Vol. 24 (2021) 57-66

Quality Control Results of Pharmaceuticals Analyzed in the Mission for Essential Drugs and Supplies (MEDS) Laboratory During the Period 2013-2017

KENNEDY O. ABUGA[1]*, STEPHEN T. KIGERA[2], MILDRED WANYAMA[2], WYCLIFFE M. NANDAMA[2] AND ISAAC O. KIBWAGE[1,3]

[1]*Department of Pharmacy, Faculty of Health Sciences, University of Nairobi, P.O. Box 19676-00202, Nairobi, Kenya.*

[2]*Mission for Essential Drugs and Supplies, P.O. Box 78040 – 00507, Viwandani, Nairobi.*

[3]*Egerton University, Njoro, P.O. Box 536, Egerton 20115, Kenya*

During the 2013-2017 period, the MEDS laboratory received and processed 6853 samples. Samples were sourced from Kenya and other sub-Saharan Africa countries. The samples submitted comprised Kenyan manufactured (31.9%) and internationally manufactured products (67.9%) while nine samples were of unknown origin. Analysis was carried out according to compendial and/or in-house specifications. The non-compliance rate was 5.1% consisting of 1.2 % local and 3.8% imports. The top ten drug classes with high failure rates were antimyasthenics (50.0%), antiseptics/disinfectants (24.7%), anthelminthics (22.0%), thyroid/antithyroid drugs (20.0%), nutrient mixtures (18.5%), uricosurics (12.5%), waters (11.6%), mixed anti-infectives (11.1%), hemostatics (10.0%) and nootropics (10.0%). Full compliance was however, recorded with laxatives, antidiarrheals, antihemorrhoidals, prokinetics, antithrombotics, antithrombocytopenia agents, vasopressors, anti-arrhythmic drugs, anti-anginal drugs, disease modifying antirheumatic drugs, antimigraine drugs, vertigolytics, muscle relaxants, bisphosphonates, joint lubricants, hormones, anticholinergics, osmotic diuretics, hypophosphatemics, lubricants, minerals, amino acids/peptides, immunomodulatory agents, choleretics, antidotes, lozenges, ear drops, proteins/glycoproteins, herbal products, X-ray contrast media, vaccines, environmental monitoring, medical devices/equipment and cleaning validation swabs. A total of 23 substandard and falsified medicines devoid of active ingredients were encountered over the five-year period. The results obtained demonstrate the need to strengthen regulatory stringency in order to curb incidences of substandard and falsified medicines.

Key words: MEDS, drug product, assay, dissolution, substandard and falsified medicine, specification

INTRODUCTION

The World Health Organization (WHO) defines quality control (QC) as the sum of all procedures undertaken to ensure that raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics [1]. Quality control is an integral part of the pharmaceutical quality system as stipulated in the International Conference on Harmonization (ICH) guidelines [2]. Quality control laboratories provide the essential technical support to drug regulatory authorities (DRAs) towards fulfilling their mandate with respect to market authorization (MA), post market surveillance (PMS) and pharmacovigilance (PV) which are the hallmarks of efficient oversight in the pharmaceuticals market. Such regulation is complicated by the existence of organized syndicates dealing in substandard and falsified medicines (SFM) in

*Author to whom correspondence may be addressed. Email address: koabuga@uonbi.ac.ke

low- and middle-income countries (LMICs). The LMICs are particularly susceptible to this vice due to weak regulatory systems resulting from resource constraints and limited legal mandate [3]. The global SFM prevalence is estimated at 10.5% with expenditure valued at about 30 million USD, attributable to poor pharmaceutical regulation, weak technical capacity, and inadequate supply chain management [4]. The pitfalls of these products towards disease prevalence, antimicrobial resistance, erosion of consumer confidence, wastage of healthcare resources, morbidity and mortality remain unevaluated [5]. Quality control plays a critical role in local and global SFM surveillance and monitoring initiatives.

In Kenya, the competent authorities charged with regulation of the drug market are the Pharmacy and Poisons Board (PPB) and the Directorate of Veterinary Medicines for human and veterinary pharmaceuticals respectively [6, 7]. Consequently, the PPB has instituted the requisite guidelines and procedures for manufacture, importation, registration, distribution, use and disposal of drugs [8]. The PPB governs the market authorization process for human medicines and technologies whereby pre-registration QC is an integral part of dossier evaluation according to the ICH Common Technical Document (CTD), module 3 [9, 10]. For this purpose, the applicants are required to submit a QC report from three accredited laboratories; National Quality Control Laboratory (NQCL), Drug Analysis and Research Unit (DARU) and Mission for Essential Drugs and Supplies (MEDS) laboratory. It is thus deductive that majority of samples submitted to these laboratories are intended for drug registration [11, 12].

The Mission for Essential Drugs and Supplies (MEDS) is a faith based not-for-profit pharmaceutical distributor established in 1986 under the auspices of the Kenya Conference of Catholic Bishops (KCCB) and Christian Health Association of Kenya (CHAK) ecumenical partnership. The organization undertakes three main functions namely, supply chain management, quality assurance and health advisory services [13]. The MEDS laboratory supports the quality assurance pillar through prequalification (PQ) of MEDS suppliers, commodity testing, PMS and PV. Quality control testing for purposes of supplier PQ is a vital part of the MEDS tender evaluation mechanism. Typical suppliers include importers, distributors, wholesalers who are agents for specific manufacturers.

Additionally, MEDS is a member of the Ecumenical Pharmaceutical Network (EPN), an alliance of faith-based organizations, majority of whom are supply chain organizations that promote QC through the Global Pharma Health Fund (GPHF)-Minilab [14]. Confirmatory testing for failed samples is performed at the MEDS laboratory. The EPN conveys confirmed non-compliant results to the WHO Global Surveillance and Monitoring System for substandard and falsified medicines, whereof public alerts are issued [4].

The MEDS laboratory attained WHO prequalification status in the year 2009 and has maintained compliance up-to-date [15]. Aside from internal analysis, the MEDS laboratory receives samples from manufacturers, importers, distributors, government institutions, regulatory authorities, non-governmental organizations, hospitals, public health programmes and international organizations. Monthly and annual reports are consistently generated for in-house appraisal. Nonetheless, this is the first published report of quality control results obtained, covering the five-year period, 2013-2017.

MATERIALS AND METHODS

Samples

Samples for analysis were received from pharmaceutical manufacturers and importers, regulatory authorities, non-governmental organizations, donor-funded programmes, government agencies and hospitals domiciled in Kenya and other sub-Saharan Africa countries. In addition, internal MEDS samples for supplier prequalification or post market surveillance were processed. Testing was requested for purposes of product registration, batch release, manufacturing

inputs, supplier prequalification, post market surveillance and pharmacovigilance investigations. Additionally, the laboratory was contracted by one manufacturer for quality assurance (QA) testing in batch release, shopfloor environmental monitoring, water quality, cleaning validation and stability.

The samples were received and processed according to the laboratory's standard operating procedure (SOP) for sample handling. Briefly, clients filled the Test Request Form (TRF) capturing information on the applicant, sample details, tests required, applicable specification, person authorizing request for analysis and visual inspection findings. Duly completed TRFs were approved by the laboratory supervisor, assigned unique laboratory numbers and entered into the sample records register. Samples were issued for analysis to the executing analyst with the required specification and working/reference standard substances. The analytical process was tracked, checked and verified through an internal mechanism until release and archival of certificates of analysis. Retention samples were stored under controlled conditions until disposal in congruence with the laboratory's instructions for waste disposal.

Samples for human use

A total of 6360 pharmaceutical samples for human use incorporating drug products and raw materials were submitted for analysis during the study period.

Veterinary samples

Ninety-four veterinary samples belonging to the anti-infectives (63) and vaccines (31) categories were received during the study period. The samples were submitted by manufacturers, distributors and importers in pursuit of market authorization.

Non-drug samples

A total of 399 non-drug samples consisting of excipients (16), solvents (1), medical devices/equipment (4), environmental monitoring (365) and cleaning validation swabs (13) were tested. Most of these samples were submitted by manufacturers for testing production inputs and hardware in line with Good Manufacturing Practices (GMP) compliance.

Specifications

Samples were subjected to compendial and/or in-house specifications. Where applicable, official monographs from current editions of the British Pharmacopoeia (BP), United States Pharmacopeia (USP), International Pharmacopoeia (Ph. Int.) and European Pharmacopoeia (Ph. Eur.) were applied [16-19]. Additionally, the GPHF-Minilab was used for PMS samples covering diverse pharmacological classes [14]. Medical devices were subjected to the ISO 4832:2006(E) specifications for coliforms count [20]. Otherwise, validated client's in-house methods were used. The results were reported in approved templates for certificates of analysis in accordance with the laboratory's procedures.

RESULTS AND DISCUSSION

The QC outcomes for the different categories of samples analyzed during the study period are presented in Table 1 while the product details are recorded in Supplementary Table S1 [21]. The total number of samples processed was 6853 consisting of 2188 (31.9%) Kenyan made and 4656 (67.9%) imports while nine samples (0.1%) were of unknown origin. The low number of locally manufactured products reflects Kenya's low manufacturing capacity for pharmaceuticals against competing imports, an observation corroborated by previous reports [11]. The number of internal MEDS samples was 1814 with the rest (5039) being clients' submissions.

Official methods were applied in 4796 samples (70.0%) while 342 samples (5.0%) were subjected to GPHF minilab (340) and ISO 4832:2006(E) (2) specifications. The remaining 1751 (25.0%) were analyzed using client's in-house specifications. In 109 cases (1.6%), a combination of two compendial specifications were applied, whereas 13 samples were analyzed using a mix of compendial and GPHF-Minilab tests. The latter are samples that underwent

confirmatory laboratory testing after failing in the GPHF-Minilab field procedures. The high level of compendial reference differs from reports from other laboratories in Kenya [11].

The overall non-compliant rate was 5.1% disaggregated into 3.9% local and 5.6% imported products respectively. This level of non-compliance is marginally higher than that reported by Abuga et al. [11] but with a reversal of the local-imported failure pattern. Similar reports from the DARU laboratory have demonstrated higher failure rates [12, 22, 23]. Antimyasthenics recorded the highest failure rate of 50.0%, followed by antiseptics/disinfectants (24.7%), anthelminthics (22.0%), thyroid/antithyroid drugs (20.0%). Failure in the assay test accounted for all non-compliant antimyasthenic drugs and 57.1% of antiseptics/disinfectants while 71.4% of anthelminthics failed in the dissolution test for albendazole, levamisole and mebendazole tablets.

Complete compliance with specifications was achieved with laxatives, antidiarrheals, antihemorrhoidals, prokinetics, antithrombotics, antithrombocytopenia agents, vasopressor agents, anti-arrhythmic drugs, anti-anginal drugs, disease modifying antirheumatic drugs, antimigraine drugs, vertigolytics, muscle relaxants, bisphosphonates, joint lubricants, hormones, anticholinergics, osmotic diuretics, hypophosphatemics, vaginal lubricants, minerals, amino acids/peptides, immunomodulatory agents, choleretics, antidotes, lozenges, ear drops, proteins/glycoproteins, herbal products, X-ray contrast media, vaccines, environmental monitoring, medical devices/equipment and cleaning validation swabs.

Among the gastrointestinal drugs, spasmolytics recorded non-compliance of 9.4% followed by anti-ulcer drugs (8.6%) and anti-emetics (7.3%) while all other drugs in this category complied with specifications. For cardiovascular drugs, four classes namely, hemostatics (10.0%), hypoglycemics (5.6%), antihypertensives (4.5%) and hypolipidemics (4.0%) exhibited quality problems. Eight eye preparations (5.9%) consisting of chloramphenicol, ciprofloxacin, prednisolone, sodium cromoglycate and tetracycline failed in assay except gentamicin which failed in deliverable volume and pH.

The anti-infectives had varying failure rates ranging from 22.0% (antihelminthics) down to 0.9% (antivirals). Majority of antiviral samples analyzed consisted of antiretroviral (ARV) drugs (86.0%) submitted by donor-funded programmes to support procurement and distribution of ARVs in their respective countries. Antimalarials showed a failure rate of 9.2% with quinine (10) and sulfadoxine/pyrimethamine (7) tablets accounting for 52.0% of the non-compliant samples. The non-compliance level for antibacterials was 4.4% covering several classes. Only three samples (3.2%) of antimycobacterials failed in weight variation and assay tests. Six antifungal samples (5.0%) composed of fluconazole capsules and griseofulvin tablets failed in the quality tests conducted.

Nootropics had a failure rate of 10.0% attributable to one sample of citicoline injection which failed in assay. Other non-compliant drugs in the neurological category were anti-epileptics (7.5%), opioid analgesics (6.0%), analgesics (4.6%), anti-inflammatory agents (3.1%), and psychotropics (2.5%). Among the anesthetics, two samples (2.8%) of thiopentone injection failed in loss on drying (LOD).

Respiratory drugs with quality issues (7.6%) included, aminophylline, (levo)cetirizine, montelukast, promethazine, salbutamol, salmeterol/fluticasone and cough syrup mixtures. This presents a high risk to patients since some of these drugs are commonly used as prescription or over-the-counter remedies.

Among the genito-urinary drugs, one sample in each category including tadalafil, levonorgestrel tamsulosin, febuxostat and clomiphene failed in the quality tests performed. For uterotonics however, two samples (misoprostol tablets, oxytocin injection) were non-compliant.

Table 1: Quality control results of samples analyzed in MEDS laboratory during the period 2013 - 2017

	Body system/ Drug class	Number of samples	Compliant samples		Non-compliant samples	
			Local	Imported	Local	Imported
1.	**Gastrointestinal system**					
	a. Antiulcer drugs	140	10	118	-	12
	b. Anti-emetics	55	4	47	-	4
	c. Spasmolytics	32	2	27	-	3
	d. Laxatives	10	3	7	-	-
	e. Anti-diarrheals	7	-	7	-	-
	f. Antihemorrhoidals	6	-	6	-	-
	g. Prokinetics	2	-	2	-	-
2.	**Cardiovascular system**					
	a. Hemostatics	20	-	18	1	1
	b. Antithrombotics	41	8	33	-	-
	c. Antithrombocytopenics	2	-	2	-	-
	d. Vasopressor agents	7	-	7	-	-
	e. Anti-arrhythmic drugs	1	-	1	-	-
	f. Anti-anginal drugs	20	-	20	-	-
	g. Antihypertensives	534	84	426	2	22
	h. Hypoglycemics	142	42	92	-	8
	i. Hypolipidemics	75	8	64	-	3
3.	**Eye preparations**	136	16	112	1	7
4.	**Anti-infectives**					
	a. Antibacterials	*1622	618	930	13	58
	b. Antimycobacterials	94	48	43	-	3
	c. Anthelmintics	127	50	49	7	21
	d. Antiprotozoals	116	31	75	4	6
	e. Mixed anti-infectives	27	-	24	-	3
	f. Antimalarials	*390	36	317	3	33
	g. Antivirals	442	29	409	-	4
	h. Antifungals	119	63	50	-	6
5.	**Nervous system**					
	a. Analgesics	*431	100	306	2	18
	b. DMARDs	4	-	4	-	-
	c. Anti-inflammatory drugs	65	24	39	-	2
	d. Opioid analgesics	84	1	78	-	5
	e. Anti-epileptics	67	11	51	1	4
	f. Psychotropics	157	45	108	2	2
	g. Nootropics	10	2	7	-	1

	Body system/ Drug class	Number of samples	Compliant samples		Non-compliant samples	
			Local	Imported	Local	Imported
	h. Anesthetics	71	-	69	-	2
	i. Antimigraine drugs	3	-	3	-	-
	j. Vertigolytics	1	-	1	-	-
6.	**Musculoskeletal system**					
	a. Antimyasthenics	8	-	4	-	4
	b. Muscle relaxants	19	-	19	-	-
	c. Bisphosphonates	8	-	8	-	-
	d. Joint lubricants	1	-	1	-	-
7.	**Endocrine system**					
	a. Thyroid/antithyroid drugs	10	2	6	-	2
	b. Hormones	19	-	19	-	-
8.	**Respiratory system**	302	87	192	8	15
9.	**Genitourinary system**					
	a. Sexual dysfunction drugs	30	-	29	-	1
	b. Ovulants	12	-	11	-	1
	c. Anti-BPH drugs	15	-	14	-	1
	d. Anticholinergics	9	-	9	-	-
	e. Uterotonics	24	-	22	-	2
	f. Contraceptives	23	-	22	-	1
	g. Uricosurics	8	-	7	-	1
	h. Osmotic diuretics	6	-	6	-	-
	i. Hypophosphatemics	2	-	2	-	-
	j. Lubricants	2	2	-	-	-
10.	**Anticancer agents**	105	-	103	-	2
11.	**Nutritional products**					
	a. Nutrient mixtures	27	9	13	4	1
	b. Vitamins	56	34	20	-	2
	c. Minerals	39	10	29	-	-
	d. Amino acids/peptides	1	-	1	-	-
	e. Electrolytes	272	175	93	4	-
	f. Waters	69	40	21	8	-
12.	**Skin preparations**	174	75	94	3	2
13.	**Miscellaneous products**					
	a. Immunomodulatory agents	14	-	14	-	-
	b. Choleretics	2	-	2	-	-
	c. Antidotes	10	-	10	-	-
	d. Lozenges	5	-	5	-	-

Body system/ Drug class	Number of samples	Compliant samples		Non-compliant samples	
		Local	Imported	Local	Imported
e. Ear drops	4	-	4	-	-
f. Antiseptics/disinfectants	81	49	12	20	-
g. Proteins/glycoproteins	2	-	2	-	-
h. Herbal products	1	-	1	-	-
i. Solvents	1	-	-	1	-
j. X-ray contrast media	2	-	2	-	-
k. Vaccines	32	-	32	-	-
l. Environmental monitoring	365	365	-	-	-
m. Medical devices/ equipment	4	-	4	-	-
n. Cleaning validation	13	7	6	-	-
o. Excipients	16	13	2	1	-
TOTAL	**6853**	**2103**	**4393**	**85**	**263**

*Includes samples of unknown origin. BPH – Benign prostatic hyperplasia, DMARDs – disease modifying antirheumatic drugs, MEDS – Mission for essential drugs and supplies.

All the anticancer drugs analyzed were compliant except two vincristine injection products that failed in content uniformity and assay. Five samples of nutrient mixtures (ferrous fumarate/folic acid) failed in weight variation, content uniformity and assay while two samples of mecobalamin had pH values outside the specified range. Four samples of dextrose infusion did not comply with acidity/alkalinity (3) and assay (1). With regard to waters, two samples of potable water failed in microbial load and limit tests while six samples of purified water were non-compliant. The dermatologicals recorded a failure rate of 2.9% owing to calamine lotion (residue on ignition) as well as hydrocortisone, silver sulfadiazine and terbinafine creams for assay. The failure rate for antiseptics/disinfectants was 24.7% owing to methylated spirit, povidone-iodine and sodium hypochlorite.

Only one sample of methanol was analyzed, which did not meet the acceptance criteria for ultraviolet (UV) absorbance and residue on evaporation. Environmental monitoring samples included swabs and plate exposures for sterility and microbial load testing for shop floor QC. Similarly cleaning validation samples were collected on site and tested for active pharmaceutical ingredient (API) residues and microbial load. The excipients analyzed included glycerine, non-pareil seeds and petrolatum of which one sample of the latter failed in the appearance specification.

During the study period, 23 samples (0.3%) including spasmolytics (2), antibacterials (6), antimalarials (13), anti-epileptics (1) and ovulants (1) did not contain the stated API as listed in Table 2. Majority (82.6%) of these samples were antimicrobials which incidentally are the mainstay treatment for infections. Therefore, use of such SFM could seriously undermine healthcare delivery due to treatment failures, antimicrobial resistance and possibly mortality. In a study dedicated to surveillance for falsified and substandard medicines in Africa and Asia similarly alarming findings were elucidated. Notably, out of 21 confirmed SFM, 12 samples consisting of antibacterials (3) and antimalarials

(9) did not have the stated API [24]. This scenario underscores the need for sustained risk-based PMS to combat the SFM circulation thus protecting the unsuspecting public from potential adverse outcomes of these products.

Table 2: List of SFM without API analyzed in MEDS laboratory during the period 2013-2017

	Brand name	Claimed API content	Therapeutic class
1.	Enscopan injection	Hyoscine butyl bromide 20 mg /ml	Spasmolytic
2.	Buscopan capsules	Hyoscine butyl bromide 10 mg	Spasmolytic
3.	Amoxverse capsules	Amoxicillin 250 mg	Antibacterial
4.	Ampiverse	Ampicillin 250 mg	Antibacterial
5.	Zinnat tablets	Cefuroxime 250 mg	Antibacterial
6.	Ciprofloxacin tablets	Ciprofloxacin 750 mg	Antibacterial
7.	Ciprofloxacin tablets	Ciprofloxacin 500 mg	Antibacterial
8.	Augmentin	Co-amoxiclav 625 mg	Antibacterial
9.	Coartem tablets	Artemether 20 mg, lumefantrine 120 mg	Antimalarial
10.	Duo-cotecxin tablets	Dihydroartemisinin 40 mg, piperaquine 320 mg	Antimalarial
11.	Duo-cotecxin tablets	Dihydroartemisinin 40 mg, piperaquine 320 mg	Antimalarial
12.	Quinine sulfate tablets	Quinine 300 mg	Antimalarial
13.	Quinine sulfate tablets	Quinine 300 mg	Antimalarial
14.	Quinine sulfate tablets	Quinine 500 mg	Antimalarial
15.	Quinine sulfate tablets	Quinine 300 mg	Antimalarial
16.	Quinine bisulfate tablets	Quinine 350 mg	Antimalarial
17.	Quinine sulfate tablets	Quinine 300 mg	Antimalarial
18.	Maloxine tablets	Sulfadoxine 500 mg, pyrimethamine 25 mg	Antimalarial
19.	Maloxine tablets	Sulfadoxine 500 mg, pyrimethamine 25 mg	Antimalarial
20.	Novidar SP tablets	Sulfadoxine 500 mg, pyrimethamine 25 mg	Antimalarial
21.	Novidar SP tablets	Sulfadoxine 500 mg, pyrimethamine 25 mg	Antimalarial
22.	Neurolin M tablets	Pregabalin 75 mg, methylcobalamin 1 mg	Anti-epileptic
23.	Clomid 50 tablets	Clomiphene	Ovulant

API – active pharmaceutical ingredient, SFM – substandard and falsified medicine

CONCLUSION

The MEDS laboratory received a relatively high sample load compared to other laboratories which have recently published QC results [11, 12]. This may be attributable to enhanced capacity, WHO PQ status and analysis of internal MEDS samples. The study findings underscore the need to strengthen post-market surveillance and pharmacovigilance programs as vital regulatory tools to ensure that good quality medicines reach the population. Such strategies and programs need to be integrated as core functions of the DRA for effectiveness and efficiency. The level of falsified medicines encountered adds impetus to the concerted efforts by regulatory authorities and international bodies towards the fight against drug fraud. More studies are required to provide data for evidence driven regulatory actions and operations. This first report of QC results in MEDS laboratory acts as baseline data for comparison in future publications.

ACKNOWLEDGEMENTS

The authors wish to thank the management of MEDS for granting approval towards publication of this paper. Gratitude also goes to Ms. Karen Kimathi and Ms. Lilian Ndegwa who consolidated the data used in this paper from the archives.

REFERENCES

[1]. https://www.who.int/publications/m/item/who-good-practices-for-pharmaceutical-quality-control-laboratories---trs-957---annex-1. Accessed on 5th April 2022.

[2]. International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use. Pharmaceutical Quality System - Q10. 2007, Step 4 Version 2008.

[3]. G. Kaddu, E. D'Amore, A. Clark and P. Nkansah Strengthening regulatory systems to improve medical product quality in low- and middle-income countries. 2018. Promoting the Quality of Medicines (PQM) program. U.S. Pharmacopeial Convention, Rockville, Maryland.

[4]. World Health Organization. WHO Global Surveillance and Monitoring System for substandard and falsified medical products. Geneva, World Health Organization, 2017. Licence: CC BY-NC-SA 3.0 IGO.

[5]. World Health Organization. Study on the public health and socioeconomic impact of substandard and falsified medical products. Geneva, World Health Organization, 2017. Licence: CC BY-NC-SA 3.0 IGO.

[6]. National Council for Law Reporting. CAP 244, Pharmacy and Poisons Act. 1956 (Revised in 2015). Government Printer, Nairobi, Kenya

[7]. Kenya Gazette Supplement No. 174. Legal notice No. 209. The veterinary surgeons and veterinary paraprofessionals act (the veterinary medicines directorate) regulations, 2015. 9th October, 2015.

[8]. https://web.pharmacyboardkenya.org/downloads/guidelines. Accessed on 5th April 2022.

[9]. International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use. Quality – M4Q(R1). 2000, Step 4 Version 2012.

[10]. Pharmacy and Poisons Board. Registration of drugs; Guidelines to submission of applications. Pharmacy and Poisons Board, Nairobi, 2010.

[11]. K.O. Abuga, S.N. Ndwigah, B.K. Amugune, D.B. Ongarora, P.M. Njogu, A.O. Okaru and I.O. Kibwage. East Cent. Afr. J. Pharm. Sci. 23(3), 2020, 79-86.

[12]. K.O. Abuga, B.K. Amugune, S.N. Ndwigah, F.N. Kamau, G.N. Thoithi, J.O. Ogeto, A.O. Okaru, J.M. Nguyo, O.K. King'ondu, H.N. Mugo and I.O. Kibwage. East Cent. Afr. J. Pharm. Sci. 16(2), 2013, 33-43.

[13]. https://meds.or.ke/about-us/. Accessed on 5th April, 2022.

[14]. https://www.gphf.org/en/minilab/index.htm. Accessed on 5th April 2022.

[15]. https://extranet.who.int/pqweb/medicines/medicines-quality-control-laboratories-list. Accessed on 5th April, 2022.

[16]. The Stationery Office (TSO). British Pharmacopoeia. TSO, London.

[17]. U. S. Pharmacopeial Convention. United States Pharmacopeia. U. S. Pharmacopeial Convention Inc., Rockville, MD, U.S.A.

[18]. World Health Organization. International Pharmacopoiea. World Health Organization, Geneva.

[19]. Council of Europe. European Pharmacopoiea. Council of Europe, Strasbourg.

[20]. International Organization for Standardization (ISO). Microbiology of food and animal feeding stuffs - Horizontal method for the enumeration of coliforms - Colony-count technique, ISO 4832:2006(E). ISO, Geneva. 2006.

[21]. http://uonjournals.uonbi.ac.ke/ojs/index.php/ecajps/article/view/966.

[22]. G.N. Thoithi, K.O. Abuga, J.M. Nguyo, O. King'ondu, G.G. Mukindia, H.N. Mugo, J.K. Ngugi and I.O. Kibwage. East Cent. Afr. J. Pharm. Sci. 11 (3), 2008, 74-81.

[23]. G.N. Thoithi, K.O. Abuga, J.M. Nguyo, G.G. Mukindia, O. King'ondu, J.K. Ngugi and I.O. Kibwage. East Cent. Afr. J. Pharm. Sci. 5 (2), 2002, 28-32.

[24]. A. Petersen, N. Held and L.Heide. PLoS ONE, 12(9), 2017, e0184165.