1. Introduction

Tanzania Medicines and Medical Devices Authority (TMDA) is a semi-autonomous agency under the Ministry of Health established under section 4(1) of the Tanzania Medicines and Medical Devices Act, Cap 219.

Due to the above-mentioned Act, TMDA is mandated to regulate quality, safety and effectiveness of medicines (human, veterinary and herbal), vaccines including other biological, medical devices, diagnostics and tobacco products.

During the course of regulating quality, safety and efficacy of medicines, TMDA receives and evaluates applications for registration of medicinal products in Tanzania. For the product to be registered, manufacturing facility of the product applied for registration must be inspected and deemed GMP Compliant by TMDA hence GMP status of the facility is among enabler of the medicine's registration process.

Before manufacturing facility is inspected, TMDA receives applications and conducts GMP Inspection to verify compliance of the facility with applicable national and international standards. This is in accordance with section 51 of the Tanzania Medicines and Medical Devices Act, Cap 219.

In the financial year, 2021-2022 TMDA set aside funds for inspection to conduct GMP inspections of 13 domestic pharmaceutical manufacturing facilities. During this year, TMDA was able to inspect seven (7) domestic pharmaceutical manufacturing facilities which account 53.84% of the target.

The inspection was conducted by seven (7) teams comprising of one (1) Lead GMP Inspector and one (1) Co-Inspector as per the SOP and appointment letters issued as per requirement. Some teams had trainee inspectors in order to impart them with GMP inspection knowledge and techniques.

TMDA had realized the importance of analyzing the inspection findings and come up with the recommendations for continuous improvement of GMP inspection process. This assure products manufactured by domestic manufacturers meet GMP standards as a result medicines of good quality, safe and efficacious are authorized to circulate in the Tanzania market.

2. Objectives

The main objective of analyzing GMP inspection findings is to assess internal systems and realize risk factors for some facilities which did not comply with the GMP requirements. High risk factors shall be shared among the TMDA inspectors or being captured during in house GMP training. Such risk factors shall include but not limited to fraud, misrepresentation or falsification of products or data.

3. Scope

The analysis of the inspection findings shall include domestic inspected facilities which engaged in manufacturing of human and veterinary medicinal products marketed or intended to be marketed in Tanzania mainland.

4. Methodology

The methodology applied was systematic analysis of both qualitative and quantitative data. In the aspect of qualitative, critical observations were categorized into two groups namely site-specific observations and QMS related observations. All these observations were quantified and analyzed through graphical representation.

Number of facilities inspected in a specified pharmaceutical quality system and their percentage compliance was systematically analyzed and represented through graphical system. Data were grouped and analyzed based on critical, major or minor non conformances observed on a particular inspection.

5. Tools for assessment and evaluation

GMP inspection reports for all facilities inspected in the specified period which had critical noncompliance observations and the list of inspected facilities was used during the assessment and analysis.

6. GMP reference materials

a. Compendium of Good Manufacturing Practices (GMP) Technical Documents for Harmonization of Medicines Regulation in the East African Community, 2014
b. Good Manufacturing Practice Guidelines for Veterinary Medicinal Products, 2016
c. TMDA (2018) Good Manufacturing Practices Enforcement Regulations, GN No.295.

7. List of facilities inspected

The list of pharmaceutical manufacturing plants inspected and their compliance status have been indicated in **Annex 1.**

8. Key quality elements

The assessment was based on seventeen (17) key quality elements as laid out in the EAC GMP Compendium, 2014. These key quality elements listed below are also part of WHO GMP Guidelines:

a. Quality assurance
b. Utilities impacting Good Manufacturing Practices (GMP)
c. Sanitation and hygiene
d. Qualification and validation
e. Complaints
f. Product recalls
g. Contract production and analysis
h. Self-inspection and quality audits
i. Personnel
j. Training
k. Personal hygiene
l. Premises
m. Equipment

n. Materials

o. Documentation

p. Good practices in production including biological, sterile and herbal medicines

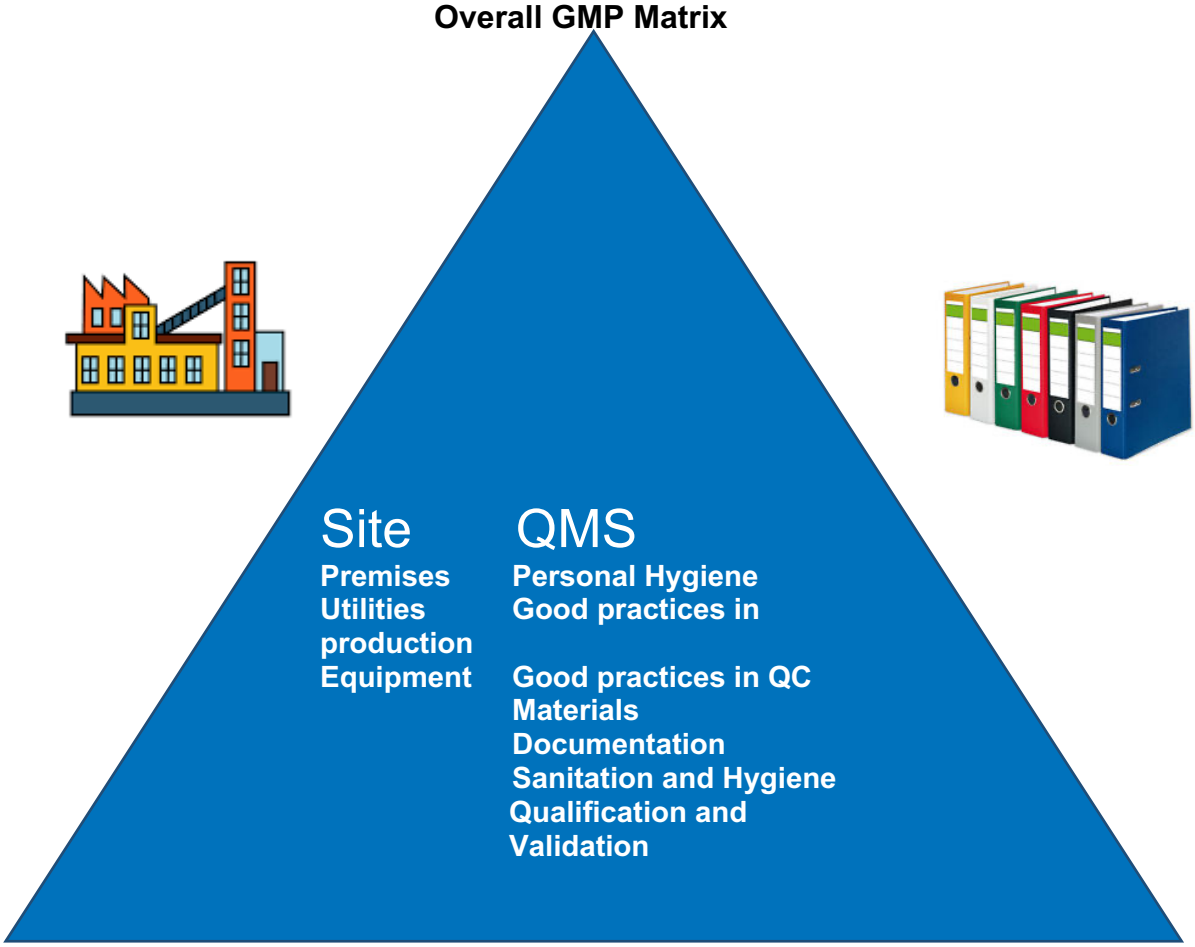
q. Good practices in quality control

The key quality elements have been assigned to two dimensions of compliance, namely 'Site' and 'QMS'. The term Site mainly refers here to physical entities which are components of the pharmaceutical manufacturing industry and comprises all elements related to premises, utilities and equipment; whereas the term QMS refers to procedures, processes, and resources needed to implement a quality management, this includes Quality Assurance, Complaints, Product Recalls, Contract production/analysis, Self-inspection and Audits, Personnel, Training, Personal Hygiene, Documentation, Good practices in production and Good practices in quality control.

However, a clear distinction is not possible for five (5) key quality elements, notably Sanitation and Hygiene, Qualification and validation, Materials, Good practices in production and good practices in quality control. These five (5) keys quality elements have been assigned to QMS for a matter of convenience and because they all focused on procedures rather than facilities or instrument. The physical parts have been already taken into account in the Site related key quality elements. Nevertheless, there is a correlation between QMS and Site, and the quality of a finished pharmaceutical product can only be assured through compliance of both the Site and QMS elements to GMP standards.

Figure 1 illustrates which elements are mainly assigned to Site and QMS

Overall GMP Matrix



9. Results and evaluation

In this period (2021/22), seven (7) facilities were inspected, four (4) facilities which is equivalent to 57.14% complied with EAC GMP guidelines standards, three (3) facilities did not comply. Furthermore, results portray that most of the major observations noted during the GMP inspection were from the utilities impacting GMP (15.79%), Premises (13.76%), Qualification and Validation (13.16%) and Quality Assurance (13.16%). Summaries of the results are also shown under the table below;

Table 1: Summarizes the results for GMP inspections

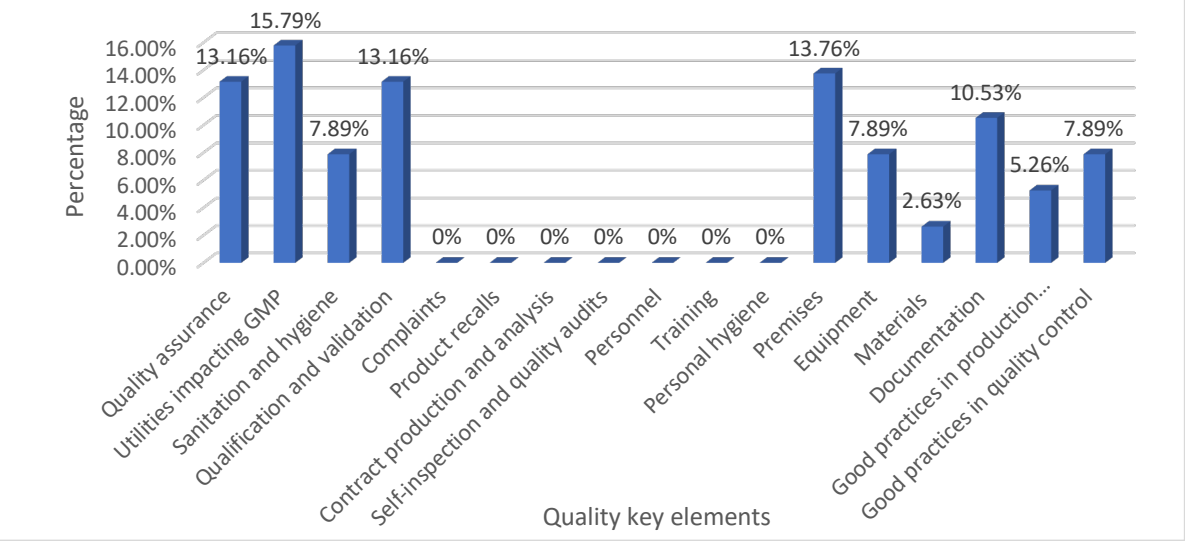
SN	No. inspected	Passed	Failed	% Compliance
1.	7	4	3	57.14%

Table 2: Summarizes the results of the major observations for GMP inspection

SN	Quality key elements	Frequency of major NCs	Percentage
1.	Quality assurance	5	13.16%
2.	Utilities impacting GMP	6	15.79%
3.	Sanitation and hygiene	3	7.89%
4.	Qualification and validation	5	13.16%
5.	Complaints	0	0%
6.	Product recalls	0	0%
7.	Contract production and analysis	0	0%
8.	Self-inspection and quality audits	0	0%
9.	Personnel	0	0%
10.	Training	0	0%
11.	Personal hygiene	0	0%
12.	Premises	6	13.76%
13.	Equipment	3	7.89%
14.	Materials	1	2.63%
15.	Documentation	4	10.53%

SN	Quality key elements	Frequency of major NCs	Percentage
16.	Good practices in production including biological, sterile and herbal medicines	2	5.26%
17.	Good practices in quality control	3	7.89%
18.	**TOTAL**	**43**	**100.00%**

Graphical presentation of results of the major observations for GMP inspection



10. Discussion of the results

Graphs above presents that out of 7 facilities inspected, 4 (57.14%) complied with the GMP requirements while 3 (42.86%) facilities did not comply with the GMP requirements. However, facilities which did not comply had major observations that were required to be readdressed and submit CAPA for assessment.

The percentage compliance of all inspected facilities indicates the importance of conducting GMP inspection before registering products and continual reassessing of GMP of the manufacturing facilities at least once in a year as required EAC GMP guidelines Part 1 section 6.1 due to the fact that 42.86 % of all inspected facilities have repeated major non-conformances observations which puts a question mark on the reliability of the firm's quality assurance systems.

Table 2 together with graphical presentation of results above portray that most of the major observations noted during the GMP inspection were from the utilities impacting GMP (15.79%), Premises (13.76%), Qualification and Validation (13.16%) and Quality Assurance (13.16%).

These indicated that utilities and premises were not designed as per GMP requirements for manufacturing of pharmaceutical products. Similarly lack of quality assurance system, qualification and validation especially validation and verification of the analytical methods was noted as a risk factor during the GMP inspection.

Nevertheless, most of the facilities inspected had improved level of compliance for personnel with relevant qualification, training and experience.

11. Conclusion

Analysis of the GMP inspection reports for the facilities inspected in the financial year 2021-2022 has been the baseline to measure the continuous improvement of such facilities and capacity of the Authority to inspect them.

The inspection percentage achieved indicating the commitment of the Management to conduct GMP inspection as a pre requisite requirement for registration of medicinal products in Tanzania and continual improvement of pharmaceuticals manufacturing quality systems for the purpose of ensuring that quality is built into the products and not tested at the end.

12. Annexes

12.1 Annexure I: List of pharmaceutical manufacturing plants inspected and their compliance status

Na.	Name of the facility	Date of GMP inspection	GMP Status
1.	Shelys Pharmaceuticals Limited	19th – 20th August, 2021	GMP Compliant
2.	Prince Pharmaceuticals Ltd	28th & 29th June, 2022	GMP Compliant
3.	Kairuki Pharmaceuticals Industry Ltd	17th & 18th March, 2022	GMP Compliant
4.	Hester Biosciences Africa Ltd	26th & 27th January, 2022	GMP Compliant
5.	Afravet/Novel Vaccines and Biological Company Ltd (NOVABI)	16th & 17th June, 2022	Pending CAPA
6.	TVI (Tanzania Vaccines Industries)	20th -21st June, 2022	Pending CAPA
7.	Biotec Laboratories Ltd	02nd March, 2022	Pending CAPA