Breaking the Barriers:
The Impact of Evergreening in the Access of HIV Treatment in Kenya

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Reclaiming Rights, Rebuilding Lives

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Abbreviations

AHD	Advanced HIV Disease
ARIPO African	Regional Intellectual Property Organization
ARVs	Antiretrovirals
BDQ	Bedaquiline
EAC	East African Community
EML	Essential Medicine List
FDA	Food and Drug Administration
GATS	General Agreement on Trade in Services
GATT	General Agreement on Tariffs and Trade
GDF	Global Drug Facility
GFATM	Global Fund to Fight AIDS, Tuberculosis (TB) and Malaria
HCV	Hepatitis C Virus
HIC	High Income Country
HIV	Human Immunodeficiency Virus
IP	Intellectual Property
IPRs	Intellectual Property Rights
J&J	Johnson & Johnson
KEMSA	Kenya Medical Supply Authority
KIPI	Kenya Industrial Property Institute
LDC	Least Developed Countries
LMICs	Low-and-middle Income Countries
MDR-TB	Multidrug-resistant Tuberculosis
MSF	Médecins Sans Frontières
NEML	National Essential Medicine List
MPP	Medicines Patent Pool
PEPFAR	US President's Emergency Plan For Aids Relief
PLHIV	People Living with HIV
RIPD	Regional IP Database
R&D	Research and Development
STBP	Stop Tuberculosis (TB) Partnership
TB	Tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UK	United Kingdom
USA	United States of America
WHO	World Health Organization
WHO PQ	World Health Organization Prequalification
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

EXECUTIVE SUMMARY

Intellectual property barriers are one of the key challenges to accessing affordable and effective lifesaving medicines. In many countries, pharmaceutical companies obtain patent extensions through various mechanisms – whether secondary patents or continuously making incremental drug changes - these drug life-cycle management strategies delay the entry of generic medicines into the market. The extensions of existing patents also prevent the innovation of new drugs, as most drugs are so recycled through such strategies that research and development have slowed scientific advancements to diseases that could already have been eliminated, such as HIV. For this study and discussions at policy, stakeholder and industry levels, the term "evergreening" has been used in parallel with "patent extension" or "secondary patent".

Objectives of the study:

The objectives of this study included the following:

i. Conducting a comprehensive literature review focusing on intellectual property and patent extension practices such as 'evergreening' within the African Regional Intellectual Property Organization (ARIPO) - is an intergovernmental organization for cooperation among African states in patent and other intellectual property matters for its member states; with a particular focus on how these impact access to essential ARVs in the Republic of Kenya.
ii. Document cases of patent extension (or evergreening) among the antiretroviral (ARVs) listed in Kenya's Essential Medicine List (EML).
iii. Evaluate the consequences of patent extension (or evergreening) on the availability, affordability, and quality of HIV treatment in Kenya and how these practices negatively impact access to essential HIV medication to various at-risk populations and vulnerable groups.

Key Findings

i. The study found evidence of patent extension (or evergreening) practices as part of pharmaceutical companies' life-cycle management of many AVRs. This practice was predominant among ARIPO member states, including Kenya, registering nearly 5628 patents (not exclusively ARVs). Patents were often extended for minor modifications or formulations of existing drugs, delaying the entry of generics to the market.

ii. Documentation of patent extension (or evergreening) information on the ARIPO Database was a significant barrier, and documentation on the database was limited to the date the patent was initially registered.

iii. Some older ARVs on Kenya's 2019 EML are either off-patent according to sources such as MedsPaL and ATSTAT and/ or may not be registered on the ARIPO Database.

iv. What was found on the ARIPO database were the following: the initial registration data, the patent number, the company registering the patent, and the date the drug was registered were found.

v. Kenya's current Industrial Property law does not explicitly address secondary patenting (patent extensions or evergreening). This allows pharmaceutical companies to exploit loopholes to extend their market exclusivity. It was noted that there is a revised Industrial Property Bill in circulation for finalizing this assignment.

vi. The Harare Protocol - the guiding instrument of ARIPO - has undergone several updates, but none of these have extensively incorporated the flexibilities provided for by the TRIPS Agreement. Many versions of the updated Protocol were found in various legitimate sources. This is problematic for the accuracy of data analysis.

Policy Recommendations

i. A review of Kenya's IP laws should accompany implementation guidance to address evergreening practices explicitly. This may prevent the unjust extension of patents for minor changes to existing drugs.

ii. The government has the Industrial Property Bill in circulation. It is recommended that the Bill incorporates most of the essential flexibilities the TRIPS Agreement provides.

iii. The need to build alliances between the ministries of Health, Finance and Trade, along with stakeholders such as KIPI, academia and civil society working on access matters, is a strong recommendation.

iv. As mentioned under recommendation three above, stakeholders should be involved in the negotiations of Free Trade Agreements which impact Kenya, or at least there should be transparency and access to documents under negotiation. This way, TRIPS-Plus measures can be actively challenged during negotiation processes, such as data exclusivity provisions of stronger intellectual property protections leading to unfavourable terms for Kenya to safeguard access to medicines for critical populations.

v. The government of Kenya should work with other EAC member states to develop a regional Access Alliance. Along with EAC, partner states must develop a regional patent examination and pre-and post-opposition system. The EAC region is encouraged to establish a database of essential diagnostic tools, medical devices and essential medicines so that countries can follow cooperative pooling processes when procuring pharmaceutical commodities.

1.0 INTRODUCTION

1.1 Background

As scientific and technological advancements have taken the pharmaceutical industry to new heights, much emphasis is being placed on developing "novelty", which encompasses inventive steps and innovation which could contribute to the industrialization agendas and the improvement of economies through, among other things, safeguarding of the overall health of citizenry as enshrined within Bill of Rights of the Constitution of the Republic of Kenya. The patent system was a form of compensation for innovators to ensure and promote continued research and development (R&D) into new and more accessible treatments and cures for diseases. These legal rights grant the exclusive right to fully use, sell, or even forbid others from using the invention while incentivizing others to come up with ground-breaking discoveries (Brown 2003).

Patents and other IP rights were thought to increase creativity significantly. Nevertheless, the profits made from allowing corporations to keep the proceeds from the use and sale of their goods are also said to be used in theory to fund new research and development (R&D), which would continuously expose the economy to a rapid boom (Atun, Harvey, and Wild 2007). It is considered a cycle in which the law guards against the appropriation of ideas and prevents the exploitation of research to advance economic development.

1.1.1 Brief Legal Overview

IP regulating laws and procedures date centuries ago. However, clear guidelines governing IP are said to have been established by the World Trade Organisation (WTO). Set up in 1995, the WTO is considered the main influential body in regulating international trade among its nation members by providing frameworks on the trade of goods and services and IP agreements (WTO, 2012). Kenya was among the founding members of the World Trade Organization (WTO) when the Marrakesh Agreement was signed in Morocco on April 15, 1994. As such, there are three mandatory agreements: GATT (the General Agreement on Tariffs and Trade), GATS (the General Agreement on Trade in Services) and TRIPS (Trade-Related Aspects of Intellectual Property Rights) agreement (Croome and Organization 1995). Like many developing and least-developing countries, the

Republic of Kenya became a member of the TRIPS on January 1, 1995.

For international jurisdictions, the TRIPS agreement is crucial for regulating IP. The agreement, which went into effect in 1995, incorporates principles from the 1880s-era Paris Convention for the Protection of Industrial Property and the Berne Convention for the Protection of Literary and Artistic Works. However, TRIPS is special. It is a component of a package of agreements that nations must obediently abide by to be accepted as WTO members. As a result, states must include a minimum level of IP protection in line with the TRIPS agreement in their domestic laws (Bhattacharya and Saha 2011). This agreement has had far-reaching negative consequences for developing and least-developed member states in the last three decades.

1.2 Unprotected through the Sword of Innovation

The globalization of IP under the TRIPS agreement has created a critical situation where patents and other mechanisms now play an unprecedented role in determining the availability and affordability of medicines. TRIPS, to put it simply, limits the freedom of States. The obligations outlined in TRIPS limit the development of an IP system that best suits the priorities of the states that are WTO members regarding public health. The implementation is carried out without considering the various nations' technological prowess or degree of development. As a result, several African countries lost the ability to provide their populace with necessary medications. In a sense, TRIPS gives the company with IP protection a double benefit: ownership and sales privileges as well as control over the commercialization and monopolization of the product on international markets (Morin and Gold 2014).

1.3 Access Inequalities

The sale of HIV medications has been where this double advantage system has had the most noticeable effect and caused the most conflict (Correa 2020). Without a doubt, research demonstrates that expensive medications are associated with limited access to health care and effective illness treatment. In many countries, regardless of their level of development and income, patents as an IP mechanism under TRIPS protect and legitimize the high cost of medicines. In the pharmaceutical industry, the justification is based on the idea that because the development of new drugs is expensive, the price should be recouped à traverse sales profits. As stated, the 'ripple effect' of IP protection that was most noticeable occurred in the late 1990s, when HIV/AIDS spread rapidly in Africa (Giaccotto, Santerre, and Vernon 2005).

1.4 Evergreening - Peeling Back the Layers of IP Systems & Pharmaceutical Exclusivity

With global and national advocacy campaigns playing a crucial role in raising awareness about the importance of access to ARV in LMICs, governments and international organizations were urged to prioritize affordable and accessible HIV treatment (Ahmad 2013). As such, these collective efforts forced pharmaceutical companies to reduce patent barriers by leveraging domestic legal systems and other advocacy pressure campaigns - leading to essential changes in increased access to HIV drugs for PLHIV globally (Hoen et al. 2011). However, despite the significant progress made in increasing access to ARVs in LMICs, there are still challenging areas in IP that demand attention and ongoing efforts.

While the development of robust IP laws and the establishment of international agreements, as mentioned above, provide exclusive rights to the inventors for a duration of typically around 20 years from the filing date, pharmaceutical companies have now sought ways of extending the patent life of their drugs. This is because once a patent expires, the drug becomes part of the public domain, allowing generic manufacturers to produce and distribute identical versions of the drug at a fraction of the price of the originator. However, to maintain their market exclusivity

and continue generating revenue, pharmaceutical companies strategically make **slight modifications to drug formulations or their delivery methods,** which often results in new patent applications, prolonging the duration of the patents beyond the 20 years as guaranteed by the TRIPS Agreement (Moir, 2021).

Even though the TRIPS Agreement and the adjoining DOHA Declaration of 2001 allowed for certain 'flexibilities' within the TRIPS Agreement to be leveraged by member states – in response to the HIV/AIDS crisis and with a long-term view of striking a balance between public health and innovation as well as the protection of research and development - it has also ***unintentionally*** created room for 'evergreening' practices. The specific provisions of the TRIPS agreement on the exigency for patentability and the lack of strict examination requirements of commercialized products have facilitated the use of extensions by pharmaceutical companies to extend their patent's life expectancy strategically. Such practices hinder competition from generic manufacturers, as the extended patents create obstacles to the production and distribution of lower-cost versions of drugs (Feldman, 2018).

A 2012 study illustrated how secondary patents could extend market exclusivity and thus delay generic competition. (Amin and Kesselheim, 2012) This study focused on two critical antiretroviral drugs used in HIV management, namely, ritonavir (Norvir) and lopinavir/ritonavir (Kaletra). They identified a total of 108 patents that could potentially postpone generic competition until at least 2028—twelve years after the expiration of the patents on the drugs' base compounds and thirty-nine years after the first patents on ritonavir were filed. Some of the secondary patents that they reviewed were found to be of questionable inventiveness. Another study conducted in Ukraine (100% LIFE, AIDSfonds, the International Treatment Coalition [ITPC] and the Scientific Research Institute of IP/National Academy of Law Sciences Ukraine, 2020) analysed 27 ARV patents. Out of those 27 patents, 15 were found to have patent extensions for various incremental changes filed by foreign applicants. These extensions have negatively impacted the affordability, accessibility, and availability of medication in the country. The same ARVs were assessed in the Kenya 2019 EML, and the same extension practices were found through MedPaL.

2.0 RESEARCH METHODOLOGY

2.1 Scope of this Report

The scope of this body of work included an extensive analysis of the state of TRIP-plus measures, in this case, patent extensions and access to medical care by people living with HIV, with a particular emphasis on the evergreening practices on existing ARVs in the Republic of Kenya. This research report aims to identify instances of HIV drug (ARV) evergreening practices used by pharmaceutical companies in Kenya, evaluate their implications for access to reasonably priced healthcare, and suggest potential strategies to mitigate these barriers. This project also seeks to shed light on the scope of evergreening practices and their impact on healthcare outcomes. This was mainly done by analyzing pertinent laws, regulations, and case studies, fostering evidence-based policy recommendations that support equitable access to necessary medications for the Kenyan population living with HIV.

The purpose is to conduct a patent landscape analysis of antiretroviral (ARV) drugs in Kenya, explicitly exploring potential evergreening practices. We used Kenya's Essential Medicines List (EML) as a reference to identify ARV drugs and examine their patent status to assess any instances of evergreening. In our desktop research to check the quality and composition of the ARV drugs, we used publicly accessible databases, including MedsPal, Patenscope, PATSTAT and ARIPO Regional IP Database. For the research on the potential evergreening practices in Kenya and the world, research was conducted through the National Library of Medicine, BMC Public Health, Jstore, Health Affairs and the Lancet (the free access version).

2.1.1 Secondary Data

An extensive review of the literature around IPRs and public health, IP, and evergreening was undertaken to appreciate the extent of evergreening practices. Intellectual property laws, rules, and case studies focused on ARV drugs and access within the healthcare system in Kenya. The data were collected from various sources, including academic journals, reports, policy documents, legal frameworks, and case studies. As such, the data has provided a broader context for understanding the historical, legal, and policy aspects of evergreening practices in Kenya. The following table provides an overview of the research methodology and sampling size:

A non-structured 110 documents (including academic papers, reports, and media articles from PubMed, Jstor, Wiley, and Health Affairs) were reviewed. Even though systematic reviews were prioritized in the hierarchy of evidence-based public health for addressing research questions, non-systematic reviews were crucial for addressing a subject in various contexts. The purpose of selecting this approach for this report was to summarize what has already been documented on the subject matter and gather adequate data to understand how this was happening within Kenya as a member of ARIPO and as a member of the EAC.

Articles were extensively referenced, using

reference management software to manage bibliographic data and related research materials. Using institutional websites, PubMed Google Scholar, and snowballing by reviewing the references in the identified publications, additional grey literature, and scholarly materials, such as working papers, dissertations, and book sections, were found. As such, included in this report were all publications that provided findings from a multi-dimensional perspective on the influence of evergreening on access to medications.

Secondary data were favoured for the development of this report as few constraints were encountered during the data collection stage. Time restrictions and the unavailability of crucial ARIPO staff members were some of the obstacles encountered during the development of this report. These limitations will further be discussed across sub-headings 3.3 of this paper.

2.1.2 Research Questions

The research aims to address the following questions:

- Which ARV drugs are listed in Kenya's EML?
- What is the patent status of these ARV drugs in Kenya?
- Are there any instances of evergreening among the listed ARV drugs, and if so, what do pharmaceutical companies employ strategies to extend exclusivity?
- Evaluate the consequences of evergreening on the availability, affordability, and quality of HIV treatment in Kenya.
- Examine how evergreening practices affect different populations and vulnerable groups.
- Discuss the implications of delayed or limited access to newer, more affordable ARV treatments.

2.1.3 Data Analysis

- Evergreening Identification: Identify ARV drugs with patents filed for new formulations, dosages, combinations, or uses beyond their original patent's expiration.
- Duration of Exclusivity: Calculate the duration of exclusivity for each ARV drug based on the original patent's grant date and any additional evergreening patents.
- Patent Trends: Analysis of evergreening practices and trends among ARV drugs over time.

2.1.4 Limitations

This research acknowledges potential limitations, including:

- Inaccessibility to ARIPO Data management or senior IP Agent – despite numerous emails, calls, and LinkedIn outreach.
- Limited visibility of comprehensive information on the ARIPO Database. There is no disaggregation of data on the database as it relates to chemical compounds of the ARV medicines and the changes that are made to extend the patent for such a medicine.
- The accessibility of the ARIPO Database in searching for evergreening information was a significant barrier, and documentation on the database was limited to the date the patent was initially registered.
- Some of the older ARVs on Kenya's 2019 EML are either off-patent according to sources such as MedPaL PATSTAT and/or not registered on the ARIPO Database. Only the initial registration data, the patent number, the company registering the patent, and the date the drug was registered were found.
- Kenya's current Industrial Property law does not explicitly address secondary patenting (or evergreening). It also does not incorporate the flexibilities inherent in the TRIPS Agreement, which the Kenya government could leverage to ensure access to diagnostic tools and newer essential HIV medicines. This allows pharmaceutical companies to exploit loopholes to extend their market exclusivity.

3.0 BEYOND LIMITS: UNRAVELING THE TIES BETWEEN "ACCESS" AND " EVERGREENING"

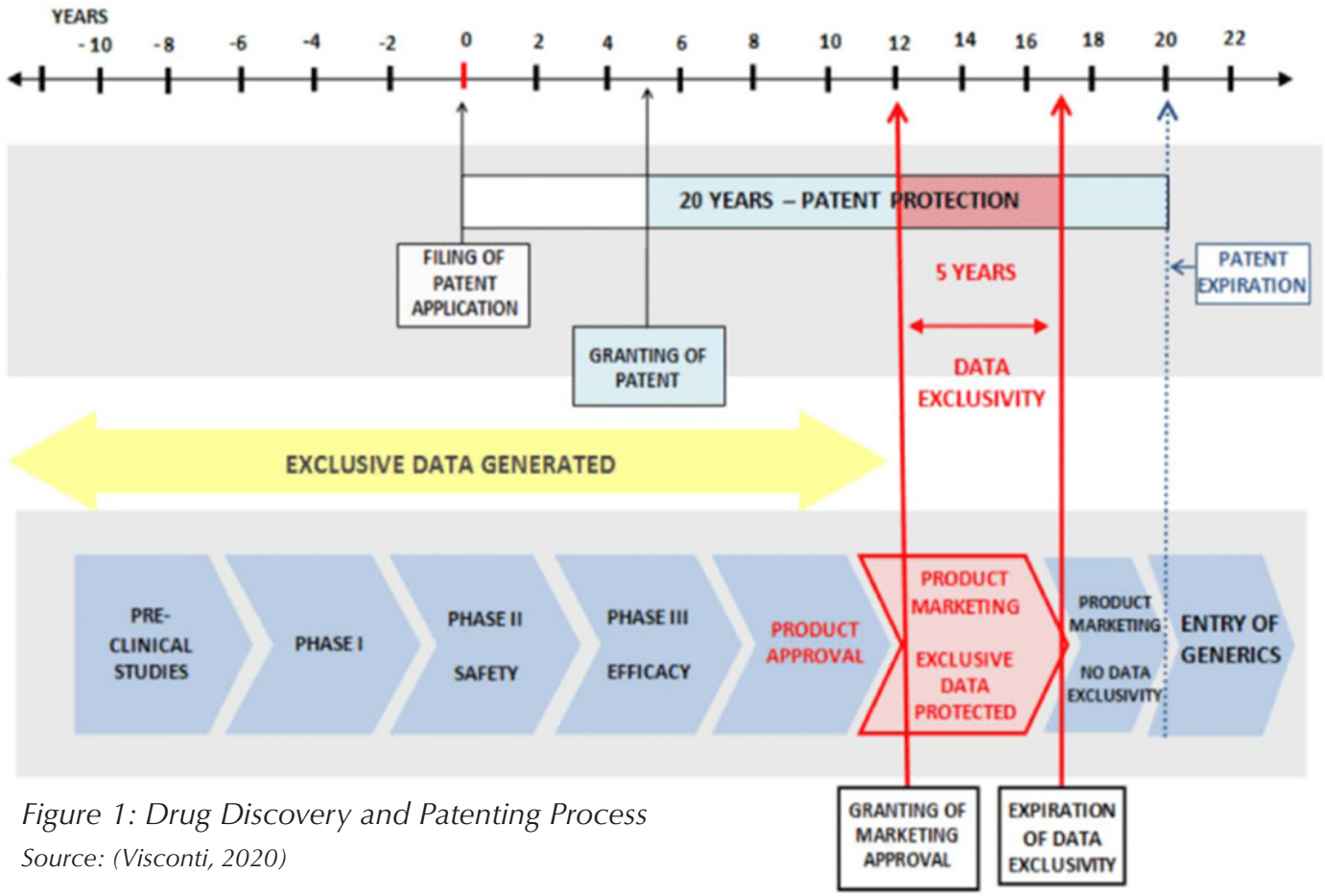


Figure 1: Drug Discovery and Patenting Process

Source: (Visconti, 2020)

3.1 Understanding Patent Filing and Extension

The legal process by which pharmaceutical companies seek to acquire exclusive rights to their new drugs, preventing others from producing, selling, or using the same drug without permission, is known as the drug patent filing process (TRIPS Agreement, Article 28).

- Discovering and developing a brand-new drug or compound is the first step in the process. To prove the drug's safety and potential efficacy, extensive laboratory research, testing, and preclinical studies are conducted (Mohs and Greig 2017).
- A patent application is drafted and filed after identifying a promising drug candidate. The chemical compound, makeup, manufacturing process and intended usage are all disclosed in the application, which must be precise, thorough and in line with the applicable national or international IP laws where the product will be marketed.
- After applying, the patent office thoroughly examines it to determine its innovativeness, non-obviousness, and utility. To determine whether the claimed invention for the drug is novel and innovative, patent examiners look at prior art (previous publications and patents)(Gurgula 2020).
- Once granted, a drug patent grants exclusivity for a predetermined time, typically 20 years from the filing date.
- It ought to be noted that the pharmaceutical company is also granted an exclusive right to the data collected. Data Exclusivity, in simple terms, protects the clinical trial data submitted by the pharmaceutical company during the drug approval process, including preclinical studies and human clinical trials. Data exclusivity periods range from 5 to 10 years (Tenni et al. 2022). Data exclusivity is distinct from patent protection. Even if a drug's patent has expired, data exclusivity can prevent

competitors from using the originator's data to gain approval for generic or biosimilar versions.
- Once the drug's patent and data exclusivity have expired, other pharmaceutical firms can manufacture and market generic versions and enter the market as competitors at a more affordable price.

3.2 Patented Drugs versus Unpatented Profits

Genuinely coming up with novel inventions, in this instance, for lifesaving medications, can be a complicated and time-consuming process. The process, from molecular discovery to clinical trials and patent filing, does not always guarantee success or product approval, which means investments that can span across decades. On the other hand, one way of shortening the process is through ***"incremental innovation,"*** where existing ideas, products, or concepts are slightly modified to create something that may appear new but lacks significant originality.

This type of innovation typically builds upon pre-existing ideas instead of starting from scratch. While this practice has been shared across other societal spheres, as a result of this citing the *Apple iPhone* is an excellent example of how evergreening and incremental innovation are used to sustain a successful product on the market over an extended period ("Incremental Innovation in iPhone" 2021), such method where minor changes to existing medications are made can undoubtedly lead to a public health crisis.

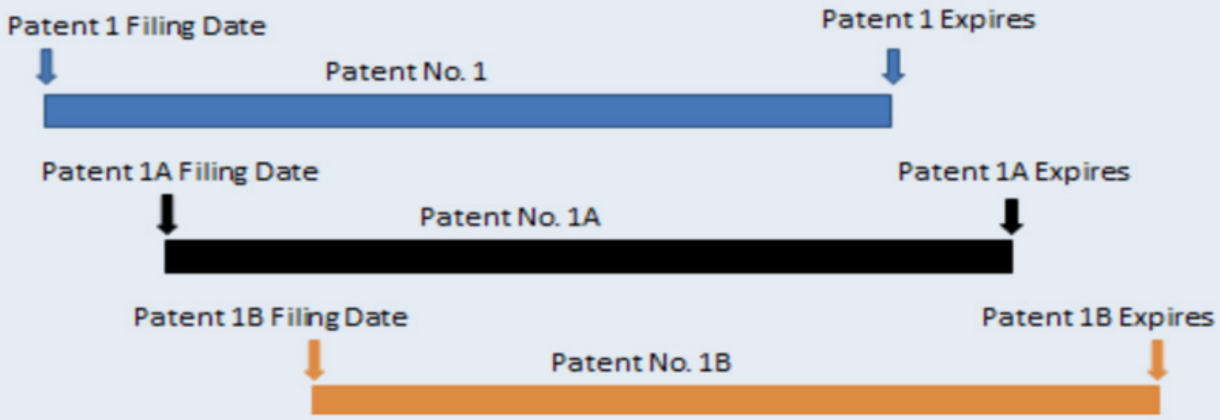


Figure 2: Patent Extension (Evergreening)

Source: (Intellectual Property Watch 2016)

While evergreening was strategically used to maintain a legal market monopoly where only one entity has near-full control over the supply of products in the global market, they have often been criticized for contributing to inequalities in accessing affordable medications (Quigley 2017). Such has been apparent among vulnerable populations in LMICs who can still not access lifesaving medicines due to the exorbitant prices at which the companies sell their products.

3.2.1 Evergreening or Life-Cycle Management

To qualify for patent protection, the TRIPS of the WTO requires an invention to be novel, non-obvious and valuable in the sense of being capable of industrial application (Correa 2020) (Art 27). In 2015, the United Nations Development Programme released the "Guidelines for Pharmaceutical Patent Examination: Examining Pharmaceutical

Patents with a Public Health Perspective" (UN Guidelines). These guidelines analyze 12 distinct types of secondary pharmaceutical patent claims from a public health standpoint. The categories include:

- Markush claims, selection patents, polymorphs, enantiomers, salts, ethers, esters, compositions, doses, combinations, prodrugs, metabolites, and new medical uses. ("Guidelines for the Examination of Patent Applications Relating to Pharmaceuticals | United Nations Development Programme" n.d.)

According to the WHO Commission on Intellectual Property, Innovation, and Public Health, the term "evergreening" was defined as "a term popularly used to describe patenting strategies when, in the absence of any apparent additional therapeutic benefits, patent holders use various strategies to extend the length of their exclusivity beyond the 20-year patent term".(Commission on Intellectual Property Rights 2006, 131)

There is disagreement about what would be considered a novel innovation, even if it is a minor variation to the original patent. According to the chair of the board of the Novartis Institute for Tropical Diseases in Singapore, Paul Herrling, "Anything you do to a molecule, as small as it could be, if it results in a clear medical advantage for patients, then it should be protected." (Collier 2013, 385)

The evergreening of pharmaceutical patents poses significant consequences for the availability of vital medications, particularly in developing nations, as it hinders or prolongs the Introduction of generic alternatives once the original drug patent has expired. Generic drugs are considerably more affordable than their patented counterparts because generic manufacturers are not required to invest in R&D costs. This situation creates challenges in accessing essential medicines, particularly in regions with limited resources (Abbas 2019, 53).

3.2.2 Life-Cycle Management

Life Cycle Management is a strategic approach adopted by pharmaceutical companies to maximize the value and potential of a drug throughout its entire life cycle, from the early stages of development to its eventual market maturity and beyond. This process involves a series of carefully planned actions and strategies to extend the drug's life and maintain its relevance in the market. The patent extension would fall into this strategy and could have multiple evergreening strategies connected to one drug. The table below summarizes extension tactics as documented across various literature:

Table 1: Extension Strategies

Strategy	Details	Example
Reformulation (Gilead, 2015)	One typical approach to evergreening is to make minor changes to the current drug and then apply for a new patent for the reformulated version of the drug. This may entail switching the dosage form—from a tablet to a liquid, or the delivery method—from immediate to extended-release.	Tenofovir Disoproxil Fumarate (TDF) was initially created as a tablet formulation and was frequently used in a variety of combination ARV therapies. When the TDF patent was about to expire, Gilead Sciences reformulated TDF into a new dosage form (fixed-dose combination tablet with other ARVs) and obtained. They obtained for the reformulated

Strategy	Details	Example
		product. As a result, they could extend their drug monopoly and keep their market exclusivity.
Combination Drugs (Gilead, 2015)	This approach entails the combination of two or more existing medications into a single product. Although these combinations may offer minimal therapeutic benefits, they can still provide grounds for new patent protection.	**Emtricitabine and tenofovir disoproxil fumarate (FTC/TDF)** were commonly used ARVs for treating HIV. Before their patents were set to expire, Gilead Sciences combined both medications into a single fixed-dose combination tablet and secured a new patent for the resulting medicines.
Paediatric Exclusivity (Clinic Info HIV, 2023) (Larru et al., 2014)	To gain additional patent protection, some pharmaceutical companies have been repurposing adult medication for paediatric studies on the drug	As its original patent was approaching expiration, the pharmaceutical company behind the Adult ARV drug **efavirenz** conducted clinical trials to demonstrate its efficacy for treating HIV in paediatric patients.
New chemical Formulae (Salts) (Goizman et al., 2016)	Pharmaceutical companies can seek new patents for different salt or stereoisomer forms of an existing medication.	Before **darunavir's** initial patent was about to expire, Janssen created a new salt form of the medication and obtained a new patent for the new modified version of the drug.

3.3 Case Study of Secondary Patenting: The actual cost of bedaquiline

In 2012, bedaquiline (BDQ) became the first new treatment from a novel class to be approved for tuberculosis in nearly five decades and became the first new tuberculosis (TB) drug from a new drug class to receive approval by the US Food and Drug Administration (FDA) in 40 years (McKenna, Frick, and Low 2018). The originator pharmaceutical company, Janssen, is owned by Johnson & Johnson (J&J). Since then, uptake of this critical drug has far exceeded expectations in high-burden TB countries, but its exorbitant price has marred its access and availability.

Burgeoning evidence showed that BDQ was likely cost-effective and cost-saving compared with the current MDR-TB standard of care. A UK study entitled Drug Regimens for the Treatment of Multidrug-Resistant Tuberculosis in the UK concluded that cost savings over one year could be realized from hospitalization length reductions, which offset the bedaquiline drug costs. The cost-benefit conclusions were held after several sensitivity analyses, thus validating assumptions and suggesting that the results would have been even if the actual price of bedaquiline in the UK were higher than in the US (Wolfson et al. 2015). The growing body of evidence contributed to updated guidelines by the World Health

Organization (WHO) in August 2018. These were designated bedaquiline as a core component of treatment regimens for rifampicin-resistant and multidrug-resistant TB (RR-/MDR-TB). ("Rapid Communication: Key Changes to the Treatment of Drug-Resistant Tuberculosis" n.d.). As a result, even broader access to BDQ is now needed to treat people with drug-resistant TB (DR-TB). Among barriers to bedaquiline entry, affordability is a significant concern, as the global donation program set up by the drug's sponsor, Janssen, a subsidiary of Johnson & Johnson, ends in March 2019.

The evolution of the price of bedaquiline has been an exciting journey. Janssen initially established a tiered pricing structure for BDQ. The price for a six-month BDQ course differed for low-, middle-, and high-income countries (US$900, $3,000, and $30,000, respectively, depending on whether the country was classified as LMIC or HIC). As the demand for BDQ increased, the price became a serious concern. Extensive literature proved that bedaquiline-based treatment regimens reduced mortality. A 2018 retrospective cohort analysis of routinely reported data in the context of high HIV and extensively drug-resistant tuberculosis prevalence showed that bedaquiline-based treatment regimens were associated with a significant reduction in mortality in patients with drug-resistant tuberculosis compared with the standard regimen (Yates 2018).

After numerous intensive negotiations with the company, an announcement was made that the price of BDQ was significantly reduced from USD$750 USD to USD$ 400 USD for a 6-month treatment course on July 23, 2018, at the 2018 Union on Lung Conference. This meant that BDQ could be procured for $USD400 for a 6-month treatment course for all TB programs procuring from the Stop TB Partnership's Global Drug Facility (GDF).

Bedaquiline, the cornerstone of most all-oral drug-resistant TB programs, was also a public good. The pharmaceutical company Janssen benefited from substantial public investments in BDQ. These publicly funded studies were necessary to inform the appropriate clinical use of BDQ, and some were even required to fulfil Janssen's regulatory requirements (McKenna, Frick, and Low 2018).

Figure 3: Bedaquiline

Jurisdiction	Product Name(s)	Disease Area(s)	Patent Description	Patent Status	Patent Application Number	Expected Expiry Date
Kenya	Bedaquiline 100 mg In EML	Tuberculosis (TB)	Bedaquiline compounds	Granted	AP2005003210	18/07/2023
			Bedaquiline to treat MDR TB and/or combinations with other antimycobacterial agents	Granted	AP2006003828	24/05/2025
			Bedaquiline to treat latent TB	Granted	AP2007004054	08/12/2025
			Bedaquiline fumarate salt and solid compositions	Granted	AP2009004870	03/12/2027

Source: MedsPal

Figure 4: Direct Public Funding of Clinical Trials

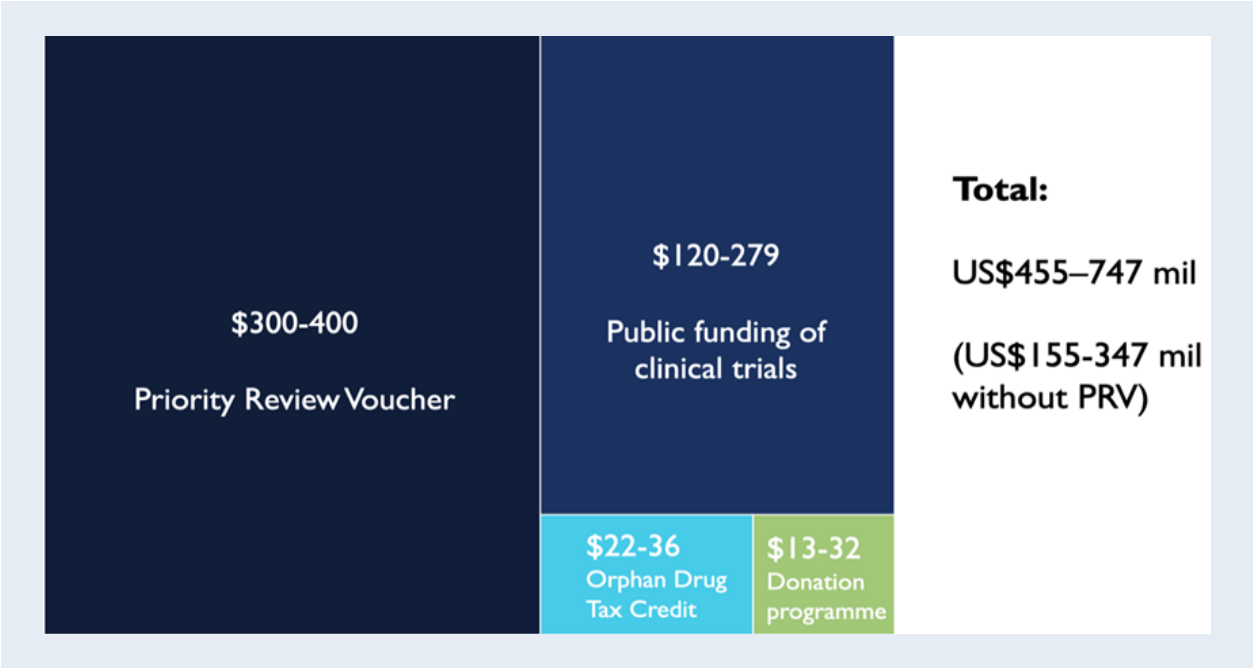
Trial phase	Short title	Sponsor(s)	Dates	Trial cost (2018 US$ million)**
1	ACTG 5267	NIAID	2009-10	0.4
1	TMC207-CL002	TB Alliance	2010-10	4.9*
1	TMC207 +/- Rifabutin/Rifampin	NIAID	2011-12	4.9*
1	TASK-002	IMPAACT, NIAID, NICHD, NIMH	2016-17	0.2
1/2	IMPAACT 1108	NIAID	2017-22	1.0
2	TMC207-CL001	TB Alliance	2010-10	16.5*
2	NC-001	TB Alliance	2010-11	16.5*
2	NC-003	TB Alliance	2012-13	16.5*
2	NC-005	TB Alliance	2014-18	16.5*
2	ACTG 5343	NIAID	2016-20	2.2
2	Janssen C211	Janssen, Unitaid	2016-25	1.5
2	IMPAACT P1108	NIAID, NICHD	2017-22	1.0
2	SimpliciTB (B-Pa-M-Z) NC-008	TB Alliance	2018-22	21.6*
2/3	NEXT	UCT, UoL, WSU, UoS, UCTLI	2015-19	3.8
2/3	TB-PRACTECAL	MSF, TB Alliance, DNDi, others	2017-21	8.0
2/3	TRUNCATE-TB	UCL, NUHS, SCRI	2018-22	7.4
3	NiX-TB	TB Alliance	2015-21	26.6*
3	STREAM Stage 2	The Union, UK MRC	2016-21	40.0
3	endTB interventional	MSF, PIH, others	2016-21	19.9
3	ZeNix (B-Pa-L) NC-007	TB Alliance	2017-22	26.6*
3	endTB-Q	MSF, PIH, others	2019-22	13.1
4	endTB observational	MSF, PIH, others	2016-20	31.0

*Costs not provided by sponsor, estimated using trial cost averages reported in Sertkaya et al. 2016.
**Costs shown here do not include adjustments for lower LMIC trial costs, or 'bedaquiline-attributable' portion of trial costs (see later).

Source: (Gotham et al. 2020)

Other public funding for the research and development of BDQ can be seen in Figure 4 below.

Figure 5: Monetary Contributions to The Clinical Development of Bedaquiline (US$ Millions)



3.3.1 Activism to Decrease the Price of Bedaquiline: A Global Public Good, "a dollar a day"

Since 2019, Médecins Sans Frontières (MSF) launched a global campaign calling on pharmaceutical corporation Johnson & Johnson (J&J) to lower the price of its anti-tuberculosis medicine BDQ to no more than US$1 per day for people everywhere who need it, to allow scale-up of drug-resistant tuberculosis (DR-TB) treatment and reduce deaths ("Johnson & Johnson Must Halve Price of Lifesaving TB Drug Bedaquiline | MSF" n.d.). This worldwide advocacy campaign was joined by organizations worldwide, including in Kenya. At the same time, a peer-reviewed modelling analysis by the Treatment Action Group (TAG) found that public investment in the development of BDQ was up to five times that of Johnson and Johnson (Gotham et al. 2020). It found that total public investments amounted to USD$ 455-747 million, while Johnson & Johnson's investments were USD$90-240 million (if capitalized and risk-adjusted, USD $647-1,201 million and USD$292-772 million, respectively). The total public investments thus exceeded the companies by a factor of 1.6-5.1 (Gotham et al. 2020). The public pressure and campaigns led to a reduction in the price of BDQ, from USD$400 to $340, for a six-month treatment, in low- and middle-income countries to scale up its use during the COVID-19 pandemic to 139 eligible countries, including Kenya, through the United Nations-hosted Stop TB Partnership's Global Drug Facility ("StopTB Partnership's Global Drug Facility (STBP/GDF) FAQs on Bedaquiline Price Reduction and Free Goods" 2020).

3.3.2 Evergreening Leading to Increased Prices

Along the same line, the patent on the tuberculosis drug bedaquiline expired on July 18, 2023. J&J started applying for extended patents to stretch its exclusive right to sell the drug. The company planned to enforce its secondary patent on a slightly altered drug version in more than 30 lower and middle-income countries, including South Africa, Kenya, Pakistan, and Indonesia. While governments, including Kenya, had approved the secondary patent - on July 13, 2023, J&J has granted Stop TB Partnership's GDF licenses that enable the GDF to tender, procure, and supply generic versions of SIRTURO® (Bedaquiline) for the majority of LMICs, including countries where the patents remain in effect. This license covers countries procuring TB drugs from the GDF, such as Kenya, that can do so at a lower price. However, the Indian patent office has rejected an application by the pharmaceutical company to extend the patent beyond July 2023, effectively ending its eight-year monopoly on tuberculosis drugs (Thiagarajan 2023). In a letter to J&J during its annual shareholder's meeting on April 26, 2023, MSF issued a statement demanding that the company publicly commit now to not enforce its secondary patents on TB drug bedaquiline in all countries with a high burden of TB - into which Kenya falls and to allow generic manufacturers to supply more affordable, quality-assured generic versions. "While J&J's patent on the base compound of Bedaquiline expires in 2023 in most countries, it has resorted to 'patent evergreening' by filing additional patents to extend its monopoly on the drug until 2027 in many high-TB-burden countries (MSF 2023).

3.3.3 Open letter requesting immediate action to ensure universal, equitable and sustainable access to Bedaquiline

On the 22nd of September 2023, an open letter addressed to Mr. Joaquin Duato, the Chief Executive Officer of Johnson & Johnson (J&J), was sent by the Unitaid. The context of the letter revolved around the accessibility and affordability of the bedaquiline. The letter emphasizes the importance of equitable access to the life-saving medicines, for individuals in low- and middle-income countries (LMICs) where TB is a significant health concern. While there has been a recent price reduction of bedaquiline through the STOP TB partnership/Global Drug Facility (GDF) tender, concerns over the enforcement of the secondary patents remains as such practice would hinder generic manufacturer competition and limit

access to the drug. The letter calls on Johnson & Johnson to take immediate action to expand equitable access to the drug by removing secondary patents or providing comprehensive licenses to generic manufacturers.

3.3.4 Equitable access to Bedaquiline

The 29th of September 2023 marks a historic day in the fight against TB when Johnson & Johnson made a significant announcement regarding SIRTURO® (bedaquiline), and its patents in low- and middle-income. As such, the pharmaceutical company confirmed that it will not enforce its patents for bedaquiline in 134 low- and middle-income countries. This decision means that generic manufacturers can now produce and sell high-quality generic versions of the drug without concerns about patent enforcement. The move comes after several advocacy groups called on the pharma giant to increase access to the drug. In a company press release made on the same day, the company emphasized that the generic versions must meet quality standards, be medically acceptable, and be used exclusively in the designated countries to benefit from this non-enforcement. The figure below is a list of sub-saharan African country where J&J will enforce the secondary parents on Bedaquiline:

(Reference: https://news. bloomberglaw.com/ip-law/j-j-wont-enforce-tuberculosis-drug-patents-in-134-countries)

SUB-SAHARAN AFRICA

[48]

Angola	Ethiopia	Niger
Benin	Gabon	Nigeria
Botswana	Gambia, The	Rwanda
Burkina Faso	Ghana	São Tomé and Principe
Burundi	Guinea	Senegal
Cabo Verde	Guinea-Bissau	Seychelles
Cameroon	Kenya	Sierra Leone
Central African Republic	Lesotho	Somalia

SUB-SAHARAN AFRICA

[48]

Angola	Ethiopia	Niger
Benin	Gabon	Nigeria
Botswana	Gambia, The	Rwanda
Burkina Faso	Ghana	São Tomé and Principe
Burundi	Guinea	Senegal
Cabo Verde	Guinea-Bissau	Seychelles
Cameroon	Kenya	Sierra Leone
Central African Republic	Lesotho	Somalia

3.4 Implications of evergreening on access to affordable HIV treatment

Despite the numerous breakthroughs in medical science and various legal frameworks, access to medicines/treatment as part of a right to health remains elusive, costing many lives. Even if the provisions of IPRs, such as patents, are viewed as a tool intended for public benefits, strict protection and evergreening have been documented to impede access to lifesaving medications. Additionally, recent research even correlates a low level of R&D towards diseases affecting LMICs and IP profit-oriented systems. This double-edged sword limits the ability of governments to import those expensive medications and restricts the creation of other similar medicines at affordable prices (Budiman 2021).

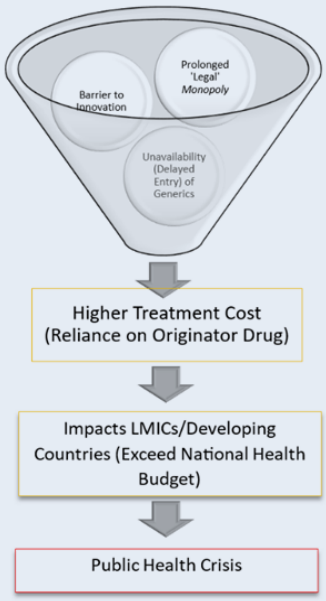


Figure 6: Cost of Evergreening

The figure above seeks to explain that evergreening effectively extends the monopoly held by the patent holder and keeps generic manufacturers from entering the market. Because of this, the cost of HIV treatment may continue to be high and unaffordable for many patients and healthcare systems. The delayed entry of generics has been viewed as a barrier to innovation. Such a system can only impact LMICs and developing countries as the cost of the originator drugs may exceed the national health budget, leading to a public health crisis (Collins et al., 2023).

3.5 The Situation in Africa (ARIPO & The Harare Protocol)

Access to essential medicines in Africa has long been severely hampered by IP laws, particularly those about pharmaceutical patents. As discussed above, patents can significantly raise the price of medications, making them unaffordable for many African populations. Additionally, IP laws also influence how technology is transferred to Africa. Developed countries and pharmaceutical companies frequently implement strict intellectual property protection to prevent their technology from being transferred to less developed countries. Africa's potential for growth and development is constrained because of this barrier to accessing and developing essential technologies (Inventa 2022).

To facilitate cooperation in IP matters among its member states in Africa, the African Regional Intellectual Property Organization (ARIPO), a regional intergovernmental organization, was established by the Lusaka Agreement in 1976. It can hear patent applications in its member states parties to the Harare (patents) protocol (1984). This critical agreement lays out the legal foundation for creating and operating ARIPO. It is the foundation for member states to harmonize their IP policies and laws to establish a more consistent and dependable IP system. By encouraging the effective use and protection of IPRs, the organization aims to promote innovation and economic growth while encouraging regional collaboration in tackling IP challenges collectively.

3.5.1 Latest Developments in Patents

ARIPO has made notable progress in promoting an efficient regional patent system. The opening in November 2017 of the ARIPO Regional Patent Examination Training Centre is one of those significant developments, aiming at unifying the patent examination system through training and capacity building for patent examiners from member states. The launch of the online ARIPO Regional IP Database (RIPD) in recent years has allowed for easy access to patent information. This digital platform enables stakeholders to search and retrieve patent data from multiple member states, promoting transparency and simplifying patent-related research.

3.5.2 Access to Essential Medications

Accessing essential and affordable medications in Africa, where many nations experience healthcare difficulties and a high burden of diseases, has been of crucial concern for ARIPO and, thus, aimed at striking a balance between IP rights and public health interests. As such, ARIPO has promoted access to medicines by addressing patent-related issues by signing a Memorandum of Understanding with the World Intellectual Property Organization (WIPO) in 2018, aiming to enhance IP services, facilitate technology transfer, and promote innovation within the region.

3.6 Background of IPR Evolution in the Republic of Kenya

Before independence in 1963, IP protection in Kenya was governed by British colonial laws and international agreements, including the Berne Convention for the Protection of Literary and Artistic Works and the Paris Convention for the Protection of Industrial Property. Following its independence, Kenya enacted the Industrial Property Act, which comprehensively addressed the country's protection of industrial property rights (Oladunni Amos et al., 2022). However, medication access remained one of the primary unaddressed issues in the 1989 Industry Property Act.

Over time, Kenya has made several amendments and revisions to its IP laws to address emerging challenges and align with international best practices. These changes aim to balance providing adequate protection to IP rights holders and promoting sufficient access to medicines. One example includes the review of the Industrial Property Act in 2001, which incorporates the majority of recognized TRIPs-compatible access to medicines safeguards (Baldeh et al. 2023). The new Act also establishes the Kenya Industrial Property Institute (KIPI) - a government parastatal under the Ministry of Industrialization, Trade and Enterprise Development. The primary function of the organization includes:

- Handling the patent application process, granting inventors exclusive rights to their inventions for a specified period, typically 20 years.
- To raise awareness of intellectual property rights and their importance to people, companies, and the country's economy, the institute also offers training courses to increase stakeholders' understanding of intellectual property.
- KIPI plays a role in shaping the IP policy framework in Kenya, contributing to developing and improving IP-related laws and regulations.
- While KIPI's primary function is the registration of IP rights, it may also assist in matters related to the enforcement of these rights, ensuring that IP owners' interests are protected (under the Kenya Industrial Property Tribunal).

3.6.1 Kenya's Essential Medicines List (EML)

The EML is a list of medicines that are the most effective and safe for addressing the priority health needs of the country's population. The first Kenyan NEML was established in 1981 and has been updated by the Ministry of Health five times. The current EML is from 2019; before, this one was in 2016. Kenya has made significant efforts to improve access to HIV treatment and care, and including ARVs in the EML plays a vital role in achieving this goal. The procurement of medicines in Kenya is the responsibility of the Kenya Medical Supplies Agency (KEMSA). However, budget limitations have led to the non-purchase of numerous medicines on the National Essential Medicines List (NEML). In 2010, KEMSA procured only 34% of the medicines listed on the NEML (Baldeh et al., 2023, 2).

The government of Kenya, with support from international organizations and donors, has implemented various programs and initiatives to address HIV/AIDS. This includes providing free or subsidized antiretroviral therapy (ART) to eligible individuals living with HIV. The expansion of HIV

testing, prevention, and treatment services has been a priority in the country's public health agenda.

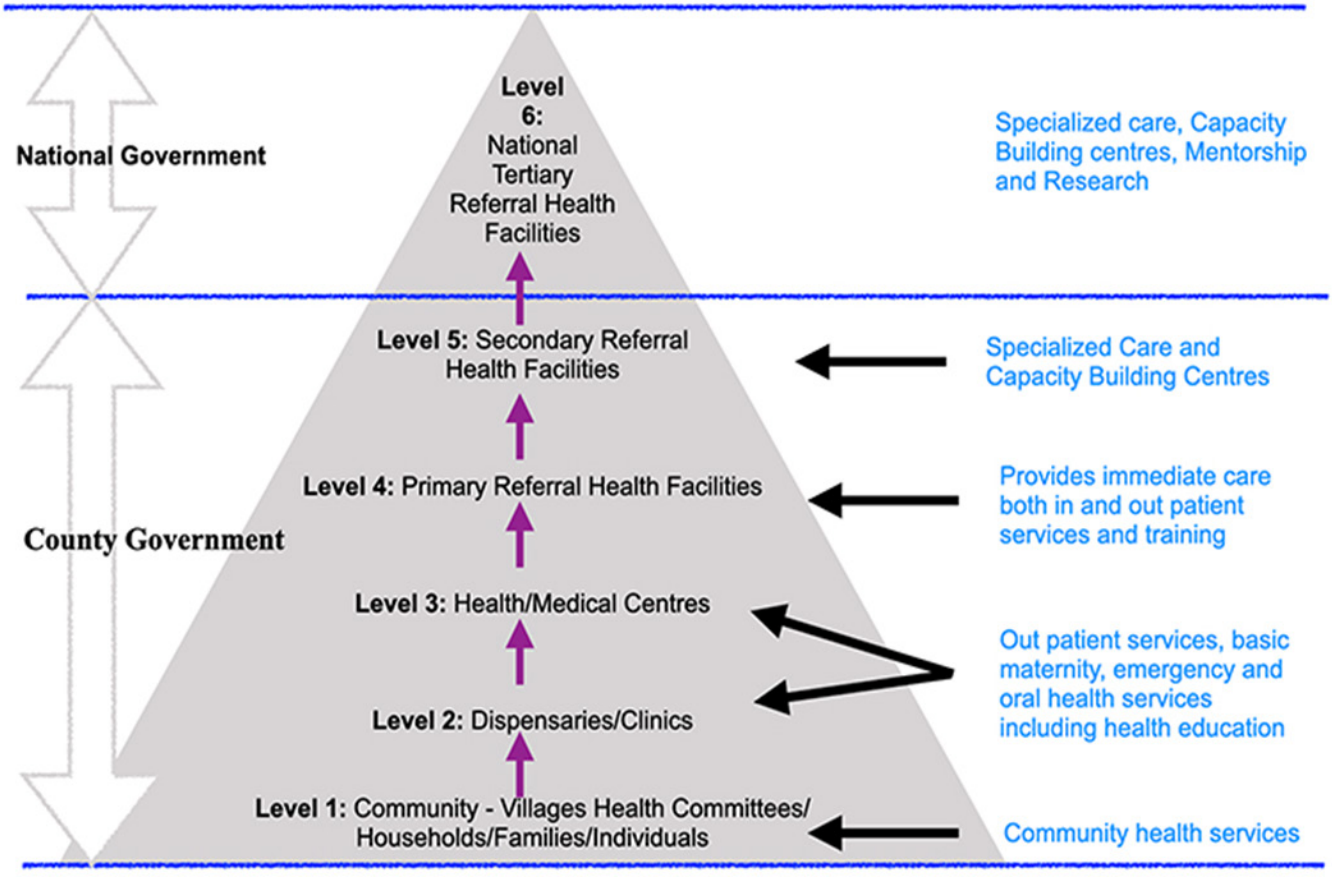
3.6.2 Access to medicines: Kenya's Healthcare systems and procurement Overview

Kenya's healthcare is anchored in its Constitution, in which health is considered a fundamental human right, and this is implemented through the rights-based approach of the right to health. ("Chapter Four - The Bill of Rights - Kenya Law Reform Commission (KLRC)" n.d.).
The government of Kenya operates through a devolved governance structure, assigned to 47 country governments, with the national government playing a coordinating and implementing role in the overall national health policy, regulatory, and technical support, as well as management of the various health institutions and related programmes (Onsomu et al. 2018). As a result, health services and access to essential pharmaceutical health commodities are managed interdependently at the county level alongside the national government.

As a result, various levels dictate how the health care system is designed. Level 6 is the national tertiary referral health facility at the government level. These specialize in care, capacity building and monitoring, and mentoring centres. Level 5 is the secondary referral health facility. They specialize in care and capacity building. Level 4 is the primary referral facility. These are in each of the 47 counties and provide immediate care with both in and outpatient services and training. Also, at the county level, there are three, two and one. Level 3 is health/ medical clinics. Level 2 are dispensaries and clinics providing primary outpatient care, essential maternity and emergency care services, and health education. Level one is the district or village-level health facilities for communities, households, families, and individuals. They provide community health services.

A summative overview of the levels of care in a schematic format is provided in Figure 6.

Figure 7: Kenya healthcare service delivery and patient referral levels



Source: Adapted from the Ministry of Health Kenya. Kenya primary health care strategy framework: 2019–2024 (Toroitich et al., 2022)

As shown in Table 2, access to diagnostic tools and medicines in Kenya consists of many variables. These are segmented into the public health sector, private (not-for-profit), and personal (for-profit) sectors. Common amongst most countries, these sectors are driven by diverse facility types and adhere to different regulatory body standards. Numerous supply entities dictate the supply and procurement of pharmaceutical commodities. For HIV, the public procurement agency is the Kenya Medical Supplies Authority (KEMSA), as shown in the table below.

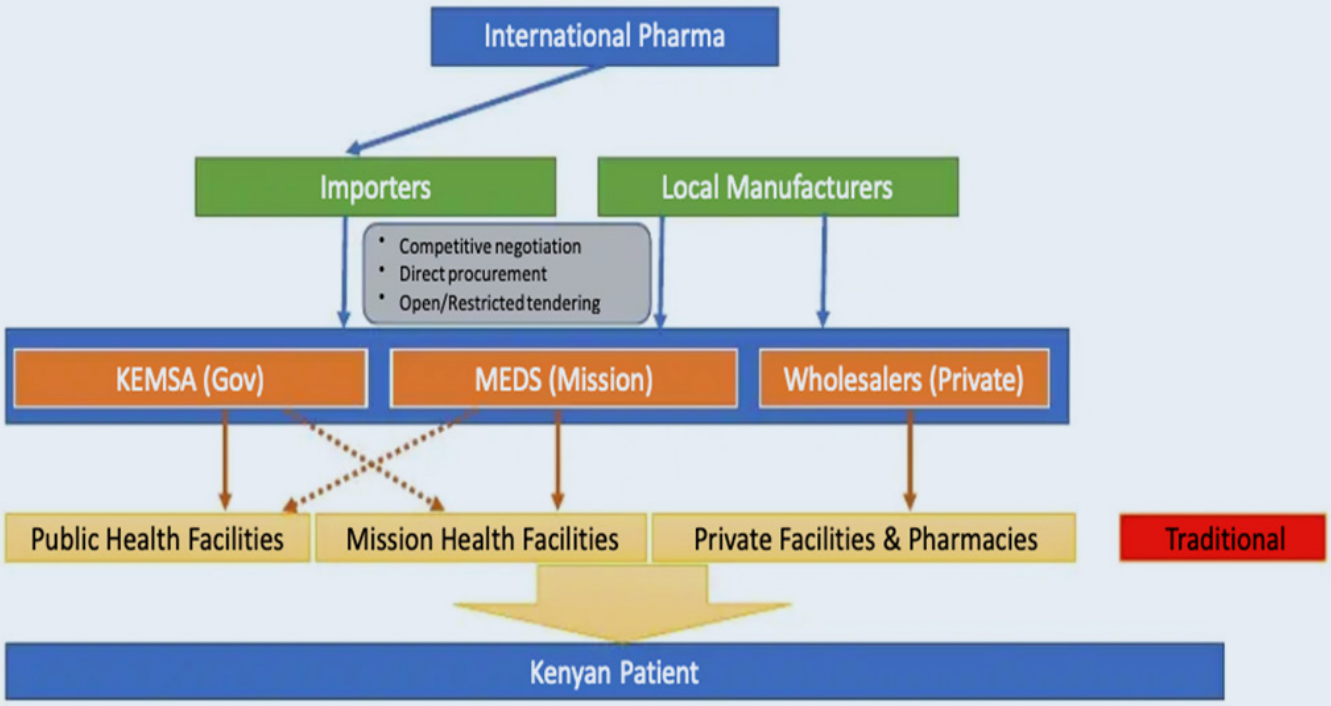
Health Sector	Health Facility Type	Regulatory Body	Main Professional Category in the Facility	Supply Entity Facilitating Medicine Access to Patients
Public health sector	Hospitals, Health Centers and Dispensaries	All regulatory authorities under MOH	All health professional category	Public procurement agency (Kenya Medical Supplies Authority [KEMSA])
Private not-for-profit health sector	Hospitals, Health Centers, Dispensaries, and Clinics	Kenya Medical Practitioners and Dentists Council	All health professional category	Private procurement agency (Mission for Essential Drugs and Supplies [MEDS]) and private pharmacies wholesalers, importers, distributors, or local manufacturers
Private for-profit health sector	Private Hospitals and Medical Centers	Kenya Medical Practitioners and Dentists Council	Medical Officers, Dentists and Pharmacists	Private pharmacies wholesalers, importers, distributors or local manufacturers, medicine pilferage from sources above
	Private Clinics	Kenya Medical Practitioners and Dentists Council	Medical Officers and Dentists	
		Clinical Officers Council	Clinical officers	
		Nursing Council of Kenya	Nurses	
	Wholesale Pharmacies	Pharmacy and Poisons Board	Pharmacists	
	Retail Pharmacies		Pharmacists and Pharmaceutical Technologists	
	Illegal health facilities including those in informal sector	All regulatory authorities	Quacks	Medicine pilferage from sources above, private pharmacies wholesalers, importers, distributors, or briefcase suppliers

Table 2: Ownership of Different Institutions within Health Sub-Sectors

Source: (Toroitich et al. 2022)

Public sector procurement of pharmaceutical products is governed by the Public Procurement and Disposal Act (2015) revised 2022, which is based on the principle of lowest bidding price and the Competition Act No. 12 (2010). According to a study from 2014, Kenya does not impose any tariffs (duty and VAT) on finished pharmaceutical products, whether locally manufactured or imported (Wamae et al., n.d.). In the fiscal year 2022/2023 budget, the Kenyan government declared that an array of medical devices and equipment would be free from Value Added Tax (VAT). This move aims to stimulate and promote further investment in Kenya's healthcare industry ("Kenya - Healthcare - Medical Devices," 2023). In the 2014 study, essential medicines were available only half the time in public healthcare facilities surveyed. The availability rate was slightly higher in hospitals, reaching up to 60%, but dropped to as low as 46% in dispensaries (Wamae et al., n.d.).

Figure 8: Pharmaceutical Landscape in Kenya



Source: : Esbon Gakuu, Kenya: Pharmaceutical Pricing Study; Policy Analysis and Recommendations

4.0 IP BARRIERS TO ACCESSING HIV TREATMENT IN KENYA: AN IMPACT ASSESSMENT

4.1 Patent Landscaping

This research has found that most patents are registered worldwide or region simultaneously, making it easier to verify whether a drug uses secondary patenting as part of its business strategy. The table below shows a list of ARV drugs found in the EML of Kenya. Some drugs are not listed in the MedsPal or the Regional ARIPO patent database. The flagged evergreening drugs are still listed since they are found in the EML or have relevance to the study. One such drug is Cobicistat. It is not on the EML list, but it is registered in Kenya and has been flagged as an evergreening practice, so we thought it pertinent to have it on the list. Tables 3 and 4 show evidence of multiple different evergreening practices.

Figure 9: Patent Descriptions, including Formulation on MedsPaL and ARIPO Database

Jurisdiction	Product Name(s)	Disease Area(s)	Patent Description	Patent Status	Patent Application Number	Expected Expiry Date	Last Updated Date
Kenya	Abacavir 20 mg/ml	HIV	Abacavir and similar compounds (Markush structure)	Expired	AP8900129	26/06/2009	08/09/2016
			Abacavir compound	Expired	AP9000234	21/12/2010	08/09/2016
			Abacavir hemisulfate salt	Expired	AP9901688	14/05/2018	19/11/2018
			Abacavir enzyme for intermediate process	Expired	AP9901721	20/08/2018	19/09/2019
			Abacavir manufacturing process	Expired	AP2000001790	14/10/2018	28/01/2019
			Abacavir oral solution	Expired	AP2000001878	04/02/2019	19/09/2019

Application Type	Aripo patent		
(10) Registration Number and Date	AP2109 2010.02.26	**Status**	Registered
(180) Expiration Date			
(20) Filing Number and Date	KE AP/P/2004/003551 2010.09.20	**(40) Publication Number and Date**	
(86) PCT Filing Number and Date		**(87) PCT Publication Number and Date**	
(85) National Entry Date			
(30) Priority Details			
(51) IPC Classes	A61K 31/52 (2006.01) A61P 31/5134 (2006.01) A61K 31/505 (2006.01)		
(71/73) Applicant	(EN) TIBOTEC PHARMACEUTICALS INC		
(72) Inventor	(EN) STOFFELS Paul		
(74) Representative Name	(EN) HONEY & BLANCKENBERG		
(54) Title	(EN) COMBINATIONS OF A PYRIMIDINE CONTAINING NNRTI WITH RT INHIBITORS.		
(57) Abstract	(EN) The present invention concerns combinations of a pyrimidine containing NNRTI named TMC278 with nucleoside reverse transcriptase inhibitors such as emtricitabine or abacavir and/or nucleotide reverse transcriptase inhibitors such as tenofovir useful for the treatment of HIV infected patients or for the prevention of HIV transmission or infection.		

Source: : MedsPal and ARIPO Regional IP Database

Table 3: Overview of Known Evergreening and Patent Status in Kenya

Drug	Patent Application Number	Patent Description	Invention Title	Patent Extension/Evergreening Explanation	Patent Status
Abacavir	AP9901688	Abacavir hemisulfate salt	Carbocyclic Nucleoside Hemisulfate And Its Use In Treating Viral Infections.	The patent safeguards the hemisulfate salt of abacavir, possessing therapeutic benefits like abacavir with improved optical purity. However, it lacks sufficient inventive advancement compared to prior patents involving abacavir compounds or abacavir salt applications like succinates	Expired 14/05/2018
Atazanavir (ATV)	Not filed	Atazanavir sulfate	HIV Protease Inhibitor Bisulfate	The invention pertains to atazanovir monosulfate and its pharmaceutical composition, with similar pharmacological properties as its free base. The atazanovir salt offers enhanced physical stability, increased water solubility compared to other salts, and improved oral bioavailability.	Expired 22/12/2018 (Ukraine)
Cobicistat	AP2010005429	Cobicistat tablets	The use of solid carrier particles to improve the processability of a pharmaceutical agent	The invention includes pharmaceutical compositions and methods of obtaining them, using cobicistat as the main compound. The innovation lies in a new pharmaceutical form of the composition based on cobicistat while retaining its original pharmaceutical properties.	Granted (National Patent Office) Not EML
Cobicistat	AP2011005857	EVG/COBI/TDF/FTC bilayer tablets	Tablets for combination therapy	The invention comprises pharmaceutical compositions in tablet form and a corresponding tablet manufacturing method. The novel aspect involves arranging the active pharmaceutical ingredients (APIs) in layers within the tablet. Notably, no synergistic effect has been observed in the pharmaceutical properties of these compositions compared to the individual administration of the same APIs.	Withdrawn
Darunavir	Not filed	Process for the preparation of (3r,3as,6ar)-hexahydrofuro [2,3-b] furan-3-yl (1s,2r)-3-[[(4-aminophenyl)		This process involves synthesizing darunavir ethanol, a known compound, and its intermediates to enhance yield, purity, simplicity, and cost efficiency. The method disclosed in US6248775B1, does not affect the pharmacological or biological activity of darunavir ethanol.	Commitment not to enforce patents on darunavir (DRV) in Sub-Saharan Africa and LDCs

Lopinavir + Ritonavir	Not file		Method for Treatment of HIV/AIDS by administration of solid pharmaceutical dosage formulation of HIV protease inhibitor in a fast state	Treating HIV/AIDS by administering a solid pharmaceutical dosage comprising lopinavir and ritonavir as a reliable solution is deemed obvious, as the specific parameters of the components and their benefits have not been proven. All features of the invention are apparent to those skilled in the art, and their selection is standard practice.	Commitment not to enforce LPV/r and Ritonavir patents
Raltegravir	Not filed	Raltegravir potassium salt		The pharmaceutical composition based on raltegravir's anhydrous crystalline potassium salt has the same pharmacological properties as the pharmaceutical composition based on raltegravir. Both compositions achieve the same technical result in terms of their pharmacological effects.	MPP licence on paediatric formulations of raltegravir (RAL)
Tenofovir/ Emtricitabine /Efavirenz	Not filed (EML in Medspal but not in EML 2019)	Single-dosage pharmaceutical form		A triple combined dosage form of known antiviral compounds (tenofovir, emtricitabine, and efavirenz) ensures their biocompatibility and product size. However, the invention does not enhance the pharmacological or biological activity of these known compounds, only improving the consumer quality of the product, which can be achieved through alternative methods.	Commitment not to enforce patents on emtricitabine (FTC), TDF/FTC and TDF/FTC/EFV

Source: : MedsPal and for patent extension/evergreening explanation ("Evergreening Patents in Ukraine" 2020)

4.2 Key Findings from the Summative Patent Landscaping

28 ARVs listed in the 29 Kenya EML 2019 were analysed to verify their current patent status. Of the 28, 10 have expired or been withdrawn, 11 have not been filed, and seven had no information registered on the MedsPaL database. The study also looked at seven previously flagged drugs as potentially evergreened in some of the literature reviewed. All of which had either expired, withdrawn, and/ or not filed at the ARIPO level or by KIPI. Cobicistat was the only instance of granting a secondary patent leading to extension. However, this drug is not currently in the Kenya 2019 EML. It was registered with WIPO in 2009, and the expected expiry date is 05/01/2029. The combination drug - Lopinavir + Ritonavir (Kaletra by Abbott) - was highlighted in the CSO proposal of 2019 to ARIPO but is not filed in Kenya ('Civil society proposals to address policy and legal incoherencies in the Harare Protocol that impact access to health technologies in ARIPO member states', 2019). Looking at the different EML drugs and the secondary patents in Table 3 above, there are multiple cases of evergreening. It is noteworthy that all these patents have either expired or withdrawn. Even with all the drugs in the EML being expired or withdrawn, there is ample evidence that ARIPO has historically approved patents that are not novel or have an inventive step. This was made possible through the granting of patents for variations of known incremental changes to the compounds. This includes their crystal forms, salts, formulations, compositions, and combinations.

Table 4: Evergreening of Expired ARV Drugs

Compound	Patent Holder	Patent Grant (Expiry Date)
Abacavir		
Abacavir compound	The Wellcome Foundation Limited	AP101A (2010/12/21)
Abacavir hemisulfate salt	Glaxo Group Limited	AP2009A (2018/05/14)
Lamivudine		
Lamivudine compound	Iaf Biochem International Inc Shire Canada Inc	AP182A (2011/05/02)
Lamivudine crystal forms	Glaxo Group Limited	AP300A (2012/06/02)
3TC+AZT tablets	Glaxo Group Limited	AP1067A (2017/10/29)
Zidovudine (AZT)		
Zidovudine compound	The Wellcome Foundation Limited	AP90A (15/09/2006)
ABC/3TC, ABC/FTC combinations with or without ZDV	The Wellcome Foundation Limited	AP652A (28/03/2016)
Tenofovir/Emtricitabine/Efavirenz		
Emtricitabine and lamivudine compounds	Iaf Biochem International, Inc	AP136A (2010/02/08)
TDF/FTC combinations	Gilead Sciences Inc	AP2089A (2024/01/13)

Source: : MedsPaL

4.3 Civil Society Organisations 2019 Recommendations to ARIPO

During the 16th Session of the Council of Ministers of ARIPO held on November 23, 2017, in Lilongwe, Malawi, it was directed that the Secretariat should investigate and create specific proposals to *address policy and legal inconsistencies affecting access to health technologies within ARIPO Member States*.

The Secretariat implemented these proposals and reported the outcomes to the Organization's member states. 90 CSO organizations from the ARIPO member countries submitted specific proposals to incorporate essential TRIPS flexibilities into the Harare Protocol and related Regulations. The objective of these proposals was to address significant gaps at the regional level concerning the implementation of TRIPS flexibilities.

In Table 5, we have looked at the proposals and compared them to the Harare Protocol on Patents and Industrial Designs of 2019 and 2023 and found no amendments following the proposals have been made. The only amendment worth noting is on grant opposition. New in the Harare Protocol 2023 *(Harare Protocol on Patents and Industrial Designs 2023 Edition 2023)* is the inclusion of observations by third parties, "any third party may, in accordance with the Implementing Regulations, present observations concerning the patentability of the invention to which the application or patent relates. That person shall not be a party to the proceedings" *(Harare Protocol on Patents and Industrial Designs 2023 Edition 2023, 11)*.

This falls short of the CSO proposal to extend from 6 to 12 months and to have administrative third-party Opposition Systems in place as well as pre-and post-grant opposition systems ("Civil Society Proposals to Address Policy and Legal Incoherencies in the Harare Protocol That Impact Access to Health Technologies in ARIPO Member States" 2019, 25).

Table 5: Recommendations from civil society organizations (CSO) in 2019 to ARIPO post-ARIPO Council Meeting in Lilongwe, Malawi 2017

CSO Proposal	2023 Harare Protocol	Amendment
To **adopt an "opt-in" approach**. This means that when the ARIPO Office notifies of its intent to grant a patent, a designated state has to make a written notification to the ARIPO Office confirming that the patent will have effect in its territory. Failure to communicate means that the patent is not applicable to the designated state. This approach is consistent with ARIPO members maintaining their own sovereignty with respect to granting of patents that are consistent with their national patent laws. It is also **proposed that the time-frame of 6 months be extended to 12 months**. To implement this proposal Section 3(6) and (7) of the Harare Protocol should be amended.	Section 3 (6) (a) If the Office decides to grant a patent, it shall notify the applicant and each designated State. The designated State shall have **6 months** within which to respond to the notification. Section 3(7) (7) After expiration of the said **6 months**, the Office shall grant the patent, whichshall have effect in those designated States which have not made the communication referred to in Sub-section (6). The Office shall publish the patent granted as provided for in the Regulations.	✕
To amend **Section 3(10)(h)** of the Protocol to **make explicit that secondary patents such as** new forms, new use, method of use, combinations etc. of known substances are not inventions andhence should not be patented. In addition, to **review & amend Section 3(10)(j)(iii)** of the Harare Protocol and Rule 7 and other Regulations/Administrative Instructions to the Harare Protocol to exclude patenting of new forms, new use, combination of known substances or any other secondary patent claims, consistent with the proposals made above.	3(10 H) The following in particular shall not be regarded as inventions within themeaning of paragraph 10(a): (i) discoveries, scientific theories and mathematical methods; (ii) aesthetic creations; (iii) schemes, rules and methods for performing mental acts, playing gamesor doing business, and programs for computers; (iv) presentations of information. 3(10)(j)(iii) methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body; this provision shall not apply to products, in particular substances or compositions,for use in any of these methods.	✕
To amend Section 2bis of the Harare Protocol to require disclosure (i) in a manner sufficiently clear and complete for it to be carried out by a person of ordinary skill in the art; (ii) to disclose the best mode known, at the date of the application or priority, for the execution of the invention and (iii) to provide a description sufficient to enable the reproduction of each embodiment of the invention for which protection is sought.	(b) Shall disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. (c) Disclosure of an invention as stipulated in Sub-section (1)(b) above shall be entirely effected by an enabling description as read in conjunction with accompanying drawings if any (2) The claims shall define the matter for which protection is sought. They shallbe clear and concise and shall be supported by the description.	✕
To add a **new section in the Harare Protocol requiring the applicant to disclose international non-proprietary names**, if available or within 30 days of the publication of INN. In addition, the proposal calls for **Rule 16 of the Regulations to be amended** so that it is mandatory for an applicant to promptly provide the ARIPO Office information about corresponding foreign patent applications filed and grants including the results of search and examination or any other information concerning prior art; any decision rejecting the foreign application; any decision refusing the grant of patent and any decision revoking the grant of patent.	(1) The applicant shall, at the request of the Office, and within the period specifiedin such request, furnish it with the date and number of any application for a patent orother title of protection filed by him with a national industrial property office or with aregional industrial property office ("foreign application") relating to the same or essentiallythe same invention as that claimed in the application being processed by theOffice.(2) (a) The applicant shall, at the request of the Office and within the period specifiedin such request, furnish it with the following documents relating to one of theforeign applications referred to in paragraph (1).	✕
It is recommended that the Harare Protocol **implements administrative third-party pre and post-grant opposition systems.** Such procedures should be simple, easy-to -use and inexpensive.Any person should have the right to file an opposition at any time and have the right to be heard shouldthe person wish to be heard. If a post grant opposition is successful, the patent should be revoked in all ARIPO members.	**Section 2quater Observations by Third Parties** In proceedings before the Office, following the publication of the ARIPO patent or utility model application, any third party may, in accordance with the Implementing Regulations, present observations concerning the patentability of the invention to which the application or patent relates. That person shall not be a party to the proceedings.	✕

4.4 Implications

Currently, it costs about Sh10,000-Sh20,000 a year to put one person living with HIV on first-line generic ARVs, according to the Kenyan Ministry of Health. About 85 per cent of that cost is through donor support, including the Global Fund to Fight AIDS, Tuberculosis (TB) and Malaria (GFATM) and the US President's Emergency Plan for Aids Relief (PEPFAR) ("Will Kenyans Afford the Once-a-Year-Year ARV?" n.d.). The accessibility, availability and affordability of HIV treatment remain critical factors that impact the physical, emotional, and mental well-being of people living with HIV in Kenya.

On the other hand, the pharmaceutical industry's evergreening practices have sparked debates about how they may affect people's ability to obtain and pay for lifesaving medications. As such, the following impacts may be experienced in Kenya:

i. Evergreening may occasionally prevent the development of innovative treatments.

If businesses concentrate on boosting the exclusivity of currently available drugs rather than making investments in R&D, innovations and advancements in HIV treatment may be stifled.

ii. The current patent system has led to little or no innovation in the research & development space. This means that scientific advancements for essential medicines or orphaned drugs have been slowed in favour of more cosmetic innovations such as bolding, weight-loss drugs and other non-essential lifestyle conditions.

iii. The absence of a variety of treatment options is regressive to the goals of eliminating HIV, Tuberculosis (TB) and Malaria. Instead, the world is seeing increasing cases of Advanced HIV Disease (AHD) and more children being born with HIV, particularly when patients experience adverse side effects or develop resistance to a particular medication. Achieving better health outcomes and managing HIV can be made more difficult by limited access to alternative medicines. Additionally, patients may receive medications with marginal improvements, raising concerns about the value and efficacy of treatment.

iv. The Introduction of generic versions of *'new technologies, HIV prevention drugs and ARVs'* into the Kenyan market may be delayed when pharmaceutical companies obtain new patents for minor alterations or combinations of already available HIV drugs. As a result, patients might not always have access to newer, more potent, and perhaps even lifesaving drugs. These essentially promote TRIPS-plus measures instead of leveraging the flexibilities provided by the TRIPS Agreement.

v. Evergreening also leads to an increased financial and socio-economic burden on the Kenyan government and out-of-pocket expenditure for clients accessing public health facilities (Siddalingaiah and Fugh-Berman 2022). What is even more problematic IP are the regulatory processes concerning procurement, which contributed to the recent ARV shortages in 2021 and 2022 through KEMSA. This was extensively documented in the media and through research reports—programmes funded by donors suffered because of the stand-off between KEMSA and USAID. In 2022, the stand-off between the United States agency (USAID) and the Kenyan government further worsened the situation because of concerns about mismanagement of funds by the Kenya Medical Supply Authority (KEMSA) and questionable tax policies. (Oladunni Amos et al. 2022).

vi. Given the shortages of accessible viral load tests and long-acting technologies, which can only be accessed through the private sector, people who would like to be placed on PrEP or long-acting injections have no hope. This has resulted in numerous human rights violations for people living with HIV who should have medications at no cost. This, in turn, can lead to treatment failure, forcing some to forego treatment or engage in cost-cutting measures that compromise treatment adherence.

vii. The government and healthcare providers may incur higher costs when acquiring patented new and emerging HIV drugs due to the limited availability of affordable generic alternatives. As a result of these rising costs, efforts to extend treatment coverage to a larger population may be hampered.

5.0 RECOMMENDATIONS AND CONCLUSION

5.1. Critical components of strengthening stakeholder engagement, coordination and collaboration

Given the above diversification of stakeholders and public health implementers, there is a need for a policy overhaul, alignment of state mechanisms, tripartite stakeholder engagement, and collaboration. To ensure a coherent and progressive trade policy, the country would benefit from revising its Patent/ Intellectual Property framework to align with its long-term industrialization and development agenda - Kenya Vision 2023 ("Kenya Vision 2030 | Kenya Vision 2030" n.d.). As a developing country, at a national level, Kenya - as a member state and signatory to the TRIPS negotiators needs to leverage the 'flexibilities' through revising and tailoring its national intellectual property regimes so that country to be TRIPS-compliant and to take advantage of the flexibilities inherent in the TRIPS Agreement. This will ensure coherence of the laws, policies, and regulations regarding competition, government procurement and medicines. Given that Kenya has not yet fully domesticated and utilized the TRIPS flexibilities nor fully taken advantage of the various instruments supporting access to affordable, productive and safe pharmaceutical commodities, there is a need to address these within a structured framework that includes stakeholder engagement as well as address some of the trade agreements, and inter- and intra-regional barriers, to which he country has acceded to; yet which continue to impede progressive and localized access to innovative medical technologies and therapeutics.

This approach includes engagement with various other stakeholders and organizations.

5.2 Government bodies and intra-relationships for the trade of goods and services

The TRIPS exists mainly centralized around the international trade of goods and services. This includes pharmaceutical products. Therefore, during trade negotiations, parameters agreed upon may often create barriers to the movement of pharmaceutical goods. Within the Intellectual Property Rights (IPRs) engagement paradigm, disharmonious engagements and collaboration at the policy level exists. This is mainly between the Ministry of Health, the Department of International Relations / Foreign Affairs, the National Treasure of Kenya, and the Ministry of Finance and Planning, the Government of Kenya. These core policy decision-making structures often dictate how and when commodities such as goods and services, including pharmaceuticals, are traded. In most cases, the State Department of Trade's negotiations do not provide preferential treatment in trading

pharmaceutical commodities, which is left to the Ministry of Health and Ministry of Finance and Planning.

Without proper coordination and collaboration of various structures at a policy and regulatory level, access to affordable pharmaceutical therapeutics will remain a 'siloed' agenda left as the mandate of the Ministry of Health and procurement bodies such as KEMSA. This requires serious consideration of better institutionalised oversight mechanisms. From a coordination standpoint, a recent Re***gional Dialogue on Utilizing Flexibilities in the TRIPS Agreement to Promote Access to Medicines*** (2021) with regulators and patent officials, such as the KIPI Nairobi, provided some salient points for consideration to promote coordination and tripartite collaboration between policymakers, civil society, and regulators to promote a progressive access agenda.

As with the findings of much of the literature reviewed, this dialogue concluded that stakeholder engagement and coordination required key components for Kenya. These included the following:

i. Fast-tracking the formation, registration, and operationalization of a stakeholders' coalition on intellectual property and access to medicines at the national level. An example of a Kenyan National Coalition on Intellectual Property and Access to Medicines was cited.
ii. The formation, registration, and operationalization of a stakeholders' Coalition on Intellectual Property and Access to Medicines at the Regional Level (e.g., EAC Regional Coalition on Intellectual Property and Access to Medicines).
iii. Addressing member states' problematic processes when engaging with ARIPO. This was poignant as ARIPO remains a weakness for its member states due to its laxity in overhauling its systems.
iv. ARIPO needs to urgently prioritize the revision of the Harare Protocol (beyond the minor amendments in the 2022 Harare Protocol on Patents and Trademarks) to incorporate the flexibility provided by the TRIPS Agreement. This includes granting pharmaceutical patents for its Least Developing Countries (LDCs) members to develop the most amicable solution to ensure that LDC member states develop and realize their national industrialization agendas to grow to a level where they can be TRIPS-compliant.
v. Further, as a regional body, ARIPO should invest in patent examiners, ensuring that member states have **more than six months** to review whether to approve a patent, including proper working professionals to access the patent innovativeness level.

5.3 Lessons from the other jurisdictions: India's Patent Law

Above all, Kenya needs to strengthen its own IP/Patent Framework in line with the country's industrial and growth aspirations. As per the recommendations from KIPI, the Introduction and formation of accountability mechanisms are vital in protecting Kenya against any future threats to access, co-create and develop its pharmaceutical industry, which could work with the East African Commission to economies of scale, market access, faster WHO PQ ensure innovative pharmaceutical therapeutics and advancing a regional local manufacturing agenda to realize Kenya's 2030 Vision of resilient industrialization agenda. Kenya's Industrial Property Act (2001, rev. 2016) remains another policy that requires improvement for innovation to thrive. With its 2016 amendment, the following was concluded:

i. The 2016 Act still lacks clarification on the definition of "invention" to avoid patents being granted for new formulations of well-known substances without any appreciable therapeutic advancement (evergreening). Even if the Act (Section 21e) mentions:

   "public health-related methods of use or uses of any molecule or other substance whatsoever used for the prevention or treatment of any disease which the

Minister responsible for matters relating to Health may designate as a serious health hazard or as a life-threatening disease."

Explicit mention of:

"mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance or the mere discovery of any new property or new use for a known substance or the mere use of a known process, machine or apparatus unless such known process results in a new product or employs at least one new reactant" as in **India patent laws** (section 3d) is missing.

ii. Article 22 of the Act defines patentable inventions as *"An invention is patentable if it is new, involves an inventive step and is industrially applicable"*. (Same standard as the TRIPS Agreement). Nevertheless, granting patents on new uses of medicines is highly undesirable and leads to evergreening practices which in turn delays the availability of generics, as seen above. Even if the EAC has directly encouraged its Partner States to exclude patents on *"new medical uses of known substances including microorganisms…."* existing regulations and KIPI Examination Guidelines still allow **new use** patents.

iii. Clear guidelines and tough standards on pre- and post-grant opposition procedures enabling interested parties to contest patents that they feel are unfairly granted or based on evergreening techniques are also missing in the Act. Such guidelines will halt unfair competition that leads to unwarranted monopolies, create a pathway for more accountability and create strong legal basis for opposition for the benefit of communities.

iv. Currently, Article 58(5) permits the limitation of the right under patents subject to compulsory licensing. Explicitly, Articles 72 – 78 legally documents the preconditions and terms that need to be satisfied before the IP tribunal for granting compulsory licenses. While these provisions can be seen as cumbersome, India has made provisions to use compulsory licensing *"if the use of the patented product is not satisfying public requirements, or the patented product is not accessible to the public at a reasonable price, or the patentee has not worked the patented product in India"* In other words, the Indian Patent Office will only impose compulsory licensing when an innovation which could be greatly beneficial to the public interest is not being used/provided – or at least not sufficiently/on reasonable terms and price – by the patent owner. Even if the Indian patent law requires that a number of criteria be respected when deciding whether a compulsory licence should be granted to a third party, the law and administrative system have until now been able to strike a balance that considers the public health interest.

5.4 Alignment in the procurement process in Kenya

On August 31, an article published in The Guardian (Ahmed 2023) and StopTB Partnership Website (Stop TB Partnership n.d.) announced a price reduction of up to 55% for Bedaquiline following an agreement with the Stop TB Partnership's Global Drug Facility (GDF), allowing the sale of generic versions of the drug for 44 LMICs. As such, J&J has agreed to drop the drug-resistant TB medication from $289 (£227) to $130 for a six-month course until December 2024. The Indian drug manufacturer Lupin has also agreed to reduce the cost of its TB treatments by a third to $194 for a six-month course, saving $8m, which should allow the purchase of 51,000 more Bedaquiline treatments. With this deal, the current cost of the

drug equates to less than a dollar a day. However, the issue remains that this deal is accessible only to countries procuring the TB drug through the GDF. Currently, the procurement system in Kenya is decentralized, with each procuring entity conducting procurement procedures separately, using standardized tender documentation. Thus, Kenya needs to improve its TB supply chain management. Improving the procurement process for medicines is a complex issue that involves multiple stakeholders, including the government, healthcare providers, pharmaceutical companies, and the general population. KEMSA has been battling with payment of orders, drug shortages, leakages in supply management and stock management issues. In 2018, the Global Fund audit was full of praise, but the 2022 audit reveals that KEMSA has become deficient ("Audit Report - Global Fund Grants in the Republic of Kenya," n.d.). An overhaul of KEMSA would ensure fewer chances of stockouts and general fund wastage. At present, transparency is not a primary tenet of Kenya's Public Procurement Law (PPL). The legislation restricts the disclosure of procurement details, citing confidentiality reasons; an amendment of the PPL would be beneficial.

5.5 Further Research (ARIPO Database Landscaping)

Ultimately, this research has shown that it has become essential to undertake property patent landscaping of ARIPO (African Regional Intellectual Property Organization) and the patents on their database. The benefits or objectives of undertaking such a study to advance this one further include:

- Understanding the existing intellectual property landscape within the ARIPO
- Obtain insights into the active patents within ARIPO member countries, including filing dates, expiration, extensions or evergreening.
- Analyzing patent trends to gain insights into market developments and emerging technologies.
- Engage in advocacy and policy change efforts through effective and evidence-based data.
- Development of IP risk-mitigation strategies on new and emerging technologies (The ring, CAB-LA, etc.).

5.6 Conclusion

Like most research on IP and evergreening, this also sheds light on one critical issue at the nexus of public health versus innovation. This report shows that evergreening practices affect affordable medicine access in real ways and may unintentionally stifle true pharmaceutical innovation.

It is necessary to approach this problem with consideration and balance, realizing the value of upholding public health interests and intellectual property protection. Kenya can promote a more equitable and sustainable healthcare system by implementing the suggested policy recommendations, ensuring that all citizens have access to essential medications without undermining the incentives for genuine innovation.

All parties involved must work together and implement these measures as the nation develops to build a more equitable and prosperous future for the health and well-being of the Kenyan people. These parties should include the government, the pharmaceutical industry, and civil society.

Additionally, the KIPI could learn from India's Patent Act, which allows for patent examination and pre- and post-examination of patent applications. In the 2023 case of the application for a secondary patent for drug-resistant tuberculosis (DR-TB) medicine bedaquiline (a fundamental medicine that has proven efficacious and safe in the treatment of drug-resistant TB) through the BPAL/M regimen, lessons can be learnt from the Indian patent office, which rejected the application as there was no 'inventive step' in the application by the company, Johnson and Johnson. (Thiagarajan 2023) While India has a stronghold against pharmaceutical companies who try to 'hoodwink' the country with such applications, Kenya, like other countries, approved the secondary patent. Above are examples of the secondary patents granted to pharmaceuticals due to incremental changes. This should not happen in a progressive region like the East African Community (EAC) or a strong country like the Republic of Kenya.

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