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Workshop

Drug lifecycle control in Subsaharan Africa

From production to responsible safe disposal and elimination in wastewater treatment plants

(Med4Africa)

PROFICIENCY TESTING SCHEMES FOR PHARMACEUTICAL QUALITY CONTROL LABORATORIES

EAST AFRICAN REGIONAL EXPERIENCE

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Drug Lifecycle Control in Subsaharan Africa
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OUTLINE

- Pharmaceutical QC laboratories **quality** assessment
- PT schemes provision
- EAC PT schemes experience
  - Design of the PT scheme
  - Steps during execution of the PT scheme
  - Results obtained so far..
  - Challenges
- Conclusion

PHARMACEUTICAL QC LABORATORIES QUALITY ASSESSMENT

LABORATORY QUALITY ASSESSMENT

Quality is....

- Invisible when GOOD
- Impossible to ignore when BAD

LABORATORY QUALITY ASSESSMENT

- **Quality assessment** (QA) is the evaluation of results obtained in the laboratory using known standards and proficiency panels in order to validate QC and QA programmes.

- QA can be
  - Internal (IQA)- Lab staff perform verification(internal audit)
  - External (EQA) – Assessment done by an agency outside lab

External quality assessment (EQA)

- Involves a comparison of the lab's testing and analysis performance to another similar lab or reference lab.

- A system of **objectively** checking laboratory results by means of an external agency

- The main objective being the establishment of **trueness** of lab results

External quality assessment (EQA)

Can be carried out through

1. **Proficiency testing (PT)**: EQA organizer provide identical material to participant labs for testing

2. **Re-testing/Rechecking**: Participant lab send material to EQA organiser

3. **On-site assessment:** periodic site visits to systematic assessment of lab practices

Benefits of EQA

1. Method validation
2. Comparing of results with other laboratories
3. Testing problem identification
4. Accreditation requirement compliance eg ISO/IEC 17025
5. Credibility

PROFICIENCY TESTING SCHEMES (PTS)

PROFICIENCY TESTING SCHEMES

- It is evaluation of participant lab performance against pre-established criteria by means of interlaboratory comparisons.

- There are three types of laboratory examination
  i. Quantitative tests: statistical analysis
  ii. Qualitative tests: Descriptive, statistical analysis not necessary
  iii. Interpretive : "PT item" is the test result (descriptive morphology)

PROFICIENCY TESTING SCHEMES

Uses of PT scheme results

- Accreditation bodies
- Other parties eg customers, subcontracting mandate
- Regulatory bodies

PROFICIENCY TESTING SCHEMES

Internal benefits of Interlab participation:

- Determination of the performance of individual labs for specific tests or measurements
- Helps to monitor labs' continuing performance
- Identify problems in labs and initiate remedial actions through root cause analysis

EAC PT SCHEME EXPERIENCE

DESIGN OF EAC PT SCHEME

- In an effort to build regional capacity for providing PT services in the pharmaceutical sector, the EAC Secretariat in cooperation with PTB, the German Metrology Institute, started to support Pharma R&D laboratory, to become a regional PT provider for pharmaceutical testing laboratories - 2013.

- Why MUHAS Pharm R&D?
  - Has capacity to perform Formulation development and Drug Testing
  - Is ISO/IEC 17043:2010 accredited since 2020!

DESIGN OF EAC PT SCHEME

- Planning and execution :ISO/IEC 17043:2010 Conformity requirement

- Statistical evaluation as per requirement ISO/IEC 13528
  - Determination of assigned value: consensus value from participants with target RSD set at 2.5 %.
  - Z-score –biased estimate of the results (mean value, assigned value and target RSD) + kernel density
    - <2 = satisfactory; 2-3 = questionable; >3 = non satisfactory
  - Cochran's test - checking for higher RSD
  - Grubbs' test – checking for outlying means

STEPS IN EAC PT SCHEME EXECUTION: ISO/IEC 17043:2010 & ISO/IEC 13528

1. Preparation of PT material and protocol
   - PT provider: homogeneity testing
2. Distribution of PT material and protocol to participants
   - PT provider: stability testing
   - Participants: sample analysis
3. Data analysis
   - Participants: send raw data
   - PT provider: statistical analysis
4. Preliminary PT report
5. Evaluation workshop: PT provider and participants
6. FINAL PT report

EAC –PT SCHEME ROUNDS

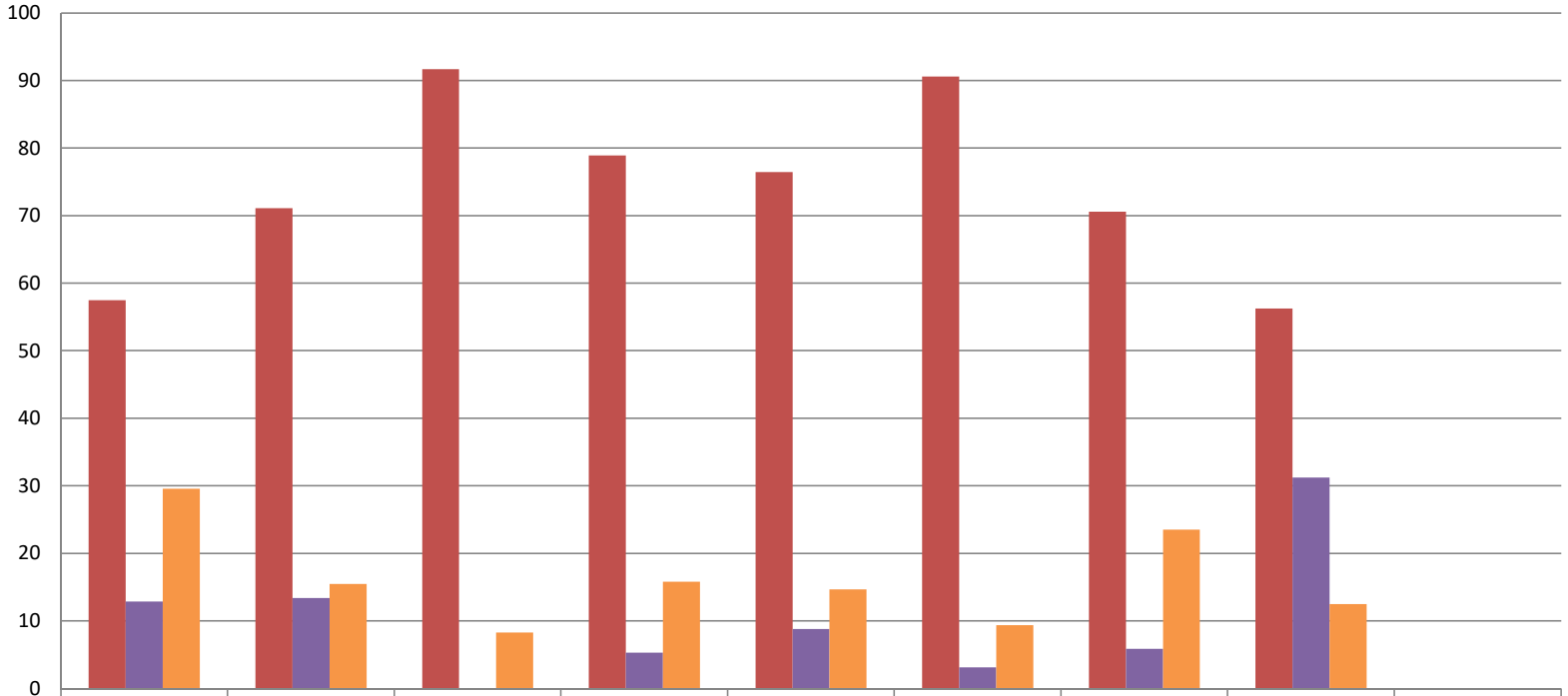
Round	Test substance /strengths	Test Parameter	Method	Number of Lab	
				Registered	Responded
4	Paracetamol • (S1-600mg, • S2-400mg and • S3- 500mg)	Assay	UV-Absorbance	20	16
5	Quinine • S1-360mg, • S2-195mg and • S3- 300mg)	Assay	Non-Aqueous Titration	16	15
6	Albendazole • S1-400mg	Assay	HPLC	15	12
7	Albendazole • S1-400mg	Dissolution	UV		
8	Metronidazole • S1-200 mg	Assay	Own Method	18	18
9	Co-trimoxazole • S1-480 mg	Assay and Dissolution	Own Method	22	17/16
10	Ciprofloxacin • S1-500 mg	Assay and Dissolution	Own method	36	17

REGIONAL DISTRIBUTION OF PARTICIPANTS

R/N	TANZANIA	KENYA	UGANDA	BURUNDI	RWANDA	OTHERS
4	6	2	4	1	2	3 (Congo DRC, Eritrea, Ethiopia)
5	6	4	1	1	2	1 (Ethiopia)
6	5	2	2	-	2	-
8	6	6	2	-	2	3 (2 Ethiopia and 1 Seychelles)
9	6	4	2	-	2	3 (1 Ethiopea, 1 Seychelles and 1 **Germany)**
10	5	2	2	-	1	7 (1 Congo DRC, 1 Seychelles, 2 Nigeria, 1 Burkina Fasso, 1 Zimbabwe and 1 Mali)

These labs are from Academia, R&D labs, Pharm industry, NRA, NBS

EAC PT SCHEMES RESULTS



	Round 4	Round 5	Round 6	Round 8	Round 9 A	Round 9 D	Round 10 A	Round 10 D
Satisfactory	57.5	71.1	91.7	78.95	76.47	90.63	70.59	56.25
Questionable	12.9	13.4	0	5.3	8.82	3.13	5.88	31.25
Nonsatisfactory	29.6	15.5	8.3	15.8	14.71	9.38	23.53	12.50

EXAMPLE

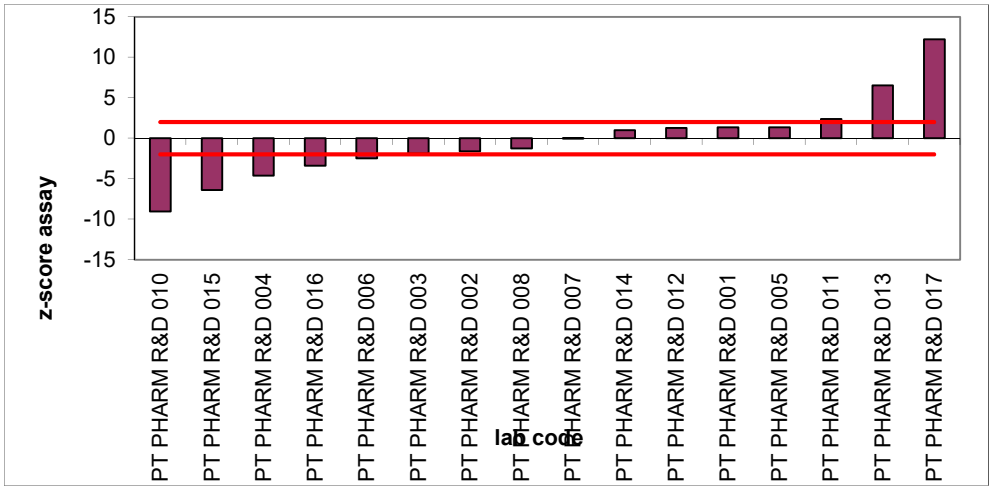
ROUND 10: ASSAY AND DISSOLUTION TESTING OF CIPROFLOXACIN TABLETS (500 mg)

Round 10: Procedure 1 - Scoring for the laboratories for assay of Ciprofloxacin sample

Assigned value		**483.45**	**Preliminary lab value**			**475.48**
Target RSD		**2.5**				
lab code	**result 1**	**result 2**	**result 3**	**mean**	**Z-score**	**Assessment**
PT PHARM R&D 001	486.92	493.22	483.92	488.02	0.4	s
PT PHARM R&D 002	502.36	500.64	501.08	501.36	1.5	s
PT PHARM R&D 003	454.00	452.40	452.80	453.07	-2.5	q
PT PHARM R&D 004	480.55	475.60	485.10	480.42	-0.3	s
PT PHARM R&D 005	490.40	490.00	490.00	490.13	0.6	s
PT PHARM R&D 006	500.70	500.60	501.00	500.77	1.4	s
PT PHARM R&D 007	471.80	470.32	470.56	470.89	-1.0	s
PT PHARM R&D 008	465.87	467.90	466.51	466.76	-1.4	s
PT PHARM R&D 009	502.34	505.86	504.11	504.10	1.7	s
PT PHARM R&D 010	384.90	386.50	384.50	385.30	-8.1	n
PT PHARM R&D 011	473.37	477.07	474.63	475.02	-0.7	s
PT PHARM R&D 012	478.16	477.84	478.48	478.16	-0.4	s
PT PHARM R&D 013	615.00	609.00	612.00	612.00	10.6	n
PT PHARM R&D 014	74.68	74.66	74.68	74.67	-33.8	n
PT PHARM R&D 015	481.83	480.46	480.60	480.96	-0.2	s
PT PHARM R&D 016	494.96	494.28	496.27	495.17	1.0	s
PT PHARM R&D 017	558.90	565.71	549.45	558.02	6.2	n
Including all results			Mean	465.58		
			STDEV	110.71		
			RSD	23.78		
			n	17		
Excluding outliers with Cochran and Grubb's Test			Mean	483.45		
			STDEV	15.07		
			RSD	3.12		
			n	13		

Round 10: Procedure 1 - Scoring for the laboratories for dissolution of Ciprofloxacin sample

			Assigned value			**119.4**	**Preliminary lab value**			**118.4**
			Target RSD			**2.5**				
lab code		**result 1**	**result 2**	**result 3**	**result 4**	**result 5**	**result 6**	**mean**	**Z-score**	**Assessment**
PT PHARM R&D 001		123.30	123.50	123.10	123.30	123.50	123.30	123.30	1.1	s
PT PHARM R&D 002		116.38	120.73	110.33	107.60	116.00	119.40	116.38	-1.2	s
PT PHARM R&D 003		112.80	112.60	112.30	112.80	112.60	112.30	112.80	-1.9	s
PT PHARM R&D 004		106.33	108.78	103.58	102.98	102.98	104.70	106.33	-4.0	n
PT PHARM R&D 005		119.80	135.00	120.40	128.00	122.90	124.00	119.80	1.6	s
PT PHARM R&D 006		111.70	111.50	112.00	111.80	111.70	112.00	111.70	-2.1	q
PT PHARM R&D 007		116.53	119.11	119.72	125.94	113.04	120.48	116.53	0.0	s
PT PHARM R&D 008		114.04	115.30	110.15	119.87	118.25	115.49	114.04	-1.0	s
PT PHARM R&D 010		92.60	92.90	91.60	92.30	91.90	92.50	92.60	-7.5	n
PT PHARM R&D 011		122.00	126.00	125.00	128.00	127.00	130.00	122.00	2.0	S
PT PHARM R&D 012		122.94	120.82	120.62	123.64	124.04	124.25	122.94	1.0	S
PT PHARM R&D 013		138.00	139.00	139.00	139.00	138.00	139.00	138.00	5.4	n
PT PHARM R&D 014		121.00	123.00	121.00	123.00	123.00	122.00	121.00	0.8	s
PT PHARM R&D 015		100.17	100.91	99.16	100.27	100.12	100.97	100.17	-5.3	n
PT PHARM R&D 016		109.29	110.41	107.37	109.77	109.77	109.13	109.29	-2.8	q
PT PHARM R&D 017		150.98	148.74	155.19	155.35	164.44	158.89	150.98	10.2	n
			Including all results				Mean	118.40		
							STDEV	14.90		
							RSD	12.59		
							n	16		
			Excluding outliers with Cochran and Grubb's Test				Mean	119.40		
							STDEV	5.29		
							RSD	4.44		
							n	09		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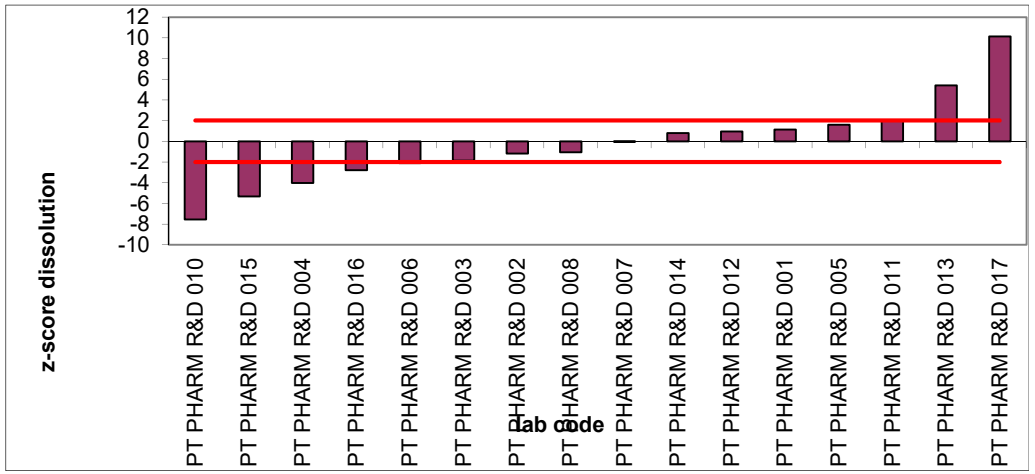
lab code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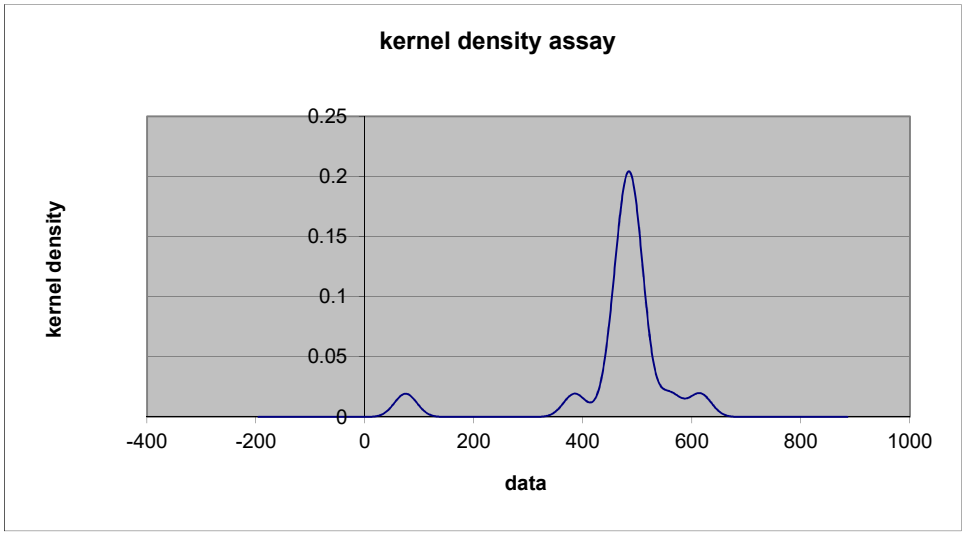
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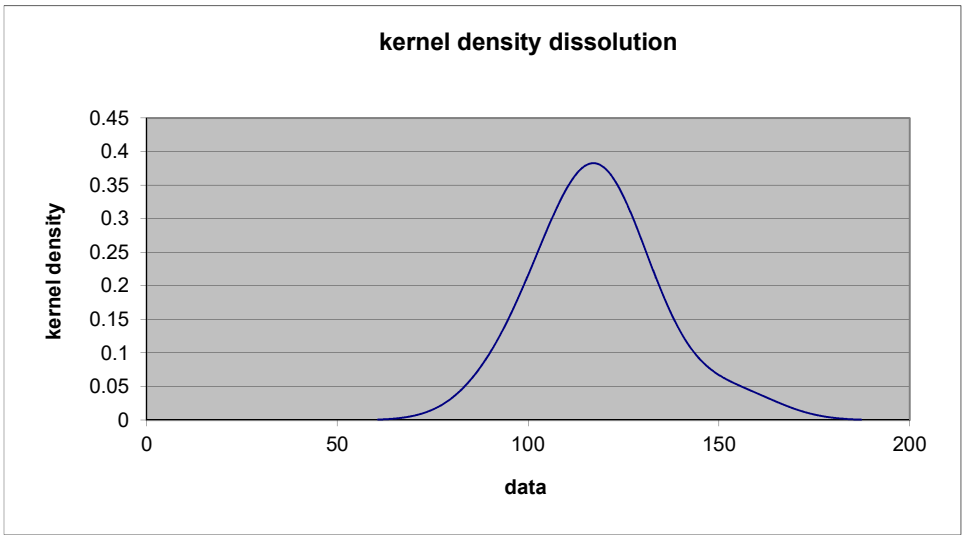
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data

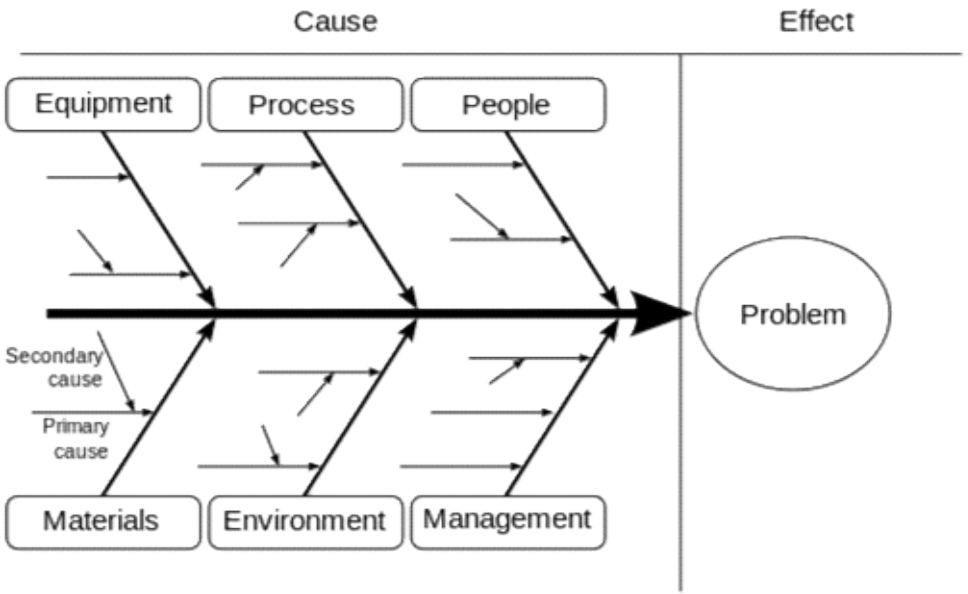
Evaluation and training workshop

- Preliminary PT report is sent to each participating laboratory
- Poor performing lab need to do investigation/root cause analysis
- Feedback evaluation workshop and training

Certificate of participation and successful completion

Possible causes of deviations

- Each participant with Z-score ≥ 2 need to perform a root cause analysis.



Possible source of errors

- Weighing errors of samples
- Dilution errors.
- Variability of response within injections.
- Use of uncalibrated HPLC, UV-VIS, etc

Comments sent by the laboratories with the results

Laboratory 012 comments on the use of mg/tab that was not included during raw results submitted before instead they submit % of the content hence recalculation was performed and included in the report.

Laboratory 009, comments on the dissolution results were not submitted because the laboratory does not perform dissolution tests as they don't have the dissolution tester.

CHALLENGES OF PT PROVISION

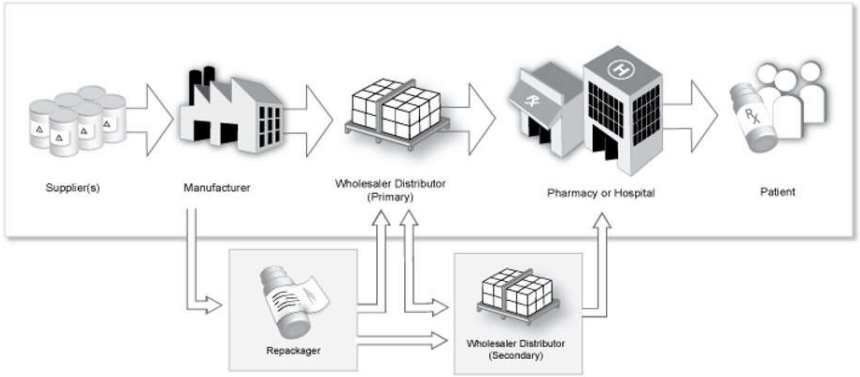
- Lack of consistency of participants: difficult to establish performance trend of individual labs

- Lack of potential funders to sustain the project (not budgeted in labs)

QUALITY LABORATORY IS MANDATORY

Right result

- First time
- Every time



This is essential because

- Reduce morbidity (detect substandard /falsified med. products with wrong amount of API)
- Reduce mortality (toxic SF)
- Reduce economic loss
- Reduce unnecessary repetition of experiments → protect the environment

CONCLUSION

- Six locally organized EAC PT scheme within pharma testing Labs
- Participation is good but variable with laboratories
- Participants are from within as well as outside EAC region
- This external quality assurance tool provides a competence assessment opportunity for the testing labs towards quality system improvement eg attaining ISO/IEC 17025 accreditation, improving lab confidence
- The experience gained was useful and had allowed Pharm R&D Lab attaining ISO/IEC 17043:2010 accreditation. Hence, more labs in Africa are encouraged to engage in this locally available PT scheme

AKNOWLEDGEMENT

- MUHAS Pharm R&D laboratory team (Kaale, Shedafa, Prosper+, Ruth, Maro, Edson)
- PTB
- EAC secretariat
- ALL Participants from testing labs
- MUHAS

Interested to participate in EAC PT Scheme?

Visit our website

https://pharmrd.muhas.ac.tz/proficiencyregister

THANKS FOR LISTERNING