12-9-2021

Improving Pharmacovigilliance Quality Management System in the Pharmacy and Poisions Board of Kenya

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IMPROVING PHARMACOVIGILLANCE QUALITY MANAGEMENT SYSTEM IN THE PHARMACY AND POISONS BOARD OF KENYA

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ABSTRACT

The purpose of this study was to explore ways of improving the pharmacovigilance quality system employed by the Pharmacy and Poisons Board of Kenya. The Pharmacy and Poisons Board of Kenya employs a hybrid system of pharmacovigilance that utilizes an online system of reporting pharmacovigilance incidences and a physical system, where a yellow book is physically filled by the healthcare worker and sent to the Pharmacy and Poisons Board for onward processing. This system, even though it has been relatively effective compared to other systems employed in Africa, has one major flaw. It is a slow and delayed system that captures the data much later after the fact and the agency will always be behind the curve in controlling the adverse incidents and events. This means that the incidences might continue to arise or go out of control. This project attempts to develop a system that would be more proactive in the collection of pharmacovigilance data and more predictive of pharmacovigilance incidences. The pharmacovigilance system should have the capacity to detect and analyze subtle changes in reporting frequencies and in patterns of clinical symptoms and signs that are reported as suspected adverse drug reactions. The method involved carrying out a thorough literature review of the latest trends in pharmacovigilance employed by different regulatory agencies across the world, especially the more stringent regulatory authorities. A review of the system employed by the Pharmacy and Poisons Board of Kenya was also done. Pharmacovigilance data, both primary and secondary, were collected and reviewed. Media reports on adverse drug reactions and poor-quality medicines over the period were also collected and reviewed. An appropriate predictive pharmacovigilance tool was also researched and identified. It was found that the Pharmacy and Poisons Board had a robust system of collecting historical pharmacovigilance data both from the healthcare workers and the general public. However, a more responsive data collection and evaluation system is proposed that will help the agency achieve its pharmacovigilance objectives. On analysis of the data it was found that just above half of all the product complaints, about 55%, involved poor quality medicines; 15% poor performance, 13% presentation, 8% adverse drug reactions, 7% market authorization, 2% expired drugs and 1% adulteration complaints. A regulatory pharmacovigilance prioritization tool was identified, employing a risk impact analysis was proposed for regulatory action.

Keywords: pharmacovigilance, poor quality medicines,adverse drug reactions, counterfeit medicines,risk mangement.

1. INTRODUCTION

The project involved the strengthening of the quality systems for the pharmacovigilance in the Pharmacy and Poisons Board of Kenya. The system proposed a data driven system that that would be more proactive in the collection of pharmacovigilance data and more predictive of pharmacovigilance incidences. The Pharmacy and Poisons Board of Kenya employed a hybrid system of pharmacovigilance that utilized an online system of reporting and a physical system where a yellow book was physically filled by the healthcare worker and sent to the Pharmacy and Poisons Board for onward processing. The previous system was slow and not quite effective in meeting the challenges of a modern pharmacovigilance system. There was poor coordination between the different departments in the Pharmacy and Poisons Board that were meant to use and act on this pharmacovigilance data to ensure safety and efficacy of registered medicines in the Kenyan market. These

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departments were the Medicines and Registration department, the GMP department, the Pharmacovigilance department and the Import/Export department. However, they often times worked independently of each other and no real time data was shared among them.For example the Pharmacovigillance department might receive a critical information that affects the quality of a product in the market, if this information is not shared with the Medicines and Registration department no regulatory action related to the registration status of the product will be taken such as deregistration or GMP inspection of the manufacturing facility. This made pharmacovigilance very reactive, causing a lot of back log. The project, as a result, sought to improve the system so that it could be more proactive than its current reactive nature. It also looked to enhance the coordination between the Medicines Registration department and Pharmacovigilance department and enhance the involvement of pharmaceutical manufacturers and distributors in the pharmacovigilance system.

Poor pharmacovigilance of medicines in Kenya will result in poor health outcomes for the general public, such as increased morbidity, poor quality of life and reduced lifespan for the people of Kenya.

Borg et al. (2011) defined pharmacovigilance as the science of, and activities relating to, the detection, assessment, understanding and prevention of adverse effects of marketed medicines; specifically, taking action to increase product benefits and reduce their risks. This is achieved by monitoring the use of medicines in normal conditions of use to identify previously unrecognized adverse effects or changes in patterns of adverse effects.

In 2014, Thompson, Komparic and Smith noted that once products are approved by regulatory authorities and used by the public in the uncontrolled context, it becomes very difficult for the responsible regulatory bodies to ensure their safety and effectiveness. As a result, regulation of pharmaceuticals and vaccines moved towards an approach that considered the full life cycle of the drug or vaccine. Therefore, new strategies are being developed to allow faster identification of high-risk interactions between marketed drugs and adverse events to enable the automated uncovering of scientific evidence behind them. Pharmacovigilance plays an important role in healthcare through assessment, monitoring and discovery of interactions amongst drugs and their effects in human beings. Post market pharmacovigilance complements the traditional premarket austere drug approval process where the National Regulatory Agencies establish guidelines for new medicine approvals.

According to Lopes et al. (2013), pharmacovigilance research is based on the analysis of ″signals.” The World Health Organization (WHO) defines signals as undisclosed assertions or direct relationships between adverse events or effects on a human organism and a drug. To generate comprehensive signal data sets, clinicians and researchers use spontaneous reporting systems (SRS). Although drug companies are required to track and manage adverse events reported by clinicians or patients, the detection process mostly relies on the physician′s ability to recognize a given trait as a drug′s adverse event. This normally results in underreporting and biased selective reporting.

Labodie (2012) noted that counterfeit or adulterated drugs have less therapeutic efficacy than the original product, even when they do not result in additional adverse reactions. However, when they do result in adverse reactions, identification of those adverse reactions, as a first indication of possible counterfeit or adulterated drugs, requires a well-organized and rigorous post market surveillance system at the national level. The pharmacovigilance system should have the capability to detect and analyze subtle changes in reporting frequencies and in patterns of clinical symptoms and signs that are reported as suspected adverse drug reactions.

The latest trends in the pharmaceutical industry strongly support the concepts of risk management and see formal risk management as playing a major role in the development of safe medicines for the public, as well as providing a mechanism to ensure that decisions concerning individual drug benefit and risk are made based on scientific evidence. Safe medicines refer to those drugs whose benefits have been found to outweigh their risks when they are used according to approved labeling. Risk management is the comprehensive and proactive application of scientifically based methodologies to identify, assess, communicate and minimize risk throughout the life cycle of a drug so as to establish and maintain a favorable benefit-risk balance in patients (Bushet al., 2005).

A key factor in the success of overall risk management is the dialogue between industry and regulators throughout the development, review and marketing of the product. It is through such dialogue that appropriate, efficient and effective risk management strategies will be developed and implemented. Pharmacovigilance has evolved over time because of increased public awareness of the potential risks of drug therapy through technology (such as the internet), globalization of the industry and changes in the industry. Consumers and media houses have come to expect ″risk free” medications,

putting pressure on the regulators and industry alike to ensure that pharmaceuticals "do no harm." Globalization has resulted in the need to communicate with multiple regulatory bodies, simultaneously, although the individual regulators may have different perspectives and requirements. As a result, regulators have increasingly placed greater importance on the issue of benefit-risk balance of pharmaceutical products, including greater focus on recognizing and, where possible, mitigating risks. Consequently, there is need to improve the current passive system of post marketing surveillance, which depends on a voluntary spontaneous reporting system.

2. METHODS

The methodology involved a review of the poor quality reports submitted to the Pharmacy and Poisons Board for the year 2015 in order to classify them based on a risk-based system. The techniques and tools utilized in the project included observations, recordings, document reviews, expert interviews, focused group discussions, interviews and questionnaires. The method involved carrying out a thorough literature review of the latest trends in pharmacovigilance employed by different regulatory agencies across the world, especially the more stringent regulatory authorities. A review of the system employed by the Pharmacy and Poisons Board of Kenya was also done. Pharmacovigilance data, both primary and secondary, were collected and reviewed. Media reports on adverse drug reactions and poor-quality medicines over the period were also collected and reviewedThe data was then analysed and presented in the tubular form below.

Table 1. Summary of Pharmacovigillance data obtained from the Pharmacy and Poisons Board for the year 2015.

NO.	PRODUCT NAME	ACTIVE INGRIEDIENTS	NATURE OF COMPLAINT	ACTION TAKEN	CLASSIFICATION
1	Aloha Liquid 200ml		The product was found to have turned from reddish brown to green and sedimented.	Asked to provide sample from MAH for comparison. Complainant filled pink form. Wrote to manufacturer to provide investigation Reported on what could have happened.	Quality
2	Lamivudine 300mg & Tenofovir Desoproxil Fumarate 300mg	Lamivudine 300mg & Tenofovir Desoproxil Fumarate 300mg	Similarity of product with related product	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.memo retrieved and given to Dr. Mohammed	Presentation
3	Sulfran suspension	Cotrimoxazole	The product had two layers, an upper light layer & darker layer at the bottom-	Sent to NQCL for analysis 09/02/2015	Quality

4	Morphine HCL BP/PH.EUR Powder	Morphine HCL BP Powder	Once the powder is reconstituted with distilled water, it forms a solution which starts sedimenting after some time.-	Clarify with the reporter. Abdi to be sent to the site.	Quality
5	Heparin Sodium Fresenius	Heparin Sodium	Four Patients had severe reactions on administration , ranging from headache, shivering, body weakness, tremors, erythematous wheal at injection site. The patients did not react to different batch of heparin procured thereafter. See yellow forms submitted.-	Wrote a letter to the company and gave reportt that we have, awaiting response.	ADR
6	Sulfran suspension	Cotrimoxazole	Black particles formed on shaking the bottle and observing under sunlight-	Sent to NQCL for analysis 09/02/2015	Quality
7	Sulfran suspension	Cotrimoxazole	Black particles formed on shaking the bottle and observing under sunlight-	Sent to NQCL for analysis 09/02/2015	Quality
8	Sulfran suspension	Cotrimoxazole	The bottle turned black-	Sent to NQCL for analysis 09/02/2015	Quality
9	Nevirapine tablets, USP	Nevirapine	The packing is similar to that of lamivudine 150mg from the same manufactuer.	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation
10	Lamivudine tablets 150mg	Lamivudine 150mg	The drug has identical packaging to Nevirapine 200mg from the same manufactuer. Thus dispensing the wrong drug is possible because they are aesthetically similar-	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation

11	Lamivudine & Tenofovir Disoproxil Fumarate tablets	Lamivudine & Tenofovir Disoproxil Fumarate	The product packaging is similar to that of lamivudine, Nevirapine, & Stavudine tablets from the same manufactuer.	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation
12	Efavirenz tablets 600	Efavirenz tablets	The reason for the ADR was due to change of formulaion. EFV Mfg by Macleods was cited as the cause of severe vomiting, dizziness, headache, & body ache, & when the old formulation was dispensed the client was comfortable. This is the EFV Mfg. by Strides Arcolab Ltd that the patient had been taking without complaint. Since then client is doing well.	Communicated to NASCOP asked NASCOP to share any information that they have on the product 03/02/15 Fill it as an ADR write to kisii a response letter.	ADR
13	Curamol	Paracetamol	Solid crystal are seen at the bottom of the container.	Abwao to write a letter to KEMSA see if they have received any complaint.	Quality
14	Cotrimoxazole	Sulfran	Tablets cracking & thus separating 30 tablets returned by client. 145 tablets had not been issued to clients & have some features. Total tabs available 175 quarantined.	Sent to GMP ask for a sample	Quality
15	Sulfran	Sulphamethoxazole Trimethoprim	Crystalization. The non - umiformity of the syrup crystal seen in the syrup.	Sent to NQCL for analysis 09/02/2015	Quality
16	Bupivacaine Hydro in dextrose		Not Potent spinal blocade not achieved after intra-thecal administration.	Sent to NQCL for analysis 24/02/2015	Poor performance

17	Efavirenz tablets 600mg	Efavirenz tablets 600mg	Formulation change related to difference in Manufactuer. The othe formulation is Mfg by Macleods and Pt well tolerated . My client a male 60 yrs PSC No. 12,275-5 Km returned drugs to clinic because of generalised rahes photos sent online 09/02/2015	Fill an ADR form	ADR
18	Curamol	Paracetamol	Crystalization Solid crystals have been deposited on the bottom of the container shaking container did not loosen or dissolve the crystals.	Confirm source with the reporter and get samples.	Quality
19	Methylated spirit		Appears to have an abnormal colour, thickness and smell	County pharmacist to supply update.	Quality
20		Tenfovir Disoproxil Fumarate & Lamivudine	Similar packaging color (blue) with Tdf/3tc/Efv/& Nvp 200mg making it difficult to differentiate the products.	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation
21		Tenofovir Disopiroxil/ Lamivudine/ Efavirenz	Similar packaging color (blue) with Tdf/3tc & Nvp 200mg making it difficult to differentiate the products.	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation
22		Nevirapine 200mg	Similar Pack color blue with Tdf/3tc/Efv and Tdf/ 3tc making it difficult to differentiate the products.	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation
23	Bactoclav-625	Amoxicillin/ Clavunate 500/125mg	Substandard	Results received from NQCL 16/04/2015 Does not Comply	Quality
24	Bactoclav-625	Amoxicillin/ Clavunate 500/125mg	Substandard	Results received from NQCL 16/04/2015 Does not Comply	Quality

25	Sulfran	Trimethoprim 40mg, Sulphathoxazole 200mg	The formulation has particles in it. It is even rough on hand.	Sent to NQCL 09/02/2015	Quality
26	Efavirenz tablets 600mgs	Efavirenz tablets 600mgs	The client cited change of formulation as the cause of the ADR. when he took his first dose of efavirenz manufactured by strides arcolab limited he developed generalized rashes the following day. Patient returned the drugs and demanded for the old formulation manufactured by macleods pharmaceutical limited which he had used since 2006 safely	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	ADR
27	N/A	Fluphenazine Deacanoate Inj. BP 1ml	The ampoule does not contain the 1ml as specified in package the ampoule line of weakness is not adequate to enable opening. At times the ampoule breaks inappropriately	To ask for samples	Quality
28	Erocin dry suspension	Erythromycin ethylsuccinate 125mg/5ml	The product should be packed in boxes of 100 packs but all boxes received had 6 packs less.	Contact pharmacist for more information.to write a memo to inspectorate.	Presentation

29		TDF 300Mg/3TC 300Mg	The two products very similar packages creating alot of confusion when dispensing at facility. AT ONE TIME 3TC/TDF WAS DISPENSED INSTEAD OF 3TC/NVP/d4t AND THE PATIENT HAD TO BE CALLED TO COME FOR THE RIGHT MEDICATION. THIS WAS REALIZED BEFORE THE PATIENT HAD USED THE MEDICATION	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation
30	Lamivudine tablets 150mg	Lamivudine 150mg	The boxes and containers are similarily colored and designed.	Memo to be retrieved and sent to drug Reg and to be provided with a sample of the photographs.	Presentation
31	Isovent 200	Misoprostol 200mcg	There has been a number of failed inductions with the product.	samples were collected on 19/03/2015 from Machakos L5 during PMS	Poor performance
32	lidocaine Injection B.P	Lidocaine Hydrochloride B.P 1% w/v	severe adverse reactions at injection site upon injection ophthalmologist reported massive oedema (orbital) extending to the face in all the patients he administered. The preparation contains Benzyl alcohol as preservative.	Is an ADR	ADR
33	Pure Soya Oil			Need to establish how these products get into the country.and then check with drug reg wether they are listed.Then to see wether we can enforce a crack down.To investigate herbmed research group to confirm where they are getting these products.	MA

34	Mens Powder Power	Ginseng root bilora ginggigo tonkatail & others		"	MA
35	B-tex Lotion	Salicylic acid ip 10% w/v denatured spirit with 1% acetone QS alcohol content 80-90%		"	MA
36	Broad Spectrum herbal chest (A) powder			"	MA
37	Broad Spectrum herbal chest (A) powder			"	MA
38	Anti typhoid Malaria Amoeba Herbal Powder			"	MA
39	Sapat Plus Lotion			"	MA
40	Purex Special Body Detox	Aloe soctrina Urtic , neem a dloca, garlic yellow dock, senna & yarrow		"	MA
41	Biodopa	Methyldopa 350mg	Moulding observed on tablets	Inform Biodeal if they have any complaints from the market. To send out an e-shot to check the magnitude of the problem then from the information received we can make a decision	Quality
42	Kinem	Imipenem & Cilastatin for injection USP	The powder does not dissolve completely in some vials.In others once the powder dissolves the solution changes colour from from yellow to dark brown.	Njeri to Contact Regulatory Pharmacist of Medox to bring the sample to come for a meeting.	Quality

43	Dawaflox	Flucloxacillin	The above product when reconstituted forms a clear solution with small black particles were seen inside reconstituted product.	An e-shot was sent out the company pharmacist brought a recall letter between 15th -25th of March 2015. Need to retrace that letter from Kabue	Quality
44	Dawaflox	Flucloxacillin	The above product when reconstituted forms a clear solution with small black particles were seen inside reconstituted product.	An e-shot was sent out the company pharmacist brought a recall letter between 15th -25th of March 2015. Need to retrace that letter from Kabue	Quality
45	Normal Saline nasal drops	Sodium Chloride 0.99% w/v	Suspected adulteration the drug has a strong pungent smell similar to organophosphate chemicals. The Nasal drops were administered to the child who developed pin point pupils. Find attached documents.	Get final investigational report from Dennis	Adulteration
46	Neladol	Paracetamol	Brownish colouration of some tablets in the 1000tab tin of paracetamol	Refer to the older investigational report for neladol and to contact the reporter	Quality
47	Salbumed	Salbutamol	The syrup is packaged in transparent plastic bottles as opposed to the recommended amber coloured bottles to protect from sunlight.	Check with drug reg what they registered and follow up with the company.To confirm with George by 16/05/15	Quality
48	Alimoxycillin Oral suspension	Alimox	Colour change.	QSE recommendations	Quality
49	Nepusolone Forte eye drops	Prednisolone Acetate 1.7m/v	Clouding lack of batch No. prescence of particulate matter in the eye drops that has caused clouding in what should have been a clear solution.	inform GMP & Inspectorate to do a follow up of the same and guide them on GMP issues.	Quality

50	Nepumiconazole Eye drops BP	Miconazole 1% m/v	Clouding crystallisation lack of batch No. prescence of particulate matter in eye drops that has caused clouding in what should have been clear cloudy & sedimentation observed.	inform GMP & Inspectorate to do a follow up of the same and guide them on GMP issues.	Quality
51	Nepucortisone eye Drops	Hydrochloride base PMCO 0.0048	Clouding. The product showed prescence of particulate matter resulting in clouding sedimentatiom & caking.	inform GMP & Inspectorate to do a follow up of the same and guide them on GMP issues.	Quality
52	Bupivacaine in Dextrose injection USP	Bupivacaine HCL	Diminished potency. The product was found to have diminished potency effective ness to the extent of requiring a repeat dose to achieve spinal anaesthesia.-	to check if they were sent to the lab Miriam	Poor performance
53	Isovent 200	Misoprostol 200mcg	Diminished potency/effectiveness the product effectiveness was found to be lower than normal to the extent of needing a repeat dose to achieve effectiveness.	same as above	Poor performance
54	Tenolol - 50	Atenolol BP 50mg	Suspected poor quality-	Checked with Drug Reg. Its Registered 13/04/2015	Quality
55	Zycet syrup	Cetrizine Hydrochloride B.P 5mg	Suspected poor quality	Not Registerd 13/04/2015	Quality
56	Zycet tablets	Cetrizine Hydrochloride tablets 10mg	Suspected poor quality	Not Registerd 13/04/2015	Quality Y
57	Enterezole	Diloxanide Furoate B.P 250mg Metronidazole Benzoate BP	Suspected poor quality	Not Registerd 13/04/2015	Quality

58	Genatamicin Eye/Ear drops	Gentamicin Sterile 10ml	Suspected poor quality	Checked with Drug Reg. Its Registered 16/04/2015	Quality
59	Cipiem Tabkets	Chlorophenaramine malelate B.P 4 mg	Suspected poor quality	Checked with Drug Reg. Not Registered 16/04/2015	Quality
60	Metronidazole Intravenous Infusion B.P		Suspected poor quality	Checked with Drug Reg. Its Registered 16/04/2015	Quality
61	Biomol	Paracetamol	Some tablets had a brownish colour	pick the previous reports look at the batches and make a decision.	Quality
62	Alimox	Amoxicillin Oral Suspension	Suspension changes color when reconstituted caking is observed.	Implement QSE recommendations	Quality
63	Alimox	Amoxicillin Oral Suspension	Colour change from white to yellow and brown when recostituted.	Implement QSE recommendations	Quality
64	Alimox	Amoxicillin Oral Suspension	Colour change from white to yellow and brown when recostituted.	Implement QSE recommendations	Quality
65	Alimox	Amoxicillin Oral Suspension	Colour change from white to yellow and brown when recostituted.	Implement QSE recommendations	Quality
66	Alfree	Cetrizine Dihydrocloride	The manufacturer describes the tablet as a white oval shaped uncoated tablet on one side and plain on the other side for oral administration. We however noted that the tablets are not white but rather creamish with yellow crystals.	Contact the Local agent get info from drug reg on what was regeistered	Presentation

67	Kinem	Imipenem & Cilastatin for injection USP	After adding 10mL of Normal saline as appropriate and shaking it vigorously, the solution does not mix. the powder quickly settles at the bottom of the bottle. ALso another bottle received from the ward had a reddish color instead of white to yellow color.	Contact the Local agent get info from drug reg on what was regeistered	Quality
68	Kemoxyl	Amoxicillin	Capsules heads breaks off and the contents spills in the container	Contact the reporter for samples then get intouch with the company.confirm if it was a government tender or private purchase.	Quality
69	Hemsyl Inj	Etamsylate BP 125	Colour change from tinge to brown. only two ampoule affected, signs of slow leakage along the neck/ scoreline as evidenced by comparatively low volume of the content and mould like substances around the necks of affected ampoules.	to Call the company on 27/05/2015 and ask them to provide a sample.	Quality
70	TDF/3TC/NVP and TDF/3TC and NVP Tablets		The complaint is about the packaging of the TDF/3TC/EFV, TDF/3TC and NVP from this company. Their outer packaging look very identical. This can cause serious dispensing errors especially in busy hospital pharmacy departments and where there are trainees in the department. they are also very confusing to our patients. The color and design of the packaging should be changed See the pictures attached,	refer above Cristabel to follow up	Presentation

			especially the ones on the shelves.		
71	Jotomol	Paracetamol	crumbling and breaking of tablets into small particles and powder	a letter to be written to be to BENMED	Quality
72	Pyremol	Paracetamol Suspension	The syrup has unpleasant smell and the labelling is different. The same product but the other one has faint label	Call the reporter to give us samples.and also call Concepts africa Ltd	Quality
73	Salol	Salbutamol	Powdering and crumbling	Check registration status and ask for samples.Biopharma to be sent for a letter	Quality
74	Chlorist	Chlorophenaramine malelate B.P 4 mg	Powdering and crumbling	Check the registration status and contact syner Med.	Quality
75	Metopride	Metoclopramide injection BP 10mg/2ml	THE AMPUOLE NEEDS TO HAVE CLEAR SOLUTION FOR INJECTION BUT THIS CONTAINS LIGHT-BLUE SOLUTION. AWAITING RECOMMENDATION N FROM YOUR OFFICE ON THE WAY FORWARD BUT TGE AMPOULE HAS BEEN QUARANTINED FOR THE TIMR BEING.	Ask the reporter to send samples then we contact the company.Get the local agent from Drug reg.	Quality
76	Heparovit-H	Heparin Injection	The patient experienced shivering, difficulty in breathing and bronchospasms on administration on a dialysis patient on two occasions	Should be reported as an ADR Cristabel to call to get more information.	ADR

77	Diclofence Sodium		THE AMPOULES HAVE SOME LEAKING POINTS THAT DRAIN GRADUALLY. SOME AMPOULES ARE COMPLETELY EMPTY. THIS HAPPENS IN AT LEAST 20-40% OF THE AMPS	Contact the reporter to send samples. Find the local distributor.to check registration status, confirm with the reporter if it was supplied by KEMSA	Quality
78	Nicardia	Nifedipine	Complaints that the product is not reducing blood pressure.	Contact the reporter to send samples. Find the local distributor.to check registration status, confirm with the reporter if it was supplied by KEMSA	Poor performance
79	Nicardia	Nifedipine	Complaints that the product is not reducing blood pressure.as required	Contact the reporter to send samples. Find the local distributor.to check registration status, confirm with the reporter if it was supplied by KEMSA	Poor performance
80	Dawa-flox	Flucloxacillin	Capsules were opened and the powder spilt. Some other capsules had different colours	Contact supplier & reporter to give us samples. Talk to Dr. Wasike about it	Quality
81	Quinine Dihydrocholoride I.V	Quinine inj 600mcl/2ml	the quantitiy of the drugs is incomplete because of the poorly packed ampoules.	contact the company and refer the company to GMP and check GMP status and check if it was supplied by KEMSA	Presentation

82	Fluphenazine Decanoate Injection BP 1ml	Fluphenazine Decanoate Injection BP 1ml	The nurses in the psychiatric ward reported several cases of patients that experienced relapses of psychosis 2 weeks after administration of the drug instead of 4 weeks.The nurses carried out an experiment where they issued the same batch under question to some patients and a different brand from another company. Those who were given the batch under question returned with psychosis while those who got the other brand came back on there appointment day after 4 weeks.	Contact the reporter for more information, ask them for samples check registrations status of what it contains.	Poor performance
83	Artesun 120mg	Artesunate injection	full course of artesunate injection drug administered to 2 patients with a positive blood smear for malaria. the MPS after treatment was still positive. patients were switched to quinine injection and they responded well.	Registration status Contact them to find if the have samples	Poor performance
84	Oxytocin 10 i.u	Oxytocin 10 i.u	Low efficacy i.e Using up to 4times the normal dosages to achieve desired results as stored at room temperature.	Send abwao an email to ask him about the outcome of the oxytocin analysis	Poor performance
85	Gripe Water	Sodium Bicarbonate	White Floating particles	Ask the reporter to provide samples and ask the manufacturer for samples.	Quality
86	Neocuron	Pancuronium	The effects wear out within a very short time (20-25 minutes), higher doses are required. Anesthetists have had to use doses as high as	To ask the reporter for samples to send to NQCL	Poor performance

			18mg for an operation of two and a half hours.		
87	Unitel -H 40	Telmsartan with HCL	Bought Expired drugs from Temple Stores Pharmaceuticals on 30/05/2015	To liaise with inspectorate.	Expired drugs
88	Artemether 20mg Lumefantrine 120mg		After taking meds experienced skin rashes & difficulty breathing feeling exhausted.Expired drug was given to patient boss. After finishing the dose the client went to hospital after which he was told to report to PPB		ADR
89	Apresoline	Hydrlazine Injection	The powder for reconstitution has changed color from yellow to white, the product has caked at the bottom of the ampule and the resultant powder after intensive shaking of the ampule is not free flowing.	to contact reporter to bring sample and to also contact manufacturer to bring sample	Quality
90	Parace	Paracetamol	The tablets crumbles /breaks easily into pieces.	To registration status and get samples from reporter	Quality
91	Dawa flox	Flucloxacillin 125mg/5ml powder for suspension	Particular bottles of the said batch started caking & color change from white to pink.	we will sample for more and sent an e-shot to the county pharmacist	Quality
92	Diclofenac Injection	Diclofenanc Inj	The drug has changed in color i.e to pink color	To confirm registration status and act from there.Call the reporter to fill a yellow form, quarantine the product and then hand over the case to inspectorate	Quality
93	Bupivacaine HCL dextrose injection	Bupivacaine HCL dextrose injection	The product does not achieve optime levels of anaesthesia @ therapeutic doses	Refer to same	Poor performance

94	Tenoretic		Sold for expired drug from on 8th July 2015	Inspectorate to give an update on this case	Expired drugs
95	Misoprostol Tablets KONTRAC 200	Misoprostol 200mcg	Lack of efficacy		Poor performance
96	Hepa	Heparine 5000iu	There is coagulation despite increase in dosage of the drug.	Take to NQCL for analysis 04/08/2015	Poor performance
97	Ceftriaxone	Ceftrimed	Patient on treatment for severe UTI.put on ceftriaxone 1gm of for 5/7.developed itchiness mild on day one of treatment and was reassured..has developed type 1 hypersensitivity reaction after finishing dose ..1later.patients has swollen face..periorbital edema and wheels....over the whole body.patient has associated intense itchiness which results to wheals after scratching.	Reporter to be advised to fill a yellow form ADR form	ADR
98	Aziagio		Overwhelmingly Repugnant spicy smell, coarse consistency and bitter pepperminty taste with a strong after-taste. Induces vomiting almost instantly even to a normal adult. Absolutely unpalatable for paediatric patient	to call the reporter ask for sample and ask the reporter what he meant.	Quality
99	Ascoril Expectorant	Salbutamol Bromhexine Guaiifenesin & Menthol	PRODUCT LABELLING/PACKAGE AND PRODUCT COMPOSITION IS UNREGISTERED. HAS TERBUTALINE SULPHATE IP 1,25MG INSTEAD OF SALBUTAMOL SULPHATE BP 2MG.	Inspectorate to do followup and provide samples.	Presentation

			IT DOES NOT HAVE A UNIT BOX OR PIL		
100	Dolomol	Dolomol	The tablets have changed colour to brown	To ask for samples and to send an eshot and get in touch with the supplier or manufacturer.	Quality
101	Nimodor -s	Sufadoxine 500mg Pyrimethamine 25mg	The tablets are said on the label to be film coated while in actual sense they are uncoated. Plus there is no literature for the product or any other information apart from the sticker on the tin. The tablets look like any other circular tablet with no engraving for identification and the description states that its film coated while onnchechikng they are uncoated white circular tablets	Get samples contact the agent Look at the submitted dossier on what was suggested.	Quality
102	Dolomol	Paracetamol	Moulding	To ask for samples and to send an eshot and get in touch with the supplier or manufacturer Edward to do the eshot Mary to follow up.	Quality
103	Hepa	Heprin Sodium BP 5000iu	The drug was found to be in-effective. Blood coagulation took place during dialysis despite it being administered in correct doses.	To follow up with the lab NQCL	Poor performance
104	Biodopa	Methyldopa 250 Mg Tablets	The yellow tablets form moulds and turn to grey in colour	Abwao to do an eshot and find out from KEMSA if there is a report on the same.Mary to contact Biodeal	Quality

105	RHZE COM	Rifampicine, isoniazid, ethambutal, pyrazinamud	The drug RHZE turned dark brown from brown and crumbling happen to a whole row in a pack. Patient complaint in change of test, feels as if has not taken any medicine (different from other similar medicine	Edward called on 23/09/2015 To ask for samples so that we can send them for analysis	Quality
106	Telmi 80H	Telmisattan 80mg Hydrochlorothiazide 12.5mg tablets	The medicine disintegrate/dissolves before swallowing	Sent to NQCL 04/08/2015	Quality
107	Cytotec	Misoprostol 200mcg	Suspected potency issue one mother experienced raptured uterus and the other one had precipitate labour is still born birth.	To liaise with Drug reg Dr Mbwiri and ministry of reproductive health	Poor performance
108	Depin E Retard	Nifedipine Retard Tabs	Batch No.Manufacturing date and Expiry date of product omitted.	write am email to MEDS Get Kingori to dispatch a team to quarantine and give the quantities and to give a list of all the places supplied.	Quality
109	Not Indicated	Not Indicated	The product was packed together with Diclofenanc tablets 50mg but not labelled	write am email to MEDS Get Kingori to dispatch a team to quarantine and give the quantities and to give a list of all the places supplied.	Quality
110	Cytotec	Misoprostal tablets 200mcgs	It is a follow up of the ADR that was reported on 31/07/2015	To contact Ministry of Reproductive Health.	ADR
111	OXYTOCIN INJECTION BP	OXYTOCIN	There was several complaints from maternity ward that the drug failed to produce the desire effect (induction of uterine contraction)	Dr. Kimathi Draft a letter to the registrar for change in storage conditions. To liaise with drug Reg	Poor performance

112	Ferrous Sulphate Tablets		The tablets are dull red instead of the usual bright red, they break in the mouth like chalk which is not what I am used to. I feel dizzy upon taking them which is odd. Something is just not right.	Edward contacted the reporter and they were to organise on how they can collect the samples from the hospital	Quality
113	Bupivit - D	Bupivacaine Hydrochloride in Dextrose injection	After spinal injection it does not pick, most of the time it fails and if lucky it picks it gives more hypotension than the block intended.	The product passes analysis so we to Write to the owner of the product/agents to explain the problem followed by a literature review contract experts to analyse the product.	Poor performance
114	Metropride	Metoclopramide injection BP 10mg/2ml	The liquid in the ampuoles have different colors, some colorless, some are bluish green. This may indicate that there is some color change.		Quality
115	Carefenac	Diclofenanc Sodium Inj	Ampoules not labelled. Severe discomfort on injection (severe pain redness & swelling) at the site of injection.		Presentation
116	Diclomed	Diclofenac Sodium	Packs contain ampoules with different colours of solution i.e Clear yellow.		Quality
117	Hartmann's Soln		Black growths spotted in the colourless soln supposedly having grown overtime suspected to be moulds.		Quality

Regulatory Pharmacovigilance Prioritisation System (RPPS) refer to appendix.

A Regulatory pharmacovigillance prioritization system adopted from Seabroke et al. (2013) was developed. This tool is prposed for adoption by the Pharmacy and Poisons Board Pharmacovigillance department. It is a risk-based system that implements regulatory action based on a weighted system, as shown in Table 2 below. The tool reviews different sources of pharmacovigillance information and weights them depending on their impact on their importance. The different categories are regulatory obligations, public health implications, strength of evidence and public perceptions. Input is the source of the pharmacovigillance data. Criteria for a positive response in the RPPS tool indicates the severity of the adverse effect and the number of points is the weight given to the criteria.

Table 2.

Category	Input	Criteria for a positive response in RPPS	Number of Points
Public health implications	Drug/vaccine exposure	Estimated number of patients prescribed medication in the past year in Kenya is[100,000 or the drug is newly marketed but with the potential for rapid uptake	3
	Frequency of ADR	Absolute frequency of the ADR is thought to be at least 1/1,000 users	2
	Health consequences	Combined case fatality rate plus non-fatal outcome score in Impact Analysis is 0.7 or greater	4
	Spontaneous case reports	In total, more than 20 cases or three fatalities have been reported spontaneously in Kenya	1
Regulatory obligations	Ministerial/public health authority concern	The Cabinet Secretary of Health or Ministry of Health has expressed concern about the drug or sent significant correspondence in the last 12 months	1
	Recent parliamentary questions	Parliamentary questions relevant to the safety of the drug have been posed in the last 12 months	1
	EAC obligations	Kenya is rapporteur or reference member state for the drug	3
	Marketing Authorisation Holder application	An application from the Marketing Authorisation Holder has some bearing on the issue, e.g. an application to reclassify from a prescription-only medicine to a pharmacy-supplied medicine	2

Strength of evidence	Disproportionality measure/ risk estimate	An EBGMb[10 (spontaneous ADR data) and/or RR[3 (RCT or epidemiological study) has been observed	2
	Data sources	More than one data source provides positive clinical evidence of a hazard (e.g. spontaneous ADR data plus an observational study)	4
	Evidence from RCT or meta-analysis	At least some positive evidence comes from a RCT or metaanalysis	4
	Biological plausibility	There is some biological plausibility for the ADR	2
Public perceptions	Media attention	There has been significant media attention for the drug in the last 12 months	3
	Factors likely to cause public anxiety	Two or more factors in the following list are present: • ADR threatens death (C5 % case fatality in spontaneous ADR data) • ADR threatens vulnerable groups (e.g. children, pregnant women) • ADR is generally unavoidable by taking precautions (few clear risk factors, no specific monitoring) • ADR involves cancer, teratogenicity, suicidality or major neurological disability • Scientific basis for ADR is poorly understood (no known biological plausibility) • Experts have publicly disagreed about the existence or scale of the problem • New first-in-class drug where the safety profile is not yet established	4
	Public misperceptions	Potential public misperceptions about the safety of the drug could be expected to cause harm through a behavior change (e.g. decreased vaccine uptake, abrupt discontinuation of medicine)	1
	Other Public concerns	Any other indication that the matter is causing public concern	

3. RESULTS AND DISCUSSION

Based on the data collected in Table 1, it was noted that the current pharmacovigilance system utilized by the Pharmacy and Poisons Board collected numerous data relevant to pharmacovigilance. On analysis of the data it was observed that just above half of all the product complaints, approximately 55%, involved poor quality medicines, 15% on poor performance, 13% on presentation, 8% on adverse drug reactions, 7% market authorization, 2% expired drugs and 1% adulteration complaints. This was good information; however, it did not give guidance on the next step to be carried in order to reduce or mitigate these pharmacovigilance incidences. A new system, Regulatory Pharmacovigilance Prioritization System, adapted from Seabroke et al. (2013) was proposed to be implemented to develop regulatory action as a result of these pharmacovigilance incidences. The tool was deemed appropriate since it utilized a weighted risk-based system, as shown in Table 2, to determine regulatory action. This tool took into account, not only the current pharmacovigilance parameters recorded by the system, but also included public health implications such as drug exposure, recent parliamentary questions, marketing authorization, public anxiety and misperceptions and other concerns, which are not captured in the current system. The weighting of the pharmacovigilance incidence will help the agency make decisions on how to handle the pharmacovigillance incidences. The higher the weight the more effort need to be put in place to mitigate or prevent such future occurences. This will make the system more proactive and responsive in regulatory actions.

4. CONCLUSION

This project gives the Pharmacy and Poisons Board a new tool that it could use to improve pharmacovigilance of medicines in the Kenyan market. The tool uses a risk-based system to weight and prioritize different pharmacovigilant relevant signals that could be used to make regulatory decisions and actions. This system is definitely more proactive and responsive to the needs of the public whose safety pharmacovigilance is supposed to protect.

5. RECOMMENDATIONS FOR NEXT STEPS

The next step would be to implement the Regulatory Pharmacovigilance Prioritization system. Since the system incorporates pharmacovigilance signals that are currently not captured, such as public health implications, public perceptions, media perceptions, recent parliamentary questions, etc., it would be necessary to redesign the pharmacovigilance information collection system to take these factors into account. The tool should be redesigned to reflect the current needs and capabilities of the Pharmacy and Poisons Board. The tool is in the form of a flow chart however it can be adapted into a mobile phone application for ease of use.

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APPENDICES

Regulatory Pharmacovigilance Prioritization System, adapted from Seabroke et al., 2013

ACKNOWLEDGEMENTS

I would like to thank all of the BIRS guest faculty from global industry and regulatory organizations for generously sharing their professional expertise and providing donated, in-kind time towards building the professional skills and technical capabilities of the students within the BIRS program. I would also like to thank my fellow peers in the BIRS MS student cohort for providing guidance and constructive feedback during the classroom group work and interactive sessions; Abigail Ekeigwe and Mercy Okezue, Purdue ABE BIRS PhD candidates, for their mentorship and input throughout the project; Professor Fran Eckenrode for providing content expertise throughout the review process on this paper; and Lauren Terruso, operations manager for BIRS Center, for all of her efforts on editing multiple iterations of the technical paper draft in preparation for publication. The international component of the Purdue BIRS program was initiated through educational support provided by the Merck Foundation and most recently through a capacity building effort funded by the Bill and Melinda Gates foundation, grant # 41000460.