TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA
Tanzania Medicines & Medical Devices Authority

GOOD MANUFACTURING PRACTICES (GMP) ANALYSIS REPORT FOR FACILITIES INSPECTED BY TMDA IN THE FINANCIAL YEAR 2019/2020

1. Introduction

Tanzania Medicines and Medical Devices Authority (TMDA) is an Executive Agency under the Ministry of Health, responsible for protecting and promoting public health by ensuring quality, safety and effectiveness of medicines and medical devices including invitro diagnostics. TMDA (formerly known as Tanzania Food and Drugs Authority) was established in 2003 after enactment by the Parliament of the Tanzania Food, Drugs and Cosmetics Act, Cap 219.

The Authority execute its responsibilities by regulating medicines (human, veterinary and herbal) and medical devices by ensuring their quality, safety and efficacy through registration of the products. During registration process, TMDA evaluates medicines dossiers along with inspection of the manufacturing facilities to verify their compliance to East Africa GMP Compendium on Good Manufacturing Practices, 2014 as required by section 51 of the Tanzania Food, Drugs and Cosmetics Act, Cap 219. Inspection is conducted based on the risk matrix prescribed in the procedure number TMDA/DMC/MCIE/SOP/007 for preparation for GMP inspection of pharmaceutical manufacturing facilities.

In the financial year, 2019/20 the Authority planned to conduct inspection of 135 overseas pharmaceutical manufacturing facilities. 77 of overseas pharmaceutical manufacturing facilities equivalent to 57% of the number of facilities initially planned, were inspected. The low number of facilities inspected was attributed by the travel

restrictions due to Covid-19 pandemic, therefore it was not possible to inspect the overseas medicines manufacturing facilities. The inspections involved a total of 40 inspectors who formed 20 teams to inspect the facilities located in Africa, Asia and Europe. Teams were composed of lead inspector and co-inspector appointed by the Director General as per procedure for preparation of GMP inspections. Inspection reports including observations and findings of inspections were reviewed by the GMP technical committee composed of DMC and managers together with the respective inspectors before approval and dispatch to the applicants.

This report provides analysis of the findings observed during inspections and recommendations for continuous improvement, including training of inspectors on the areas found with most critical non-compliances so as to assure the quality, safety and efficacy of the medicines circulating in the Tanzania market.

2. Objectives

2.1. General Objective

To assess inspection outcome 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 our in-house GMP trainings. Such risk factors shall include but not limited to fraud, misrepresentation or falsification of products or data.

2.2. Specific Objectives

i. To calculate percentage of inspected facilities in different countries;
ii. To identify percentage of manufacturing facilities which complied by having minor non-compliances only after inspection;
iii. To identify percentage of inspected manufacturing facilities with major non-compliances;
iv. To identify percentage of inspected manufacturing facilities with critical observations;

v. To calculate percentage of manufacturing facilities which were found to have critical observation in premises, personnel, production, equipment, quality control, purified water system, HVAC and documentation;

vi. To identify location/ country of facilities found to have critical non conformances; and

vii. To identify type of products manufactured in facilities found with critical non conformances.

3. Scope

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

4. Methodology

Analysis of GMP inspection reports involved systematic analysis of qualitative and quantitative data obtained in the GMP inspection reports for the 77 facilities inspected in the year 2019/20. Number and percentage of facilities found with non-compliances in minor, major and critical categories were calculated. Furthermore, analysis was conducted for the critical non-compliances found in various principles of Good Manufacturing Practices as prescribed in the EAC GMP compendium, 2014. The results were graphically presented for evaluation.

5. Assessment and evaluation tool

GMP inspection reports for all facilities inspected in 2019/20 financial year.

6. GMP references

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. Company site master files

7. List of facilities inspected

The list of pharmaceutical manufacturing facilities inspected from July, 2019 to March 2020 and their compliance status at the time of inspection is attached as **Annex 1.**

8. Good Manufacturing Practices Principles

The assessment was based on the different chapters of the EAC GMP Compendium, 2014 which underline various GMP principles. Among others, the following GMP principles were selected;

a. Pharmaceutical Quality Systems;
b. Premises;
c. Personnel;
d. Heating, Ventilation and Air Conditioning (HVAC);
e. Water Treatment Plant;
f. Quality Control;
g. Equipment;
h. Production; and
i. Documentation

The selected principles were based on the non-compliances observed during inspection of manufacturing facilities in the financial year 2019/20

9. Discussion of the results

The fundamental reason for inspection of the manufacturing facilities is to verify their compliance to GMP requirements as stipulated in the GMP guidelines to ensure that the products are consistently manufactured and controlled to the quality standards.

During inspections, the non-compliances were classified into three classes namely minor, major and critical non-compliances.

Minor non-compliances are those with low probability of affecting the quality or usability of the product. Major non-compliances are those which may cause reduction in the usability of the product without causing harm to the consumer and they have no impact on the strength, identity, purity or safety of the product. On the other hand, critical non-compliances may cause a significant impact on strength, identity, purity and safety of the product and may cause adverse physiological response to a consumer.

As described above, GMP inspection is very important in ensuring that the products registered and circulating in the market are of good quality, efficacy and safe for the patients. TMDA use the data obtained from its inspections to develop trainings on the areas mostly found with critical non-compliances in order to equip inspectors with more knowledge and updated information on respective GMP principles. Majority of the facilities inspected in 2019/20 were located in India (61%) followed by other countries as shown in Table 1 below;

Table 1 Number and Percentage of the pharmaceutical manufacturing facilities inspected in the various countries in 2019/20

Country	*No. inspected*	*% Inspected*
Bangladesh	4	5.2
China	4	5.2
Egypt	2	2.6
India	47	61.0
Indonesia	2	2.6
Jordan	2	2.6
Kenya	2	2.6
Pakistan	4	5.2
Palestine	2	2.6
Singapore	2	2.6
South Africa	2	2.6
Turkey	1	1.3
Vietnam	3	3.9

Total	**77**	**100**

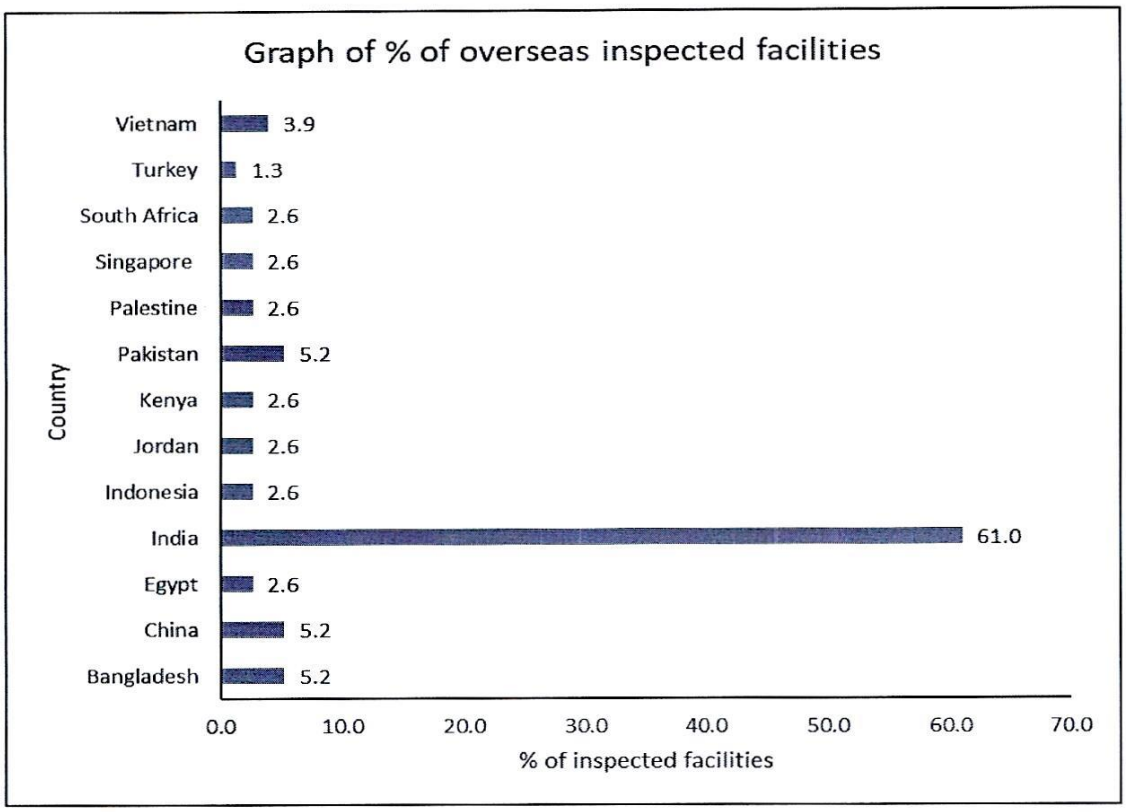

Figure 1 Percentage of pharmaceutical manufacturing facilities inspected in the various countries in 2019-2020

Table 2 below indicates that out of 77 facilities inspected, 26 (34%) complied with the GMP requirements compared to 37% in 2018/19. This difference may be attributed by the increase in inspectors' knowledge in the area of production and/ or non-adherence of the manufacturing facilities to Good Production Practices.

Table 2 Number and Percentage of the pharmaceutical manufacturing facilities found with minor non-compliances in 2018/19

Country	*Number of facilities with minor NCs only*	*% of facilities with minor NCs only*
China	1	3.8
Egypt	1	3.8
India	19	73.1
Kenya	1	3.8
Singapore	1	3.8
South Africa	2	7.7
Vietnam	1	3.8
Total	26	100

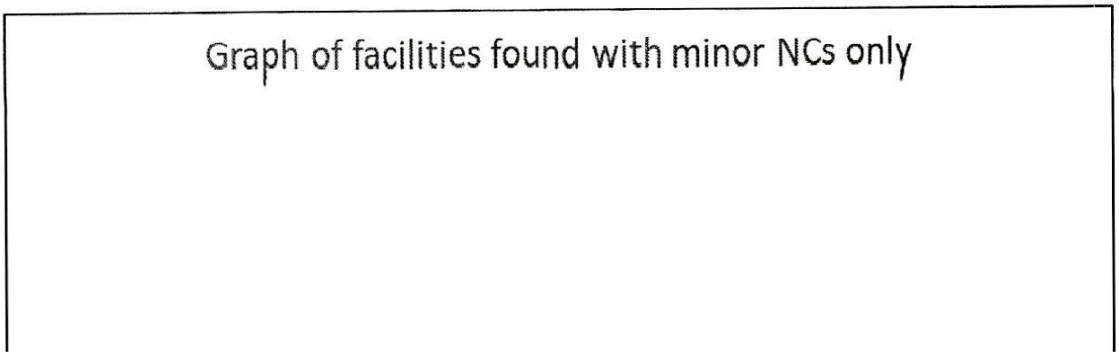

Table 2 Number and Percentage of the pharmaceutical manufacturing facilities found with minor non-compliances in 2018/19

Country	*Number of facilities with minor NCs only*	*% of facilities with minor NCs only*
China	1	3.8
Egypt	1	3.8
India	19	73.1
Kenya	1	3.8
Singapore	1	3.8
South Africa	2	7.7
Vietnam	1	3.8
Total	26	100

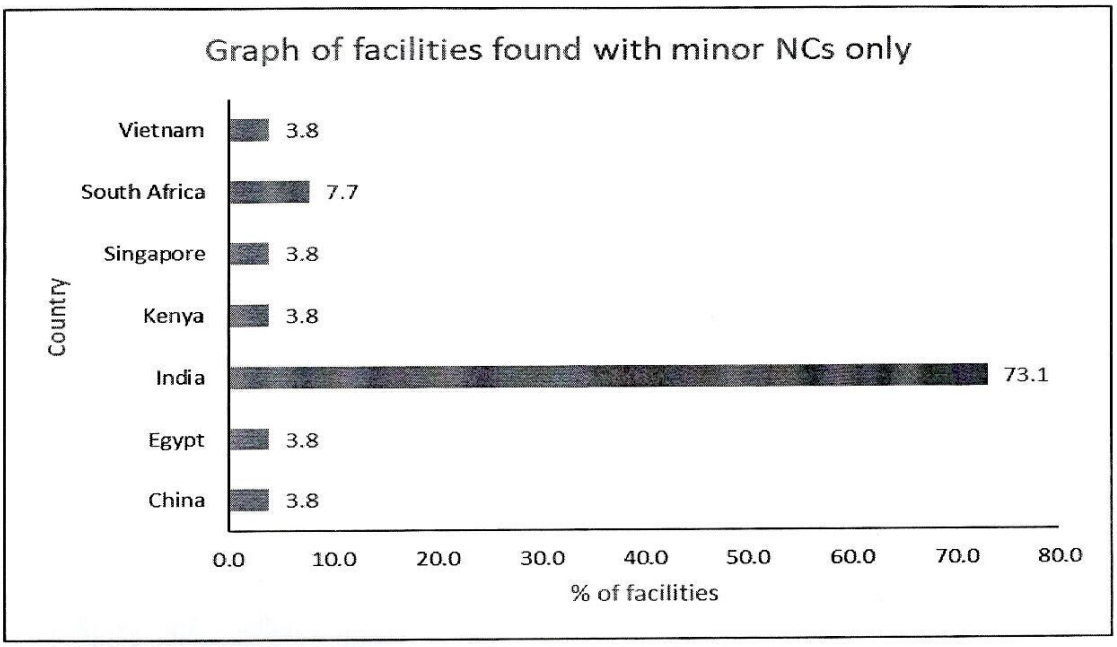

Figure 2 Percentage of pharmaceutical manufacturing facilities found with minor non-compliances only in 2019/20

Table 3 below indicates that, a high percentage (51.2%) of the facilities found with major non-compliances were located in India. This may be because large number of facilities inspected were located in India compared to other countries.

Table 3 Number and percentage of pharmaceutical manufacturing facilities found with major observations in 2019 – 2020

Country	No. of facilities with major NCs	% Facilities with major NCs
Bangladesh	4	9.3
China	3	7.0
Egypt	1	2.3
India	22	51.2
Indonesia	2	4.7
Jordan	2	4.7
Kenya	1	2.3
Pakistan	4	9.3
Palestine	2	4.7
Turkey	1	2.3
Vietnam	1	2.3
Total	**43**	**100**

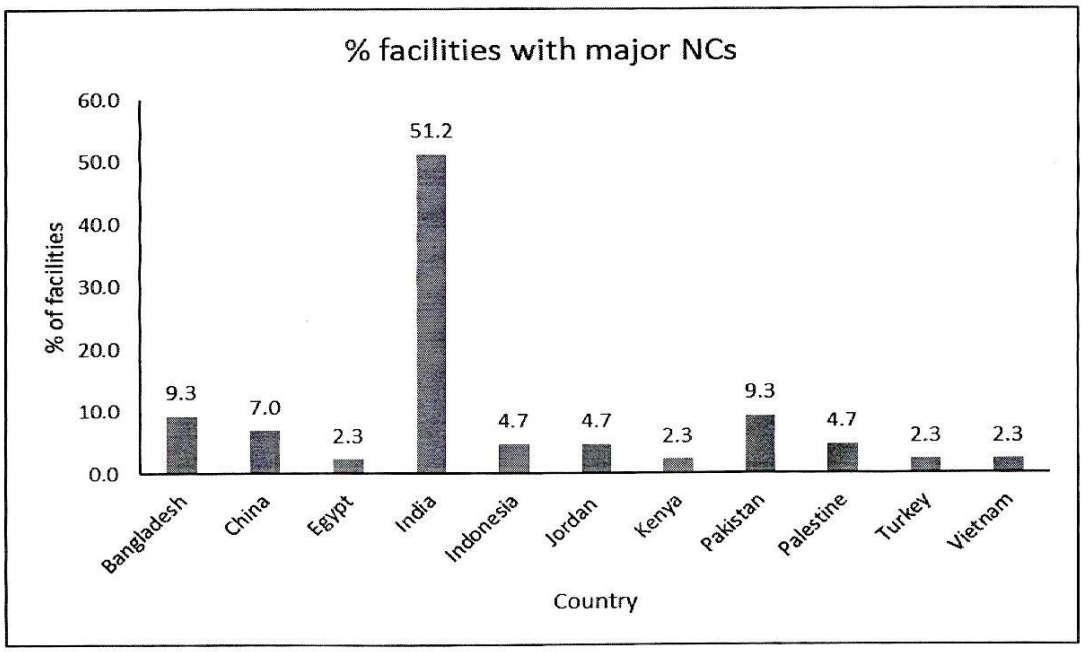

Figure 3 Percentage of pharmaceutical manufacturing facilities found with major non-compliances in 2019/20

Table 4 Summary of number and percentage of pharmaceutical manufacturing facilities found with non-compliances in minor, major and critical non-compliances

Category of no-conformance	*Number of facilities*	*% of facilities*
Minor Only	26	33.8
Major and Minor	43	55.8
Critical/ Major and Minor	8	10.4
Total		**100**

The average percentage critical non-compliance of all inspected facilities was 10.4% which indicates the importance of conducting GMP inspection before registering products. These facilities have high risk issues related to the safety, quality and efficacy of the products manufactured due to the critical non-compliances observed.

Table 4 below shows percentage of facilities found with critical non-compliance in various countries. India was found with many facilities with critical non-compliances (6) this may be because many facilities in India (47) were inspected in 2019/20. The facilities with critical non-compliances were further analyzed to identify the products manufactured in these facilities as well as the GMP principles against which the critical non-compliances were found.

Table 5 Number and percentage of pharmaceutical manufacturing facilities found with critical non-compliances in various countries

Country	Total inspected	No. of facilities with critical NCs	% Facilities with critical NCs
India	47	6	12.8
Vietnam	3	1	33.3
Singapore	2	1	50

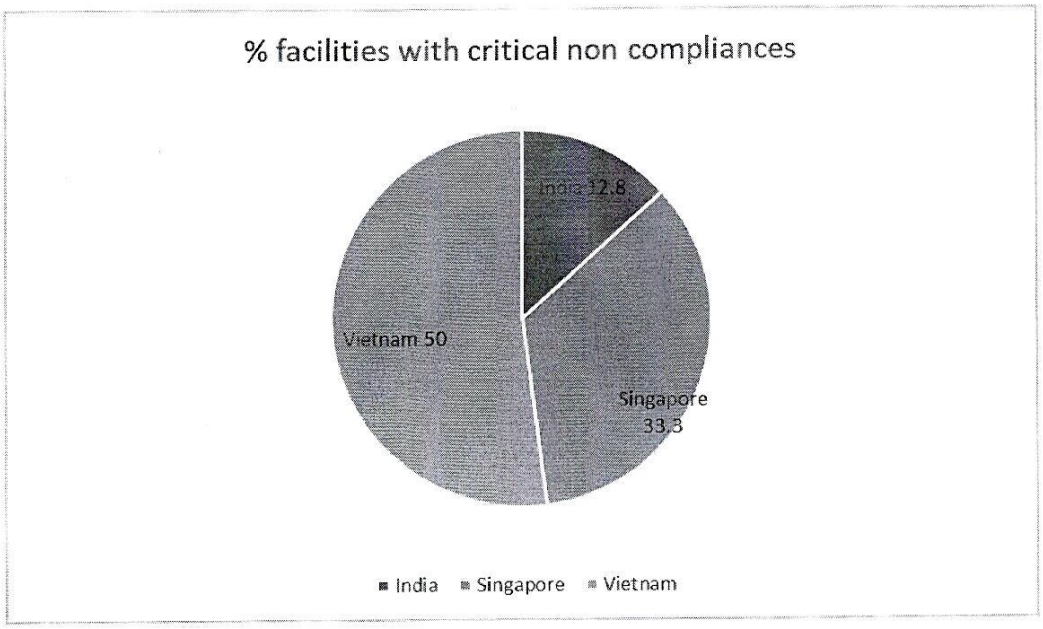

Figure 4 Percentage of pharmaceutical manufacturing facilities found with critical non-compliances in various countries in 2019/20

Table 6 below indicates that most of the critical observations noted during the GMP inspections were related to Production (27.3%) followed by HVAC (18.2%).

These indicated that production activities were not carried out as per required Good Production Practices. High rate of non-compliances observed may be attributed by the inspectors' knowledge on the area, however since few inspectors were involved in the inspection of these facilities, topic on Good Practices in Production and HVAC systems should be included in the GMP trainings to equip inspectors with more knowledge and inspection techniques on the same.

Moreover, risk factors were also observed for premises, water treatment plant, quality control, equipment, pharmaceutical quality systems and vendor audits and approval.

Table 6 Number and percentage of pharmaceutical manufacturing facilities found with critical non-compliances in various GMP principles in 2019/20

GMP Systems/ Principles	*Number of facilities*	*Percentage %*
Pharmaceutical Quality Systems	1	4.5
Premises	3	13.6
HVAC	4	18.2
Water Treatment Plant	1	4.5
Quality Control	3	13.6
Equipment	3	13.6
Production	6	27.3
Vendor Approval	6	4.5

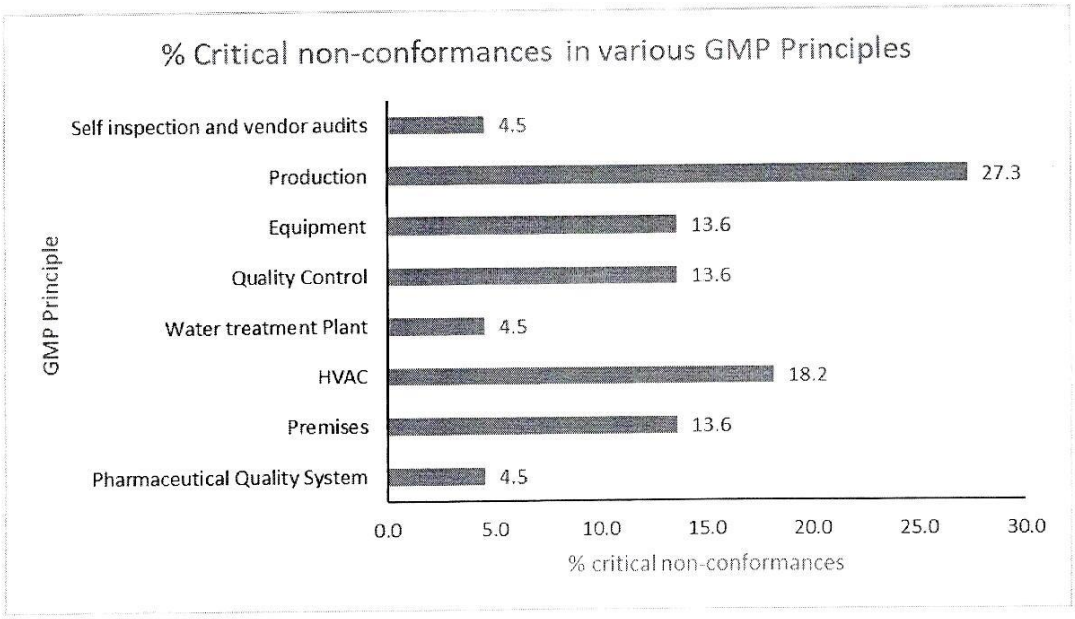

Figure 5 Percentage of pharmaceutical manufacturing facilities found with critical non-compliances in 2019/20

All facilities found with critical non conformances in 2019-2020 were manufacturing general pharmaceutical products. There were different formulations such as tablets, capsules, small volume parenteral, dry powder for injection, suspensions and external preparations. There is no direct relationship between the critical non-compliances found and the category of the product manufactured.

10. Conclusion

Results obtained from the analysis of GMP inspection reports for the facilities inspected in the financial year 2019/20 will be used for continuous improvement and capacity building of GMP inspectors. The observations will be used in developing GMP trainings for the inspectors.

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