

Quality of the Combined Oral Contraceptive
pill (0.15mg levonorgestrel and 0.03mg
ethinylestradiol) in the private retail pharmacies
of Nyeri Town, Kenya. Results from a
postmarket quality study

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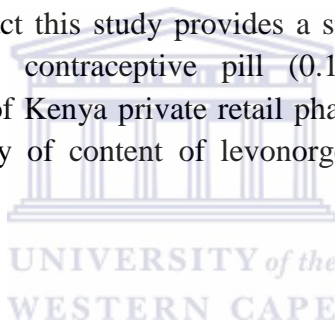
Abstract

Background: The effectiveness of the combined oral contraceptive pill as a family planning method is dependent on its quality. The quality of medicines on the healthcare market is established through postmarket quality studies.

Methods: The quality of the combined oral contraceptive pill was established through the collection of samples from 17 (62%) private retail pharmacies in the Nyeri town of Kenya. Their quality was then determined through the assay of content of levonorgestrel and ethinylestradiol and the levonorgestrel dissolution test at the National Quality Control Laboratory.

Findings: 13 of the 17 pharmacies were licensed with the Pharmacy and Poisons Board while 4 were unlicensed. Femiplan® was available in all the 17 pharmacies while Microgynon® was available in only 4 pharmacies. 17 samples of Femiplan® and 4 samples of Microgynon® were collected. None of the samples was counterfeit or falsely labeled. All the samples passed the assay of content of levonorgestrel and ethinylestradiol and the levonorgestrel dissolution test.

Conclusion: Notwithstanding the fact this study provides a snapshot in time, it is reasonable to conclude that the combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg ethinylestradiol) in the Nyeri town of Kenya private retail pharmacies is of the right quality with respect to the quality tests of assay of content of levonorgestrel and ethinylestradiol and the levonorgestrel dissolution test.



Declaration

I declare that this thesis that I now submit for assessment on the programme of study leading to the award of Master of Science in Pharmacy Administration and Pharmacy Policy Specialising in Regulatory Sciences has not been submitted as an exercise for a degree at this or any other university. It is entirely my own work and has not been taken from the work of others, save the extent that such work has been cited and acknowledged within the text of my work.

I agree to deposit this thesis in the University of the Western Cape and Hibernia College institutional repositories or allow their libraries to do so on my behalf, subject to South Africa's and Irish Copyright Legislation and the University of the Western Cape and Hibernia College libraries conditions of use and acknowledgement.

Signed. **TOM MWANGI KAUKI**

Dated. **30TH JULY 2015.**



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1. Introduction

Pharmaceutical services in Kenya are provided through the private and public sector (Ministry of Medical Services – Kenya 2010, p. 17). As of June 2015 there were 38 pharmaceutical manufacturers, approximately 250 wholesale pharmacies, 5,000 retail pharmacies and 12,000 medicines registered in Kenya (Ministry of Medical Services – Kenya and World Health Organization 2010, p. 17). Public sector pharmaceutical services are provided through the Ministries of Health located at the National Government and the 47 County Governments (Ministry of Medical Services 2008). The Kenya Medical Supplies Agency, the Pharmacy and Poisons Board and the National Quality Control Laboratory are government agencies established for public sector medical supplies, medicines regulation and medicines quality testing respectively (Kenya Medical Supplies Agency 2015; National Quality Control Laboratory 2015).

It is the responsibility of governments to promote and protect public health by ensuring that the medicines on the healthcare market are not of poor quality. A medicine is deemed to be of poor quality if it fails to meet the pharmacopoeial specifications it claims to comply with (Shakoor, Taylor and Behrens 1997; Kaur et al 2008; Hadi et al 2010). A poor quality medicine can have the wrong ingredients, inadequate amounts of the right ingredients, excess amounts of the right ingredients or the right ingredients in the right quantities but with a poor dissolution profile (Almuzaini, Choonara and Sammons 2013).

The use of poor quality medicines leads to therapeutic failure and for antimicrobials this leads to spurious reporting of resistance (World Health Organization 2003; Newton et al 2006; Keoluanghot et al 2008; World Health Organization 2012). Money spent on poor quality medicines is wasted (World Health Organization 2003; Alfadl et al 2006). Poor quality antimicrobials lead to development of antimicrobial resistance (World Health Organization 2003; Alfadl et al 2006; Newton et al 2006). Public confidence in healthcare systems is eroded by the finding of poor quality medicines in the healthcare market (World Health Organization 2003; Newton et al 2006; World Health Organization 2012). It is an exercise in futility to translate evidence from clinical trials into treatment protocols if the medicines actually used are of poor quality (Newton et al 2006; Newton et al 2009).

The quality of medicines on the healthcare market is established through **postmarket quality studies**. Due to financial constraints, it is impossible for medicines regulatory authorities to collect samples of all medicines on the healthcare market at a given time and test their quality and therefore they adopt a risk and impact on public health approach in determining which medicines to sample.

75% of all women in Kenya using contraceptives opt for hormonal contraceptives with 32% of them going for combined oral contraceptives (Republic of Kenya, Division of Reproductive Health 2009, p. 69). The combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg

ethinylestradiol) is listed in the 2013 World Health Organization Essential Medicines List and the 2010 Kenya Essential Medicines List (Republic of Kenya, Ministry of Medical Services and Ministry of Public Health and Sanitation 2010; World Health Organization 2013).

The purpose of this project was to establish the quality of the combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg ethinylestradiol) in the private retail pharmacies of Nyeri Town, Kenya. This was with respect to the quality tests of assay of content of active pharmaceutical ingredients and dissolution.

2. Literature review

2.1. Medicines. Not your ordinary consumer product

Medicines are not your ordinary consumer product owing to the asymmetry of information about medicines which exists between prescribers and consumers (Brundtland 1999; Rago and Santoso 2008, p.66). Consumers find themselves not in a position to make decisions about when to use medicines, which medicines to use, how to use medicines and to weigh the potential benefits of medicines against their risks (Brundtland 1999; Rago and Santoso 2008, p.66). Healthcare professionals also do experience difficulties in making informed decisions on all aspects of medicines unless specially trained (Nikiema 2014).

Therefore, medicines needs to be regulated with an aim of protecting and promoting public health and this is achieved through the following mutually reinforcing activities: the assessment of quality, safety and efficacy of medicines during market authorisation and postmarket, the licensing of manufacture, import, export, distribution and promotion of medicines, the inspection and surveillance of manufacturers, importers, wholesalers and retailers of medicines and last but not least the provision of independent medicines information to healthcare workers and the general public (World Health Organization 2003; Rago and Santoso 2008, p.67).

2.2. Medicines regulation. Historical perspectives

Human beings have been taking medicines since history began (Penn 1979). The regulation of medicines is also not of recent origin. The ancient Egyptians had a flourishing medical profession in which physicians administered their medicines in accordance with a written law called the sacred book (Penn 1979). The Hippocratic Oath which originated after the 5th Century BC enjoined the physician then and now against the giving of 'pharmacon oudeni' meaning lethal drug (Penn 1979; National Institutes of Health, National Library of Medicine, History of Medicine Division 2012). The medieval Muslim countries, in the early part of the 9th century, established the office of the hisba headed by the muhtasib as the official responsible for enforcing public health regulations (Levey 1963). The muhtasib had specific instructions to inspect the drugs of the syrup makers while cautioning them not to flout medicines related public health regulations (Levey 1963).

Unfortunate events have played a significant role in the evolution of medicines regulatory frameworks (Rago and Santoso 2008, p.65). The enactment of the Federal Food, Drug and Cosmetic Act in the United States of America was hastened following the 1937 sulfanilamide disaster in which more than 100 people died after consuming an elixir sulfanilamide laced with diethylene glycol as the solvent (Bowie and McKenzie 1972; Ballentine 1981; Rago and Santoso 2008, p.65). The thalidomide tragedy also had a major role in catalysing developments within the medicines regulatory frameworks (Rago and Santoso 2008, p.65-66). Thalidomide, a sedative and hypnotic drug, widely used as a morning sickness treatment between 1958 and 1960, resulted in an estimated 10,000 babies being born with phocomelia worldwide (Rago and Santoso 2008, p.66; Tantibanchachai 2014). In 1963 the Australian Government formed the Australian Drug Evaluation Committee to evaluate the safety of medicines before they are offered for sale to its citizens in response to the thalidomide tragedy (Therapeutic Goods Administration 2014). The Drug Amendments of 1962 were enacted requiring that the United States Food and Drug Administration approve all new drug applications following demonstration of safety and efficacy (Rago and Santoso 2008, p.66; Tantibanchachai 2014). In the United Kingdom the Committee on the Safety of Medicines was established in 1963 following the thalidomide tragedy (Rago and Santoso 2008, p.66).

Regrettably, unfortunate events are still catalysing developments in the medicine regulatory frameworks. In November 2013, President Barrack Obama signed into law the Compounding Quality Act to regulate the compounding of human drugs following the death of 64 people from meningitis contracted after receiving a fungi-contaminated methylprednisolone acetate injection produced by a Massachusetts-based compounding pharmacy (Gaffney 2013; The Lancet 2013 Dennis 2014; Outterson 2014; United States Food and Drug Administration 2014).

2.3. Modern medicines regulatory frameworks

Modern medicine regulatory frameworks are laid down by legislation to be enforced by government agencies known as **medicines regulatory authorities**. Medicines regulatory authorities regulate the trade in medicines (human, veterinary and herbal) and a host of other products such as nutraceuticals, medical devices, in vitro diagnostics, food, cosmetics and tobacco products as provided for by legislation (Food and Drugs Authority Ghana 2014; Medicines and Healthcare Products Regulatory Agency 2014; Medicines Control Council 2014; Pharmacy and Poisons Board 2014; Therapeutic Goods Administration 2014; United States Food and Drug Administration 2014). The Pharmacy and Poisons Board of Kenya also regulates the practice of pharmacy. This is in contrast to other countries such as South Africa where we have the Medicines Control Council for medicines regulation and the South African Pharmacy Council for pharmacy practice regulation (Medicines Control Council 2014; South African Pharmacy Council 2014).

The most important function of medicines regulatory authorities is to ensure that the medicines on the healthcare market are not compromised with respect to **quality, safety and efficacy**. The quality of a medicine is of special significance since its compromise subsequently compromises the safety and/or efficacy of the medicine. Keoluangkhhot and colleagues describe the case of an adult in Laos with uncomplicated malaria who failed to improve clinically following treatment with an artemether injection whose artemether content was 74% of the manufacturer's label claim, a clear case of quality failures compromising the efficacy of medicines (Keoluangkhhot et al 2008). The poor quality isosorbide mononitrate contaminated with a heavy dose of the antimalarial pyrimethamine supplied to patients in Pakistan in the year 2012 had a compromised safety evidenced by the death of 120 patients who used it (Arie 2012; The Lancet 2013).

2.4. What is a poor quality medicine?

Before we delve further into matters 'quality of medicines' it is important that we gain an understanding of what is meant by the quality of a medicine. A medicine is deemed to be of poor quality when it fails to meet the pharmacopoeial specifications it claims to comply with (Shakoor, Taylor and Behrens 1997; Kaur et al 2008; Hadi et al 2010). A poor quality medicine can have the wrong ingredients, inadequate amounts of the right ingredients, excessive amounts of the right ingredients or the right ingredients in the right quantities but with a poor dissolution profile (Almuzaini, Choonara and Sammons 2013).

Poor quality medicines can be genuine medicines produced by authorized manufacturers in which case they are referred to as substandard or out of specification medicines (Bate, Mooney and Milligan 2012; European Directorate for the Quality of Medicines and Healthcare of the Council of Europe 2013; World Health Organization 2012). They can also be medicines that are illegally manufactured and fraudulently mislabeled with respect to identity or source in which case then they are referred to as counterfeit medicines (Bate, Mooney and Milligan 2012; World Health Organization 2012).

2.5. Poor quality medicines. Historical perspectives

Human beings have been taking medicines since history began and poor quality medicines are perhaps as old as the medicines themselves (Penn 1979; World Health Organization 1999; Newton et al 2006; Rago and Santoso 2008, p.64). Dead flies adulterating the ointment of the apothecary, a person who prepares and sells medicines, appears as a comment in the Bible (Ecclesiastes 10:1, King James Version; Oxford Dictionaries 2014). The 17th century witnessed the deliberate adulteration of the cinchona bark, the first effective treatment for malaria, with other astringent barks precipitated by the huge demand of the cinchona bark in the then malaria endemic Europe (Newton et al 2006; Cambridge University Library 2014).

Our concern for the quality of medicines is also not of recent origin with the concepts for assuring the quality of medicines having evolved gradually over time (World Health

Organization 1999; Newton et al 2006; Rago and Santoso 2008, p.64). The first century AD, witnessed the Greek physician Pedanius Dioscorides advising on the dangers of adulterated medicines (World Health Organization 1999). The *Materia Medica* of Dioscorides highlighted some organoleptic tests for the detection of adulterated medicines (Penn 1979). The fine clay ‘terra sigillata’ used from early Greek times for the treatment of wounds was made into round cakes and stamped with designs alluding to its authenticity and quality (Penn 1979). In the medieval Muslim countries we had the muhtasib, official in charge of enforcing public health regulations, vested with powers to inspect the shops of the syrup makers (Levey 1963). The development of obligatory pharmacopoeial standards dates back to the 16th century and the 1498 New Compound Dispensatory issued by the Florentine guild of physicians and pharmacists for the apothecaries of Florence is regarded as the first official pharmacopoeia of a specific political unit in Europe (Penn 1979).

2.6. Need for the concern for quality of medicines

The agenda of assuring the quality of medicines on the healthcare market should zealously be pursued by governments due to the following reasons. Firstly, the use of poor quality medicines can result in therapeutic failure with a subsequent increase in morbidity and mortality (World Health Organization 2003; Newton et al 2006; Keoluangkhhot et al 2008; World Health Organization 2012). Secondly, the use of poor quality antimicrobials leads to development of resistance and this is especially undesirable among the sub-Saharan Africa high public health priority diseases specifically malaria, tuberculosis and the Acquired Immune Deficiency Syndrome (World Health Organization 2003; Alfadl et al 2006; Newton et al 2006). Thirdly, the detection of poor quality medicines on the healthcare market leads to erosion of public confidence in healthcare systems which can compromise the uptake of high public health priority healthcare services such as immunization (World Health Organization 2003; Newton et al 2006; World Health Organization 2012). Fourthly, it is a waste of resources to spend money on poor quality medicines whether individually or by governments (World Health Organization 2003; Alfadl et al 2006). Fifthly, the use of poor quality medicines leads to spurious reporting of resistance which can lead to unwarranted alterations of treatment protocols (Newton et al 2006). Lastly, it is an exercise in futility to translate evidence on drug treatment outcomes into treatment policy when the medicines actually used have inferior efficacy due to poor quality compared to the medicines originally tested during clinical trials or bioequivalence studies (Newton et al 2006; Newton et al 2009).

2.7. Poor quality medicines. Now and recently

Since the 17th century adulteration of the cinchona bark, the world is still grappling with the problem of poor quality medicines notwithstanding the modern medicine regulatory frameworks. An Institute of Medicine of the National Academies report estimated that in the year 2011 substandard or falsified medicines were sold in at least 124 countries worldwide (Institute of

Medicine of the National Academies 2013). Poor quality medicines are a problem for both the high and low income countries affecting both the expensive brands and cheap generics (World Health Organization 2012). Poor quality medicines have been witnessed in the medicines for the treatment of life-threatening conditions such as tuberculosis, medicines for the treatment of neglected tropical diseases such as visceral leishmaniasis and even in cheap generic versions of painkillers and antihistamines (Senior 2008; Dorlo et al 2012; World Health Organization 2012; Division of Malaria Control, Pharmacy and Poisons Board and National Quality Control Laboratory 2013). The problem of poor quality medicines appears to burden the low income countries more compared to the high income countries (Institute of Medicine of the National Academies 2013; The Lancet Editorial 2013).

The world is still witnessing deaths occasioned by the use of medicines laced with diethylene glycol as the solvent and to mention a few: 7 deaths in South Africa in 1969, 14 deaths in India in 1986, 5 deaths in Spain in 1987, 85 deaths in Haiti in 1995, 33 deaths in India in 1998, 12 deaths in China in 2008 and 57 deaths in Nigeria in 2008 (Bowie and McKenzie 1972; Singh et al 2001; Sosa et al 2014). 81 people died in the United States of America during the 2007-2008 heparin crises after using a heparin batch contaminated with oversulfated chondroitin sulfate (Briones 2008; Harris 2008). Avastin without active pharmaceutical ingredient was detected in the United States of America in the year 2012 (World Health Organization 2012). In June 2014, the United States Food and Drug Administration instituted a product recall of metoprolol succinate 100mg manufactured by Wockhardt Limited, India and metoprolol succinate 25mg manufactured by Dr. Reddy's Laboratories Limited, India after the two products failed **dissolution tests**, one of the basic tests of medicines quality (United States Food and Drug Administration 2014).

In August 2008, health authorities in South Africa withdrew from the healthcare market two brands of antituberculosis medicines after World Health Organization accredited quality control tests indicated inadequate concentrations of rifampicin and isoniazid (Senior 2008). The lack of a substantial financial incentive in the market for medicines for Neglected Tropical Diseases has also not protected these medicines from poor quality batches (Dorlo et al 2012). In 2008, a generic miltefosine without the active pharmaceutical ingredient emerged in Bangladesh for use in the national leishmaniasis elimination programme (Senior 2008; Dorlo et al 2012).

2.8. Reasons for the availability of poor quality medicines

There are various reasons for the availability of poor quality medicines on the healthcare market. The first one is the failure of medicine manufacturers to adhere to Good Manufacturing Practices (Bate, Mooney and Milligan 2012). The second reason is the pharmaceutical manufacturers' use of poor quality pharmaceutical raw materials (Shakoor, Taylor and Behrens 1997). The third reason is the degradation of finished pharmaceutical products and pharmaceutical raw materials due to poor storage practices coupled with the high temperatures and humid conditions that

prevail in the tropical countries (Shakoor, Taylor and Behrens 1997; Taylor et al 2001). Lastly, we have the unscrupulous businessmen who guided by criminal greed engage in the production of poor quality medicines facilitated by lack of legislation criminalizing the production and marketing of poor quality medicines and if existent the failure of enforcement by government authorities and if enforced light penalties being imposed by the judiciary on the culprits (Newton et al 2006 and Onwujekwe et al 2009).

2.9. Measures for ridding the healthcare market of poor quality medicines

There are various measures which medicine regulatory authorities can adopt to rid the healthcare market of poor quality medicines. The first one is the implementation of a robust marketing authorisation process encompassing a thorough evaluation of the quality data as presented on the Common Technical Document. The second measure is the conduct of regular and thorough inspection of pharmaceutical manufacturers to ensure that the manufacture of active pharmaceutical ingredients and finished pharmaceutical products adheres to Good Manufacturing Practices.

The third measure entails the routine inspection of medicines distribution outlets in order to ensure that the medicines offered for sale are registered and that medicines distributors adheres to Good Distribution Practices by having for instance a system for batch tracing in case of poor quality medicinal product recall. The fourth measure entails having a paper and online based platform through which healthcare providers and the general public can report incidents of poor quality medicines. An example is the Pharmacy and Poisons Board poor quality medicinal product reporting form, also called the pink form, through which healthcare workers and the general public alert the Pharmacy and Poisons Board of any incidents of poor quality medicines (Pharmacy and Poisons Board 2014). The last and very important measure entails the conduct of regular **postmarket quality studies**.

2.10. Postmarket quality studies

Postmarket quality studies entail the collection of medicines samples within a given geographical area and subjecting them to quality tests mainly the assay of content of active pharmaceutical ingredient(s) and dissolution. Postmarket quality studies can be conducted on a routine basis, following a complaint of a poor quality medicine or through sentinel site monitoring which entails the monitoring of the quality of medicines at a given site over a certain period of time.

The benchmark for the postmarket quality of a medicine lies in its compliance with the laid down pharmacopoeial specifications it claims to comply with (Taylor et al 2001). A pharmacopoeia is an official book of medicines quality standards and the term is derived from the Greek word *pharmaco-poios* meaning drug-maker (United States Pharmacopoeial Convention 2000; Rago and Santoso 2008, p.64; Rago and Santoso 2008, p.72). A pharmacopoeia is legally binding and contains the recommended quality specifications for the analysis and determination of medicinal

substances, specific dosage forms, excipients and finished pharmaceutical products (Rago and Santoso 2008, p.72). Quality specifications are composed of appropriate tests for confirming the identity and purity of medicinal products, ascertaining the amount of active pharmaceutical ingredients and the performance characteristics of medicinal products (Rago and Santoso 2008, p.72). The **assay of content of active pharmaceutical ingredient(s)** and the **dissolution test** are two quality specifications which find application in postmarket quality studies (Shakoor, Taylor and Behrens 1997; Taylor et al 2001; Laroche et al 2005; Alfadl, Abdoon, Elamin and Elnabi 2006; Kaur et al 2008; Onwujekwe et al 2009; Hadi et al 2010; Bate, Mooney and Milligan 2012; Evans et al 2012; Boateng 2013).

Postmarket quality studies are also conducted by researchers affiliated to academic institutions and organizations such as the World Health Organization. The Promoting the Quality of Medicines program funded by the United States Agency for International Development and implemented by the United States Pharmacopeial Convention assists medicines regulatory authorities in the conduct of postmarket quality studies through financing and provision of technical assistance (Ghana Food and Drug Authority and The Promoting the Quality of Medicines Program 2013; United States Pharmacopeial Convention 2014).

The Medicines Information and Pharmacovigilance Directorate of the Pharmacy and Poisons Board is the unit responsible for the conduct of postmarket quality studies in Kenya. This unit has for instance been monitoring the quality of antimalarials since the year 2011 with the results indicating that a significant proportion of antimalarials in the Kenyan healthcare market are of poor quality (Division of Malaria Control, Pharmacy and Poisons Board, National Quality Control Laboratory and The Promoting the Quality of Medicines Program 2011; Division of Malaria Control, Pharmacy and Poisons Board, National Quality Control Laboratory and The Promoting the Quality of Medicines Program 2012; Division of Malaria Control, Pharmacy and Poisons Board, National Quality Control Laboratory and The Promoting the Quality of Medicines Program 2013).

Table 1: Antimalarials postmarket quality studies results. Kenya

PARAMETERS	YEAR	2011	2012	2013
Samples collected		536	499	545
Percentage of samples registered with the Pharmacy and Poisons Board		94	97	99
Samples analysed using minilab in the field – Level 1		519	496	514
Percentage of samples that passed Level 1 minilab testing		92	97	95
Samples analysed using minilab at the National Quality Control Laboratory – Level 2		80	65	71
Percentage of samples that passed Level 2 minilab testing		76	100	90
Samples analysed using compendial methods at the National Quality Control Laboratory – Level 3		44	25	20
Percentage of samples that passed Level 3 compendial testing		84	76	90

The average results are 5% failure at Level 1 minilab testing, 11% failure at level 2 minilab testing and 16% failure at level 3 for compendial testing.

The Ghana Food and Drug Authority over the months of August and September 2012 assessed the postmarket quality of uterotonic (oxytocin injection, ergometrine injection and ergometrine tablets) in the Ghanaian healthcare market and found that a significant proportion of them failed the assay of content of active pharmaceutical ingredient (Ghana Food and Drug Authority and The Promoting the Quality of Medicines Program 2013).

Table 2: Uterotonics postmarket quality study results. Ghana

PARAMETERS	MEDICINE	Oxytocin injection	Ergometrine injection	Ergometrine tablets
Samples collected		185	103	15
Samples subjected to the assay of content of active pharmaceutical ingredient		169	99	11
Percentage of samples which failed the assay of content of active pharmaceutical ingredient		56	74	100

The Medicines and Healthcare Products Regulatory Agency, United Kingdom's medicines regulatory authority, regularly identifies high risk medicines in need of postmarket quality surveillance based on a criteria such as patient exposure, product stability and impact and likelihood of risk (Medicines and Healthcare Products Regulatory Agency 2014). The postmarket quality of these medicines is then surveyed on a one off basis or continually sampled from pharmacies for authentication using a variety of analytical quality testing techniques (Medicines and Healthcare Products Regulatory Agency 2014).

In the European Union, postmarket quality surveillance of centrally authorized and mutually recognized medicines is done by the General European Official Medicines Control Laboratory Network on behalf of the European Directorate for the Quality of Medicines and Healthcare (European Directorate for the Quality of Medicines and Healthcare of the Council of Europe 2013). 20-25 Official Medicine Control Laboratories from 15-20 Member States participate in the scheme every year and the scheme results indicate a high level of quality is present in the medicines that are in use within the European Union since out of specification parameters have so far being found in only 2% of the medicines subjected to the surveillance programme (European Directorate for the Quality of Medicines and Healthcare of the Council of Europe 2013).

Postmarket quality studies published in various journals point toward a significant proportion of medicines circulating in the healthcare market of the low income countries been of poor quality. 1912 antimalarials and antibiotics samples were collected from 11 African cities (Accra, Addis Ababa, Cairo, Dar es Salaam, Kampala, Kigali, Lagos, Luanda, Lubumbashi, Lusaka and Nairobi), 3 Indian cities (Delhi, Chennai and Kolkata) and 5 middle income countries cities (Sao Paulo, Moscow, Bangkok, Istanbul and Beijing) in 2012 and subjected to quality tests (Bate, Mooney and Milligan 2012). 3.8% of them failed quality tests performed with the Global Pharma Health Fund e.V. Minilab and 5.2% failing product authentication by Raman spectrometer (Bate, Mooney and Milligan 2012). 58% of 77 samples of antimalarials sampled in Guyana over the period of June and August 2009 failed quality control tests (Evans et al 2012). 18% of 104 antibiotic samples collected from pharmacies in Indonesia in the year 2010 failed quality control tests (Hade et al 2010). Out of 713 samples of isoniazid and rifampicin purchased at community pharmacies in 19 cities of 17 countries, 65 (9.1%) had insufficient active pharmaceutical ingredient with the failure rate being 9.1% in Africa, 10.1% in India and 3.9% in other middle-income countries (Bate et al 2013; Binagwaho et al 2013).

Postmarket quality studies conducted in the low income countries have tended to focus more on antimicrobials most probably due to the high burden of infectious and communicable diseases. A search of medical literature on EMBASE, MEDLINE, Google Scholar, PubMed and International Pharmaceutical Abstracts for postmarket quality studies on combined oral contraceptives yielded no results. It is imperative that postmarket quality studies are conducted to

establish the quality of the combined oral contraceptives circulating in the Kenyan healthcare market.

2.11. Combined oral contraceptives

Contraception, also referred to as birth control, entails the use of various medical devices, drugs, sexual practices or surgical procedures to prevent pregnancy (Nordqvist 2012; The State of Queensland 2014). Contraception is achieved either by prevention of fertilization of the female egg by the male sperm or by prevention of implantation of the fertilized egg in the uterus (Kimathi, Micheni and Muriithi 2002, p.87).

There are various methods of contraception available in Kenya and these include: the natural family planning method also called periodic abstinence or fertility awareness method, the barrier methods such as the male condom, female condom, diaphragm and sponges, the surgical contraception method through tubal ligation for women and vasectomy for men, the intrauterine contraceptive devices which can be copper based or hormonal and lastly we have the hormonal contraceptives administered as combined oral contraceptives, progestogen only contraceptives, intramuscular shots and implants or delivered through the transdermal patch, the vaginal ring and the hormonal intrauterine contraceptive device (Kimathi, Micheni and Muriithi 2002, p. 91-92; Crouch 2009, p. 489-490; Republic of Kenya, Division of Reproductive Health 2009 p. 21).

Hormonal contraceptives can either be progestogen-only or combined hormonal contraceptives (Amin et al 2012, p. 514). The progestogen-only contraceptives are classified into oral progestogen only contraceptives, intra-uterine progestogen-only devices and the parenteral progestogen-only contraceptives which are administered through deep intramuscular injections or as subcutaneous implants (Crouch 2009, p. 493, Amin et al 2012, p. 521; McEvoy et al, 2013, p. 3118). The combined hormonal contraceptives combine an oestrogen and a progestogen and are administered through the combined oral contraceptive pill, the vaginal contraceptive ring or the transdermal contraceptive patch (Amin et al 2012, p. 515; McEvoy et al 2013, p. 3103).

Majority of the combined oral contraceptive pills contain ethinylestradiol as the oestrogen component with the progestogen component being one of the following progestogens: levonorgestrel, norgestrel, ethynodiol, desogestrel, gestodene, drospirenone, norethisterone, norethindrone, norgestimate or dienogest (Amin et al 2012, p. 519-520; McEvoy et al 2013, p. 3116-3117). The readily available brands of the combined oral contraceptive pills in Kenya are composed of 0.15mg levonorgestrel and 0.03mg ethinylestradiol. The combined oral contraceptive pills can also be monophasic or phasic (Amin et al 2012, p. 515; McEvoy et al 2013, p. 3104). The monophasic ones contain a fixed amount of an oestrogen and a progestogen in each of the active tablets in a cycle while the phasic ones contain varying amounts of the two hormones in a cycle and in that case they can be biphasic, triphasic or estrophasic (Amin et al 2012, p. 515; McEvoy 2013, p. 3104).

The combined oral contraceptive pills achieve their contraceptive effect through an interplay of several factors with the most important being the inhibition of ovulation and the thickening of the cervical mucus thus providing a physical barrier to spermatozoa (Crouch 2009, p. 491; Bayer Pharma AG 2011; McEvoy et al 2013, p. 3114). They also make the endometrium too thin for implantation (Crouch 2009, p. 491). The inhibition of ovulation is through suppression of the hypothalamic-pituitary system with the oestrogen component suppressing secretion of the follicle-stimulating hormone and the progestogen component inhibiting the preovulatory rise of the luteinizing hormone (McEvoy 2013, p. 3114).

It is the responsibility of governments to ensure that the medicines and medical devices employed as methods of contraception are not quality compromised since this has an impact on their effectiveness as methods of contraception. Contraception is the platform through which we practice family planning (World Health Organization 2014). Family planning enables us to bring forth life when it is wanted, expected and welcome (Kimathi, Micheni and Muriithi 2002, p 87; Crouch 2009, p. 488). In addition, a woman's ability to utilize contraception to space and limit her pregnancies has a direct impact on her health and the outcome of each pregnancy (World Health Organization 2014). Family planning plays a central role in the achievement of the Millennium Development Goals reiterated by the 2005 revision of the Millennium Development Goal number 5 through addition of Target 5.B on attainment of universal access to reproductive health under which we have two direct family planning indicators namely: the contraceptive prevalence rate and the unmet need for family planning (Republic of Kenya, Division of Reproductive Health 2009 p. 1; United Nations 2014). Family planning is an essential priority component in the Kenya Essential Package for Health and the Kenya National Reproductive Health Policy 2009-2015 (Crouch 2009, p. 488; Republic of Kenya, Division of Reproductive Health 2010, p. 2).

A particular method of contraception for which governments should be concerned about its postmarket quality is the **combined oral contraceptive pill containing 0.15mg levonorgestrel and 0.03mg ethinylestradiol**. This is due to the following reasons. Firstly, a significant number of women in Kenya use the combined oral contraceptive pill as a family planning method. Nearly 75% of all women in Kenya using contraceptives opt for hormonal contraceptives with 32% of them going for the combined oral contraceptive pill (Republic of Kenya, Division of Reproductive Health 2010, p.69). Secondly, the combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg ethinylestradiol) is listed as an essential medicine in the 2013 World Health Organization Essential Medicines List and the 2010 Kenya Essential Medicines List (Republic of Kenya, Ministry of Medical Services and Ministry of Public Health and Sanitation 2010; World Health Organization 2013). Thirdly, every Kenyan has a right under the Constitution of Kenya to access the highest attainable standards of healthcare. This includes the right to access family planning methods which are of the right quality. Lastly, the combined oral contraceptive pill is also used in emergency contraception and has non-contraception uses such

as the treatment of acne, hirsutism and premenstrual mood syndrome (Crouch 2009, p.492; Republic of Kenya, Division of Reproductive Health 2010, p.71; Republic of Kenya, Division of Reproductive Health 2010, p.105; McEvoy et al 2013, p.3106).

In Kenya various healthcare providers are engaged in the provision of the combined oral contraceptive pill as a family planning method with one of the main providers being the private retail pharmacies where it is sold without prescription (Republic of Kenya, Division of Reproductive Health 2010, p.21).

3. Methodology

3.1. Background.

Medicines regulatory authorities conduct postmarket quality studies either on a routine basis, following a poor quality medicinal product complaint or through sentinel site monitoring. Sentinel site monitoring entails the monitoring of the quality of a medicine in a given site over a certain period of time. Postmarket quality studies entail the collection of medicines samples from the healthcare market which are then subjected to pharmacopoeial based quality tests mainly the assay of content of active pharmaceutical ingredients and the dissolution test.

Informed decisions on the minimum number of samples to be collected in postmarket quality studies so as to be representative for a given geographical area are hindered by a lack of reliable data on the prevalence of poor quality medicines and on the proportion of pharmacies selling poor quality medicines. This is especially so for combined oral contraceptives where a search of medical literature revealed not a single postmarket quality study on the combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg ethinylestradiol).

The Pharmacy and Poisons Board employs two methods in the collection of samples during postmarket quality studies. The first one entails the collection of samples from a randomly selected list of pharmacies in a given geographical area. The second one is through the convenience sampling method which is potentially flawed by bias since the sample collectors target the more geographically accessible pharmacies. The covert (simulation-client) and overt methods of sample purchase are applied as the case may be.

After consultation with the Pharmacy and Poisons Board, it was decided that samples be collected from the private retail pharmacies only as this was part of a study been conducted by the Pharmacy and Poisons Board targeting a wider range of reproductive health medicinal products available in the private and public pharmaceutical sectors of Kenya. This explains why samples were not collected from the public sector as had been stated in the research proposal.

The readily available brands of the combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg ethinylestradiol) in the private pharmaceutical sector of Kenya are Femiplan® and Microgynon®. This project therefore focused on these 2 brands.

3.2. Geographical area of study

The geographical area of focus in this project was the Nyeri town of Kenya. Nyeri town is the headquarters of Nyeri County. Nyeri is one of the 47 counties in Kenya.

3.3. Selection of private retail pharmacies for sample collection

All the 27 private retail pharmacies in Nyeri town were mapped by noting down their names and locations. The Pharmacy and Poisons Board was consulted on their licensure status and it was established that 23 are licensed while 4 are unlicensed. The 4 unlicensed premises were selected for sample collection and from the remaining 23 pharmacies 13 were randomly selected for sample collection. A total of 17 private retail pharmacies were therefore selected for sample collection representing 62% of the total number of private retail pharmacies in Nyeri town.

3.4. Samples collection

A sample was defined as that number of tablets bearing the same proprietary name, with similar content and strength of active pharmaceutical ingredients, bearing the same batch number and procured from a given pharmacy. Collection of samples was done on the 28th and 29th of August, 2014 through the covert/simulation-client method. Two covert shoppers were engaged to pose as customers. The typical user of the combined oral contraceptive pill as a family planning method is a female aged 20-40 years and the 2 covert shoppers fitted this profile. 1 covert shopper was engaged in the purchase of Femiplan® pills and the other one for the purchase of Microgynon® pills. The covert shoppers were trained on what to say while making the purchases and were also under instruction to purchase 3 cycles of either Femiplan® or Microgynon® as the case may be. 3 cycles provided 63 tablets of the combined oral contraceptive pill.

Sample coding and filling of the sample collection form was done immediately the covert shopper left a given retail pharmacy and before the next purchase was done. The sample collection forms were dated and indicated the name and location of the pharmacy concerned and the following details regarding the sample: proprietary name, name and strengths of active pharmaceutical ingredients, quantity collected, batch number, date of manufacture, expiry date, name and address of the manufacturer as indicated on the pack and lastly the name and address of the marketing authorisation holder as indicated on the pack. The nomenclature used to code the samples was COC/xxx/yyy with COC being combined oral contraceptive abbreviated, xxx being the facility code incremental from 001 as the pharmacies are visited and samples collected and yyy being the sample number also incremental from 001 as the samples are collected and coded.

3.5. Samples submission to the Pharmacy and Poisons Board

All the samples were checked to confirm that they had more than 6 months left to their expiry date. The samples were then digitally photographed using a Sony Digital Still Camera model number DSC-W350 and all the pertinent sample details tabulated in a Microsoft Office Excel 97-2003 worksheet. All the samples package colour and writings were visually inspected for obvious signs of counterfeiting. The samples were retained in their point-of-purchase packaging, sealed in individual plastic bags, packed in a carton and stored in a lockable cabinet at room temperature prior to transport to the Pharmacy and Poisons Board.

A form for submitting samples to the Pharmacy and Poisons Board was duly filled indicating the following sample details: sample code, facility name, brand name, stated manufactured by, batch number, expiry date and the quantity. The samples were delivered and received at the Pharmacy and Poisons Board on 21 September 2014.

3.6. Samples submission to the National Quality Control Laboratory

A sample analysis request form was filled for each of the samples requesting for identification, assay and dissolution tests for levonorgestrel and ethinylestradiol. The samples were submitted to the National Quality Control Laboratory on 16 October 2014.

3.7. Assay of the content of levonorgestrel and ethinylestradiol

The average of the 10 individual results obtained in the test for uniformity of content was used in the assay.

The test for uniformity of content was conducted through the High Performance Liquid Chromatography method in accordance with the British Pharmacopoeia 2012 Volume V Appendix XII C. The internal standard method was applied using the following stock solutions: Solution A containing 0.0625% weight/volume of levonorgestrel British Pharmacopoeia Chemical Reference Substance, Solution B containing 0.025% weight/volume of ethinylestradiol British Pharmacopoeia Chemical Reference Substance, Solution C containing 0.020% weight/volume of 2-hydroxybiphenyl (internal standard) and Solution D from dilution of 1 milliliter of Solution C to 20 milliliter with the solvent mixture.

Solutions for the chromatography were then prepared as follows: Solution 1 by mixing the volumes of solutions A and B as specified in the compendia with 5 milliliter of solution C and diluting to 100 milliliter with a mixture of 40 volumes of water and 60 volumes of acetonitrile and Solution 2 by adding 4 milliliter of solution D to one tablet and heating at 60 degrees centigrade in an ultrasonic bath for 25 minutes and then shaking for a repeat ultrasound treatment. This was then cooled and the clear supernatant fluid used.

The chromatographic procedure was then carried out using a stainless steel column (15 centimetres by 4.6 millimetres) packed with octadecylsilyl silica gel (5 micrometre), a mixture of 49 volumes of acetonitrile and 51 volumes of water as the mobile phase with a flow rate of 1.5 millilitres per minute and a detection wavelength of 215 nanometres.

The content of levonorgestrel and ethinylestradiol in each tablet was calculated using the declared content of levonorgestrel in the British Pharmacopoeia Levonorgestrel Chemical Reference Substance and the declared content of ethinylestradiol in the British Pharmacopoeia Ethinylestradiol Chemical Reference Substance.

The specification for levonorgestrel and ethinylestradiol was 90.0 - 110.0 % of the label claim.

3.8. Levonorgestrel dissolution test

Poor manufacturing practices, degradation due to poor storage and the use of incorrect excipients results in medicines with poor dissolution and a subsequent compromised bioavailability.

The ethinylestradiol dissolution analysis was not done due to lack of a spectrofluorometric detector. Levonorgestrel dissolution analysis utilizes an Ultraviolet 247 nanometres detector which was available.

The levonorgestrel dissolution test was carried out through the High Performance Liquid Chromatography method with compendia adopted from the United States Pharmacopoeia 37 National Formulary 32 Volume 3 page 3542. The medium consisted of polysorbate 80 (5 micrograms/gram) in water with acetonitrile and water (6:4) as the mobile phase. The United States Pharmacopoeia Levonorgestrel Reference Standard solution was prepared in medium having known concentrations that would be obtained by dissolving 1 tablet in 500 millilitres of the medium. The sample solution was prepared by withdrawing 15 millilitres portions of liquid from each vessel and passing through a polyvinylidene filter and discarding the first 10 millilitre of the filtrate. The chromatographic system consisted of a column of 4 millimeters by 15 centimeters with a flow rate of 1 milliliter per minute and an injection size of 100 microliters.

The percentage of levonorgestrel dissolved was calculated using the below formulae

$$\text{Result} = (rU / rS) \times (CS / CU) \times 100$$

rU = peak response of the corresponding analyte from the Sample solution

rS = peak response from the corresponding analyte from the Standard solution

CS = concentration of the appropriate United States Pharmacopoeia Reference Standard in the Standard solution (micrograms/milliliter)

CU = nominal concentration of the corresponding analyte in the Sample solution (micrograms/milliliter)

The tolerance limit for levonorgestrel was that not less than 65% of the labeled amount of levonorgestrel should be dissolved.

4. FINDINGS, ANALYSIS AND DISCUSSION

4.1. Pharmacies, samples availability and registration status

There were 27 private retail pharmacies in Nyeri town at the time of sample collection. 23 were licensed with the Pharmacy and Poisons Board while 4 were unlicensed. 17 (62%) pharmacies were selected and visited for sample collection. Femiplan® was available in all the 17 pharmacies while Microgynon® was available in 4 pharmacies. 17 samples of Femiplan® and 4 samples of Microgynon® were collected giving a total of 21 samples. 20 of the samples had 63 hormone-containing tablets each while 1 sample had 42 hormone-containing tablets. Femiplan® and Microgynon® are registered with the Pharmacy and Poisons Board.

4.2. Pertinent sample descriptors

1 cycle of Microgynon® consisted of 21 hormone-containing beige coated tablets and 7 hormone-free brown coated tablets while that of Femiplan® consisted of 21 hormone-containing yellow tablets and 7 hormone-free brown tablets.

The hormone-free tablets contained 75mg of ferrous fumarate.

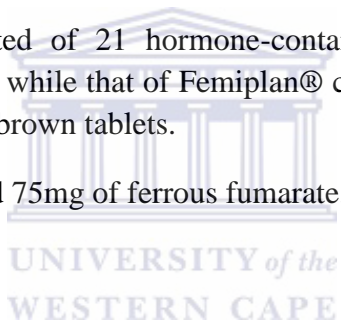


Table 3: Pertinent sample descriptors (N = 21)

SAMPLE CODE	BATCH NUMBER	EXPIRY DATE	SAMPLE SIZE (TABLETS)
COC/001/001	FN306	Feb 2018	63
COC/002/002	FN301	Dec 2017	63
COC/003/003	FN204	Nov 2017	63
COC/004/004	FN304	Jan 2018	63
COC/005/005	FN301	Dec 2017	63
COC/006/006	FN304	Jan 2018	42
COC/007/007	FN303	Jan 2018	63
COC/008/008	FN304	Jan 2018	63
COC/009/009	FN304	Jan 2018	63
COC/010/010	FN302	Dec 2017	63
COC/011/011	FN304	Jan 2018	63
COC/012/012	FN306	Feb 2018	63
COC/013/013	FN304	Jan 2018	63
COC/014/014	FN303	Jan 2018	63
COC/015/015	FN304	Jan 2018	63
COC/005/016	32375A	Mar 2018	63
COC/008/017	32375A	Mar 2018	63
COC/017/018	FN304	Jan 2018	63
COC/002/019	381A	Mar 2017	63
COC/016/020	FN304	Jan 2018	63
COC/012/021	32375A	Mar 2018	63

4.3. Visual inspection of the samples

A visual inspection of the samples did not reveal any counterfeit or falsely labeled batches.

4.4. Assay and dissolution test results

The label claim for Femiplan® and Microgynon® was 0.15mg levonorgestrel and 0.03mg ethinylestradiol. Femiplan® label claim specified the British Pharmacopoeia while that for Microgynon® was not specific on the pharmacopoeia.

Levonorgestrel and ethinylestradiol assay was done in accordance with the British Pharmacopoeia while the levonorgestrel dissolution test was adopted from the United States Pharmacopoeia. Both pharmacopoeias are recognized in Kenya for testing the quality of medicines.

All the samples passed the identification test, the assay of content of levonorgestrel and ethinylestradiol and the levonorgestrel dissolution test. **NOTE** - The ethinylestradiol dissolution test was not conducted due to the laboratory lacking a spectrofluorometric detector for the liquid chromatographic system.



Table 4: Results of assay of content of levonorgestrel and ethinylestradiol and the levonorgestrel dissolution test (N = 21)

Sample code	Assay Specification: 90.0 – 110.0% of the labeled amount			Dissolution Specification: No tablet with less than 65% of the labeled amount is dissolved	
	Levonorgestrel determination (%)	Ethinylestradiol determination (%)	Remarks	Levonorgestrel determination (%)	Remarks
COC/001/001	97.2	97.2	COMPLIES	96.2	COMPLIES
COC/002/002	96.9	105.7	COMPLIES	95.7	COMPLIES
COC/003/003	95.2	94.0	COMPLIES	97.2	COMPLIES
COC/004/004	98.3	99.6	COMPLIES	97.6	COMPLIES
COC/005/005	97.1	97.3	COMPLIES	97.8	COMPLIES
COC/006/006	103.9	104.1	COMPLIES	105.3	COMPLIES
COC/007/007	97.2	98.5	COMPLIES	98.7	COMPLIES
COC/008/008	97.9	98.5	COMPLIES	98.1	COMPLIES
COC/009/009	96.8	96.9	COMPLIES	97.3	COMPLIES
COC/010/010	97.1	99.8	COMPLIES	97.2	COMPLIES
COC/011/011	97.4	98.7	COMPLIES	98.1	COMPLIES
COC/012/012	97.9	100.2	COMPLIES	98.3	COMPLIES
COC/013/013	97.6	98.8	COMPLIES	98.9	COMPLIES
COC/014/014	102.2	101.2	COMPLIES	101.8	COMPLIES
COC/015/015	96.7	96.9	COMPLIES	96.6	COMPLIES
COC/005/016	103.1	101.4	COMPLIES	102.9	COMPLIES
COC/008/017	104.5	101.1	COMPLIES	104.3	COMPLIES
COC/017/018	102.8	103.6	COMPLIES	99.4	COMPLIES
COC/002/019	102.0	101.8	COMPLIES	101.9	COMPLIES
COC/016/020	105.8	103.5	COMPLIES	105.4	COMPLIES
COC/012/021	103.8	100.2	COMPLIES	103.1	COMPLIES

NOTE: For 3 samples, the laboratory reported that they were insufficient samples to carry out an out of specification investigation for the test of uniformity of content for ethinylestradiol (sample COC/002/002, COC/006/006 and COC/010/010) and levonorgestrel (sample COC/006/006). These did not impact on the assay since as earlier stated the assay was determined from the average of the 10 individual results obtained in the test for uniformity of content.

4.5 Discussion

Due to financial constraints, it is virtually impossible for a medicines regulatory authority to conduct laboratory quality tests on all samples of medicinal products available in the healthcare market. Therefore, a likelihood of risk and impact on public health approach is adopted in determining which medicinal products to routinely sample and test for quality.

The aim of this research project was to establish the quality of the combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg ethinylestradiol) in the private retail pharmacies of Nyeri town, Kenya. This was as part of a larger study by the Pharmacy and Poisons Board covering a wider range of reproductive healthcare products circulating in the private and public pharmaceutical sector of Kenya. The quality determination was to be pegged on the quality tests of assay and dissolution for levonorgestrel and ethinylestradiol.

This research project reports positive results. None of the samples was found to be counterfeit and they all passed the levonorgestrel and ethinylestradiol assay and the levonorgestrel dissolution test. Regrettably, it was not possible to characterize the quality of the samples with respect to the ethinylestradiol dissolution test due to a technical hitch at the laboratory occasioned by the lack of a spectrofluorometric detector in the liquid chromatographic system which indicates some capacity issues at the National Quality Control Laboratory.

These positive results indicate that the manufacturers of the concerned sample brands adhere to Good Manufacturing Practices and that the products are handled and stored well throughout the distribution chain. Poor manufacturing and distribution practices have been identified as causes of substandard medicines in the healthcare market (World Health Organization 2015). There are no studies in literature on the postmarket quality of combined oral contraceptives in Kenya for comparison purposes. Therefore, this and the wider study to be reported by the Pharmacy and Poisons Board would be useful for comparing with future studies.

This project was not without **limitations** and it is imperative that we appreciate them as we draw our conclusions. Firstly, the quality of the combined oral contraceptive pills was not characterized with respect to the ethinylestradiol dissolution test. Secondly, a cross-sectional study such as this research project provides a snapshot in time about the quality of medicines on the healthcare market. Thirdly, the Marketing Authorisation Holders of the sample brands were not contacted to authenticate the samples. Authentication relied wholly on the visual inspection of the samples by the researcher. Fourthly, lack of previous studies on the postmarket quality of

combined oral contraceptive pills in the Kenyan private retail pharmaceutical sector was a hindrance to the determination of appropriate sample sizes. Lastly, the number of tablets available per sample was not sufficient enough to have samples reserved for retesting. This was due to the limited number of tablets a mystery shopper could purchase without arousing suspicion. This is one of the limitations of using the covert as opposed to the overt method in the purchase of samples.

5. Conclusions and recommendations

Considering that none of the samples was counterfeit and that they all passed the levonorgestrel and ethinylestradiol assay and the levonorgestrel dissolution test, it is **reasonable to conclude** that the combined oral contraceptive pill (0.15mg levonorgestrel and 0.03mg ethinylestradiol) circulating in the Nyeri town of Kenya private retail pharmacies is of the right quality. This conclusion is drawn only with regard to the quality tests of levonorgestrel and ethinylestradiol assay and the levonorgestrel dissolution analysis. The ethinylestradiol dissolution analysis was not conducted.

There are various recommendations which can be made from this research project. Firstly, postmarket quality studies on reproductive healthcare products including but not limited to combined oral contraceptive pills should routinely be conducted by the Pharmacy and Poisons Board covering both the private and public pharmaceutical sectors. In consideration of the financial burden of analysis, a criterion of likelihood of risk and impact on public health would be useful in determining which medicines to sample. Secondly, the Ministry of Health Government of Kenya needs to consider how it can subsidize the cost of analysis at the National Quality Control Laboratory. It cost approximately 7,500 United States Dollars to analyse the 21 samples in this research project. This huge cost of analysis is the main impediment to the conduct of postmarket quality studies on a routine basis by the Pharmacy and Poisons Board.

Thirdly, for three of the samples (sample codes COC/002/002, COC/006/006 and COC/010/010) which the laboratory reported that they were insufficient samples to conduct a uniformity of dosage unit out of specification investigation, it is recommended that those samples with those specific batch numbers be overtly purchased from the market and submitted for analysis at the National Quality Control Laboratory. Fourthly, the National Quality Control Laboratory needs to be equipped with a spectrofluorometric detector in the High Performance Liquid Chromatography system. Lastly, all the unlicensed private retail pharmacies in Nyeri town should be closed down and criminal sanctions be imposed on the owners.

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7. Appendices

7.1. Research proposal

Title

An assessment of the quality of Combined Oral Contraceptive pills containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg in the Nyeri Town of Kenya pharmaceuticals market.

Introduction

It is the ultimate responsibility of drug regulatory authorities to ensure that pharmaceuticals in the healthcare market are of the right quality. In this regard, various strategies are adopted by drug regulatory authorities in this quest and they include among others implementing a robust initial marketing authorisation regime, conducting regular Good Manufacturing Practices audits of pharmaceutical manufacturers, conducting regular Good Distribution Practices audits of pharmaceutical distributors and lastly conducting regular postmarket surveillance of pharmaceuticals in the pharmaceuticals market in order to single out the poor quality pharmaceutical products with or without a market authorisation.

A class of pharmaceutical products deserving of postmarket surveillance in spite of the limited resources that the drug regulatory authorities in the developing countries such as Kenya have is the Combined Oral Contraceptive pill containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg. This is due to the following factors. Firstly, in Kenya nearly 75% of all women using modern contraceptives choose hormonal methods with 32% opting for the Combined Oral Contraceptive pill (Republic of Kenya 2010). Secondly, the Combined Oral Contraceptive containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg is listed as an essential drug in the Kenya Essential Medicines List which makes it readily available in both the public and private healthcare markets (Republic of Kenya 2010). Lastly, Combined Oral Contraceptives containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg have other health benefits apart from family planning and are prescribed for dysmenorrhoea, irregular cycles, emergency contraception and premenstrual mood syndrome (Republic of Kenya 2010).

Pursuant to the foregoing, the researcher is seeking approval of his research proposal which will entail an assessment of the quality of sampled Combined Oral Contraceptives containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg in the Nyeri town of Kenya pharmaceutical market. The assessment of quality will be through assay and dissolution tests and the proposed site of analysis will be the National Quality Control Laboratory in Kenya.

Methodology

Nyeri town in Kenya is home to 26 identified distribution points for the Combined Oral Contraceptives containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg and these include 3 public hospitals, 1 private hospital, 2 wholesale dealers in pharmaceuticals, 3 private medical centres and 17 retail pharmaceutical outlets.

In this regard, this research will entail collection of samples of Combined Oral Contraceptives containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg at the following 13 sampling sites / distribution points: 3 public hospitals, 2 wholesale dealers in pharmaceuticals, 1 private hospital, 3 private medical centres and 4 retail pharmaceutical outlets.

It is envisaged that a sample will consist of a minimum of 100 tablets and a sample will be regarded as distinct based on the batch/lot number. The researcher targets a total of 12 samples as a minimum. It is worth noting, and this has a bearing on the determination of the sample size, that there are 3 brands of Combined Oral Contraceptives containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg which are registered with the Pharmacy and Poisons Board and thus authorized to be in the Kenyan market.

The samples will be subjected to quality tests specifically assay and dissolution tests at the National Quality Control Laboratory. The National Quality Control Laboratory is mandated by the Pharmacy and Poisons Act (2002) of the Laws of Kenya as a testing facility for pharmaceuticals.

Ethical considerations

This research does not entail the collection of samples from research participants so there is no ethical approval issues envisaged. The researcher will foot the bill for the cost of analyzing the samples the National Quality Control Laboratory. The results of the research will be forwarded to the Pharmacy and Poisons Board of Kenya, the Division of Reproductive Health Ministry of Health, the Director of Health Nyeri County and lastly the owners of the pharmaceutical outlets where the Combined Oral Contraceptive pills containing Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg will be sampled from.

7.2. Sample collection form

RESEARCH PROJECT TITLE.

An assessment of the quality of the Combined Oral Contraceptive pill - Ethinylestradiol 0.03mg and Levonorgestrel 0.15mg in the Nyeri Town of Kenya pharmaceuticals market.

SAMPLE COLLECTION FORM.

1. Date
2. Name and address of health facility
.....
P.O. Box Postal code
- Physical location
3. Facility code
4. Sample code
5. Sample brand name
6. Sample active pharmaceutical ingredients including strength
.....
.....
7. Dosage form
8. Sample quantity collected
9. Batch number
10. Date of manufacture
11. Expiry date
12. Name and address of the manufacturer (as indicated on the pack).
.....
.....
13. Country of origin of the product (as indicated on the pack).
.....
14. Name and address of the marketing authorisation holder.
.....
.....



Sample collection done and witnessed by.

S/N	NAME	DESIGNATION	SIGNATURE
1			
2			

7.3. Sample photos

Sample code: COC/001/001



Sample code: COC/002/002



Sample code: COC/003/003



Sample code: COC/004/004



Sample code: COC/005/005



Sample code: COC/006/006



Sample code: COC/007/007



Sample code: COC/008/008



Sample code: COC/009/009



Sample code: COC/010/010



Sample code: COC/011/011



Sample code: COC/012/012



Sample code: COC/013/013



Sample code: COC/014/014



Sample code: COC/015/015



Sample code: COC/005/016



Sample code: COC/008/017



Sample code: COC/017/018



Sample code: COC/002/019



Sample code: COC/016/020




Sample code: COC/012/021




7.4. Certificates of analysis

Sample code: COC/001/001



Republic of Kenya
Ministry of Health
National Quality Control Laboratory

Hospital Road, KNH Complex, P.O. Box 29726, 00202 Nairobi - Kenya
Telephone: 2726963, +254 - 020 - 3544525/30 | Fax: 2718073
Email: info@nqcl.go.ke Website: www.nqcl.go.ke



CERTIFICATE OF ANALYSIS
CERTIFICATE No: CAN/2014/1061

PRODUCT: FEMPLAN™ TABLETS **REF. NO:** NDQA201410849

DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)

BATCH NO: FN306 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.

MFG. DATE: Mar. 2013 **MANUFACTURER:** FAMy Care Ltd.

EXP. DATE: Feb. 2018 **ADDRESS:** 1608/1609, G.I.D.C, Sarigam - 396 155, Valsad, Gujarat, INDIA.

CLIENT REF NO: COC/001/001 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.

TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.

TEST	METHOD	COMPENDIA	RESULTS		
			SPECIFICATION	DETERMINED	
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 4	COMPLIES
				Ethinylestradiol: AV = 5	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 96.2% (n=6; RSD=3.2%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 95.5% (n=6; RSD= 4.7%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 97.2% (n=10; RSD=1.4%) Ethinylestradiol: 97.2% (n=10; RSD=1.8%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 96.2% (n=3; RSD=0.9%)	COMPLIES


CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE **DATE:** 31/12/2014

ANALYST: DR. G. WANG'ANG'A **DATE:** 31/12/2014

ANALYST: DR. M. KWENA **DATE:** 31/12/2014

DIRECTOR: DR. H. K. CHEPKWONY **DATE:** 31/12/2014



Quality Medicines Protect

Sample code: COC/002/002

CERTIFICATE OF ANALYSIS
CERTIFICATE No: CAN/2014/1057

PRODUCT:	FEMPLAN™ TABLETS	REF. NO:	NDQA201410853
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron).	
BATCH NO:	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
MFG. DATE:	MANUFACTURER:	FAMY Care Ltd.	
EXP. DATE:	ADDRESS:	1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA.	
CLIENT REF NO.	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.	
COC/002/002	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution, Assay by Uniformity of Content and Titration	



RESULTS

TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 7	COMPLIES
				Ethinylestradiol: AV = 36	OoS INVESTIGATION NEEDED
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 95.7% (n=6; RSD=2.8%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 97.7% (n=6; RSD= -)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 96.9% (n=10; RSD=2.5%)	COMPLIES
				Ethinylestradiol: 105.7% (n=10; RSD=12.6%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 96.0% (n=3; RSD=0.5%)	COMPLIES

CONCLUSION: The product complies with the specifications for the Identification, Dissolution and Assay tests performed. However, there were insufficient samples to carry out an out of specification investigation for the Uniformity of Dosage Unit test for Ethinylestradiol.

ANALYST:	MR. M. SANGALE		DATE:	31/12/2014
ANALYST:	DR. G. WANG'ANG'A		DATE:	31/12/2014
ANALYST:	DR. M. KWENA		DATE:	31/12/2014
DIRECTOR:	DR. H. K. CHEPKWONY		DATE:	31/12/2014




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CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1060

PRODUCT: FEMIPLAN™ TABLETS **REF. NO:** NDQA201410850
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg. (Equivalent to 24.375 mg of Ferrous Iron)

BATCH NO: FN204 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.

MEG. DATE: Dec. 2012 **MANUFACTURER:** FAMY Care Ltd.

EXP. DATE: Nov. 2017 **ADDRESS:** 1608/1609, G.I.D.C, Sarigam - 396 155, Valsad, Gujarat, INDIA.


CLIENT REF. NO: COC/003/003 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.

TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay


RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App X17 C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 9	COMPLIES
				Ethinylestradiol: AV = 12	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 97.2% (n=6; RSD=1.5%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 92.5% (n=6; RSD= 3.9%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 95.2% (n=10; RSD=2.4%)	COMPLIES
				Ethinylestradiol: 94.0% (n=10; RSD=3.4%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 98.2% (n=3; RSD=0.4%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A **DATE:** 31/12/2014
ANALYST: DR. M. KWENA **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONYI **DATE:** 31/12/2014



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CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1058



PRODUCT: FEMIPLANTM TABLETS **REF. NO:** NDQA201410852
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)
BATCH NO: FN304 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MFG. DATE: Feb. 2013 **MANUFACTURER:** FAMY Care Ltd.
EXP. DATE: Jan. 2018 **ADDRESS:** 1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA.
CLIENT REF. NO: COC/004/004 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.
TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 7	COMPLIES
				Ethinylestradiol: AV = 6	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 97.6% (n=6; RSD=2.9%)	COMPLIES
				Ferrous Fumarate: 95.5% (n=6; RSD= -)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 98.3% (n=10; RSD=2.7%)	COMPLIES
				Ethinylestradiol: 99.6% (n=10; RSD=2.5%)	COMPLIES
Assay	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 97.1% (n=3; RSD=1.1%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A **DATE:** 31/12/2014
ANALYST: DR. M. KWENA **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY **DATE:** 31/12/2014

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CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1059

PRODUCT: FEMIPLAN™ TABLETS **REF. NO:** NDQA201410851
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg, Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)
BATCH NO: FN301 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MEG. DATE: Jan. 2013 **MANUFACTURER:** FAMY Care Ltd.
EXP. DATE: Dec. 2017 **ADDRESS:** 1608/1609, G.I.D.C, Sarigam - 396 155, Valsad, Gujarat, INDIA.
CLIENT REF NO: COC/005/005 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.
TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 5	COMPLIES
				Ethinylestradiol: AV = 5	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT. Value: 6.6 ± 10% min. present in the sample preparation Ethinylestradiol: Super-imposable peak at RT. Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 97.8% (n=6; RSD=2.9%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 92.1% (n=6; RSD= 3.3%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 97.1% (n=10; RSD=1.4%) Ethinylestradiol: 97.3% (n=10; RSD=1.7%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 95.8% (n=3; RSD=0.5%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A **DATE:** 31/12/2014
ANALYST: DR. M. KWENA **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY **DATE:** 31/12/2014



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Sample code: COC/006/006


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CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2015/155

PRODUCT: FEMPLAN™ TABLETS **REF. NO:** NDQA201410856

DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron).

BATCH NO: FN304 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.

MFG. DATE: Feb. 2013 **MANUFACTURER:** FAMY Care Ltd.

EXP. DATE: Jan. 2018 **ADDRESS:** 1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA.

CLIENT REF NO: COC/006/006 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.



TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.

TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content, Acceptance Value of the 10 dosage units ≤ 15 (AV)	Levonorgestrel: AV = 23	CoS Investigation Needed
				Ethinylestradiol: AV = 23	CoS Investigation Needed
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the assay sample preparation corresponds to that in the assay standard preparation	Levonorgestrel: Super-imposable peak at RT 5.2 ± 10% min. present in both the assay sample and standard preparations.	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT 3.8 ± 10% min. present in both the assay sample and standard preparations.	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 105.3% (n=6; RSD=9.3%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 95.5% (n=6; RSD= 2.1)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 103.9% (n=10; RSD=8.2%)	COMPLIES
				Ethinylestradiol: 104.1% (n=10; RSD=8.1%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 96.5% (n=3; RSD=0.4%)	COMPLIES

CONCLUSION: The product complies with the specifications for the Identification, Dissolution and Assay tests performed. However, there were insufficient samples to carry out an Out of Specification investigation for the Uniformity of Dosage Unit test.

ANALYST: MR. C. ROTICH *[Signature]* **DATE:** 16/02/2015
ANALYST: DR. G. WANG'ANG'A *[Signature]* **DATE:** 16/02/2015
ANALYST: DR. N. MWAURA *[Signature]* **DATE:** 16/02/2015
DIRECTOR: DR. H. K. CHEPKWONY *[Signature]* **DATE:** 16/02/2015




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CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1056

PRODUCT:	FEMIPLAN™ TABLETS	REF. NO:	NDQA201410854
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)	
16.10.2014	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
BATCH NO:	MANUFACTURER:	FAMY Care Ltd.	
FN303	ADDRESS:	1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA.	
MFG. DATE:	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.	
Feb. 2013	CLIENT REF. NO:	COC/007/007	
EXP. DATE:	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution and Assay	
Jan. 2018			

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 6	COMPLIES
				Ethinylestradiol: AV = 5	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 98.7% (n=6; RSD=2.5%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 91.0% (n=6; RSD= -)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 97.2% (n=10; RSD=1.9%) Ethinylestradiol: 98.5% (n=10; RSD=2.2%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 100.9% (n=3; RSD=0.5%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST:	MR. M. SANGALE	DATE:	31/12/2014
ANALYST:	DR. G. WANG'ANG'A	DATE:	31/12/2014
ANALYST:	DR. M. KWENA	DATE:	31/12/2014
DIRECTOR:	DR. H. K. CHEPKWONY	DATE:	31/12/2014



Quality Medicines Protect

Sample Code: COC/008/008

CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1054

PRODUCT: FEMIPLAN™ TABLETS **REF. NO:** NDQA201410857
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg, Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)
BATCH NO: FN304 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box
MFG. DATE: Feb. 2013 **MANUFACTURER:** FAMY Care Ltd.
EXP. DATE: Jan. 2018 **ADDRESS:** 1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA.
CLIENT REF. NO: COC/008/008 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.
TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 7	COMPLIES
				Ethinylestradiol: AV = 7	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 98.1% (n=6; RSD=1.8%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 92.5% (n=6; RSD= 2.5%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 97.9% (n=10; RSD=2.6%) Ethinylestradiol: 98.5% (n=10; RSD=2.9%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 96.2% (n=3; RSD=1.0%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A **DATE:** 31/12/2014
ANALYST: DR. M. KWENA **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY **DATE:** 31/12/2014



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Sample Code: COC/009/009

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CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1055

PRODUCT:	FEMIPLAN™ TABLETS	REF. NO:	YDQA201410855
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg, Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)	
16.10.2014	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box	
BATCH NO:	MANUFACTURER:	FAMY Care Ltd.	
EN304	ADDRESS:	1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA	
MEG. DATE:	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA	
Feb. 2013	CLIENT REF. NO.	COC/009/009	
EXP. DATE:	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution and Assay	
Jan. 2018			

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V, App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 5	COMPLIES
				Ethinylestradiol: AV = 6	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III, Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT. Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT. Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 97.3% (n=6; RSD=3.0%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 92.1% (n=6; RSD= 1.3%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 96.8% (n=10; RSD=1.5%) Ethinylestradiol: 96.9% (n=10; RSD=1.9%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 97.9% (n=3; RSD=0.4%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE	DATE: 31/12/2014
ANALYST: DR. G. WANG'ANG'A	DATE: 31/12/2014
ANALYST: DR. M. KWENA	DATE: 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY	DATE: 31/12/2014



Quality Medicines Protect

Sample code: COC/010/010



Republic of Kenya
Ministry of Health

National Quality Control Laboratory



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Email: info@nqcl.go.ke | Website: www.nqcl.go.ke

CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1069

PRODUCT:	FEMIPLAN™ TABLETS	REF. NO:	NDQA201410858
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg. (Equivalent to 24.375 mg of Ferrous Iron)	
16.10.2014	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
BATCH NO:	MANUFACTURER:	FAMY Care Ltd.	
FN302	ADDRESS:	1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA.	
MFG. DATE:	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.	
Jan. 2013	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution, Assay by Uniformity of Content and Titration	
EXP. DATE:			
Dec. 2017			
CLIENT REF NO.			
COC/010/010			

RESULTS



TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 7	COMPLIES
				Ethinylestradiol: AV = 18	OOS INVESTIGATION NEEDED
Identification	HPLC	B.P. 2012 Vol III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 97.2% (n=6; RSD=1.5%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 95.4% (n=6; RSD= 0.0)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 97.1% (n=10; RSD=2.6%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ethinylestradiol: 99.8% (n=10; RSD=7.5%) Ferrous Fumarate: 97.2% (n=3; RSD=1.1%)	COMPLIES

CONCLUSION: The product complies with the specifications for the Identification, Dissolution and Assay tests performed. However, there were insufficient samples to carry out an out of specification investigation for the Uniformity of Dosage Unit test for Ethinylestradiol.

ANALYST:	MR. M. SANGALE	<i>[Signature]</i>	DATE:	31/12/2014
ANALYST:	DR. G. WANG'ANG'A	<i>[Signature]</i>	DATE:	31/12/2014
ANALYST:	DR. M. KWENA	<i>[Signature]</i>	DATE:	31/12/2014
DIRECTOR:	DR. H. K. CHEPKWONY	<i>[Signature]</i>	DATE:	31/12/2014



Sample Code: COC/011/011


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CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1051


PRODUCT:	FEMIPLAN™ TABLETS	REF. NO:	NDQA201410861
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg. (Equivalent to 24.375 mg of Ferrous Iron)	
16.10.2014	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
BATCH NO:	MANUFACTURER:	FAMY Care Ltd.	
FX304	ADDRESS:	1608/1609, G.I.D.C, Sarigam - 396 155, Valsad, Gujarat, INDIA.	
MFG. DATE:	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.	
Feb. 2013	CLIENT REF NO:	COC/011/011	
EXP. DATE:	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution and Assay	
Jan. 2018			

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 5	COMPLIES
				Ethinylestradiol: AV = 4	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 98.1% (n=6; RSD=1.4%)	COMPLIES
				Ferrous Fumarate: 93.6% (n=6; RSD=4.1%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 97.4% (n=10; RSD=1.7%)	COMPLIES
				Ethinylestradiol: 98.7% (n=10; RSD=1.7%)	COMPLIES
Assay	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 98.1% (n=3; RSD=0.5%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE	DATE: 31/12/2014
ANALYST: DR. G. WANG'ANG'A	DATE: 31/12/2014
ANALYST: DR. M. KWENA	DATE: 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY	DATE: 31/12/2014




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CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1052



PRODUCT:	FEMIPLAN™ TABLETS	REF. NO.:	NDQA201410860
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg, Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)	
16.10.2014	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
BATCH NO.:	MANUFACTURER:	FAMY Care Ltd.	
FN306	ADDRESS:	1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA	
MEG. DATE:	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA	
Mar. 2013	CLIENT REF NO.:	COC/012/012	
EXP. DATE:	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution and Assay	
Feb. 2018			

TEST	METHOD	COMPENDIA	RESULTS		
			SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V, App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 6 Ethinylestradiol: AV = 9	COMPLIES
			RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Super-impossible peak at RT Value: 6.6 ± 10% min, present in the sample preparation Ethinylestradiol: Super-impossible peak at RT Value: 4.5 ± 10% min, present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 98.3% (n=6, RSD=1.7%)	COMPLIES
			No tablet less than 75%	Ferrous Fumarate: 95.5% (n=6, RSD=2.1%) Levonorgestrel: 97.9% (n=10, RSD=2.5%) Ethinylestradiol: 100.2% (n=10, RSD=3.7%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III, Page 2987	90.0 - 110.0%	Levonorgestrel: 98.0% (n=3, RSD=0.4%)	COMPLIES
			90.0 - 105.0%		COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE	DATE: 31/12/2014
ANALYST: DR. G. WANG'ANG'A	DATE: 31/12/2014
ANALYST: DR. M. KWENA	DATE: 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONYI	DATE: 31/12/2014




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CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1053

PRODUCT: FEMIPLAN™ TABLETS **REF. NO:** NDQA201410859
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg, Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)
BATCH NO: FN304 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MFG. DATE: Feb. 2013 **MANUFACTURER:** FAMY Care Ltd.
EXP. DATE: Jan. 2018 **ADDRESS:** 1608/1609, G.I.D.C. Sarigam - 396 155, Valsad, Gujarat, INDIA.
CLIENT REF. NO: COC/013/013 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.
TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPHPLC	B.P. 2012 Vol. V - App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 6	COMPLIES
				Ethinylestradiol: AV = 5	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Super-imposable peak at RT. Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT. Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 98.9% (n=6; RSD=0.9%)	COMPLIES
				Ferrous Fumarate: 97.7% (n=6; RSD= .)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 97.6% (n=10; RSD=2.1%)	COMPLIES
				Ethinylestradiol: 98.8% (n=10; RSD=2.2%)	COMPLIES
Assay	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 98.2% (n=3; RSD=0.2%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A **DATE:** 31/12/2014
ANALYST: DR. M. KWENA **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY **DATE:** 31/12/2014



Quality Medicines Protector

Sample Code: COC/014/014

CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1071

PRODUCT: FEMIPLAN™ TABLETS **REF. NO:** NDQA201410864
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg. (Equivalent to 24.375 mg of Ferrous Iron)
BATCH NO: FN303 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MFG. DATE: Feb. 2013 **MANUFACTURER:** FAMY Care Ltd.
EXP. DATE: Jan. 2018 **ADDRESS:** 1608/1609, G.I.D.C., Sarigam - 396 155, Valsad, Gujarat, INDIA.
CLIENT REF NO: COC/014/014 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.
TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.



RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V, App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 7	COMPLIES
				Ethinylestradiol: AV = 10	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III, Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT. Value: 5.5 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT. Value: 3.8 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 101.8% (n=6, RSD=2.0%)	COMPLIES
	Titration	B.P. 2012 Vol. III, Page 2816	No tablet less than 75%	Ferrous Fumarate: 97.7% (n=6, RSD= 1.4%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III, Page 2987	90.0 - 110.0%	Levonorgestrel: 102.2% (n=10, RSD=2.7%) Ethinylestradiol: 101.2% (n=10, RSD=3.9%)	COMPLIES
	Titration	B.P. 2012 Vol. III, Page 2816	90.0 - 105.0%	Ferrous Fumarate: 96.9% (n=3, RSD=0.9%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. C. ROTICH *[Signature]* **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A *[Signature]* **DATE:** 31/12/2014
ANALYST: DR. M. KWENA *[Signature]* **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY *[Signature]* **DATE:** 31/12/2014



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CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1050

PRODUCT:	FEMIPLAN™ TABLETS	REF. NO:	NDQA201410862
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron).	
16.10.2014	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
BATCH NO:	MANUFACTURER:	FAMY Care Ltd.	
FN304	ADDRESS:	1608/1609, G.I.D.C, Sarigam - 396 155, Valsad, Gujarat, INDIA.	
MFG. DATE:	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.	
Feb. 2013	CLIENT REF NO:	COC/015/015	
EXP. DATE:	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution and Assay.	
Jan. 2018			


RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 5	COMPLIES
				Ethinylestradiol: AV = 5	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-impossible peak at RT. Value: 6.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-impossible peak at RT. Value: 4.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 96.6% (n=6; RSD=1.4%)	COMPLIES
				Ferrous Fumarate: 93.6% (n=6; RSD=4.1%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 96.7% (n=10; RSD=1.4%)	COMPLIES
				Ethinylestradiol: 96.9% (n=10; RSD=1.7%)	COMPLIES
Assay	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 95.6% (n=3; RSD=0.3%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. M. SANGALE	DATE: 31/12/2014
ANALYST: DR. G. WANG'ANG'A	DATE: 31/12/2014
ANALYST: DR. M. KWENA	DATE: 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONYI	DATE: 31/12/2014



Sample Code: COC/005/016


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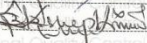

CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1088

PRODUCT:	MICROGYNON® Fe TABLETS	REF. NO:	NDQA201410865
DATE RECEIVED:	LABEL CLAIM:	1 beige coloured tablet contains Levonorgestrel 0.15 mg, Ethinylestradiol 0.03 mg, 1 brown coloured tablet contains Ferrous fumarate 75 mg	
16.10.2014	PRESENTATION:	Beige coloured (21 tablets) & Brown coloured (7 tablets), circular shaped, biconvex tablets, plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
BATCH NO:	MANUFACTURER:	BAYER Schering Pharma AG,	
32375A	ADDRESS:	13342 Berlin, GERMANY.	
MFG. DATE:	CLIENT:	Pharmacy and Poisons Board,	
Apr. 2013	CLIENT REF NO:	P.O. Box 27663 - 00506, Nairobi, KENYA.	
EXP. DATE:	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution and Assay.	
Mar. 2018			
COC/005/016			

RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than .85%, or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 6	COMPLIES
				Ethinylestradiol: AV = 10	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 12.6 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 7.5 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 102.9% (n=6; RSD=0.9%)	COMPLIES
				Ferrous Fumarate: 96.6% (n=6; RSD= 3.2%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 103.1% (n=10; RSD=1.7%)	COMPLIES
				Ethinylestradiol: 101.4% (n=10; RSD=4.1%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 98.3% (n=3; RSD=1.7%)	COMPLIES



CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST:	MR. C. ROTICH		DATE:	31/12/2014
ANALYST:	DR. G. WANG'ANG'A		DATE:	31/12/2014
ANALYST:	DR. M. KWENA		DATE:	31/12/2014
DIRECTOR:	DR. H. K. CHEPKWONY		DATE:	31/12/2014



Quality Medicines Protect

Sample Code: COC/008/017


 Republic of Kenya
 Ministry of Health
National Quality Control Laboratory


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CERTIFICATE OF ANALYSIS

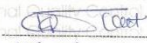

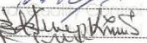

CERTIFICATE No: CAN/2014/1079


PRODUCT: MICROGYNON® Fe TABLETS **REF. NO:** NDQA201410866
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** 1 beige coloured tablet contains Levonorgestrel 0.15 mg, Ethinylestradiol 0.03 mg, 1 brown coloured tablet contains Ferrous fumarate 75 mg
BATCH NO: 32275A **PRESENTATION:** Beige coloured (21 tablets) & Brown coloured (7 tablets), circular shaped, biconvex tablets, plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MFG. DATE: Apr. 2013 **MANUFACTURER:** BAYER Schering Pharma AG.
EXP. DATE: Mar. 2018 **ADDRESS:** 13342 Berlin, GERMANY
CLIENT REF NO: COC/008/017 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.

TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.

TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 7	COMPLIES
				Ethinylestradiol: AV = 5	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-impossible peak at RT Value: 6.7 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-impossible peak at RT Value: 4.4 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.E. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 104.3% (n=6; RSD=2.1%)	COMPLIES
				Titration	B.P. 2012 Vol. III Page 2816
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 104.5% (n=10; RSD=1.6%)	COMPLIES
				Titration	B.P. 2012 Vol. III Page 2816

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. C. ROTICH  **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A  **DATE:** 31/12/2014
ANALYST: DR. M. KWENA  **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONYI  **DATE:** 31/12/2014



Quality Medicines Protect

Sample Code: COC/017/018

CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1072

PRODUCT:	FEMIPLAN™ TABLETS	REF. NO:	NDQA201410867
DATE RECEIVED:	LABEL CLAIM:	Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg, Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg, (Equivalent to 24.375 mg of Ferrous Iron)	
BATCH NO:	PRESENTATION:	Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.	
MFG. DATE:	MANUFACTURER:	FAMY Care Ltd.	
EXP. DATE:	ADDRESS:	1608/1609, G.I.D.C. Sarigam - 396 155, Valsad, Gujarat, INDIA.	
CLIENT REF. NO:	CLIENT:	Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.	
COC/017/018	TEST(S) REQUESTED:	Uniformity of Dosage Unit, Identification, Dissolution and Assay	


RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 5	COMPLIES
				Ethinylestradiol: AV = 6	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-impossible peak at RT Value: 5.5 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-impossible peak at RT Value: 3.8 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 99.4% (n=6; RSD=2.3%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 97.0% (n=6; RSD= 1.2%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 102.8% (n=10; RSD=1.6%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ethinylestradiol: 103.6% (n=10; RSD=1.5%) Ferrous Fumarate: 97.1% (n=3; RSD=0.5%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST:	MR. C. ROTICH		DATE:	31/12/2014
ANALYST:	DR. G. WANG'ANG'A		DATE:	31/12/2014
ANALYST:	DR. M. KWENA		DATE:	31/12/2014
DIRECTOR:	DR. H. K. CHEPKWONY		DATE:	31/12/2014



Quality Medicines Protect


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CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1080


PRODUCT: MICROGYNON TABLETS **REF. NO:** NDQA201410868
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each beige tablet contains levonorgestrel 0.15 mg and 0.03 mg ethinyl estradiol, each brown tablet contains 75 mg ferrous fumarate.
BATCH NO: 381A **PRESENTATION:** Beige coloured (21 tablets) & Brown coloured (7 tablets), circular shaped, biconvex tablets, plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MFG. DATE: Apr. 2012 **MANUFACTURER:** BAYER Schering Pharma AG.
EXP. DATE: Mar. 2017 **ADDRESS:** 13342 Berlin, GERMANY.
CLIENT REF NO: **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.

TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.



RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 2 Ethinylestradiol: AV = 3	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 5.5 ± 10% min. present in the sample preparation Ethinylestradiol: Super-imposable peak at RT Value: 3.8 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 101.9% (n=6, RSD=1.2%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Ferrous Fumarate: 98.4% (n=6, RSD= 2.3%) Levonorgestrel: 102.0% (n=10, RSD=0.8%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Ethinylestradiol: 101.8% (n=10, RSD=1.0%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 97.1% (n=3, RSD=0.5%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. C. ROTICH **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANGA **DATE:** 31/12/2014
ANALYST: DR. M. KWENA **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONY **DATE:** 31/12/2014


 Quality Medicines Protect

Sample Code: COC/016/020


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CERTIFICATE OF ANALYSIS


CERTIFICATE No: CAN/2014/1070

PRODUCT: FEMIPLAN™ TABLETS **REF. NO:** NDQA201410869
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** Each sugar coated yellow pill contains: Levonorgestrel B.P. 0.15 mg, Ethinylestradiol B.P. 0.03 mg. Each sugar coated brown pill contains: Ferrous Fumarate B.P. 75 mg. (Equivalent to 24.375 mg of Ferrous Iron)
BATCH NO: FN304 **PRESENTATION:** Cream coloured (21 pills) & Brown coloured (7 pills), circular shaped, biconvex tablets plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MFG. DATE: Feb. 2013 **MANUFACTURER:** FAMY Care Ltd.
EXP. DATE: Jan. 2018 **ADDRESS:** 1608/1609, G.I.D.C. Sarigam - 396 155, Valsad, Gujarat, INDIA.
CLIENT REF NO: COC/016/020 **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.
TEST(S) REQUESTED: Uniformity of Dosage Unit, Identification, Dissolution and Assay.


RESULTS					
TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V, App XII C	Not more than 1 unit is less than 85% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 11	COMPLIES
				Ethinylestradiol: AV = 7	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Super-imposable peak at RT Value: 6.7 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.4 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.F. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 105.4% (n=6; RSD=2.7%)	COMPLIES
				Ferrous Fumarate: 97.3% (n=6; RSD= 0.9%)	COMPLIES
Assay	HPLC	B.P. 2012 Vol. III Page 2987	90.0 - 110.0%	Levonorgestrel: 105.8% (n=10; RSD=2.8%)	COMPLIES
				Ethinylestradiol: 103.5% (n=10; RSD=2.1%)	COMPLIES
	Titration	B.P. 2012 Vol. III Page 2816	90.0 - 105.0%	Ferrous Fumarate: 98.0% (n=3; RSD=0.7%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. C. ROTICH *[Signature]* **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A *[Signature]* **DATE:** 31/12/2014
ANALYST: DR. M. KWENA *[Signature]* **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONYI *[Signature]* **DATE:** 31/12/2014



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CERTIFICATE OF ANALYSIS

CERTIFICATE No: CAN/2014/1078

PRODUCT: MICROGYNON® Fe TABLETS **REF. NO:** NDQA201410863
DATE RECEIVED: 16.10.2014 **LABEL CLAIM:** 1 beige coloured tablet contains Levonorgestrel 0.15 mg, Ethinylestradiol 0.03 mg, 1 brown coloured tablet contains Ferrous fumarate 75 mg
BATCH NO: 32375A **PRESENTATION:** Beige coloured (21 tablets) & Brown coloured (7 tablets), circular shaped, biconvex tablets, plain on both faces packed in a blister strip of 28 tablets contained in a printed box.
MFG. DATE: Apr. 2013 **MANUFACTURER:** BAYER Schering Pharma AG
EXP. DATE: Mar. 2018 **ADDRESS:** 13342 Berlin, GERMANY
CLIENT REF NO: **CLIENT:** Pharmacy and Poisons Board, P.O. Box 27663 - 00506, Nairobi, KENYA.

COC/012/021 **TEST(S) REQUESTED:** Uniformity of Dosage Unit, Identification, Dissolution and Assay

TEST	METHOD	COMPENDIA	SPECIFICATION	DETERMINED	REMARKS
Uniformity of Dosage Unit	HPLC	B.P. 2012 Vol. V App XII C	Not more than 1 unit is less than 83% or greater than 115% of the average tablet content. Acceptance Value of the 10 dosage units is ≤ 15	Levonorgestrel: AV = 13	COMPLIES
				Ethinylestradiol: AV = 11	COMPLIES
Identification	HPLC	B.P. 2012 Vol. III Page 2987	RT of the Major Peak in the sample preparation corresponds to that in the standard preparation	Levonorgestrel: Super-imposable peak at RT Value: 6.7 ± 10% min. present in the sample preparation	COMPLIES
				Ethinylestradiol: Super-imposable peak at RT Value: 4.4 ± 10% min. present in the sample preparation	COMPLIES
Dissolution	HPLC	Adopted U.S.P. 37 N.E. 32 Vol. 3 Page 3542	No tablet less than 65%	Levonorgestrel: 103.1% (n=6, RSD=4.8%)	COMPLIES
				Ferrous Fumarate: 96.6% (n=6, RSD= 1.3%)	COMPLIES
Assay	Titration	B.P. 2012 Vol. III Page 2816	No tablet less than 75%	Levonorgestrel: 103.8% (n=10, RSD=4.6%)	COMPLIES
				Ethinylestradiol: 100.2% (n=10, RSD=4.9%)	COMPLIES
				Ferrous Fumarate: 98.2% (n=3, RSD=0.8%)	COMPLIES

CONCLUSION: The product complies with the specifications for the tests performed.

ANALYST: MR. C. MWANGI **DATE:** 31/12/2014
ANALYST: DR. G. WANG'ANG'A **DATE:** 31/12/2014
ANALYST: DR. M. KWENA **DATE:** 31/12/2014
DIRECTOR: DR. H. K. CHEPKWONYI **DATE:** 31/12/2014

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