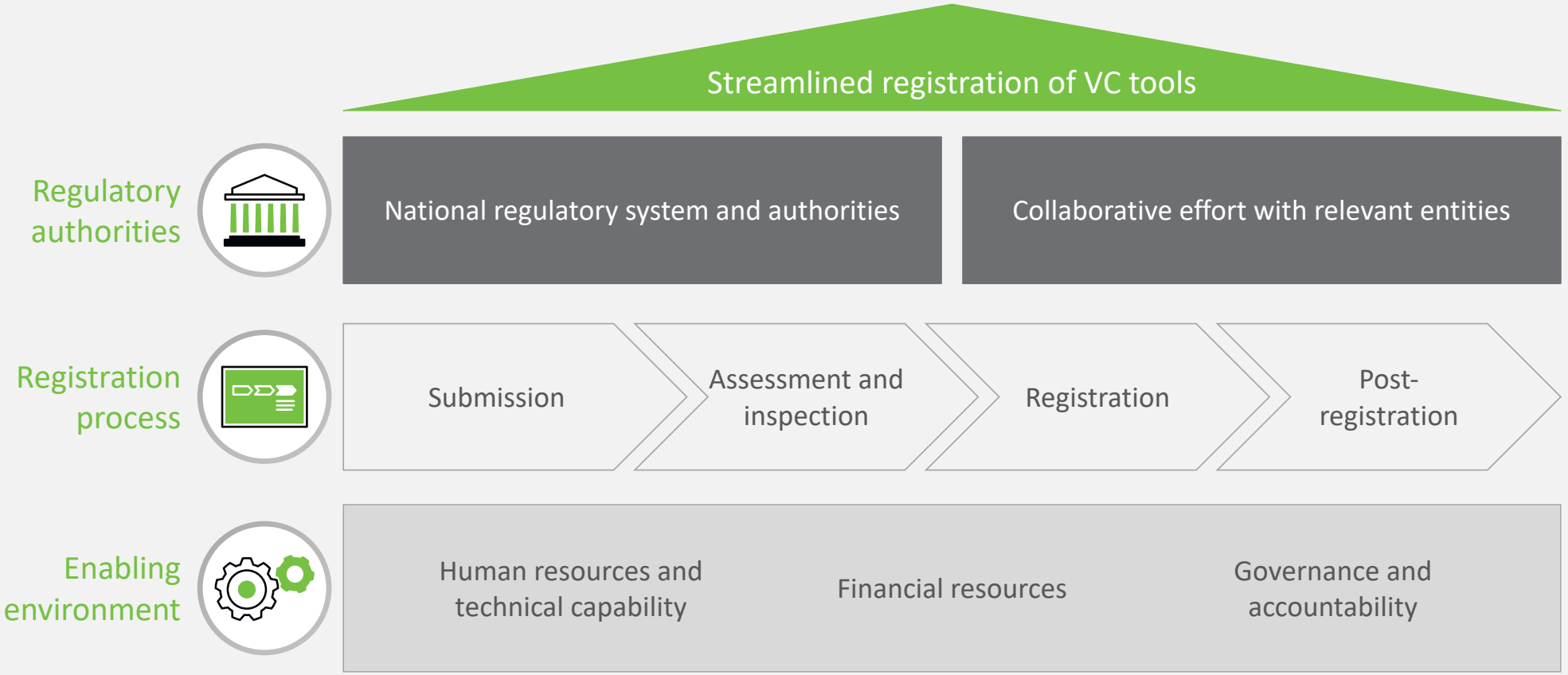
13 countries selected for in-depth analysis based on malaria burden, and regional balance/influence

Sub-region	Selected countries *( ) : Ranking in malaria burden in 2017*
Southern Africa	Mozambique (3) South Africa (38) Zambia (17)
Central Africa	DRC (2)
West Africa	Burkina Faso (5) Ghana (6) Nigeria (1) Senegal (29)
East Africa	Ethiopia (22) Kenya (16) Rwanda (11) Tanzania (10) Uganda (4)



Source: WHO World Malaria Report 2018, number of malaria cases 2017 (point); BCG Analysis

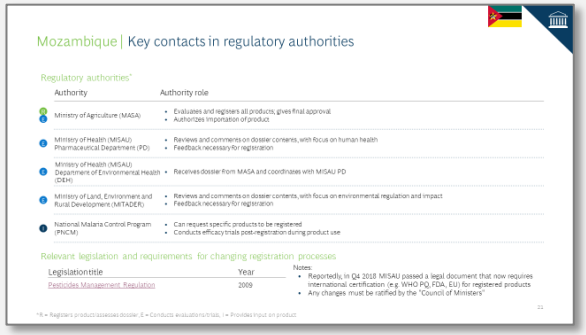
Assessment was conducted along three key dimensions …



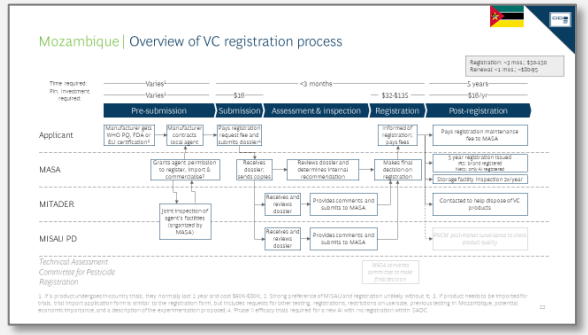
… generating robust fact-base for each country

Please see "Selected African Country Registration Processes for Vector Control Tools" database for full set of materials

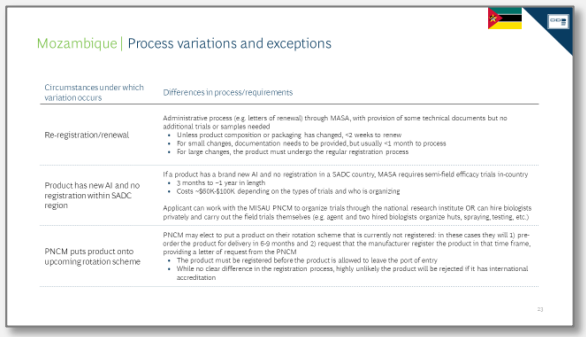
Summary of vector control tool registration



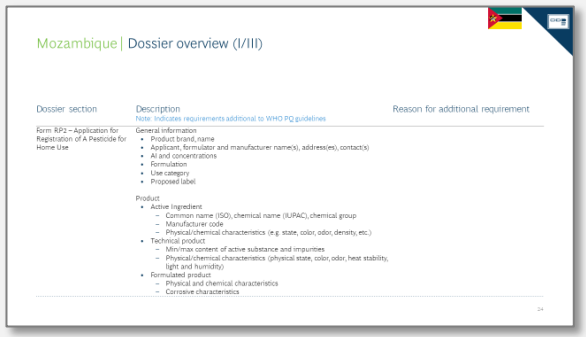
Key authorities and legislation



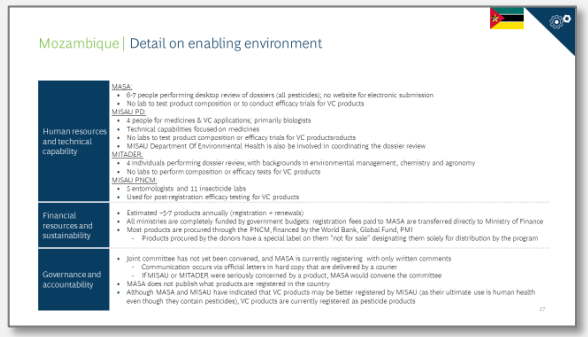
Overview of registration process



Descriptions of process variations and exceptions



Dossier overview



Detail on enabling environment

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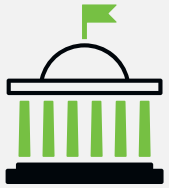
Registration landscape differs by country, but we can broadly classify countries based on two dimensions



Overseeing ministry

- Frame of reference for VC (e.g. as agricultural, environmental or public health products)
- May imply different processes / requirements and ease of communication with similar ministries across countries

Registration requirements

- Illustrates use of globally recognized norms (e.g. use of WHO PQT-VC guidelines)
- Illustrates complexity of the registration process for manufacturers (e.g. local trial requirements)
- May imply ease of collaborating with other similar models

Please see the next slide for an illustration of the WHO PQT-VC process and guidelines used as a comparison during our research

Note | Throughout this document, country application requirements are compared to those of the WHO PQT-VC process

WHO prequalification team (PQT-VC) is set up to aid in regulating VC products

- PQT-VC replaces WHOPES[1] as the WHO review source for VC products
- PQT-VC's vision is to enable access to effective, safe and good-quality vector control products to prevent the transmission of vector-borne diseases
- PQT-VC fulfils this vision by assessing vector control products and their manufacturing sites against uniform standards of efficacy, safety and quality

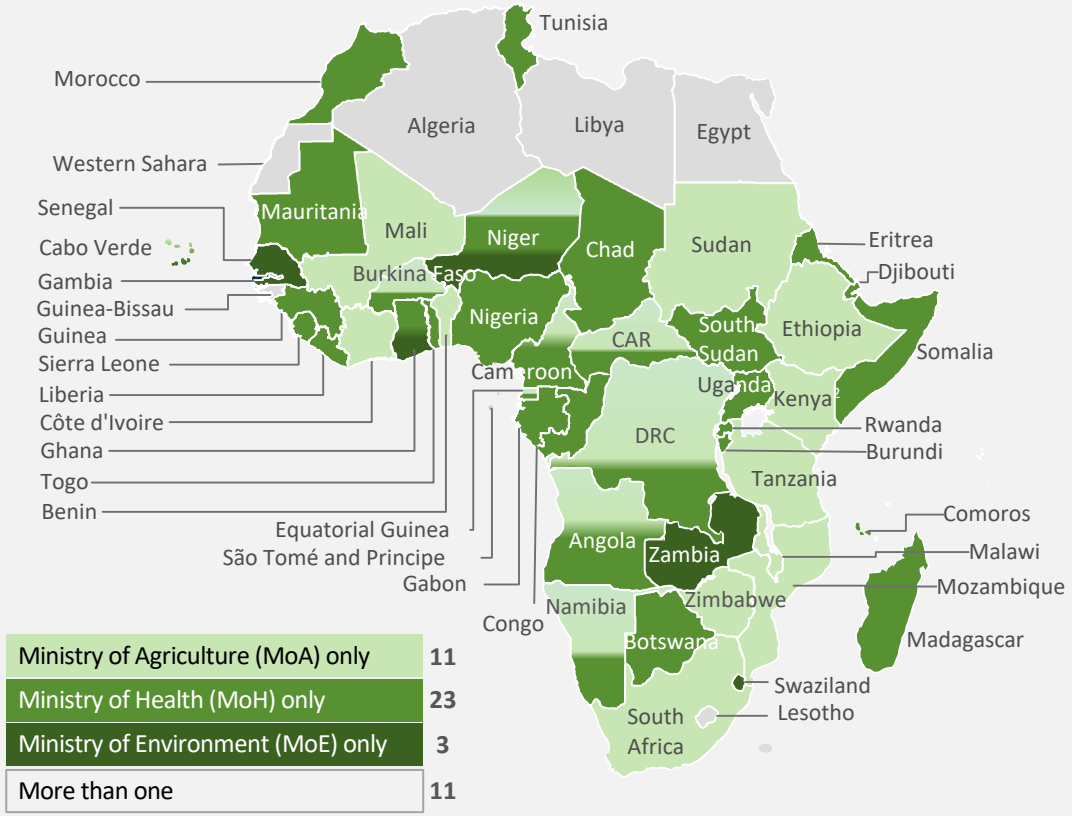
WHO PQT-VC dossier includes the following modules

1	Administrative information & labelling	• Cover letter • Application form • Table of Contents • Letter(s) of authorization • Letter(s) of access • Declaration of Labelling (includes the affixed label, leaflets, and product marketing materials)
2	Discipline summaries	• Summarized data and manufacturer conclusions (separately for quality, safety and efficacy dossier)
3	Quality dossier	• Physical/Chemical Data • Declaration of Product Formulation • Description of Manufacturing Process • Declaration of Manufacturing Sites • Confidential Appendices
4	Safety dossier	• Toxicology: Acute inhalation, oral, dermal; Primary eye irritation, skin irritation, dermal sensitization (hazard, exposure and risk characterization) • Product risk assessment • AI-specific hazard assessment (or publically available information)
5	Efficacy dossier	• Data generated from Phase I (lab studies), Phase II (semi-field conditions) and Phase III (large scale field trials (3 years)),[2] where applicable
6	Inspection dossier	• Site master file(s) with all relevant data and reports

1. WHO Pesticide Evaluation Scheme; 2. New PQT requirements for LLIN: https://www.who.int/pq-vector-control/resources/170626pqvc_020_info_note_llin_longevity.pdf?ua=1
Source: https://www.who.int/pq-vector-control/resources/dossier_req/en/

Overseeing ministry varies significantly across the continent

Overseeing ministry[1]



Ministry of Agriculture (MoA) only	11
Ministry of Health (MoH) only	23
Ministry of Environment (MoE) only	3
More than one	11

Registration authority most commonly under Ministry of Health, but high degree of fragmentation across the continent

Registration ministry	*% of countries**
Ministry of Agriculture	23%
Ministry of Health	48%
Ministry of Environment	6%
More than one	23%

** of the 48 African countries for which data on the registering authority was available*

1. Most commonly, split authorities register different products (e.g. IRS under MoA/MoE and nets under MoH) but not always; 2. Kenya's authority (PCPB) is a semi-autonomous agency
Note: From this point, Ministry of Agriculture will be abbreviated as MoA, Ministry of Health as MoH, Ministry of Environment as MoE.
Source: 2017 ALMA; BCG analysis

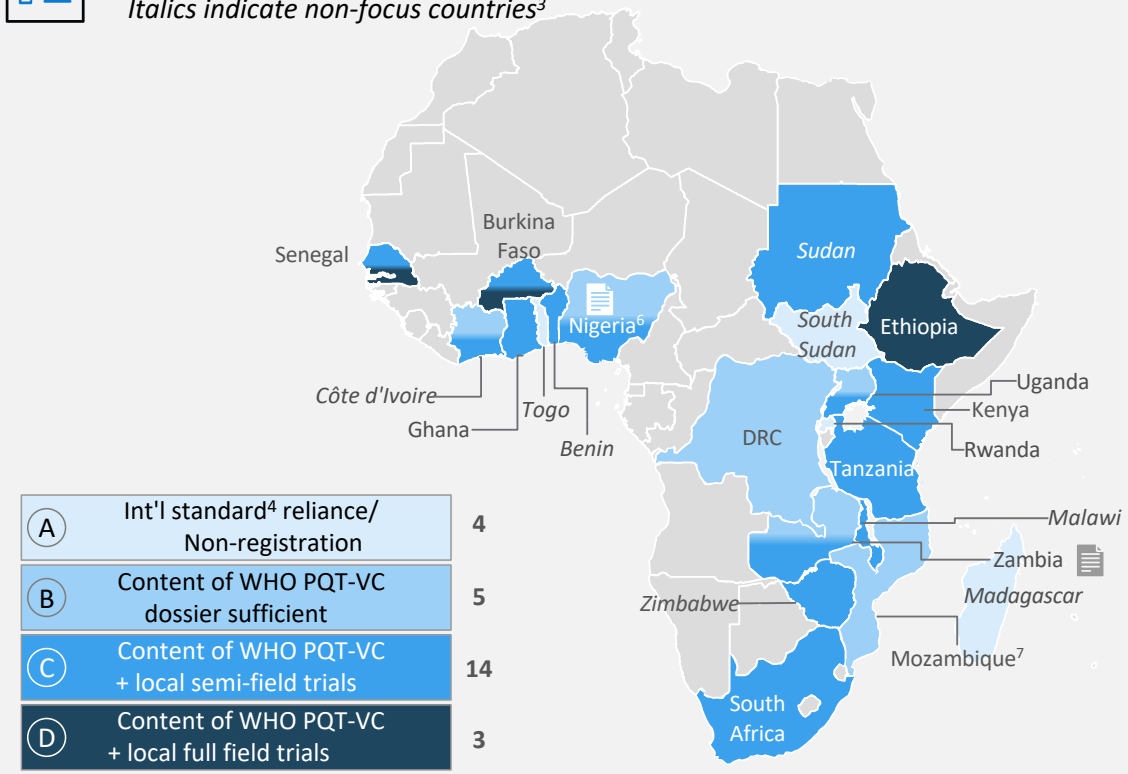
Significant variation in registration requirements as well

There is no universal set of dossier requirements specifically for vector control

The largest requirement that varies is the length of in-country field trials, which can have major ramifications for registration speed

Registration requirements

Italics indicate non-focus countries[3]



A	Int'l standard[4] reliance/ Non-registration	4
B	Content of WHO PQT-VC dossier sufficient	5
C	Content of WHO PQT-VC + local semi-field trials	14
D	Content of WHO PQT-VC + local full field trials	3

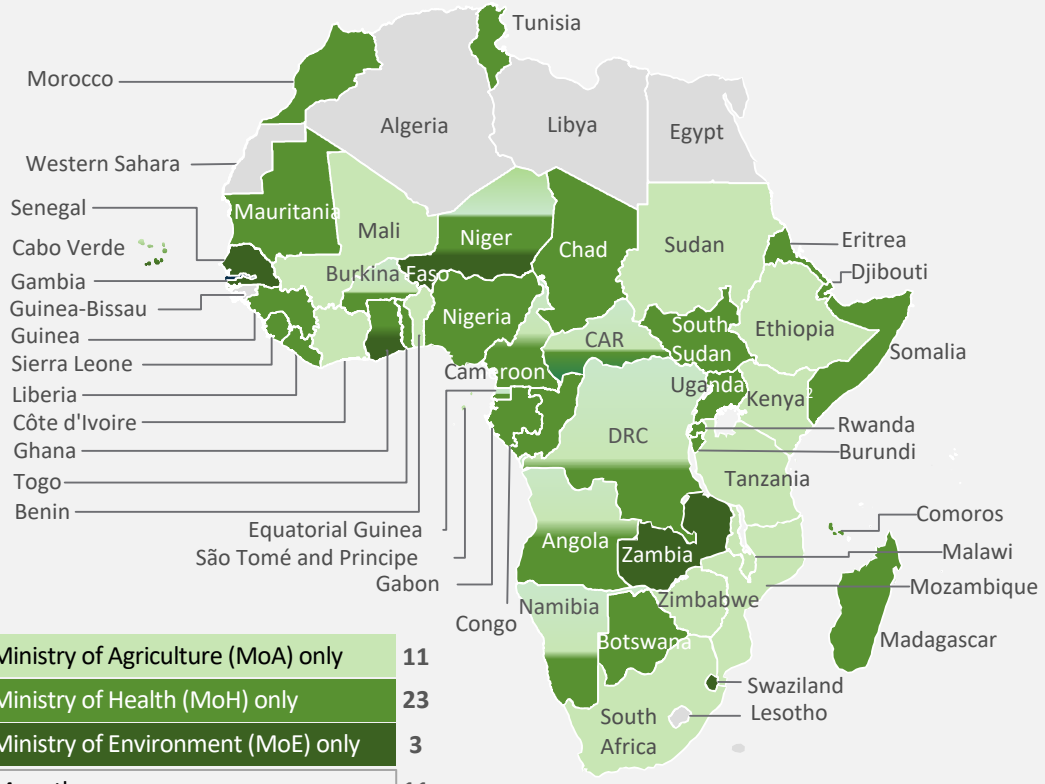
Significant additional documentation required [5]

3. Country regulators were not interviewed; understanding based on interviews with int'l orgs, manufacturers, etc.; 4. e.g. WHO, US FDA, etc.; 5. Documentation varies, but can include additional safety certificates, environmental dossiers, labels and others requiring a significant investment from the applicant. 6. Trials are required only for new AI; 7. Trials are technically required for new AI, but no

Source: 2017 ALMA; BCG analysis

In summary, African VC registration is a complex landscape

Overseeing ministry[1]



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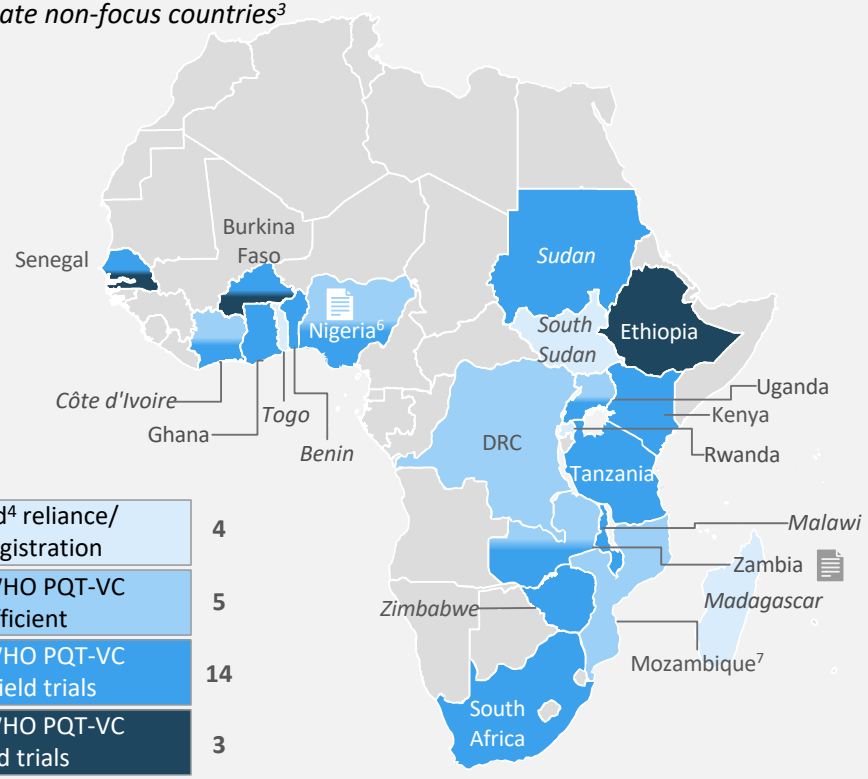

A	Int'l standard[4] reliance/ Non-registration	4
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Significant additional documentation required [5]

1. Most commonly, split authorities register different products (e.g. IRS under MoA/MoE and nets under MoH) but not always; 2. Kenya's authority (PCPB) is a semi-autonomous agency; 3. Country regulators were not interviewed; understanding based on interviews with int'l orgs, manufacturers, etc.; 4. e.g. WHO, US FDA, etc.; 5. Documentation varies, but can include additional safety certificates, environmental dossiers, labels and others requiring a significant investment from the applicant. 6. Trials are required only for new AI; 7. Trials are technically required for new AI, but no historical instance of this occurring for VC products: unclear if enforced. Note: FDA is classified as MoH. Source: 2017 ALMA; BCG analysis

Emerging challenges for VC product registration in most African countries

1 Unclear/overlapping mandates between national authorities

Multiple national authorities with a mandate to register VC products, or lack of clarity on which authority is best positioned to register (largely due to the dual nature of VC as both a pesticide and human health product), which can lead to variation in standards and manufacturer confusion about where/how to register

2 Lack of resources to ensure adequate evaluation or quality control

Funds not available 1) for the required expertise/technical capacity to evaluate products, 2) to convene the registration body, or 3) to adequately monitor quality or safety post-registration, causing variation in product review and/or reliance on external support

3 Requirements aren't tailored for Vector Control products

E.g. pesticide-focused processes from MoE / MoA can result in superfluous requirements (e.g. residue studies), while some relevant dossier sections (e.g. efficacy studies, toxicology studies) observed as missing in some MoH dossier requirements

4 Delayed communication between authorities

Back and forth efforts, slow processes in appointing committees or lack of good forums can lead to delays and less familiarity between registering/evaluating bodies

5 Insufficient transparency on registration process/requirements

Unclear or insufficient communication of requirements and process steps can increase roadblocks and delays for applicants

Note: MoA = Ministry of Agriculture, MoH = Ministry of Health as MoH, MoE = Ministry of Environment

Double click | Selected quotes from stakeholder interviews

1 Unclear/overlapping mandates between national authorities

- **MoA regulator:** *"VC products are either chemical products managed by the MoA, or as medical products managed by the MoH. However, we know the Ministry of Health has granted Marketing Authorizations for LLINs and even IRS, which are our jurisdiction."*

2 Lack of resources to ensure adequate evaluation or quality control

- **Research institute affiliated with the MoH:** *"There are often delays when the applicant cannot pay for trials upfront, and we cannot always make up the full teams. We rely on partners like PMI, etc. and interns to support the trials."*
- **MoH regulator:** *"We only conduct a review and a chemical composition test, and don't have the appropriate capabilities to conduct efficacy trials and other laboratory tests."*

3 Requirements aren't tailored for Vector Control products

- **Global manufacturer:** *"There's always a long back and forth with [country] because they require residue studies, which are simply irrelevant for a bed net."*

4 Delayed communication between authorities

- **MoH regulator:** *"Sometimes the Ministry of Agriculture will take several months to answer our questions regarding the dossier, if they answer them at all."*

5 Insufficient transparency on registration process/requirements

- **Global manufacturer:** *"If we knew exactly what to submit, we would have no problem doing so. But registration for VC is often a lengthy process with back-and-forth discussions for months about the necessary documentation and requirements."*

Note: MoA = Ministry of Agriculture, MoH = Ministry of Health as MoH, MoE = Ministry of Environment
Source: Expert interviews Dec 2018-May 2019; Source: BCG analysis

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Summary table | Vector Control product registration processes (I/II)

	Overseeing ministry	Ministries providing input	Registration Fees	Registration Process (in months, excl. trials)	Duration of registration (years)	Renewal Process (months)	Renewal Fees	In-country trials required?	Details on local efficacy trial requirements[5]
Burkina Faso	MoA[1] (CILSS[2] pathway)	MoH,[3] MoE[4]	$2,040	2 – 3	3 (provisional); 5 (full)	TBD	$2,040	Always	Semi-field trials completed in a CILSS country for provisional registration, full field trials required for subsequent registration
	MoH (National pathway)	n/a	$90	5 – 7	5	TBD	$45	No	Contents of WHO PQT-VC sufficient
Democratic Republic of Congo	MoH (overlapping mandate)	n/a	$685 – $3,000[6]	0.5 – 4	5	0.5 – 4	$685 – $3,000[6]	TBD	Efficacy trials not listed under dossier requirements
	MoA (overlapping mandate)	n/a	$250 – $400	3 – 4	2	3 – 4	$250 – $400	TBD	Efficacy trials not listed under dossier requirements
Ethiopia	MoA	n/a	$50	7	5	0.5	$20	Always	Local full field trials required
Ghana	MoE (Chemical formulation – all products)	MoH	~$2,400	3 – 12	3	1 – 12	~$800	Always	Local semi-field trials required
	MoH (Nets and personal use products)	n/a	Varies by product	3 – 6	3	2	Varies by product	Sometimes	Semi-field trials can be completed in a country with similar mosquito strains
Kenya	MoA	MoH	~$400	4 – 12[7]	3	< 1[8]	~$200	Always	Local semi-field trials and/or lab tests required

1. MoA= Ministry of Agriculture; 2. CILSS= Comité Inter-Etate pour la Lutte contre la Sécheresse au Sahel; 3. MoH= Ministry of Health; 4. MoE= Ministry of Environment 5. One average, Semi-field trials range from 1-2 years; Full field trials are usually 3 years or longer; 6. Excludes the cost of site visits, which do not always occur but can cost up to $10K; 7. Depends on manufacturer's response and length of application backlog which is 6 months as of August 2019; 8. Depends on completion and correctness of renewal application.

Note: Where two registration timelines are listed, applicants have the option of using either pathway; Source: Industry and regulator interviews; Regulator websites and documentation; BCG Analysis

Summary table | Vector Control product registration processes (II/II)

	Overseeing ministry	Ministries providing input	Registration Fees	Registration Process (in months, excl. trials)	Duration of registration (years)	Renewal Process (months)	Renewal Fees	In-country trials required?	Details on local efficacy trial requirements[5]
Mozambique	MoA[1]	MoH,[2] MoE[3]	$50 – 150 +$16/yr maintenance	3	5	<1	$80 – $95	Sometimes	Required for new AIs[5] that have not been registered in another SADC country
Nigeria	MoH	n/a	$760	4 – 10	5	4 – 10	$760	Sometimes	Local semi-field trials are required if a new AI[5] is being registered
Rwanda	MoH	n/a	n/a	4 – 8	Indefinite	n/a	n/a	No	Contents of WHO PQT-VC sufficient; local lab may conduct composition tests
Senegal	MoE (CILSS[6] pathway)	MoH, MoA	$2,040	2 – 3	3 (provisional); 5 (full)	TBD	$2,040	Always	Semi-field trials completed in a CILSS country for provisional registration, full field trials required for subsequent registration
South Africa	MoA	MoH, MoE	$690	15 – 30[7]	3	3 – 9[7]	$360	Always	WHO PQT-VC required plus local semi-field trials and stability tests
Tanzania	MoA	MoH, MoE	$1,150	7 – 13	5	1	$300	Always	Semi-field trials required
Uganda	MoH	MoE	n/a	3 – 12	TBD	n/a	n/a	Sometimes	Local lab or semi-field trials may be required on request
Zambia	MoE	MoH	$305	5 – 15	3	2 – 12	$305	Sometimes	Semi-field required, but data from similar ecologies may be accepted

1. MoA= Ministry of Agriculture 2. MoH= Ministry of Health 3. MoE= Ministry of Environment; 4. One average, Semi-field trials range from 1-2 years; Full field trials are usually 3 years or longer; 5. Active Ingredient; 6. CILSS=Comité Inter-Etate pour la Lutte contre la Sécheresse au Sahel; 7. Lower bound is official timeline; upper bound is wait time given application backlog as of Feb 2019

Source: Industry and regulator interviews; Regulator websites and documentation; BCG Analysis

Thank you