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Pharmaceutical Industry in Uganda: A Review of the Common GMP Non-conformances during Regulatory Inspections

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ABSTRACT

The prevalence of substandard medicines in Africa is high but not well documented. Low and Middle-Income Countries (LMICs) are likely to face considerable challenges with substandard medications. Africa faces inadequate drug regulatory practices, and in general, compliance with Good Manufacturing Practices (GMP) in most of the pharmaceutical industries is lacking. The majority of pharmaceutical manufacturers in developing countries are often overwhelmed by the GMP requirements and therefore are unable to operate in line with internationally acceptable standards. Non-conformances observed during regulatory inspections provide the status of the compliance to GMP requirements.

The study aimed to identify the GMP non-conformances during regulatory inspections and gaps in the production of pharmaceuticals locally manufactured in Uganda by review of the available 50 GMP reports of 21 local pharmaceutical companies in Uganda from 2016. The binary logistic generalized estimating equations (GEE) model was applied to estimate the association between odds of a company failing to comply with the GMP requirements and non-conformances under each GMP inspection parameter. Analysis using dummy estimation to linear regression included determination of the relationship that existed between the selected variables (GMP inspection parameters) and the production capacity of the local pharmaceutical industry.

Oral liquids, external liquid preparations, powders, creams, and ointments were the main categories of products manufactured locally. The results indicated that 86% of the non-conformances were major, 11% were minor, and 3% critical. The majority of the non-conformances were related to production (30.1%), documentation (24.5%), and quality control (17.6%). Regression results indicated that for every non-conformance under premises, equipment, and utilities, there was a 7-fold likelihood of the manufacturer failing to comply with the GMP standards (aOR=6.81, P=0.001). The results showed that major non-conformances were significantly higher in industries of small scale (B=6.77, P=0.02) and medium scale (B=8.40, P=0.04), as compared to those of large scale.

This study highlights the failures in quality assurance systems and stagnated GMP improvements in these industries that need to be addressed by the manufacturers with support from the regulator. The addition of risk assessment to critical production and quality control operations and establishment of appropriate corrective and preventive actions as part of quality management systems are required to ensure that quality pharmaceuticals are manufactured locally.

KEYWORDS

Pharmaceutical Industry, Good Manufacturing Practices, Inspections, Quality of medicines

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1. INTRODUCTION

Pharmaceutical manufacturing is a capital-intensive venture that requires a lot of financial investment to establish a facility that meets internationally acceptable Good Manufacturing Practice (GMP) standards (UNIDO, 2013). There were 21 registered pharmaceutical industries in Uganda in 2019, of which the majority are small scale industries. Uganda pharmaceutical market imports 90 percent of the medicines from mainly India and China, implying that 10 percent of the drugs are by local manufacturers (Gilbert O. et al., 2015). Therefore, the industries in Uganda cannot meet the required pharmaceutical market demands; and worse still, the quality of medicines manufactured cannot be guaranteed. The effects of inadequate pharmaceutical production capacity including substandard medicines are not only limited to Uganda but directly impact the poor especially in African, Asian, and Latin American countries, on a global scale.

Universal Health Coverage, target 3.8 of the United Nations post-2015 Sustainable Development Goals (SDGs) incorporates access to safe, effective, quality, and affordable essential medicines by 2030 (WHO, 2015). However, substandard and falsified medical products represent a severe problem for public health, especially in Africa, South-East Asia, and Latin America. United Nations Industrial Development Organization (UNIDO) believes that strengthening the pharmaceutical manufacturing industry in Africa contributes directly to improved access to quality-assured, affordable, safe, and efficacious essential medicines (UNIDO, 2010).

Adherence to Good Manufacturing Practices (GMP) in addition to establishment of quality assurance systems contribute to the consistent manufacture of high-quality drugs. National Medicine Regulatory Authorities (NMRA) are mandated to inspect facilities regularly to ensure compliance with these GMP practices. The GMP inspection process may include but not limited to the following parameters: pharmaceutical quality management; qualification and validation; product market complaints and recalls; self-inspection, quality and supplier audits; personnel; premises, equipment and utilities; documentation; production, outsourced activities and quality control (WHO, 2007).

Pharmaceutical companies located in developing countries, including Uganda, frequently feature operating environments and procedures that fall below acceptable standards. These are depicted in the non-conformances noted during GMP regulatory inspections. According to the WHO multi-country study of 2002 on effective drug regulation, Uganda pharmaceutical manufacturing plants inspected had 60% GMP violations, which reflected serious problems regarding GMP compliance and implementation. This has been attributed to the lack of robust quality assurance systems among local pharmaceutical companies to manufacture quality products. The concept of quality culture in most of these companies is almost non-existent. As a result, locally made pharmaceuticals are generally perceived to be of low quality compared to imported ones.

Substandard medicines are manufactured through poor production practices and controls not following GMP and could also be deliberately done for commercial gains with disregard to the safety of the patient. Johnston and Holt, 2013 noted that substandard drugs may have variable formulations between different batches of the same drug or between generic and branded drugs, incorrect amounts of API in the drug, drug related impurities and degradation products. The extent of knowledge of health workers and consumers to be able to identify substandard drugs is unknown.

Data from different studies on the quality of medicines in Uganda and Africa, in general, has been collated to provide evidence on substandard drugs, including those manufactured locally. According to WHO, about 10% of the medications in the global medicine market, and more than 25% in developing countries, are substandard/falsified with antibiotics and antimalarials being the most frequent. A systemic review and meta-analysis of databases on the prevalence and estimated economic burden of substandard and falsified medicines in low and middle-income countries indicated that 19.1% of the antimalarials and 12.4% of antibiotics were falsified, with an estimated economic impact within a range of $10-$200 billion (Ozawa S., 2018). In a study on the quality of antimalarials in six African countries, Bate et al., (2008), reported 35% of the tested medicines from Uganda were substandard.

High infant mortality rates in Uganda, among other things, are caused by substandard and falsified drugs, stock outs of essential drugs, and provision of pharmaceutical services through unlicensed pharmacies and drug shops by unqualified practitioners (Gilbert O. et al., 2015). In a survey by Renschler (2015), there were 120,000 deaths of children under-five, annually, that may be associated with the consumption of poor-quality antimalarials in sub-Saharan Africa alone. The risk of harm from receiving substandard or falsified medicines is high in vulnerable populations and patients with comorbidities. In 1990, 109 Nigerian children died as a result of administering them adulterated Paracetamol syrup by their parents, and the incidents happened due to the manufacturer's negligence by replacing genuine solvent with the counterfeit solvent that contained a deadly level of Diethylene Glycol, which is a known human toxicant and is commonly used in industries for non-edible items (Aminu and Gwarzo, 2017). The effects of substandard and falsified medicines imply that even the rich may not survive the health consequences given the complex supply chain systems among African countries.

Failure to comply with GMP leads to medications that are

not safe, efficacious and are of poor quality. These medicines lead to poor treatment outcomes, antimicrobial resistance and sometimes adverse drug reactions. This indirectly increases the treatment costs and hence becomes a burden to the general population (Geyer et al., 2019). The burden of substandard medicines is therefore linked to the wastage of resources which could have benefitted public health and increase economic productivity.

Failure to comply with GMP and subsequent production of substandard drugs may also have a direct effect on the reputation of the company as there would be increased customer complaints, recalls and production waste. The company may also face regulatory penalties and the summation of all this leads to decreased profitability and loss of market share (Geyer et al., 2018).

Failures are inevitable in any company; however, systems have to be established that provide for detailed investigation to identify the root cause for the reported non-conformance or failure in order to take appropriate corrective and preventive actions (CAPA) to avoid recurrence and improve the system. Biswas K., 2007 highlighted that about 30-50% of FDA-483 forms raised were related to CAPA deficiencies and the situation is not any better in developing countries.

National Medicines Regulatory Authorities (NMRA's) have a direct bearing on GMP implementation by local pharmaceutical industries to manufacture safe and quality medicines. In Uganda, the National Drug Authority inspects local pharmaceutical industries for GMP compliance. Therefore, improvements have to be made in the regulatory systems of the country which would directly translate into a strong regulated pharmaceutical industry boosting production of quality medicines locally.

This study identified the non-conformances during regulatory inspections and gaps in the production of local pharmaceuticals with the overall objective to promote the growth of the domestic pharmaceutical industry in Uganda through improved compliance to GMP requirements

2. METHODS

This study adopted a quantitative study design with categorization and quantification of the non-conformances obtained from a review of the available 50 GMP inspection reports for 21 local pharmaceutical companies in Uganda since 2016. The non-conformances were categorized as per the GMP inspection parameters defined by the WHO GMP guidelines, and guidance to GMP by Pharmaceutical Inspection Cooperation Scheme (PIC/S). All data were entered into an Excel database and analyzed.

Binary logistic generalized estimating equations (GEE) model was applied to estimate the association between odds of a company failing to comply with GMP requirements and non-conformances under each GMP inspection parameter. Based on the GMP requirements, nine variables (GMP inspection parameters) were selected for testing their association with failure to comply. Based on the likelihood-ratio (LR), a stepwise forward selection was used to build a multivariable model from the nine variables, retaining those variables with p-values < 0.2. The primary outcome of this model was the conclusion on GMP, as "failed=1" and "passed=0". Six variables remained significant after adjusting for other related factors. These included:

1) Pharmaceutical quality management;
2) Personnel;
3) Premises, equipment, and utilities;
4) Quality control;
5) Self-inspection; quality and supplier audits and
6) Complaints and recalls.

Dummy estimation to linear regression was used to analyze the relationship that existed between the selected variables (GMP inspection parameters) and the production capacity of the local pharmaceutical industry. The dummies for production capacity, which were the independent variables, were created holding a "large scale" as the base variable. The model was run independently across all the selected variables. A total of 9 variables (GMP inspection parameters) were tested for the relationship with the production capacity of the industry

3. RESULTS AND DISCUSSION

3.1. Production Capacity

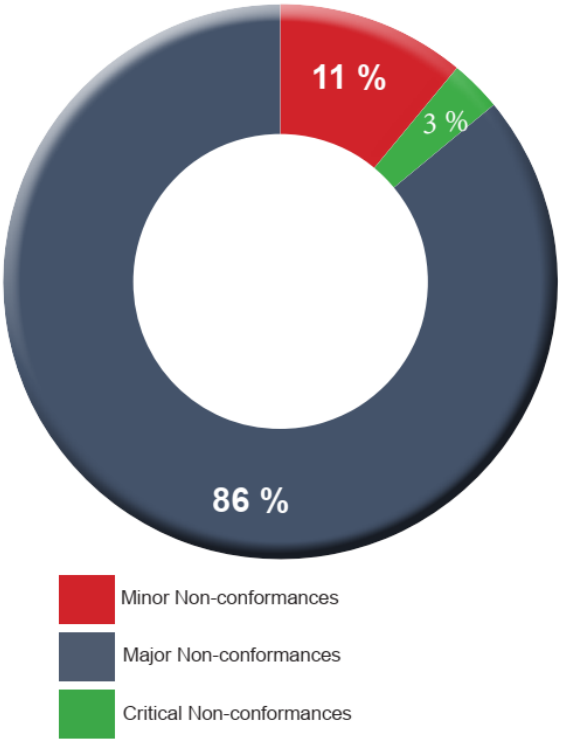
The production capacity for the local pharmaceutical companies in Uganda was classified based on the number of employees, the criteria used by Söderbom & Teal (2004) in the classification of African firms. The results indicated that 52% of the surveyed local manufacturers were small scale, 29% medium scale, and 19% large scale as shown in **Table 1**.

Table 1: Production Capacity of Local Pharmaceutical Industries in Uganda, 2019

Type of Industry	No. of Employees	No. of Industries
Small Scale	Below 30	11(52%)
Medium Scale	31-99	6(29%)
Large Scale	Above 100	4(19%)

The number of local pharmaceutical manufacturers increased from 11 in 2009 (UNIDO, 2010) to 21 in 2019. There has been a significant increase in the industries at a small-scale level from 9% in 2009 to 52% in 2019 and a decrease in medium-scale and large-scale industries from 55% to 29% and 36% to 19% respectively, in comparison to the UNIDO 2010 report.

Figure 1: Criticality of GMP Non-conformances during Regulatory Inspections



Data from the 2nd East African Community Region Pharmaceutical Manufacturing Plan (EACRPMP), according to the 2014 estimates, indicated that Uganda had a pharma size market of about 450 Million USD at 8.5% annual growth. Therefore, the potential for a booming and economically viable pharmaceutical industry is high. However, as per the results, only small-scale investments have been attracted over the past nine years in the Uganda pharma industry. Worse still, two medium-scale pharma companies have since closed business in the same time period, which needs to be analyzed further to seek possible remedies to this unbecoming trend.

3.2. Scope of manufacturing

Two facilities manufactured Beta-Lactam products, specifically Penicillins. According to the NDA GMP guidelines on medicinal products, INS/GDL/001, highly sensitizing materials (e.g., Penicillins) are required to be manufactured in dedicated and self-contained facilities. The two facilities had segregated facilities where these products were produced. However, reviewed reports had critical non-conformances related to inadequate containment systems of the air handling units on the Beta-Lactam sections, which posed a potential threat of cross-contamination.

Three manufacturing units were established in hospitals and lacked quality control facilities that were required for the products manufactured. Besides, one of the medical devices' manufacturing facility also had no quality control laboratory. In all these facilities, there was no clear policy on the outsourcing of quality control activities, which increased the possibility of the release of products not meeting specifications onto the market. This is in contradiction with the quality control requirements as per GMP guidelines.

Five facilities manufactured medical devices. However, there are no laws and regulations on the manufacturing of medical devices in Uganda although a unit to work on these gaps has since been established.

There were three manufacturing facilities for veterinary products, including a specialized facility for veterinary vaccines. The non-conformances, some critical, of the facility have demonstrated the struggles in the establishment of sterility assurance systems and maintenance of the required environmental conditions during production.

Only one large scale manufacturer was WHO accredited under the prequalification program for medicines (Antimalarials and Anti-Retroviral Drugs), which translates into the high level of GMP compliance compared to other non-accredited pharmaceutical companies in the country. Prequalification increases the market share beyond the country to other regional markets; and, participation in global procurements, as the quality of products manufactured, is guaranteed (WHO,2014). Pharmaceuticals manufactured in Uganda are exported to regional markets under the East African Community with support of the Uganda Investment Authority (UIA). This expanded market provides an opportunity to develop the pharmaceutical industry (UNIDO,2010).

The majority of these companies manufactured oral liquids (9), liquids for external use (8), powders, creams and ointments (5), and tablets (4); while large volume parenterals were manufactured in only one facility. The results are not different from the UNIDO, 2010 report, where the majority of local manufacturers specialized in oral and topical liquid preparations. The number of facilities that manufactured a given dosage form was proportional to the complexity of the manufacturing process. For example, only one facility was involved in the production of parenteral products. Specialized medical products like oral morphine and Anti-Retroviral Drugs (ARVs) were each manufactured in at least one facility while one of the hospital manufacturing units had sterile eye preparations.

3.3. GMP Non-conformances

All GMP inspection reports for local pharmaceutical industries completed from 2016-2019 had non-

Table 2: Regression results using dummy estimations comparing pharmaceutical production capacity and criticality of Non-conformances

Variable	D_large	D_small	P-Value	D_medium	P-value
Critical Non-conformances	1.0	1.40	0.34	0.84	0.120
Major Non-conformances	1.0	6.77	0.02	8.40	0.040
Minor Non-conformances	1.0	-4.12	0.03	-0.38	0.001

conformances totaling 1,758, an average of 35 non-conformances per the report, or approximately 84 non-conformances per inspected facility. Routine inspections were done once a year unless special investigations were required. In the follow up investigations by the regulator, there was scanty evidence of implementation of Corrective Action and Preventive Actions (CAPA) by majority of the local manufacturers. This demonstrated inadequate commitment and exposed laxity to improving domestic production through regulatory compliance.

Of the non-conformances, 86% were categorized as Major, 11% were Minor, and 3 % were Critical, as shown in **Figure 1**. The regression results, as per **Table 2**, showed that major non-conformances were significantly higher in small scale industries, (B=6.77, P=0.02) and medium scale industries (B=8.40, P=0.04) as compared to large scale industries. It was also revealed that large scale industries had significantly higher minor non-conformances as compared to small scale (B=-4.12, P=0.03) and medium scale industries (B=-3.8, P=0.001). The majority of the non-conformances were under the categorization of "Major." Some of the non-conformances were incorrectly classified in comparison to the GMP guidelines. Numerous "Major" non-conformances would indicate a failure in quality assurance systems and these would otherwise be critical, leading to the closure of the facilities. However, this was not the case and implied that the acceptable cGMPs were not adequately enforced in a bid to promote the local pharmaceutical manufacturers, a critical balance that may result in negative consequences on the quality of locally pharmaceutical products.

Weak enforcement of GMPs directly leads to production of substandard and or falsified medicines. Therefore, in agreement with Johnston & Holt, 2013, the key to ensure quality of drugs manufactured locally is the implementation of robust regulatory systems by the NMRA.

Table 3: GMP Inspection Outcomes/Conclusions

Type of Industry	No. of GMP reports approved	No. of GMP reports for CAPA before approval	No. of GMP reports with failure conclusion
Small Scale	2	13	6
Medium Scale	0	12	1
Large Scale	0	16	0
Total	2(4%)	41(82%)	7(14%)

3.4. GMP Inspection outcomes/conclusions

GMP inspection outcomes/conclusions for the reviewed reports in **Table 3** indicate that only 4% were GMP approved after the initial inspection, but the majority (82%) had to submit CAPA before approval, while 14% failed meeting GMP requirements. Manufacturers that fail to meet GMP standards have to cease operations since this puts the public in danger of exposure to substandard drugs. Failure to comply with GMP is not a criminal offense as per the Uganda National Drug Policy and Authority Act (NDP/A Act, Cap 206) compared to the USA, where FDA defines the minimum Good Manufacturing Practice standards, upheld by law (21 CFR part 211). Therefore, the enforcement of GMPs among the local pharmaceutical industry in Uganda need to be strengthened. Furthermore, licensing of a local manufacturing facility was not directly tagged to the results of the GMP inspection, which needs to be reviewed following the associated possible risks.

Figure 2: Percentage of non-conformances per GMP Inspection parameter

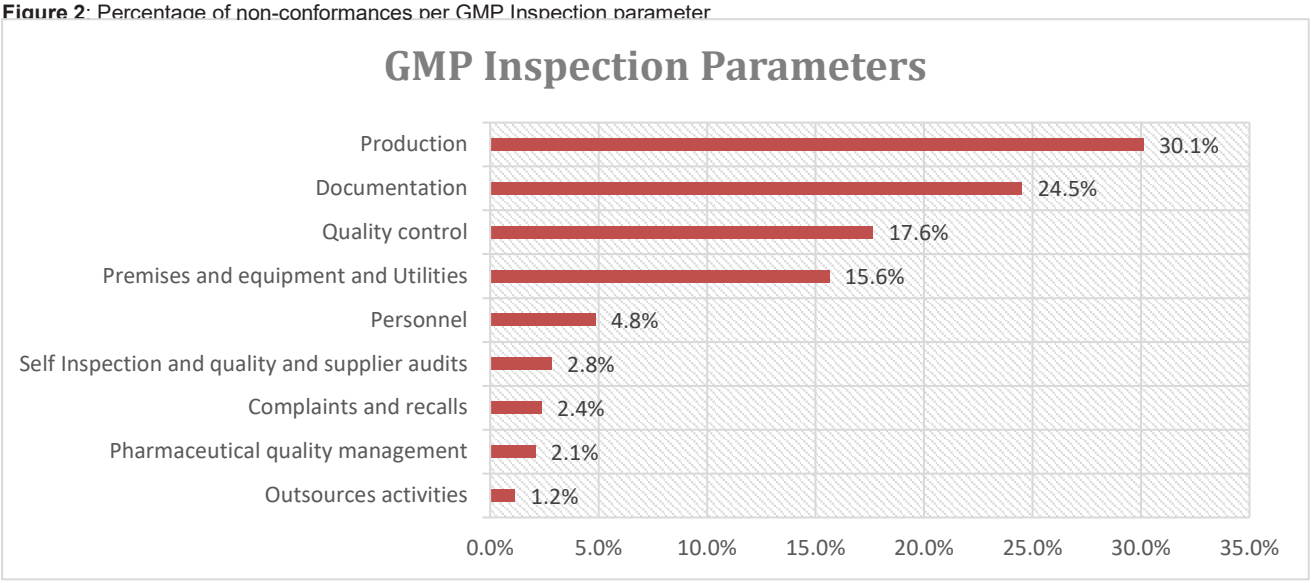


Table 4: Logistic regression model showing likelihood of failure to comply with GMP due to non-conformances per given GMP parameter

Variable/GMP inspection parameter	Average	cOR	P-Value	aOR	P-Value
Pharmaceutical quality management	0.72	2.21	0.013	3.26	0.003
Personnel	1.68	3.86	0.016	5.73	0.001
Premises and equipment and utilities	5.42	4.20	0.034	6.81	0.001
Documentation	8.50	1.11	0.399	-	-
Production	10.44	1.06	0.213	-	-
Quality control	6.12	3.14	0.021	5.32	0.003
Outsources activities	0.40	0.85	0.74	-	-
Complaints and recalls	0.82	2.23	0.019	3.82	0.023
Self-inspection and quality and supplier audits	0.98	2.26	0.029	5.97	0.001

cOR= Crude Odds Ratio, aOR= adjusted Odds Ratio

3.5. GMP Inspection Parameters and associated Non-conformances

The common areas of non-conformances were Production (30.1%), Documentation (24.5%), Quality control (17.6%), and premises, equipment and utilities (15.5%) as per **Figure 2**. Results contrast to a similar study carried out in Brazil by Geyer et al., 2019, where the most common areas of deficiency were qualification and validation (35.1%), documentation (32.2%), premises (26.4%), and quality control (23.5%). For the case of this study in Uganda, non-conformances under qualification and validation were incorporated under documentation. The two studies indicate similarities in problems faced by manufacturers regarding documentation and quality control. Documentation non-conformances have also been highlighted in most of the FDA-483 forms and this appears to be a challenging fact for the pharmaceutical manufacturers globally (Geyer et al, 2019).

Non-conformances related to quality control activities are highly cited in Uganda due to lack of adequate human resources, equipment, and technology to meet the current standards, for example, no laboratory among local pharmaceutical manufacturers is accredited to ISO 17025 standard. Quality control analysis of medicines is critical in confirmation of the quality of the medicine as per the defined pharmacopeial specifications.

Non-conformances under production were the major violations for Uganda, mainly due to the basic methods employed in the processes with minimal technological advancements to meet current developments. Poor raw and packaging materials quality and storage, poor equipment designs and maintenance, inadequate procedures, incompetent personnel, lack of validated cleaning processes, poor premises maintenance, and lack of process validations among others directly affected the production processes. A full commitment is required by the local manufacturers to address these problems in order to produce quality products.

The results from the logistic regression model in **Table 4** significantly showed that for every non-conformance under premises, equipment, and utilities, there was a 7-fold likelihood of failing to comply with the GMP requirements (aOR=6.81, P=0.001); and, there was also a five times likelihood that a firm was unable to conform to GMP, for any non-conformance related to quality control (aOR=5.32, P=0.003). The majority of the medium and small scale industries had poor controls for the manufacturing environments, which impacted directly on the quality of the products. Many even lacked air handling units to provide recommended manufacturing environments.

Furthermore, per the results in **Table 5**, it was found that the non-conformances relating to premises, equipment, and utilities were significantly higher in small-scale (B=2.29, P=0.04) and medium-scale industries (B=2.02,

Table 5: Regression results using dummy estimations comparing pharmaceutical production capacity and non-conformances per given GMP inspection parameter

Variable/GMP inspection parameter	D_large	D_small	P-Value	D_medium	P-value
Pharmaceutical quality management	1.0	0.43	0.52	0.49	0.879
Personnel	1.0	1.16	0.38	0.70	0.208
Premises and equipment and utilities	1.0	2.29	0.04	2.02	0.045
Documentation	1.0	0.99	0.26	-0.31	0.729
Production	1.0	2.83	0.84	3.22	0.428
Quality control	1.0	-1.41	0.03	1.89	0.008
Outsources activities	1.0	-0.92	0.02	-1.17	0.005
Complaints and recalls	1.0	0.22	0.20	0.81	0.162
Self-inspection and quality and supplier audits	1.0	0.57	0.318	0.10	0.219

P=0.045) compared to large-scale industries. The majority of medium and small-scale industries had poorly designed premises. Conversely, large-scale industries had significantly more non-conformances relating to quality control as compared to small scale (B=-1.41, P=0.03) and the medium scale industries (B=1.89, P=0.008). The quality control laboratories in large-scale facilities were not in tandem with the testing requirements for manufactured products. However, for some medium and small-scale industries, quality control activities can be considered non-existent. Finally, the non-conformances in outsourced activities were significantly more in large-scale industries than small-scale (B=-0.92, P=0.02) and medium-scale industries (B=-1.17, P=0.005).

Generally, the number of non-conformances per GMP inspection parameters observed during regulatory inspections has increased over the past three years since 2016, per the trending results shown in **Figure 3**. Evidence of recurring GMP problems among the local pharmaceutical industries also demonstrated weak corrective and preventive actions (CAPA) implementation systems.

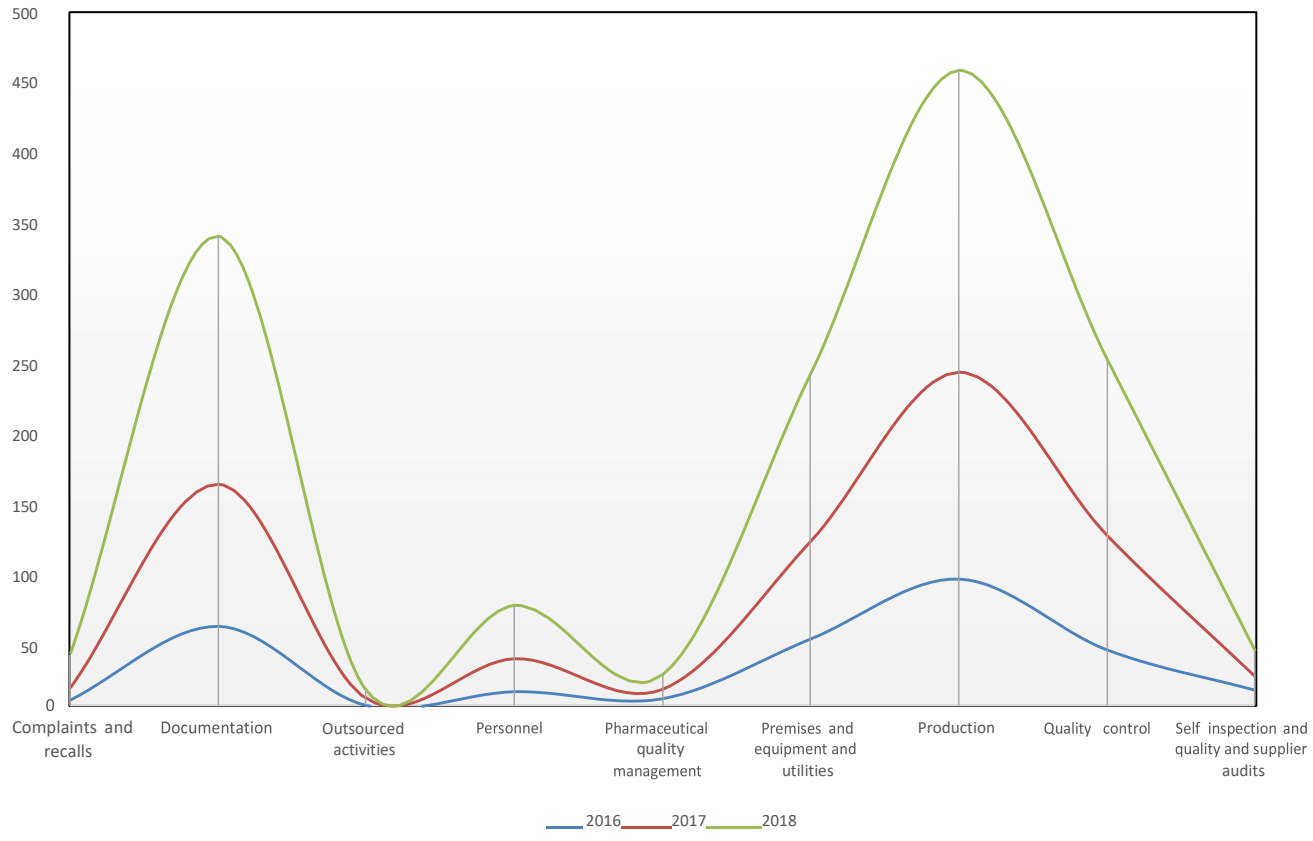
Quality risk assessment of critical production and quality control of pharmaceuticals provides guidance on the appropriate CAPA. However, the principles of root cause analysis and risk assessment with linkage to the effect on the final consumer (patient) are often not exploited by the local manufacturers as emphasis is often on correction of the non-conformances instead of CAPA. A robust CAPA system would include identification of the non-conformances with trend analysis followed by evaluation of the potential impact using risk assessment tools on the quality of the product. Investigations including root cause analysis with adequate supportive data would be conducted to guide development of the CAPA plan which has to be verified for its effectiveness (Menon N. et al, 2016).

3.6. Local pharmaceutical production – Gaps and opportunities

Caudron et al., (2008) noted that, much efforts have been geared towards the fight against counterfeit drugs but the problem of substandard drugs has been given less attention. Post market surveillance for such drugs is inadequate as few samples of locally manufactured pharmaceuticals are analyzed in a given period. Locally based pharmaceutical industries are also challenged with poor recall systems in cases of failure following laboratory analysis and this exposes patients to substandard drugs.

The 2nd East African Community Regional Pharmaceutical Manufacturing Plan (EACRPMP) 2017-2027 highlights that local pharmaceutical production in sub-Saharan Africa contributes only 30% of the medicinal products demand. The inability to meet this demand at local level is attributed to but not limited to; unfair competition of locally manufactured products with imported ones, especially from India and China; gross

Figure 3: GMP non-conformance trends from 2016 to 2018



violations to GMPs by local pharmaceutical manufacturers, inadequate human and financial resources; lack of modern technologies and equipment and weak regulatory systems, and a lack of enabling policies (including policy coherence) among various sectors (both nationally and regionally). These are the same findings as per the report on local pharmaceutical production by Bate R., (2008).

Overcoming these barriers would boost local pharmaceutical manufacturing and offer several advantages, including continuous supply of pharmaceuticals, reduction on overdependence on importations, increased technical capacity, availability of labor and increased revenue. Sufficient local production of quality medicines would contribute to reduced morbidity and mortality rates and overall growth of the pharmaceutical industry to the benefit of the final consumer- the patient as quality medicines would be available at affordable rates. Dansie et al., 2019 reported that Uganda had introduced a 12% import tax on a selected drugs that Ugandan pharmaceutical industries already manufactured under the “Buy Uganda, Build Uganda” as one of the policies to boost local production of pharmaceuticals. The regulator is also required to continue with the efforts of building capacity of the local manufacturers to meet GMP requirements and build quality into their products during the entire manufacturing cycle.

4. CONCLUSION

Domestic pharmaceutical manufacturers’ challenges with regards to the implementation of cGMPs and quality assurance systems, are enormous. They would require the regulator to design a special risk-based inspection and supervision model on the follow-up of GMP non-conformances during regulatory inspections among local manufacturers.

Commitments to GMP compliance with timelines have to be made in a phased manner and adhered to between the manufacturers and the regulator to boost the domestic production of quality pharmaceuticals in Uganda. Again, the regulators have to put in place appropriate legal framework to enforce GMPs among local pharmaceutical manufacturers. This would go a long way in building confidence of the general population in locally manufactured pharmaceuticals and in the work of the regulator.

5. RECOMMENDATIONS FOR NEXT STEPS

The regulator has to collect and analyze data based on implementation science to determine the extent of substandard drugs manufactured locally in Uganda. This would provide national medicine regulatory authorities with information on the scale of the problem for reference to base practical and applicable regulatory decisions to local pharmaceutical manufacturers.

National Medicine Regulatory Authority (NMRA) has to engage local pharmaceutical manufacturers on the development of the short-term, medium-term, and long-term strategies to address the non-conformances observed in regulatory inspections with defined timelines for implementation and follow-up. The strategies may include facilitation of GMP upgrades among local industries or amendment of the NDP/A Act to provide for explicit legal consequences against GMP violations.

Manufacturers would be required to conduct a risk assessment on critical production and quality control processes based on the GMP non-conformances and thereafter develop a CAPA plan whose effectiveness would be monitored by the regulator. Local pharmaceutical manufacturers should also be supported to build quality management systems that would guide implementation of CAPA plans in a sustainable way.

Refresher GMP training for the local pharmaceutical manufacturers need to be conducted more frequently based on the findings on GMP non-conformances during inspections.

NMRA should continue to participate in harmonization initiatives in medicine regulation including the East African Community to achieve regulatory convergence not only in GMP inspections but also medicine dossier assessments and registration, quality control analysis, post market surveillance and pharmacovigilance within the region and optimally benefit from sharing the available limited resources. WHO has recently introduced a system of evaluation of NMRA’s using a Global Benchmarking Tool (GBT) as a means of strengthening regulatory systems on medical products and this would also be beneficial to the NMRA.

A study on the quality of locally manufactured products should be undertaken to determine the extent of substandard products on the market

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