Quality Control Report of Drugs Analyzed in the Drug Analysis and Research Unit During the Period 2016-2020

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During the five-year period covering 2016-2020, the Drug Analysis and Research Unit (DARU) received and processed 326 drug samples. Of these samples, 32.5% were locally manufactured, 65.7% imported and 1.8% of undeclared origin. Samples were analyzed according to compendial and/or in-house specifications. The overall non-compliance rate was 1.8% (0.6% locally manufactured, 0.9% imported and 0.3% drugs of undeclared origin). Full analytical compliance was recorded with anti-emetics. spasmolytics, antihypertensives, ophthalmics, anti-infectives, analgesics, anti-inflammatory agents, anti-epileptics, nootropics, anaesthetics, respiratory drugs, genitourinary drugs, anticancers, dermatologicals, immunomodulatory drugs, vaccines and excipients. However, one sample each of anti-ulcers, hypoglycemics, opioids and herbals as well as two samples of antiseptics did not comply with specifications. This represents the lowest failure rate of samples analyzed in DARU and presented as pentad reports since the year 1991.

Key words: DARU, specifications, drug class, market authorization, adulteration, substandard and falsified medicine

INTRODUCTION

The pharmaceutical industry operates stringent quality assurance (QA) systems for production, distribution (including storage) and dispensing of medicines in order to safeguard consumer interests. The requisite regulatory guidelines are categorized into Good Manufacturing Practices (GMP), Good Distribution Practices (GDP) and Good Dispensing Practices (GDSP).[1–3] These 'good practices' engender a code of conduct and operational measures aimed at consistently producing high quality products and preserving this attribute down the distribution chain to the end users. In this context, quality control (QC) is a critical part of QA concerned with testing of inputs, intermediates and final products for conformity with specifications.[4] Consequently, pharmaceutical QC laboratories support pharmaceutical manufacturing, market authorization, post-market surveillance (PMS) and pharmacovigilance (PV) activities. For optimal performance, QC laboratories require in-built procedures that ensure traceable, transparent and verifiable processing of samples during analysis in tandem with International Conference on Harmonization (ICH) and World Health Organization (WHO) guidelines.[4,5]

Market authorization (MA) for new drug products is granted after rigorous dossier evaluation to which a QC report from an accredited laboratory is integral.[5,6] In Kenya, the competent authorities mandated with MA are the Pharmacy and Poisons Board (PPB), and Veterinary Medicines Directorate (VMD) regarding medicines for human use and veterinary products, respectively.[7,8] Nonetheless, MA *per se* may not guarantee consistent supply of quality products into the market due to potential batch to batch variations and post distribution degradation.[9] Thus, robust PMS and PV systems appropriately managed by national medicines regulatory authorities (NMRAs) are necessary to detect any substandard and falsified (SF) medicines in circulation.[2,10] Several PMS

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studies have demonstrated existence of poor quality medicines in low- and middle-income countries (LMICs) including Kenya.[9,10] In some instances, the products do not contain the labeled active pharmaceutical ingredient (API).[11,12] Consumption of SF medicines portends adverse patient outcomes (including mortality) as well as degraded professional and consumer confidence. The NMRAs are charged with the mandate of ensuring that quality medicines are accessible to consumers.

The Drug Analysis and Research Unit (DARU) is domiciled in the Department of Pharmaceutical Chemistry, Pharmaceutics & Pharmacognosy of the University of Nairobi. The laboratory carries out QC for clients towards approval of raw materials, in-process and batch release testing, in addition to market authorization, pharmacovigilance and post market surveillance. Since 1991 the results obtained in DARU have been regularly published in pentad reports as part of QC performance monitoring and policy input.[13–17] This paper presents the quality control results of samples analyzed in the DARU laboratory during the 2016-2020 period.

MATERIALS AND METHODS

Samples

The samples analyzed in DARU during the study period were submitted by manufacturers, importers, wholesalers, non-governmental organizations, regulatory bodies and hospitals. The samples consisted of human medicines, veterinary products, vaccines, herbals and excipients. Majority of the clients were manufacturers and importers who requested analyses in support of MA submissions. Other reasons for analysis included batch release, stability studies and PV investigations. Procedures for sample submission to the DARU laboratory have been described previously.[17]

Drugs for human use in various therapeutic classes accounted for 89.0% of the samples submitted with the top five being anti-infectives (110), neurological drugs (72), respiratory drugs (20), cardiovascular agents (14) and dermatologicals (10). On the other hand, a total of 36 (11.0%) veterinary samples were submitted for analysis consisting of anthelminthics (20), antibacterials (12), antiprotozoals (3) and antiseptics (1). One herbal sample claimed to possess aphrodisiac activity was investigated for adulteration with phosphodiesterase type 5 (PDE-5) inhibitor drugs usually marketed for erectile dysfunction.

Methods

Compendial methods were applied for products with monographs in current versions of the British Pharmacopoeia[18] and United States Pharmacopeia.[19] Where official methods were unavailable, in-house specifications were utilized. All methods were verified prior to application. Analyses were performed according to the specific tests requested by clients.

RESULTS AND DISCUSSION

Table 1 displays the summary results obtained for samples analyzed during the study period. Product details and quality performance in the tests carried out are listed in Supplementary Table S1.[20]

A total of 326 samples were analyzed during the 2016-2020 period comprising 106 (32.5%) locally manufactured, 214 (65.7%) imported and six (1.8%) samples of undeclared origin (Table 1). Five samples in the latter category were capsule shells intended as manufacturing inputs while one sample was an isopropyl alcohol-based sanitizer. The 326 samples reported represented a decline from those analyzed in the preceding pentad.[17] The previously observed pattern of a lower proportion of locally manufactured samples as compared to imports was still evident. The underlying causes of low local manufacturing capacity in Kenya have been cited in the literature.[11,13–17]

Compendial methods were applied in analysis of 120 samples (36.8%) distributed between the BP (71) and USP (49), while the rest were subjected to in-house specifications. The implications of lack of official specifications were previously discussed by Abuga et al.[16]

Table 1: Quality control results of samples analyzed in DARU during the period 2016–2020

	Body system/Drug class	Number of samples	Compliant samples		Non-compliant samples	
			Local	Imported	Local	Imported
1.	**Gastrointestinal system**					
	a. Antiulcer drugs	5	1	3	-	1
	b. Anti-emetics	2	2	-	-	-
	c. Spasmolytics	1	-	1	-	-
2.	**Cardiovascular system**					
	a. Antihypertensives	10	4	6	-	-
	b. Hypoglycemic agents	4	-	3	-	1
3.	**Eye preparations**	9	-	9	-	-
4.	**Anti-infectives**					
	a. Antibacterials	104	13	91	-	-
	b. Anthelmintics	18	9	9	-	-
	c. Antiprotozoals	8	4	4	-	-
	d. Mixed antimicrobials	7	2	5	-	-
	e. Antimalarials	4	-	4	-	-
	f. Antivirals	2	-	2	-	-
	g. Antifungals	2	2	-	-	-
5.	**Nervous system**					
	a. Analgesics	18	5	13	-	-
	b. Anti-inflammatory agents	1	-	1	-	-
	c. Opioid analgesics	45	38	6	1	-
	d. Anti-epileptics	2	2	-	-	-
	e. Nootropics	1		1	-	-
	f. Anaesthetics	3		3	-	-
6.	**Respiratory system**	20	14	6	-	-
7.	**Genitourinary system**					
	a. Erectile dysfunction drugs	5	3	2	-	-
	b. Anti-BPH drugs	1	-	1	-	-
	c. Uterotonics	2	-	2	-	-
	d. Uricosurics	2	2		-	-
	e. Osmotic diuretics	1	-	1	-	-
8.	**Anticancer agents**	9	-	9	-	-
9.	**Nutritional products**					
	a. Nutrient mixtures	3	-	3	-	-
	b. Vitamins	4	-	4	-	-
	c. Minerals	1	-	1	-	-
	d. Electrolytes	2	-	2	-	-

	Body system/Drug class	Number of samples	Compliant samples		Non-compliant samples	
			Local	Imported	Local	Imported
10.	**Skin preparations**	10	-	10	-	-
11.	**Miscellaneous products**					
	a. Immunomodulatory agents	4	-	4	-	-
	b. Excipients	*6	-	1	-	-
	c. Antiseptics & disinfectants	**5	3	-	1	-
	d. Herbal products	2	-	1	-	1
	e. Vaccines	3	-	3	-	-
	Total	**326**	**104**	**211**	**2**	**3**

BPH – Benign prostatic hyperplasia, DARU – Drug Analysis and Research Unit, *includes 5 samples of undeclared origin, **includes 1 sample of undeclared origin.

The overall non-compliance rate was 1.8%, consisting of 0.6% local, 0.9% imported and 0.3% undeclared origin samples, respectively. This represents the lowest failure rate for samples tested in the DARU laboratory since 1991. Six samples comprising one each of anti-ulcers, hypoglycemics, opioids and herbals as well as two antiseptics failed to comply with quality specifications. These findings are a clear contrast to reports in literature where the proportion of substandard or falsified medicines in LMICs is usually >10%[21,22] with anti-infectives recording the highest failure rates.[15,16,21]

All of the ophthalmic, anti-infective, respiratory, genitourinary, anticancer and dermatological drugs complied with specifications. Additionally, drugs in the anti-emetics, spasmolytics, antihypertensives, analgesics, anti-inflammatory agents, anti-epileptics, nootropics, anaesthetics, immunomodulatory drugs, vaccines and excipients subclasses were compliant with corresponding specifications. The high compliance level is a pointer to improved adherence to current Good Manufacturing Practices (cGMP) by manufacturers in the pharmaceutical sector.

The non-compliant samples included omeprazole capsules (dissolution), empagliflozin tablets (weight uniformity) and iodine tincture (assay). One sample of morphine solution under accelerated stability study (zone 4 conditions) failed in assay in the sixth month of sampling. An isopropyl alcohol (IPA) sanitizer (70% v/v) was found to contain a mixture of IPA and ethanol which further failed assay of total alcohols. One herbal sample marketed as an aphrodisiac was found to be razed with tadalafil. Widespread adulteration of herbals promoted for erectile dysfunction with PDE-5 inhibitors has been reported in the literature.[23]

CONCLUSION

The study period, 2016-2020 recorded a drop in the number of samples analyzed at the DARU laboratory compared to the immediately preceding period. The results obtained demonstrate an improvement in the quality performance of the drugs processed, especially the anti-infectives which recorded poor quality performance in previous reports. This could predict desirable treatment outcomes on users and positive impacts on drug resistance patterns.

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