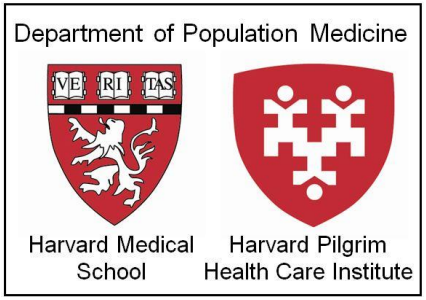
Sustainable Drug Seller Initiatives Partners



Survey of the Quality of Selected Essential Medicines in Districts Covered by the ADDO Program in Tanzania

Vicky Manyanga, PhD, Consultant

SDSI Dissemination Meeting
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Arusha

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Broad objective

- Develop a cost-efficient strategy for ongoing monitoring of the quality of products and services provided in the ADDOs

Specific objective

- Characterize the analytical quality of products available during the surveys in ADDOs and private pharmacies

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Sample criteria (1)

Type of Medicine	Rationale	Samples
Antibiotics		
Amoxicillin trihydrate capsules	Commonly used, high demand	40
Amoxicillin trihydrate suspension	Frequently prescribed, high demand	23
Co-trimoxazole suspension	High demand , low price, anti-opportunistic infection (OI)	23
Co-trimoxazole tablets	high demand , low price, anti- OI	36
Anti-Inflammatory/analgesic		
Paracetamol tablets	cheap, frequent use	24

Sample criteria (2)

Anti-malarials		
Quinine tablets (sulfate or bisulfate)	Previous experience with counterfeiting	30
Quinine injection (as dihydrochloride)	Previous experience with counterfeiting	12
Artemether + lumefantrine tablets	Expensive, high demand	39
Oxytocics		
Ergometrine injection (maleate)	Expensive, temperature and light stability concerns	16

Sample testing

- Pharm R&D lab
- 8 products analyzed using validated analytical techniques employing high performance thin layer chromatography
- One product had to undergo tier two testing:
    - Tier 1: a GPHF-Minilab® testing
    - Tier 2: LC prescribed in the International Pharmacopea

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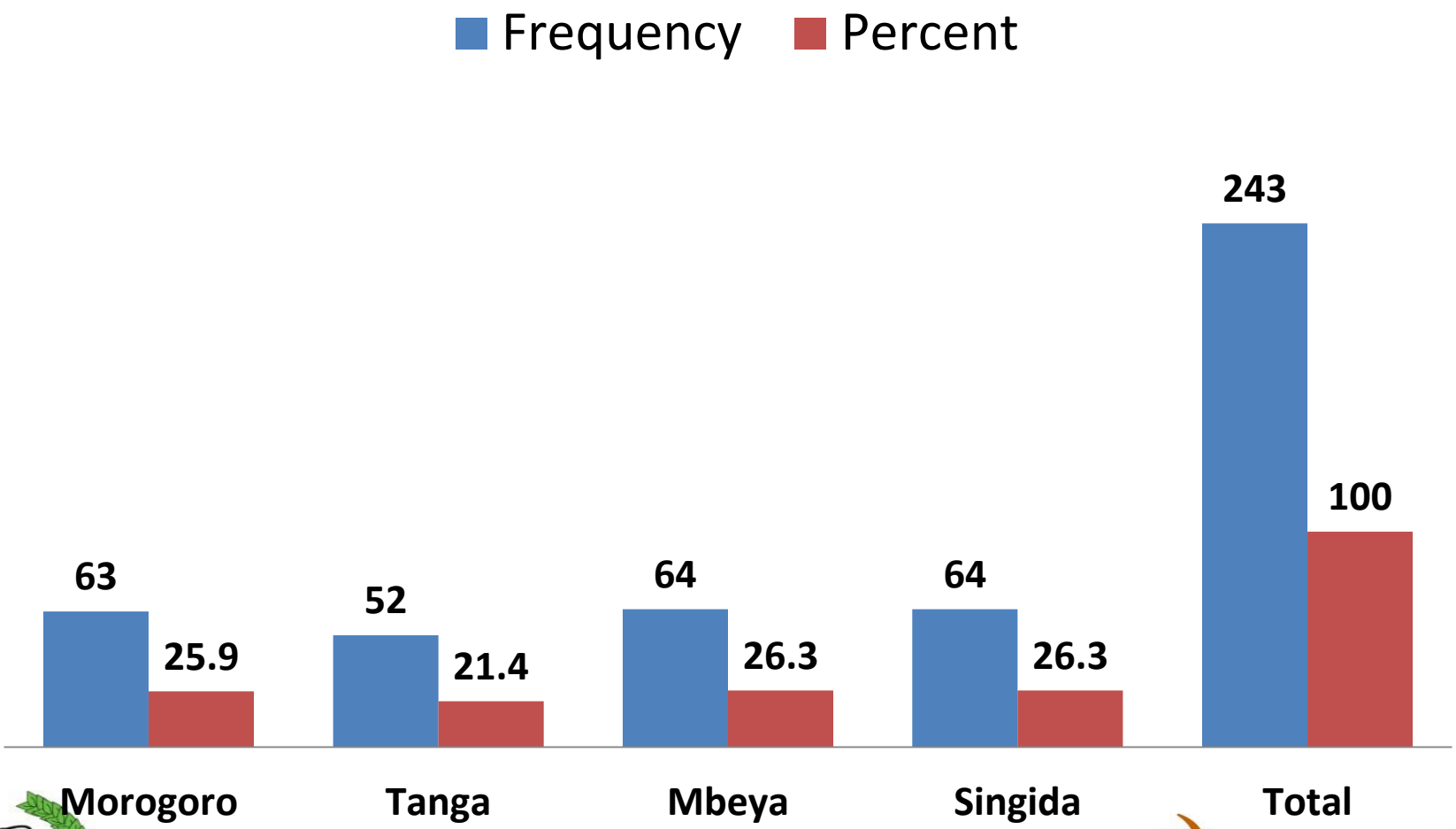
Number/percentage of samples collected in regions surveyed



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Distribution of samples by facility types and regions

Facility type	Morogoro (%)	Tanga (%)	Mbeya (%)	Singida (%)	Total (%)
ADDO	54 (22.2)	40 (16.5)	54 (22.2)	55 (22.6)	203 (83.5)
Pharmacy	9 (3.7)	12 (4.9)	10 (4.1)	9 (3.7)	40 (16.5)
Total	63 (25.9)	52 (21.4)	64 (26.3)	64 (26.3)	243 (100)

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Dosage forms of samples by facility types

		Facility type		Total
		ADDO Shop	Pharmacy	
Dosage form Type	Tablets	111	16	127
	Injections	21	7	28
	Syrups	6	2	8
	Suspensions	25	7	32
	Dry granules	5	3	8
	Capsules	35	5	40
Total		203	40	243

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Physical inspection (1)

- Appearance
- Packaging
- Labeling
- Expiry

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Physical inspection (2)

- **All samples passed except ergometrine**

- Color variations of ergometrine samples from same manufacturers collected from different locations
- Darker samples indicate less active ingredient

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Disintegration test

98.8% of the samples passed the test; two paracetamol samples did not pass (1.2%)

			Compliance		Total
			Yes	No	
Average disintegration Time	Less than 15 min	Count	159	0	159
		% of Total	98.1%	0.0%	98.1%
	Between 16 and 30 min	Count	0	2	2
		% of Total	0.0%	1.2%	1.9%
Total		Count	161	2	161
		% of Total	99.4%	1.2.%	100.0%

ALU Minilab thin-layer chromatography outcome

- Of 38 artemether-lumefantrine samples, 7 (18.4 %) failed or gave inconclusive drug content test results
- The inconclusive samples were sent for confirmatory test using *International Pharmacopeia Monograph* for ALU
- All 7 doubtful samples passed the confirmatory test

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Active ingredient analysis

- 16 (6.6%) samples did not conform to quality standard for active ingredient:
  - Ergometrine (100% of sample)
  - Other (methylergometrine)
- Ergometrine results could be anticipated

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Assay values of ergometrine by region

Ergometrine assay %

Region	Morogoro	Mbeya	Tanga	Singida
Sample 1	43.41	65.97	51.71	69.65
Sample 2	29.90	65.95	74.43	46.17
Sample 3	15.56	62.63	31.83	-
Sample 4	82.67	57.17	63.99	-
Sample 5	-	85.90	-	-
Sample 6	-	72.87	-	-
Average	**42.90**	**68.40**	**55.50**	**57.90**

Findings agree with Hogerzeil et al. that when ***unrefrigerated and exposed to light,*** ergometrine may lose up to 20% of its potency per month

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Ergometrine assay failure by facility

- 13/13 ergometrine samples from ADDOs failed
  - ADDOs are not required to have refrigerators
- 3/3 ergometrine samples from pharmacies failed
  - Likely that pharmacies were not following good storage practices

Failure rates by facility type

- Failure rate in ADDO samples: 6.4% (13/203)
- Failure rate in pharmacy samples: 7.5% (3/40)

The Z-Score is -0.635. The p-value is 0.52218.

- No statistically significant difference ($p<0.05$) between ADDO and pharmacy failure rates
- **Overall failure rate: 6.6% (16/243)**

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Summary

- Risk-based assessment focused on:
  - Identity and content
  - Quality attributes like dissolution test and test for related substances were not performed
- Large number of samples of 9 different medicines collected from ADDOs and pharmacies met quality standards (92.6%)
- Two paracetamol samples failed disintegration test
- All ergometrine injection samples failed the assay; other heat-sensitive products to investigate?
- Study gives confidence in the **right medication** and **right amount**

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Aknowledgement

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- ADDOs
- MSH