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Improving the Outcome of GMP Inspections by Improving Proficiency of Inspectors through Consistent GMP Trainings

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ABSTRACT

Approximately 90% of the pharmaceutical inspectors in a pharmacy practice regulatory agency in West Africa have not updated their training on Good Manufacturing Practice (GMP) inspection in at least eight years. However, in the last two years the inspectors relied on learning-on-the job skills. During this time, the agency introduced about 17% of its inspectors to hands-on GMP trainings. GMP is the part of quality assurance that ensures the production or manufacture of medicinal products is consistent in order to control the quality standards appropriate for their intended use as required by the specification of the product. Inspection reports on the Agency's GMP inspection format in-between 2013 to 2019 across the six geopolitical zones in the country were reviewed retrospectively for gap analysis. Sampling was done in two phases. During the first phase sampling of reports was done by random selection, using a stratified sampling method. In the second phase, inspectors from the Regulatory Agency from different regions were contacted on phone to send in four reports each by email. For those that forwarded four reports, two, were selected. However for those who forwarded one or two, all were considered. Also, the Agency's inspection format/checklist was compared with the World Health Organization (WHO) GMP checklist and the GMP practice observed. The purpose of this study was to evaluate the reporting skills and the ability of inspectors to interpret findings vis-à-vis their proficiency in inspection activities hence the efficiency of the system. Secondly, the study seeks to establish shortfalls or adequacies of the Agency's checklist with the aim of reviewing and improving in-line with best global practices. It was observed that different inspectors have different styles and methods of writing reports from the same check-list/inspection format, leading to non-conformances. Interpretations of findings were found to be subjective. However, it was also observed that inspection reports from the few inspectors with the hands-on training in the last two year were more coherent. This indicates that pharmaceutical inspectors need to be trained regularly to increase their knowledge and skills in order to be kept on the same pace. It was also observed that there is a slight deviation in placing sub indicators under the GMP components in the Agency's GMP inspection format, as compared to the WHO checklist.

Keywords: pharmaceutical, checklist, inspection, non-conformances, regulatory, sampling, manufacturing

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1. INTRODUCTION

There are a number of systems that heavily regulate the pharmaceutical industry (Plumb, 2005). It is required by the World Health Organization (WHO), and the major markets, that products be manufactured in-line with Good Manufacturing Practice (GMP) for acceptability into both local and international market place (World Health Organization, 2007). GMP is defined as “a part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization and products specifications” (Sarvari et al., 2020). The major role of GMP is to prevent particulates and micro-organism contamination of the product, especially from the operatives of the plant in the manufacturing cubicle, particulates from the equipment, chemicals leached from the product contact parts and from other products being manufactured (Plumb, 2005). GMP also entails performing qualifications and validations, availability of all the needed resources with clear instructions and procedures written. In addition GMP requires that all the personnel are trained to carry out their functions correctly with proper records keeping from the beginning of the manufacturing to the distribution. Proper storage and recall systems and feedback mechanisms must be put in place (Chaudhari et al., 2014). GMP is a tool used to prevent contamination and cross contamination of products from other products produced within the same pharmaceutical manufacturing facilities. Because of this, extensive and regular cleaning is required (Plumb, 2005).

Good Manufacturing Practice is a system put in place to guarantee the safety of the end user of a product (Hewitt et al., 2007). There are practices that require conformity to the guidelines recommended by the regulatory agencies. For these guidelines to be implemented in manufacturing industries there must be inspections and monitoring of such industries by the regulatory bodies. There is, therefore, a need for the regulators to be knowledgeable and competent in order to effectively inspect and monitor industries for the implementation of the GMP and/or enforcement of its compliance. The World Health Organization (WHO) developed a universally appropriate and flexible competency frame work for inspectors, which is to support and strengthen pharmaceutical regulators. On this account, “competency” was

defined as the knowledge, skills, attitude and behavior developed through education, training and experience (World Health Organization, 2019b). Competence here connotes independent gathering of information through objective review, observation and open communication that guides one to determine acceptability of information by comparing with the established criteria. As time went on, WHO, in their guide on quality system requirement for GMP proposed specified competency requirement of an inspector as follows:

- a GMP inspector should be able to perform his or her duties with tact, integrity and character
- be qualified academically and knowledgeable in a pharmaceutically related discipline like scientific/technology.
- have a requisite working knowledge and should be conversant with the GMP guidelines of WHO for pharmaceutical products.
- should also be familiar with procedures of GMP inspection of the relevant national regulatory authority.
- must have completed a relevant training course on quality management system and auditing.
- before conducting an inspection, the inspector must have been appropriately trained on the techniques and current procedures of GMP inspection (World Health Organization, 2019a).

Due to the constant emerging trends in the pharmaceutical manufacturing sector, untrained/non-regular trained regulators on GMP inspections may not be up-to-date with such new trends therefore lagging behind the regulated pharmaceutical companies. Improper and/or inadequate regulation leads to non-compliance to GMP and subsequent availability of poor quality/counterfeit medicines.

Basic qualifications to be an Inspector

A GMP inspector is a member of personnel that is trained in all areas relevant to quality assurance and quality control (QA/QC) management, including production procedures, distribution, inspection methodology and drug control (Tomić et al., 2010). A qualified inspector should be a pharmacist graduate, chemist or scientist with practical manufacturing experience or industrial back ground in pharmaceutical production and should be a team player (HPRA, 2018)

Role of the inspector

The primary responsibility of an inspector is to inspect and present a detailed factual report on standards of manufacturing and controls applied to specific products. Inspection also applies to all the manufacturing processes and the facility itself. Inspection should not just be a compilation of an inventory of faults, irregularities and discrepancies but should also advise the pharmaceutical industry being inspected in a manner, which in the opinion of the inspector will serve the interest of the public (World Health Organization, 2007). In summary:

- GMP compliance guarantees safety of the end user of a product (Hewitt et al., 2007).
- GMP inspections promotes GMP compliance.
- For effective GMP inspection, the inspector must be knowledgeable and because GMP is evolving, the GMP inspectors need regular GMP trainings to enable them carry out effective inspections.

It is no longer news that about 70% to 90% of drug needs in most countries in Sub-Saharan Africa are imported (Conway et al., 2019). Yet, most African leaders have policies on paper that are made to encourage an increase in local production of pharmaceuticals in their respective countries. Whether these policies are genuine and meant for implementation is another major concern.

The National Drug policy (NDP) for Nigeria encourages increased local production of essential drugs as its major goal amongst others (www.wjrp.net). However, in reality, there seems to be no concrete mechanism put in place to achieve this. Inadequate power supply has been one of the main challenges to manufacturers and is not being addressed.

In the recent past the Pharmaceutical society of Nigeria called on the Federal Government of Nigeria to increase local production of essential drugs from the present 45% to at least 75% by injecting funds into the Pharmaceutical manufacturing sector (www.niropharm.org).

Furthermore, the World Health Assembly initiated "Improving Access to medicines in developing countries through technology transfer and local production" (Anderson et al., 2012). Also, at the International Conference on Primary Healthcare in Alma-Ata in 1978, the availability of quality medicinal products was identified as an important component for healthcare delivery (Gouveia et al., 2015). However, the success of local production hinges on some vital factors like infrastructure and effective

regulation. The primary problem is the high taxation on the Active Pharmaceutical Ingredients (APIs) and other raw materials. Both APIs and drug products are subject to high taxes and tariffs, causing increased prices and decreased incentives to manufacture drugs (Ubajaka et al., 2016).

Challenges of building and operating manufacturing industries in the sub-Saharan Africa

Both the private and public sectors have roles in building and successfully running industries in any country. To the private sector, the drive to do business is the market feasibility, or the market demand. Unlike the private sector, the public sector has enormous responsibilities including but not limited to providing infrastructures, provision of subsidies and reduction in tax, issuing tenders as incentives to local producers, creating and investing in talent and skill building programs to create an enabling environment for investors (Conway et al, 2019). In some countries in Africa, donors have taken charge of the development of pharmaceutical facilities by way of financing to encourage local production of medicines in Africa. For now it appears that local production is not yet efficient in Africa. This may be due to issues like foreign exchange insufficiency which will negatively impact purchase of raw materials and cause high price of finished product compared to importers such as China (Vogel & Stephens, 1989). In addition, WHO prequalification requires a quality standard and the high operational cost to implement that standard adversely affects local manufacturers (Anyakora et al., 2017). Local manufacturers are especially affected when tenders don't come in the support to incentive from donor agencies. However, there is recent reason for optimism that the pharmaceutical manufacturing situation is changing in Sub-Saharan Africa. Out of Uganda, a country amongst the least developed countries, a local Pharmaceutical manufacturing company known as CIPLA Quality Chemical Ltd has achieved internationally recognize standards of quality. Uganda was the first in Sub-Saharan Africa apart from South Africa, to gain WHO prequalification (Anderson, 2010). Currently the company produces for international agencies. Effective regulation also plays a very important role in the manufacture of quality and safe medicines. It can only arise from sufficient knowledge of Good Manufacturing Practice (GMP). Good Manufacturing Practice is meeting quality standard by making sure that products are consistently produced and controlled to serve their appropriate intended use and as required by marketing authorization, clinical trials authorization and product specification (Gouveia et al., 2015). The guiding principle of GMP is building

quality into a product. It is not just assurance about meeting specification but more importantly, it's also about the product being made by the same procedure under the same condition every time (Chaloner-Larsson et al., 1999). GMP comprised of the following activities amongst others:

- i. There should be a clear definition of procedures and processes with a systematic review in place for risk management for the purpose of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications. Also procedures and instructions must be written in an unambiguous and clear language (World Health Organization, 2007).
- ii. All aspects of manufacturing, including facilities, should undergo qualification and/or validation (World Health Organization, 2007).
- iii. All aspects of a quality manufacturing system should be addressed including, appropriately qualified and trained personnel, adequate premises and space, suitable equipment and services, appropriate materials, containers and labels, approved procedures and instructions, suitable storage and transport, adequate personnel, laboratories and equipment for in-process controls (World Health Organization, 2007).
- iv. Personnel must be trained to ensure that procedures are carried out correctly, (Chaloner-Larsson et al., 1999).

Inspection and licensing

Pharmaceutical manufacturing facilities must be inspected prior to licensure and certified as compliant by regulatory authority prior to manufacturing products for sale. Inspection and licensing are also a fulcrum or basis on which the World Health Organization operates in regards to certification programmes on the quality of pharmaceutical products to gain access into the international market. Inspection is meant to assist and motivate a manufacturer to correct deficiencies and comply with GMP. The process of inspection of pharmaceutical facilities is an activity that is meant to help the industry comply with guidelines that are recognized internationally for GMP (Garg et al., 2013). GMP inspections can have enormous consequences on a company's viability and may result in stiff regulatory actions. Regulatory actions like product recalls can result in negative corporate image and loss of sales

by halting a manufacturing line or placing an entire facility on "hold" for gross violations (Woodcock, 2012). GMP inspections are also tools for assessment of manufacturers of pharmaceuticals by regulatory agencies (Vaishnavi et al., 2011). There are different types of audits and inspections (routine or formal, concise or abbreviated, follow-up, special inspections and quality system reviews (www.slideshare.net; Garg et al., 2013) and varying roles of individuals within regulatory agencies and the pharmaceutical industry. The approaches to inspections can be centered on the process, the product, the system or all of these (Kate, 2002).

The inspection report writing follows the inspection activity. A well written inspection report must be effective in order to observe deficiencies (Dosland., 2015). An inspection report should describe the facts, the observation and the action needed to correct the observations. The reporter should be objective (www.who.int).

Creating knowledgeable and skilled regulators that will translate to good inspection practices including report writing. Developing regulators with good inspection activities requires consistent training in the GMP aspect of inspection. Training enables inspectors to learn the GMP concepts and regulations that apply to what they do. For the US Food and Drug Administration (FDA), European Medicines Agency (EMA), and Health Canada there are periodic (annual) "refreshers" of GMP requirements that are relevant to what the personnel do (Vesper., et al 2018). Generally, the benefits of trainings cannot be over- emphasized. They also save costs in the sense that trained personnel will be more efficient for effective regulation which will lead to availability of safe, efficacious and quality medicine to the public. This explains why some organizations organize extensive and vigorous trainings for their staff immediately after employment. A study to evaluate the effectiveness of GMP training in enhancing awareness and building capability of employees was carried out in Malaysia. The study showed that the employees after exposure to different areas of GMP training namely personnel practice, premises and equipment, documentation, production and product quality control, improved their knowledge base about GMP. Thus the report emphasized that training is critical in improving the employee's knowledge about GMP in order to help improve the quality of product manufactured (Singh et al., 2018). There is therefore an absolute need for extensive and appropriate GMP training for inspectors in developing countries (Garg et al., 2013). An effective training programme is critical as demonstrated by CIPLA chemical quality Ltd, a successful pharmaceutical manufacturing company in

East Africa. CIPLA, Uganda, exposes their new employees to a six month, vigorous training with a series of written tests to assess the understanding of the new employees into their prospective schedules of duty. Those who do not perform well after six months are given an extension of three months and then dropped if considered incompetent after the training for the additional period. However, at this time, full salaries are not paid. The company is doing well and the training forms part of their success story, as indicated by the outcome of the several inspections it has had. The company has been inspected several times by WHO and have retained their WHO prequalification.

Background information about the research problem

Regulators are an essential part of the health workforce and effective regulatory systems are an essential component of health care systems, contributing to better public health outcomes (World Health Organization, 2010). It has been observed that some of the regulated industries are ahead of the regulators. It is also observed that about 90% of the pharmaceutical inspectors of a Pharmacy Practice Regulatory Agency in West Africa have not updated their training on current good manufacturing practice (cGMP) inspection in at least eight years except the last two years (2017 & 2018) but have relied on learning-on-the job skills by themselves without proper mentorship for the same said period. The agency is a statutory organ of the Federal government established by an Act and charged with the responsibility for regulation of Pharmacy practice in all aspects and ramifications (Usar et al., n.d.). This includes regulating and controlling pharmacy education, practice and training. The duties of the agency include but are not limited to

- registration and licensure of all pharmacists;
- registration and licensure of pharmaceutical premises (manufacturing, importation, distribution, wholesale, retail and hospital pharmacies);
- registration of pharmacy technicians and issuance of permit to the registered pharmacy technicians and finally, registration and licensure of patent and proprietary medicine vendors.

This means that anybody who wants to register or own a pharmaceutical premises/business of any kind, including Patent and Proprietary Medicine Vendor shop or is seeking to be registered as a pharmacist or pharmacy technician in the country must be

registered and certified by the agency. (www.pharmapproach.com, www.pcn.gov.ng). It also means that the agency inspects all the pharmaceutical facilities including manufacturing industries, for the purpose of licensure. The agency has several departments including inspection and monitoring (I&M) department. The I&M department is in charge of inspections. For inspections of new manufacturing facilities and multinationals, the lead inspector is always the Head of Department of the I&M. For subsequent routine inspections and others, it becomes the responsibility of the state officers (staff of the agency in charge of that state) where the facilities are domiciled, coordinated by the zonal officers. These State Officers handle other regulatory activities of the agency in their respective states in addition to the GMP inspections. There are different categories of practice of pharmacy and these include; retail, wholesale/distribution, importation and manufacturing. Except for manufacturing, the process of registration for pharmacies is the same. The first thing the applicant completes is application for a location inspection. Location inspection and subsequent approval is a prerequisite to a pre-approval or facility inspection. The second step, if the location is given approval is for the applicant to apply for a pre-approval inspection/ registration. After the pre-approval inspection, any compliance directive issued must be fully attended to by the applicant and the corrective measures put in place before approval is given. Nonetheless in some states, after the location is approved, the applicant may be told to submit an application letter for pre-approval/facility inspection. When this happens and the facility is approved, the applicant often is tempted to continue with business as usual, without recourse to proper registration. In this case, the premises/company can be regarded as an illegal premise because due process was not followed before commencing business. In some states, applicants are told to apply for both location and facility inspection simultaneously, in which case the inspector attempts inspecting the location and the facility at the same time, again without recourse to the fact that the location inspection and subsequent approval is a prerequisite to the facility inspection.

Aim of the study

This research was aimed at a retrospective study of the GMP inspection report of a Regulatory Agency in West Africa that regulates the pharmacy practice, to ascertain conformances with the GMP inspection format which determines the proficiency of the inspectors and the system. This was done through gap analysis of the inspection report within a given period of time.

Objectives

- To identify gaps in inspector training that should be addressed to improve quality and insure uniformity of inspection activities
- Identify if gaps are attributable to the system or individual inspectors
- To compare the WHO GMP checklist with that of the Agency with the intention of reviewing the latter
- To evaluate the report writing skills and competency of the inspectors
- To determine the effect of inspector GMP training and make appropriate training recommendations.

Research questions

- What implication, if any did non conformances and non-uniformity in GMP inspection activities have on the regulatory system?
- What implication if any, did the contents of the GMP report have on the regulatory function of the agency and the industry or the regulated?

2. METHODS

Inspection reports from States are kept in the head office and are physically filed, state by State. State offices also keep records of the reports they sent to the head office.

Sampling took place in two phases;

Files from the six geopolitical zones domiciled at the head office of the agency were evaluated. In one of the zones there was no manufacturing industry at the time of this study. Even in those geopolitical zones that have manufacturing industries, some States do not have manufacturing industries. Sampling was randomly done (the first report then after every five report the sixth was considered). For every file that was sampled, it was sampled exhaustively. For the first phase, a total of 35 reports from the six geopolitical zones were studied as follows;

For South-South zone, two reports were considered each for Edo and Rivers states. For South - East zone, the state that have manufacturing industries were; Enugu, Anambra and Imo states. Three reports were sampled from Enugu state and four each from Anambra and Imo states respectively. In the north-west zone, five reports were sampled from Kano state and one from Kaduna state. North Central zone has only one state, Kwara where four inspection reports were sampled. In the south-west, four and six inspection reports were sampled from Ogun and

Lagos states respectively. North East had no pharmaceutical manufacturing industry at the time of this research. The report studied covered a period of 2013 to 2019.

For the second phase, four soft copies of inspection reports report were requested from officers of the agency manning the states (state officers). For those that forwarded the four reports, two reports were randomly selected. For those that sent one or two, all were considered making a total of 15 reports as shown below:

South-West;- Ogun State two reports, Lagos State two reports;

South-East; two reports each for Anambra and Imo states;

South-South: one report each for Edo and Rivers States;

North-Central: one inspection report each for Niger and Kwara States.

North-West: Kano State two inspection report;

North-East: has no manufacturing industry.

This phase looked at the proficiency of the inspection activities and the inspectors themselves. The indicators or components of the inspection checklist were considered and awarded one mark each. In assessing the report, an indicator that was attended to appropriately had a full mark and that which was not fully attended to was awarded 0.5. Indicators are items on the inspection checklist. Fully attending to an indicator meant everything that an item is required to project during inspection may have been captured in the report of an inspection without ambiguity (www.who.int). All indicators and sub indicators were assigned a mark of 1 each. For example, if the sub indicators were 8, the number of sub indicators attended to will be divided by the total number of sub indicators under that major indicator or GMP component as shown here $8/8 = 1$. The percentage per report was obtained.

3. RESULTS AND DISCUSSION

Phase 1

The components of the GMP checklist of the agency and the indicators under those components were reviewed as per the proficiency of the activities of the inspectors as it affects the quality of the inspection report. Observations made on all of the sub indicators under the major indicators/components (general information, factory layout, organizational chart, building and premises, packaging materials, good

practice in production, equipment, quality control, sanitation and hygiene, safety measures and distribution) were considered during the gap analysis

Figure 1. Number of indicators under components against the major GMP components

Figure 1 shows the major indicators (GMP components) and the total number of sub-indicators under them, with building and premises having the largest number of sub indicators under it. The reviewed agency's checklist in relation with the World Health Organization (WHO) checklist indicated that there is a need to rearrange the sub-indicators and place some under their appropriate GMP components⁸. For example, health requirements for personnel was placed under "organization and personnel" instead of GMP component "personal hygiene" (www.mchrdrdi.gov.in)

Figure 2. A histogram showing a plot of percentage of non-conformance against indicators under general information component of the GMP inspection format indicators

Under general information (Fig 2), it was observed that 34.29% of the report did not address the licensure status of the superintendent or supervising pharmacists and the pharmacist director respectively.

31.43% of the accessed and assessed reports did not address the issue of the licensure of the company. 28.57% ignored batch size. This shows that attention was not given to the full indicators by other inspection reports.

Figure 3. A histogram showing a plot of percentage of non-conformance against indicators under factory layout component of the GMP inspection format indicator.

Under the factory layout component, (Figure 3) 28.47% of the reports ignored the B-lactam sensitivity test for staff which was a critical area that could affect the product and the patients. Also 37.14% under this component ignored the drainage system which is also critical and may result in a source of contamination. The design of a manufacturing plant should be done in such a way to prevent contamination or unsanitary condition. 57.14% of the total report assessed did not make more observations in addition to the guide captured by the check list. This indicated the level of competency and proficiency of the inspectors in inspection activities

In region of West Africa where this study was done, it was observed that the major source of water for

pharmaceutical factories was boreholes. It is pertinent to note that the Medicine Regulatory Agency (MRA) in the country pegs the depth of boreholes at not less than 150ft and 50m from a cesspool (www.nafdac.gov.ng), probably because the depth of a borehole and its proximity to a septic tank may affect the product (Chove et al., 2017). This showed that the source of water and its treatment was a critical point in production of pharmaceuticals and must be closely monitored during inspection to make sure that specifications are strictly adhered to. Any borehole short of the above standards cannot be recommended for use in the production of pharmaceutical products.

Figure 4. A histogram showing a plot of percentage of non-conformance against indicators under building and premises component of the GMP inspection format.

Unfortunately, Fig 4 indicates that 34.29% of the total reports assessed did not say anything about the depth of boreholes, 40% of the report did not indicate whether the water was given primary or secondary treatment. 37.14% provided no information about the availability of trained personnel for water treatment. This is an indication that the companies may not be guided appropriately at the end of such inspection activities. Again, the majority of the reports assessed

were for routine inspections that supposedly covered the whole factory. Figure 4 also showed a trending line which indicated that non conformances were increasing steadily with time.

Figure 5. A histogram showing a plot of percentage of non-conformance against indicators under packaging material/good practice in production component of the GMP inspection format

Figure 5 above indicates that 34.29% did not report on vendor supplier audit and line clearance respectively. In the current GMP regulation, the pharmaceutical manufacturer is expected to take responsibility for the entire manufacturing process including quality of components like APIs, excipients and packaging materials (Patel & Chotai, 2010). This implies that the manufacturer of the finished product must be sure of the source of materials and this calls for vendor audit and qualification. 20% of the reports did not report on the qualification and calibration of equipment which is also very critical and may be a source of error (Losada-Urzáiz et al., 2015). One of the essences of Quality Assurance (QA) is to ensure that adequate controls for all materials including

packaging materials and processes are put in place (Chaudhari et al., 2014). Unfortunately, 42.86% of the inspectors or reports ignored records of packaging materials and did not give any report on the indicator as indicated in Figure 5.

Figure 6. A histogram showing a plot of percentage of non-conformance against indicators under equipments, quality and control and sanitation and hygiene component of the GMP inspection format.

Figure 6 covers indicators under three major indicators or components of the GMP check list. These include equipment, quality control and sanitation/hygiene; 37.14% of the reports did not give any report on validations and standard operating procedures respectively. Validation is a key parameter of the GMP (Kumar & Bharat, 2013). Standard Operating Procedures (SOP) are a regulatory requirement in the pharmaceutical industries. One of their aims is to ensure that consistent quality control of processes and products are maintained through the operations performed. (Bhattacharya & Phill, 2015). Thus validation and SOPs are vital components of GMP and should not be ignored during inspections. Under these same GMP components, 31.45% of the reports ignored the preventive maintenance records and Batch Manufacturing Records. Preventive maintenance is defined as an activity of maintenance that focuses on retaining the workability of a part of a technical system while corrective maintenance rather focuses on restoring the part of a system to its workable state (Percy et al., 1997). Preventive maintenance improves the reliability of the manufacturing system and lowers cost (Meller & Kim, 1996) and this is achieved because preventive maintenance greatly

reduces the down time. Batch manufacturing records are also critical parameters never to be ignored during routine inspections. A batch is a specific quantity of a drug or other materials that is intended to have uniform character and quality within specified limits and is produced according to a single manufacturing order during the cycle of manufacture (Chatterjee, 2012). Also, in manufacturing, batch processing is the processing of raw materials with the end points determined in advance. So fraud, as regards to the quality of the process and subsequently the end product can be detected through a well-developed process control technique for batches (Tsung et al., 2007).

Inspection reports depicts what happened during inspection activities. The above results show discretionary inspection activities by inspectors in different or same zones. There were no reasons provided in the report in those circumstances where indicators/sub indicators were not attended to during the inspections. This depicted subjective interpretation rather than being objective. The manufacturers will be confused, especially in a situation where different inspectors had different approaches to inspection activities and ignored other

GMP indicators and vice versa without reasons. The concern here was whether non-conformity can be addressed in companies when inspectors themselves do not conform to the GMP inspection format or check list.

Phase 2

In the second phase, a scoring format was developed.

Figure 7. Scores (%) from the different inspection report assessed in the second phase samples.

Figure 7 represents the scores of the inspection reports. Different inspection reports had different scores ranging from 35.64 to 89.40. The wide discrepancies in the inspection reports, was a confirmation that the inspectors are not on the same page.

Figure 8. Scores and year inspections were done

It was significant the reports that scored 80% and above were inspection reports that were done in 2018 and 2019 (Figure 8). It was noteworthy that in year 2017, 2018 and 2019, about 17 % of the inspectors were trained. Coincidentally a majority of those reports for the second phase came from those regions where inspectors were recently trained. 4% out of the 17% trained inspectors produced the reports that scored 80% and above. However, behavioral changes following trainings may be short lived without activities to support transfer (Martin, 2010). In view of this and in order to make the training effective and impactful on the organization there was the need to promote transfer of skills and knowledge from trainings to the work place. To make training impactful, there are variables that must be taken into consideration as follows; program design, trainee characteristics, work place environment and follow-up activities. In designing the training program, the trainees may have to be carried along by assuring them that they will practice the acquired skills or apply the knowledge gained during the training. The self-efficacy and motivation (characteristics) of the staff involved in training also played a role. Additionally, work place environment like the employee supervisor attitude, technical support and consequences of using training on the job affected training transfer. It had been observed that an unfavorable or unfriendly post training environment can jeopardize the transfer of training (Tannenbaum & Yukl, 1992). Follow-up activities are the most important in transferring training to the workplace. Example of follow-up activities includes action plan, performance assessment, supervisory consultations and technical support from the supervisors and/or the management.

4. CONCLUSION

The results of the study showed non-conformances across 35 inspection reports reviewed retrospectively which inferred non-conformances in inspection activities across the country as shown in Figures 1 – 6 as per percentage non-conformances of varying degrees in the indicators under various components of the GMP inspection report format. In Figure 4, the straight line cutting across the histograms was called the trending line. The trend line showed increasing non conformances with time. This trend is expected to continue if no action is taken. Also, there was a slight deviation in placing sub indicators under their GMP components in the Agency's GMP inspection report format as compared

to the WHO GMP check list and the GMP practices observed at a manufacturing company in East Africa, during my internship, with the existing checklist of the Agency.

In order to eliminate the non-conformances, there is a need to regularly and consistently train inspectors in regards to inspection activities and inspection report writing to make sure they are on the same page. The work reported here demonstrates that, training will be an effective solution to reduce non-conformances. The goal was to reduce or eliminate non conformances in inspection activities as it reflected in the inspection reports. Effective training lead(s) to an enthusiastic, more satisfied and engaged workforce which finally translates to the efficiency of the system (Training, 2019). In order to produce quality-assured medicines in Africa, capabilities must be built both for Regulators and pharmaceutical industries (Fortunak et al., 2010).

The guidelines on training and qualification of GMP inspectors provided that, inspectors should be well trained in all the relevant areas and be knowledgeable in topics of manufacturing processes, control and distribution of medicinal products, quality assurance management, investigational inspection and inspection methodology (www.ec.europa.eu). Again, the Pharmaceutical Inspection Convention (PIC) or Pharmaceutical Inspection Cooperative Scheme (PIC/S) in one of their annual report stated that in order to achieve uniform interpretation and application of GMP, training of GMP inspectors remains an essential tool. The report stressed that only harmonization of GMP requirement through PIC/S GMP guide was not sufficient to achieve that (www.picsheme.org). The populations of every country on the globe have right to access of safe, efficacious, good quality and affordable medicines, which can only be ensured through competent and effective regulations by the National Medicines Regulatory Agencies (NMRAs) of those countries (Ndomondo-Sigonda et al., 2017). This indicated that the importance of training cannot be overemphasized. Figure 8 demonstrated the benefit of training as most of the reports that scored high marks in the second phase of the study were from the regions where inspectors were recently trained, indicating the importance and benefits of training. However, there was a Lack of objective interpretations in reporting which was an indication of lack of proficiency and or competence in inspection activities, reporting skills and the ability to interpret findings. Inspections are tools for assessment put in place by Regulatory Authorities and other standard

bodies to monitor external organization e.g. pharmaceutical premises, under their jurisdiction (Vaishnavi K., 2011). The primary goal for any pharmaceutical inspector is to achieve GMP compliance as regards market authorization (Vaishnavi K., 2011). An inspection should be corrective, motivational and educational to the regulated. Inspection activities should be beyond disclosure of faults, deficiencies and discrepancies. To achieve the goal of inspections, that are, corrective, motivational and educational, there is an absolute need for trainings and retraining not only in the inspection activities but in inspection-report writing and interpretation of observations because of the evolving nature of the GMP.

Furthermore, there is need to review the Agency's GMP checklist and make it more robust in line with best global practices in GMP.

5. RECOMMENDATIONS FOR NEXT STEPS

In order to minimize and or eliminate non conformances, the following actions are recommended:

1. Train and re-train inspectors in inspection activities because of the evolving nature of GMP;
2. Train inspectors on interpretation of observations or findings and GMP inspection report writing;
3. Review the GMP inspection format in line with the WHO GMP inspection check list to make it more robust and uniform;
4. Number the pages of the reviewed GMP inspection format to prevent tampering in terms of removal or addition of information except by authorized committee;
5. Provide periodic training for key industrial personnel to keep them abreast of evolving GMP issues. This will contribute to more friendly and interactive inspections;
6. Require all submitted report must to be signed by the inspectors that participated in the inspection;
7. Develop rubrics for rating GMP inspectors.

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