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World Health Organization

Identifying Potential African Manufacturers of Amoxicillin DT and Beta-Lactam Products to Expand Access to Quality-Assured Products

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Presentation outline

- **Background**
- **Study Objectives and Study Questions**
- **Methodology**
- **Key findings**
  - Status of amoxicillin DT and penicillin manufacturers surveyed
  - Sources of amoxicillin API
  - GMP inspection
  - Technical capabilities
  - Regulatory challenges and firms' capacity to meet requirements
- **Recommendations for support to produce quality-assured amoxicillin DT**
- **Acknowledgments**

Background

Global Impact of Pneumonia on Children: Annually, around 800,000 children under five die worldwide due to pneumonia.

Amoxicillin as an Effective Treatment: Clinical evidence supports amoxicillin, particularly in its broad-spectrum antibiotic form, as effective for treating children with pneumonia.

Preferred Dosage Form - Amoxicillin DT: Among various forms of amoxicillin (syrup, dry powder for suspension, dispersible tablets), dispersible tablets (DT) are the most convenient for administration, shipping, and storage.

UNICEF and WHO Advocacy: The United Nations Children's Fund (UNICEF) advocates for amoxicillin DT, and the World Health Organization (WHO) included it in the expression of interest (EOI) list in 2015.

Challenges in Adoption in Africa: Despite global efforts, the adoption of amoxicillin DT for treating pneumonia in Africa has been slow.

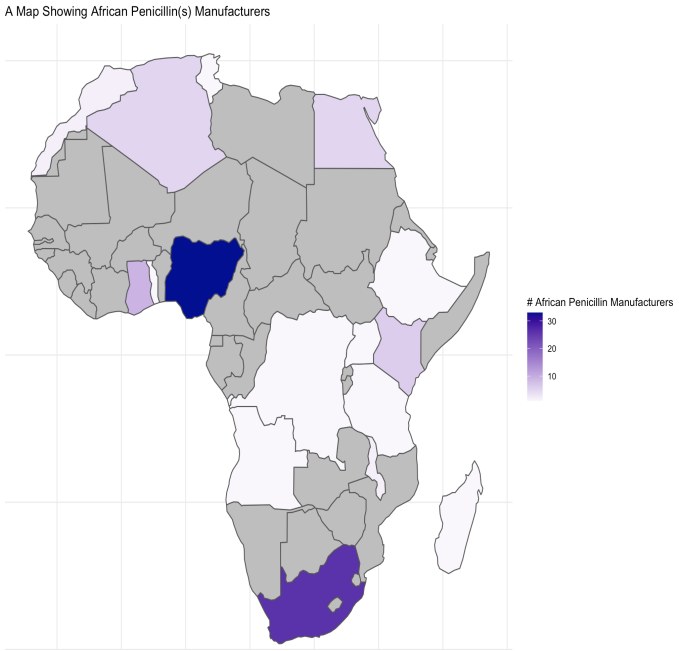
Study Objectives, and Study Questions

PQM+ partnered with Muhimbili University to conduct an analysis of amoxicillin suppliers in Africa.

The purpose of the study was to understand bottlenecks that prevent the manufacture of amoxicillin DT in Africa and to identify manufacturers and potential manufacturers who could increase future supplies of the drug.

1. Who are the current producers of amoxicillin (in any dosage form) in Africa?
2. What level of manufacturing capacity do these companies possess?
3. What are their technical strengths and weaknesses and understanding of good manufacturing practices (GMP) and regulatory requirements?
4. How do manufacturers manage the supply chain to ensure drug quality?

Methodology



Study Methodology Overview

1. Database Construction:

- Developed a comprehensive database of African manufacturers specializing in amoxicillin and penicillin-related products.

2. Semi-Structured Interviews:

- Conducted interviews with manufacturers to gather in-depth insights.

Database Inclusion Criteria:

Included both producers of amoxicillin DT and potential manufacturers (capable of producing beta-lactam products like penicillin and amoxicillin).

Data Collection Methods:

Internet searches with relevant phrases.

Sourced contact information from company websites.

Categorized firms as manufacturers of amoxicillin/penicillin and non-penicillin.

Additional Sources of Information:

Contacted the Federation of African Pharmaceutical Associations for member details.

Requested lists of manufacturers from national medicines regulatory authorities (NMRAs).

Database Composition:

Created a database of 540 pharmaceutical manufacturers.

Classified 96 firms (18%) as involved in amoxicillin/penicillin manufacturing

Survey Findings on Amoxicillin DT and Penicillin Manufacturers

Respondent Overview:

- 13 firms responded to the survey

Amoxicillin DT Manufacturers:

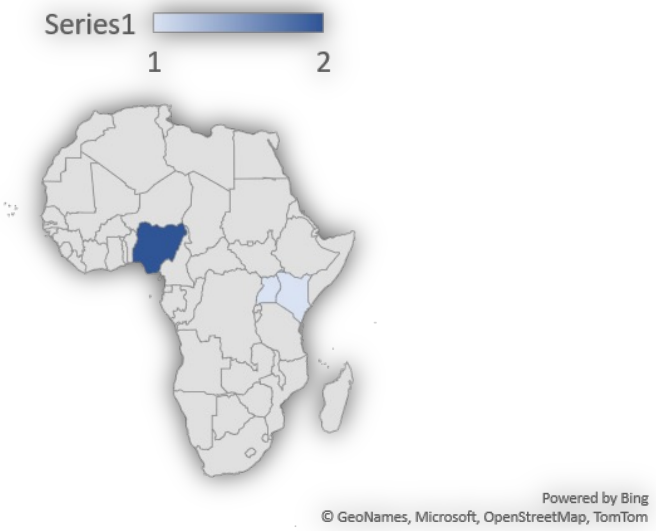
- 4 firms are actual manufacturers: 2 in Nigeria, 1 in Kenya, 1 in Uganda.

Firms in Developmental Stages:

- 2 firms (Kenya and Tanzania) in varying stages of generic formulation R&D.
- One company (Kenya) facing discoloration issues in stability studies.
- Anticipated development time for amoxicillin DT: 3-4 years.

Challenges and Progress:

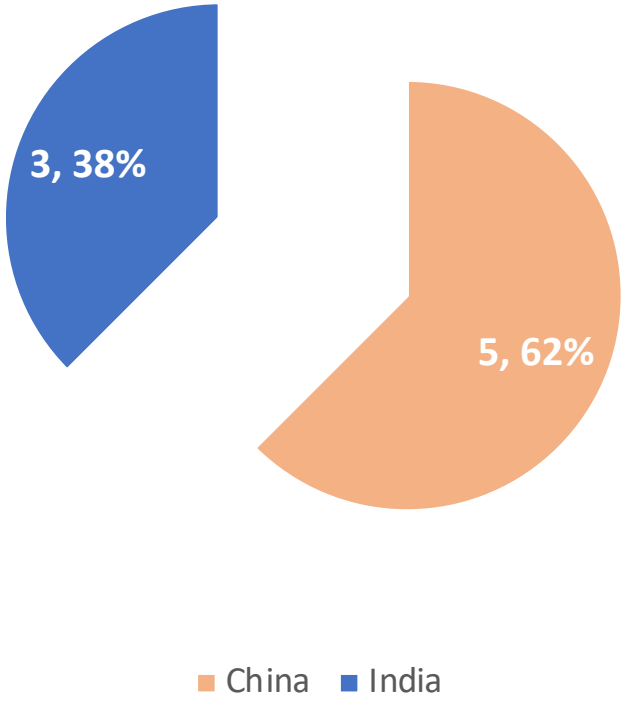
- Company 5 reported ongoing challenges with discoloration.
- Recent positive results in addressing color changes.
- Expressed need for support during formulation stage.

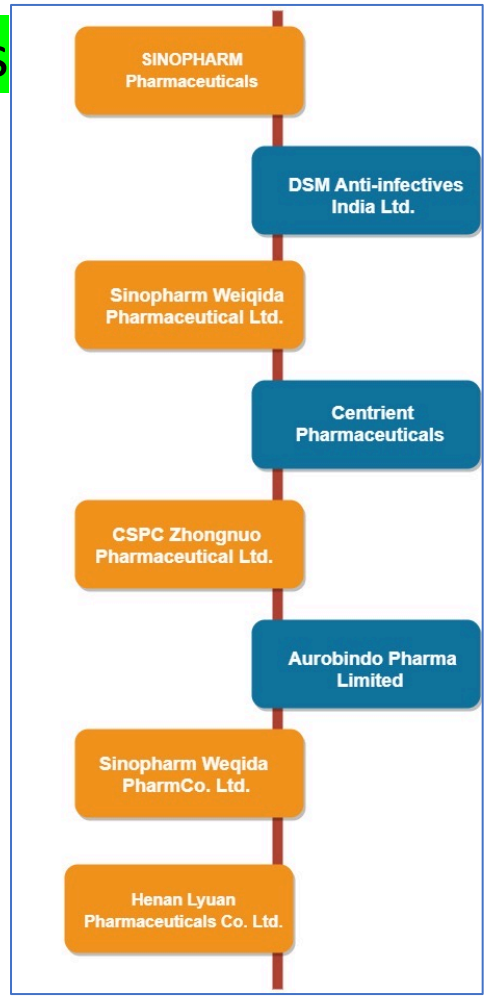


Source of API

- All pointed to approved manufacturers in either China or India Or
- source amoxicillin API from local vendors

Key sources & and proportions





GMP inspection status

Company	Country	Inspected by:	NRA certification status
		Amoxicillin DT manufacturers	
Company 1	Nigeria	National Agency for Food & Drug Administration and Control (NAFDAC) Nigeria , Pharmacy Council of Nigeria (PCN), and international procurement agencies	Certified
Company 2	Kenya	Pharmacy and Poison Board (PPB)-Kenya, Tanzania Medicines and Medical Devices Authority (TMDA)-Tanzania, NDA-Uganda, ZMRA-Zambia, and the NRAs of Burundi, Rwanda, and DRC	Certified
Company 3	Nigeria	NAFDAC and PC (UNIDO compliance)	Certified
Company 4	Uganda	NDA-Uganda, NRAs of Burundi and Rwanda, TMDA-Tanzania	Certified
		In development stage	
Company 5	Kenya	PPB-Kenya, TMDA-Tanzania, NDA-Uganda, NRAs of Burundi and Rwanda	Certified
Company 6	Tanzania	TMDA-Tanzania	Certified
		Potential producers	
Company 7	Kenya	PPB-Kenya	Certified
Company 8	Kenya	PPB-Kenya, TMDA-Tanzania, NDA-Uganda, ZMRA-Zambia, NRAs of Burundi, Rwanda, and DRC	Certified
Company 9	Nigeria	NAFDAC, PCN	Certified
Company 10	Nigeria	NAFDAC, PCN	Certified
Company 11	Tanzania	TMDA-Tanzania	Not Certified
Company 12	Nigeria	NAFDAC, PCN	Certified
Company 13	Zimbabwe	Botswana Medical Regulatory Authority (BoMRa)	Certified

Installed capacity versus utilization

Company 2 is only utilizing 15, 80, and 20 percent of its capacity to produce tablets, capsules, and bottles, respectively;

Company 3 uses only half its capacity to produce tablets; and

Company 4 uses only 75 percent of its capacity to manufacture tablets and 93 percent to produce capsules.

Company	Country	Investment, revenue, and annual growth rates
Amoxicillin DT manufacturers		
Company 1	Nigeria	-
Company 2	Kenya	Investment: US$30 m Annual revenue: US$25 m at CAGR 12%
Company 3	Nigeria	-
Company 4	Uganda	Investment: US$18 m Annual growth: 40%
In development stage		
Company 5	Kenya	Investment: US$18 m Annual growth: 10%
Company 6	Tanzania	Investment: US$5 m, Revenue: 20 billion Tsh. Annual growth: 10%
Potential producers		
Company 7	Kenya	Investment: over US$5 m
Company 8	Kenya	Annual growth: approx. 20%
Company 9[a]	Nigeria	1 billion capsules in 24-36 months
Company 10	Nigeria	Annual revenue: US$250,000 Annual growth: 20%
Company 11	Tanzania	Revenue: 7 billion Tsh.
Company 12	Nigeria	Revenue: 300-360 m Naira Annual growth: 100%
Company 13	Zimbabwe	Annual revenue: 12 m

Regulatory challenges and firms' capacity to meet requirements

Country	Challenges	Impact
Nigeria	Compilation of CTD dossier	Prolongs acquisition of marketing authorization
	Submission of API manufacturer information Inadequate documentation from API manufacturers Sourcing of quality API and its full characterization	Inability to provide data promptly
	High registration and annual retention fees	Increases costs generally and cost of products produced
	Long evaluation lead times	Delays in acquiring marketing authorization
	Lack of local capacity to perform bioequivalence studies Cost of performing BE studies	Delays in generating bioequivalence data
	Limited number of NRA assessors	Prolongs registration time
	Insufficient analytical equipment at the NRA	Inability to perform important tests on time
	Formulation optimization to make stable products	Prolongs development timelines
Kenya	Long registration time in Kenya Variable registration time in Tanzania Unable to produce bioequivalence data when requested (BCS Class 2 and Class 4)	Delays in acquiring marketing authorization
Uganda	Approval takes long due to compilation of CTD dossier	Delays in acquiring marketing authorization
Tanzania	Registration takes a long time due to delays in getting information from the API manufacturer	Delays in acquiring marketing authorization

Average lead times for registration of amoxicillin DT and related products

- Specific challenges associated with certain products or countries' specific regulatory requirements.
- Company 2 indicated that the requirement for bioequivalence data is common in Uganda, Tanzania, and Rwanda.

Company	Country	Average NRA lead times	Average lead times encountered
Amoxicillin DT manufacturers			
Company 1	Nigeria	3-4 months	-
Company 2	Kenya	Local: 9 months Foreign: 12 months	-
Company 3	Nigeria	3 months	Vary depending on how busy NRA is
Company 4	Uganda	Local: 3-12 months Foreign: 18-48 mths.	-
In development stage			
Company 5	Kenya	24-36 months	-
Company 6	Tanzania	Not yet submitted	-
Potential producers			
Company 7	Kenya	-	-
Company 8	Kenya	-	-
Company 9	Nigeria	3 months	6 Months
Company 10	Nigeria	-	-
Company 11	Tanzania	6 months	12 Months
Company 12	Nigeria	6-12 months	-
Company 13	Zimbabwe	15 months	-

Recommendations

01 Local Manufacturing and Protectionism

- Prioritize local products for market authorization
- Encourage and protect local manufacturing through government policies.
- Review the import prohibition list to reduce the influx of pharmaceutical products and expensive imported raw materials.

02 Taxes and Fees

- Advocate for import verification fees on finished products to protect against imports
- Address government tariffs on analytical equipment and value-added taxes on APIs hindering production
- Streamline importation requirements for raw materials through permits from government agencies.

03 Guaranteed Patronage

- Propose greater patronage with authorities guaranteeing purchases from local manufacturers
- Seek inclusion as a government supplier to increase production

04 Priority Medicines

- Prioritize regulatory reviews for MCH products, particularly amoxicillin DT on the Essential Medicines List (EML).

World Health Organization

Recommendations

05 Market Authorization

- Reduce registration times by increasing the pool of trained assessors and applying risk-based testing
- Abbreviate the application pathway for generic products with similar compositions
- Support local manufacturers in addressing review queries
- Implement regional harmonization approaches for the review process

06 Infrastructure and Technology Transfer

- Seek funding for machinery to increase production capacity
- Request specific hardware for manufacturing activities
- Advocate for affordable and reliable power, as well as incentives for infrastructural development.

07 Training

- All companies require training, including advanced technologies, formulation optimization, regulatory affairs, and GMP
- Emphasize the need for continuous training to meet international standards

08 Technical Assistance /Bioequivalence

- Address challenges in bioequivalence, especially for class II and class IV products.
- Seek support for document submission through CRO assistance.
- Advocate for the creation of local or regional capacity in bioequivalence
- Call for harmonized bioequivalence data accepted in the region

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Thank you!