The Role of Intellectual Property Rights and Access to Medical Products in the WHO African Region: 25 Years After the Trips Agreement

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Abstract

Background

It is now 25 years since the adoption of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and the same concerns raised during its negotiations such as high prices of medical products, market exclusivity and delayed market entry for generics remain relevant as highlighted recently by Ebola and COVID-19 pandemics. The World Health Organization's mandate to work on the interface between intellectual property, innovation and access to medicine has been continually reinforced and extended to include providing support to countries on the implementation of TRIPS flexibilities in collaboration with stakeholders. This study analyses the role of intellectual property on innovation and access to medical products in the African Region.

Methods:

We analyze patent data from the African Regional Intellectual Property Organization (ARIPO) and Organisation Africaine de la Propriété Intellectuelle (OAPI) to show trends and to identify the main diseases covered and how they correspond with top causes of morbidity and mortality. We also review legislation to assess how TRIPS flexibilities are implemented in countries.

Results

Patenting was low for African countries. Only South Africa and Cameroon appeared in the list of top ten originator countries for ARIPO and OAPI respectively. Main diseases covered by African patents were HIV/AIDS, cardiovascular diseases, cancers and tumors. 39 countries have applied TRIPS flexibilities, with the most common being compulsory licensing and LDC transition provisions. A third of the compulsory licensing application were not executed following voluntary licensing agreements. No country had legislated on research and regulatory review exceptions and patent term extension.

Discussion

There's modest alignment between innovation and health challenges. Compulsory licensing applications may have served to encourage voluntary licensing arrangements. Countries have enacted laws that allow them to deploy TRIPS flexibilities for public health needs.

Conclusions

There's need to develop and strengthen health innovation systems in the region. Opportunities exist for WHO to work with ARIPO and OAPI to support countries in reviewing their legislation to be more responsive to public health needs.

Background

The adoption of the Agreement on Trade-Related Aspects of Intellectual Property (TRIPS Agreement) in 1994 by Member States of the World Trade Organization (WTO) was a watershed event, which gave rise to a new global intellectual property protection (IPP) regime with significant effects on access to medical products. Some of these effects include high prices of medicinal products, prevention of local manufacture of generic products through reverse engineering of patented products, importation of cheaper medicinal products from off-patent countries or under licensing agreements and delayed market entry for generic products.

The potential impact of the TRIPS Agreement on access to medical products in developing and least developed countries, has caused debate with some commentators arguing that IPP makes it possible for pharmaceutical companies to recoup their Research and Development (R&D) costs and hence act as an incentive for investment in biopharmaceutical research and innovation. However, this incentive structure has failed to spur R&D investments for diseases that predominantly affect poor people, leading to the emergence of alternative product development partnership (PDP) models such as the Drugs for Neglected Diseases Initiative (DNDi), proposals for a global R&D treaty, and the promotion of public health interests by using existing TRIPS flexibilities or through revisions of the TRIPS Agreement.

Although this paper focuses on the role of intellectual property rights on access to medicines, it is recognized that limited access to medicines in countries of the WHO African Regionis a multidimensional problem. It is affected by other factors such as lack of public financing for health care and over-reliance on out of pocket expenditure, fragile logistics, storage challenges and high transport and distribution costs and inadequate or inappropriate medicines regulatory frameworks. These factors are further exacerbated by insufficient scientific, technological and local manufacturing capabilities in the Region.

The occurrence of public health emergencies of global concern such as Ebola and COVID19, have served to highlight further the tensions between IPP, innovation and access to medical products. For example, in March 2020, Gilead Sciences, the makers of remdesivir which is a drug initially studied in clinical trials for Ebola Virus Disease (EVD) and has received US FDA emergency use authorization for the treatment of adults and children hospitalized with severe COVID-19 disease, made an application for orphan drug status for the drug, which has since been rescinded. Orphan drug designation for remdesivir would have granted seven years of market exclusivity in addition to the standard 20 years of patent protection guaranteed by the TRIPS Agreement. Gilead Sciences has since signed non-exclusive license agreements with manufacturers in Egypt, India and Pakistan for the supply of remdesivir in 127 low and middle-income countries including all countries of the African Region.

The earliest articulation of the World Health Organization's (WHO) mandate to work on the interface between access to medical products, R&D in rare and tropical diseases, and trade can be traced back to 1996, in a World Health Assembly (WHA) resolution on the Revised Drug Strategy which requested the WHO Director-General (DG) to support Member States in their efforts to improve access to essential drugs; to encourage the promotion of R&D of drugs for rare and tropical diseases; and to report on the impact of WTO concerning national drug and essential medicines policies and make recommendations for

collaboration between WTO and WHO as appropriate. This mandate has been continually reinforced through assembly resolutions. It has been extended over time to include upon request, providing technical and policy support to Member States, on formulating coherent trade and health polices and the implementation of TRIPS flexibilities in collaboration with other relevant international organizations.

Most recent are assembly decisions WHA 71(8) of 2018 on 'Addressing the global shortage of, and access to, medicines and vaccines', which requested the DG to "elaborate a roadmap report, in consultation with Member States, outlining the programming of WHO's work on access to medicines and vaccines including activities, actions and deliverables for the period 2019–2023; and WHA71(9) of 2018 on the 'Global strategy and plan of action on public health, innovation and intellectual property (GSPOA-PHI): overall programme review', which requested the DG to "implement the recommendations addressed to the Secretariat … in an implementation plan, consistent with the global strategy and plan of action on public health, innovation and intellectual property". Additionally, in 2019 resolution WHA72.8 on 'Improving the transparency of markets for medicines, vaccines, and other health products', requested the DG to "continue supporting existing efforts to determine patent status of health products and promote publicly available user-friendly patent status information databases for public health actors, in line with the GSPOA-PHI and to work with other relevant international organizations and stakeholders to improve international cooperation, avoid duplication of work, and promote relevant initiatives". These WHO commitments and the fact that it is 25 years since the adoption of the TRIPS Agreement provide an excellent setting for reviewing the experiences of WHO African Region Member States in implementing the Agreement for public health gains.

This 2019 study aimed at providing an up to date analysis of the role of IPR on innovation and access to medical products in countries of the WHO African Region. The study analyses patent data from the African Regional Intellectual Property Organization (ARIPO) and the Organisation Africaine de la Proprieté Intellectuelle (OAPI), the two African regional patent depositories as an indicator of innovation and knowledge production to address priority health challenges in the Region. The analysis sought to understand the level of patenting activity by African Region countries at ARIPO and OAPI, to identify the main diseases covered by patents granted at ARIPO and OAPI and how these correspond with the top causes of morbidity and mortality in the Region. The study also provides an assessment of the Region's preparedness to respond to public health emergencies using available TRIPS flexibilities. The study also provides an analysis of how WHO African Region countries have implemented the TRIPS flexibilities and hence provides a baseline for the work of WHO towards the implementation of the Health Assembly's decision WHA 71(8) and resolution WHA72.8 mentioned above.

Methods

a. **Patenting trends**

The patent data used in this study was obtained from the ARIPO and OAPI offices in April 2019. Face-to-face meetings were organized with officers of the two organizations to explain the objectives of the study and to clarify that the data required was in the areas/fields that can potentially be applied in medical innovations using the World Intellectual Property Organization (WIPO) international patent classification (IPC) codes. Table 1 presents the codes for patents falling within the scope of this study.

Table 1: IPC Codes of patents with potential application in the pharmaceutical sector

IPC Classification	Description
A61K	Preparations for medical purposes
A61P	Therapeutic activity of chemical compounds or medicinal preparation
A61B	Diagnosis - analyzing biological material covering processes for diagnostics.
A01N	Medicinal preparations (for pharmaceutical use) containing materials from mammals or birds
C07H	Sugars, derivatives thereof; nucleosides, nucleotides, nucleic acids with therapeutic activity further classified in subclass A61P, which covers DNA or RNA concerning genetic engineering, vectors or the isolation, preparation or purification
C12N	Micro-organisms or enzymes; compositions thereof; propagating, preserving or maintaining micro-organism, mutation or genetic engineering; culture media
C12P	Fermentation or enzyme using processes to synthesize a desired chemical compound or composition or to separate optical isomers from racemic mixture; particularly processes for producing enzymes, DNA or RNA concerning genetic engineering, vectors e.g. plasmids or their isolation.
C12Q	Measuring or testing processes involving enzymes or micro-organisms (immunoassays) compositions or test papers thereof; processes of preparing such composition; condition responsive control in microbiological or enzymological process.
C08B	Polysaccharides, derivatives thereof- those with therapeutic activity are further classified in subclass A61P.
C07F	Acyclic, carbocyclic, or heterocyclic compounds containing elements other than carbon, hydrogen, halogen, oxygen, nitrogen, sulfur, selenium or teleum. Therapeutic activity in A61P
C01G	Compounds containing metals and whose therapeutic activity is further classified under A61P
C07J	Steroids particularly those whose therapeutic activity is further classified in subclass A61P.
C08L	Compositions of macromolecular compounds which include pharmaceuticals under A61K
C07G	Organic chemistry/compounds of unknown constitution. Those with therapeutic activity further classified in subclass A61P
C07B	General methods of organic chemistry; apparatus therefore (preparation of carboxylic acid esters by telomerization)
C07C	Acyclic or carbocyclic compounds
C07D	Heterocyclic compounds. Those with therapeutic activity further classified in subclass A61P
C08G	Macromolecular compounds obtained otherwise than by reactions only involving carbon-to-carbon unsaturated bonds.
G01N	Investigation or analyzing materials by determining their chemical or physical properties.
C01B	Non-metallic elements; compounds thereof; whose therapeutic activity is further classified in A61P
C08F	Macromolecular compounds obtained by reactions only involving carbon-to-carbon unsaturated bonds; which include therapeutic activity under A61K, A61P

Officers of both patent offices conducted a data search using parameters defined and provided the requisite data as downloaded files in MS Excel. The total number of health-related patents registered in ARIPO and OAPI databases as of April 2019 was 3458 and 2811 respectively. This study only reviewed and analysed patents that had been granted within the past 20 years and were, therefore, within their validity period per Article 33 of the TRIPS Agreement. Consequently, the patents covered in this analysis are 960 (28%) for ARIPO and 2274 (81%) for OAPI. In order to identify the specific disease(s) a patent can be associated with, we used the patent short title, and in instances where the short title did not mention the disease, the patent abstract was consulted. Those that did not mention a specific disease were left out of the analysis. In doing the analysis the diseases covered by the patents were clustered in broad categories namely: inflammatory diseases, cancers, tumors and abnormal cell proliferation, cardiovascular diseases viral infections, neurodegenerative diseases, diabetes and diabetes-related conditions, infections, pain, HIV/AIDS, tuberculosis, malaria, mental disorders, nervous system disease, digestive system disease, weight related disorders, lung diseases, eye diseases and vaccines.

b. **Application of TRIPS flexibilities**

This study conceptualizes flexibilities as understood within the context of the TRIPS Agreement, its amending Protocol and the Doha Declaration on the TRIPS Agreement on Public Health (Doha Declaration)[1]. We define TRIPS flexibilities through the lens of Articles 1.1[2] and 8.1[3], which provide policy space for countries to implement the Agreement in a manner appropriate and responsive to their contexts, as different options which consider national interests and can be transposed into national law.

The study used data from The TRIPS Flexibilities Database, found on http://tripsflexibilities.medicineslawandpolicy.org/, which is a searchable publicly accessible database maintained by the Medicines Law and Policy group[4]. The database contains records of instances when national authorities of WTO member countries have invoked the application of a TRIPS flexibility for public health reasons since 2001 to present.

The TRIPS Agreement uses the term flexibility in paragraph 6 of the preamble and in Article 66.1 in the context of the need for least developed countries (LDC) to create a viable technological base and their readiness to implement it. Paragraph 4[5] of the Doha Declaration reaffirms the right of WTO members to use full provisions of the TRIPS Agreements and provides a contextual basis for understanding flexibilities while Paragraph 5 clarifies that they include;

- applying customary rules of interpretation of public international law so that all provisions of the TRIPS Agreement are read in light of the object and purpose as expressed in its objectives (Article 7) and principles (Article 8);
- the right of each member to grant compulsory licenses and the freedom to determine the grounds for granting such licenses;
- the right of each member to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises include those relating to HIV/AIDS, tuberculosis, malaria and other epidemics; and
- the freedom of each member to establish its exhaustion of IPR regime without challenge subject to the national treatment (Article 3) and most-favored-nation treatment (Article 4) provisions.

Given that Paragraph 5 does not provide an exhaustive enumeration of flexibilities, table 2 below provides a summary of TRIPS flexibilities, as well as the legal basis and how and why they should be implemented that can be used by African Region countries.

Table 2: Summary of available TRIPS flexibilities

Flexibility	Legal Basis	How and Why to Implement the Flexibility
Patentability criteria and exemption from patentability based on what constitutes novelty.	Article 27.1 of TRIPS does not specify what constitutes "new" or how the novelty requirement should be met. According to Para 4 of the Doha Declaration countries may interpret provisions of this Article in a manner that seeks to protect public health and ensure access to medicines.	Countries may opt to interpret 'novelty' in domestic legislation in a manner that excludes new and second uses of medicines. This flexibility is applied to prevent patents from new uses of known or previously patented medicines.
Research exception	Article 30 of TRIPS states that "Members may provide *limited exceptions* to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking into account of the legitimate interests of third parties.	The terms *limited exceptions* have been defined by the WTO Dispute Settlement Panel as "exception under which use of the patented product for scientific experimentation, during the term of the patent without consent is not infringement" Countries can therefore allow this exception in their national law in order to allow for the development of local scientific and technological knowledge and competencies to reverse engineer pharmaceutical products for generic production and for developing them further to better suite local conditions.
Regulatory review exception (Bolar exception)	This is also anchored in Article 30 of TRIPS.	This exception allows the use of a patented invention during the patented term without consent of the patent holder for purposes of developing information to obtain market approval. It allows generic producers to use patented knowledge for purposes of attaining regulatory approval for generic products before expiry of the patent(s), while the patent holder has the right to request, within specified conditions, an extension of the patent term to compensate for the delay in the drug regulatory and market approval process. This exception facilitates market entry by competitors immediately after the end of the patent term and is therefore an instrument that is specifically designed to ensure early access to generic medicines.
Compulsory licensing	Article 31 of TRIPS allows exploitation of patented subject matter through government authorization without the patent holder's consent, for the supply of the domestic market of the member authorizing such license, for reason of national emergency and public non-commercial use. Paragraph 6 of the Doha Declaration and Article 31(bis) of TRIPS makes it possible, under specific conditions for compulsory licensing for export through regional trade areas (RTAs), which make it possible for bulk purchases and economies of scale. Para 5 (b) the Doha Declaration clarifies that each member has the right to grant compulsory licenses and the freedom to determine the grounds upon which such licenses are granted.	Article 31 of TRIPS stipulates conditions for the issuance of a compulsory license by a member state. Provisions of Article 31 (f) and (h) make it impossible for countries with insufficient or no manufacturing capacity to use this flexibility. Questions of market viability for a single national market made it unattractive to use this flexibility. Para.6 of the Doha Declaration sought a solution to situations where a foreign producer can supply patented pharmaceutical products, which are not available in a country with no sufficient manufacturing capacity. This has been addressed through Article 31(bis).
Exhaustion of rights and parallel importation	Article 6 of TRIPS states that "For the purpose of dispute settlement under this Agreement, subject to the provisions of Articles 3 and 4 nothing in this Agreement shall be used to address the issue of the exhaustion of intellectual property rights" Para 5(d) of the Doha Declaration reaffirms that countries are free to determine their own regimes for exhaustion of patent rights without challenge	This provision allows importation and resale in a country without consent of the patent holder of a patented product put on the market of the exporting country by the patent holder or in a legal manner. International level of exhaustion provides the most flexibility, followed by regional and lastly national. It is a legal doctrine according to which an IP right holder cannot prevent further distribution or resale of goods after consenting to the first sale. In such a situation the right holder is considered to have exhausted its right over those goods.
Patent term extension	Article 33 of TRIPS provides that the patent term is 20 years from the filing date.	Countries may consider limiting patent term extension in national law for pharmaceutical products.
Limits on test data protection	Article 39.3 of TRIPS states that "Members, when requiring, as a condition of approving the marketing of pharmaceuticals …which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves considerable effort shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use."	This provision allows countries to determine how to protect test data in the public interest. This provision does not demand data exclusivity, which has the potential of blocking entry of generic versions of patented medicines. Rather, it demands protection from unfair commercial use. TRIPS does not define unfair commercial use nor does it provide guidance on how protection can be achieved. Countries may therefore incorporate in domestic legislation the right of regulatory authorities to rely on available data to assess new drugs for market entry.
Transition periods for LDCs	Article 66.1 of TRIPS states that "In view of the special needs and requirements of least developed country Members, their economic, financial and administrative constraints, and their need for flexibility to create a viable technological base, such Members shall not be required to apply the provisions of this Agreement, other than Articles 3, 4 and 5, for the period of 10 years from the date of application as defined under paragraph 1 of Article 65. The Council of TRIPS shall, upon duly motivated request by a least-developed country Member in order to enable them to create a sound an viable technological base"	In 2013 the TRIPS Council decided to extend the transition period for LDC members to fully comply with the TRIPS Agreement to 1 January 2021. LDC Members are exempt from the patentability requirement under Article 27.1 of TRIPS covering pharmaceutical products until 2033.

TRIPS Council decision of 2013 for the extension of transition period for LDCs under Article 66.1 to 1 January 2021.

TRIPS Council decisions IP/C/73 and TRIPS General Council decision WT/L/971 stating that LDC members are not obliged to protect pharmaceutical patents or to provide means for filing patents and provide patent protection and exclusive marketing rights until January 2033.

The TRIPS Flexibilities Database analysed for this study only has data on the use of compulsory license provisions (TRIPS Art. 31), patent exceptions (TRIPS Art 30) Least Developed Countries (LDC) transition periods (Para 7 Doha Declaration) and parallel importation (Para 5d Doha Declaration). The database includes instances when flexibilities were executed, pending, not executed or suspended. The study retrieved all the available data on countries of the WHO African Region. Additionally, we conducted a desk review of available patent laws of different countries to analyze how they have implemented these flexibilities within their national legal frameworks.

Results

a. **Patenting trends**

Graph 1 below depicts health-related patent application trends at ARIPO and OAPI. Data shows that there was a sharp increase in patent applications at both offices from 1994 to 1999, which started to decline in the period 1999 - 2000.

According to the 2018 Report on the State of Health in the WHO African Region[1], the main five causes of morbidity and mortality in the Region, are lower respiratory infections, HIV/AIDS, diarrheal diseases, malaria and tuberculosis. Other top causes of morbidity and mortality include stroke and ischemic heart diseases, preterm birth complications, birth asphyxia and congenital anomalies.

An analysis of the top 10 diseases covered by patents granted at ARIPO and OAPI corresponds to a certain extent, with the top 10 causes of morbidity as illustrated by graphs 2 and 3 below. In both repositories the three top categories of diseases covered by granted patents were inflammatory diseases; cancers, tumors and abnormal cell proliferation; and cardiovascular diseases. Within the inflammatory diseases category, there were patents for lower respiratory diseases such as chronic obstructive pulmonary disease and asthma. HIV/AIDS, which was the second cause for morbidity and mortality, was 7th among the top 10 ARIPO patents and 10th for OAPI. Stroke and ischemic heart diseases which ranked 4th and 5th as causes of mortality respectively, fall within the broad category of patents covering cardiovascular diseases, which ranked 3rd on the list of top 10 diseases covered by patents at ARIPO and OAPI.

These observations point to modest alignment of pharmaceutical knowledge production (through R&D and innovation) with addressing health challenges in the Region. Diarrheal diseases, tuberculosis and malaria, which are among top causes of mortality and morbidity did not appear among the top diseases covered by patents in the Region. There were only 23 TB patents at ARIPO and 25 at OAPI, while there were only 37 malaria patents at ARIPO and 47 at OAPI.

The top 10 categories of diseases covered by patents taken at ARIPO and OAPI were the same, the only difference being in the ranking. Another interesting finding is the ranking of cancer-related patents, which was found to rank 2nd at both patent offices indicating an increase in cancer research.

An analysis of the countries of origin of health-related patents at ARIPO and OAPI shows that the top 10 sources of patents at ARIPO were USA, Great Britain, the European Patent Office, France, India, China, South Africa, Germany, Italy and Denmark. South Africa was the only African country in the top 10 list. The top 10 sources of patents at OAPI were USA, France, Great Britain, Germany, India, Belgium, Japan, Cameroon, Switzerland and Ireland. Cameroon was the only African country in the top 10 list. The African Region countries that had health-related patents at ARIPO were Kenya, Mauritius, Namibia, Zambia, and Zimbabwe and Egypt from the Eastern Mediterranean Region (EMRO) of the WHO. While in OAPI the African Region countries were Burkina Faso, Benin, Central African Republic, Congo Republic, Cote d'Ivoire, Cameroon, Guinea, Mali, Mauritius, Namibia, Nigeria, Senegal, Togo, South Africa and Egypt and Morocco from EMRO.

An analysis of the African country patents shows that the top three disease categories covered are HIV/AIDS, cardiovascular diseases, and cancer and tumors. Table 3 below provides a summary of the main diseases covered by African country patents. The fact that HIV/AIDS, cardiovascular diseases, malaria and tuberculosis which were mentioned as top causes of mortality and morbidity in the Region also feature among African country patents highlights a modest alignment between research and health challenges of the Region.

Table 3: Summary of main diseases covered by African country patents

Disease	Number of mentions in patents	Disease	Number of mentions in patents
HIV/AIDS	20	Tuberculosis	5
Cardiovascular diseases	18	Bacterial infection	5
Cancer and Tumors	14	Antimicrobial	4
Diabetes	14	Antiviral	4
Malaria	13	Ulcers	4
Skin	10	Hemorrhoids	4

b) Application of Flexibilities

An analysis of the TRIPS flexibilities database summarized in Table 4 below shows that 39 out of the 47 African Region Countries have used one or more TRIPS flexibility, with all applications being between 2002 and 2009. African Region countries that were not recorded as having applied any flexibility are Algeria, Botswana, Madagascar, Mali, Mauritius, Namibia, Nigeria, and Seychelles. Majority of the applications were for sourcing treatments for HIV/AIDS, except in the cases of Angola, Cape Verde, Chad, Gambia, Kenya, Lesotho, Malawi, Niger, Rwanda, South Sudan, Tanzania and Togo that applied flexibilities for sourcing all medicines.

The analysis shows that only three flexibilities were applied, namely Article 31 of TRIPS which allows for compulsory licensing including for non-commercial use; paragraph 7 of the Doha Declaration on LDC country transition periods and paragraph 5 (d) of the Doha Declaration allowing for parallel importation. The most commonly applied flexibility is paragraph 7 of the Doha Declaration on transition provisions with 27 countries having applied it, followed by Article 31, allowing compulsory licensing, which has been applied by 16 countries. Parallel importation has only been used by Kenya once (in 2002) for the importation of generic medicines.

Some countries have applied flexibilities more than once; the highest being five times by Kenya, four times by Zimbabwe, and three times by Benin, Congo, Gabon, Ivory Coast, Mozambique, Togo and Zambia. Central African Republic, Chad, the Gambia, Guinea, Lesotho, Malawi, Niger, Rwanda and Sierra Leone have all applied flexibilities twice respectively. Guinea, Mozambique and Zambia adopted a mixed approach of using both Article 31 and paragraph 7, and Kenya both Article 31 and paragraph 5 at different times. In the case of Kenya, it did not execute 4 of its applications which were under Article 31 for HIV/AIDS medications. The pharmaceutical companies involved in these cases GSK and Boehringer Ingelheim entered into voluntary license agreements with a Kenyan manufacturing company Cosmos Ltd. The 5th application by Kenya, and only one to be executed was under paragraph 5 and related to sourcing of generic drugs.

Cameroon and South Africa too did not execute their flexibilities applications which were both under Article 31 and were both for HIV/AIDS drugs. The database does not record why Cameroon did not execute its application. In the case of South Africa, the concerned pharmaceutical companies GSK and Boehringer Ingelheim entered into a voluntary license with Cipla, an Indian manufacturing company.

Table 4: Summary of application of TRIPS flexibilities by African Region countries

Country	Date	Flexibility	Product	Patent filed/granted	Disease	Executed	Reason if not executed
Angola	2005	Par7	All medicines	Yes	All	Yes	
Benin	2004	Par7	ARVs	Yes	HIV/AIDS	Yes	
Benin	2007	Par7	ARVs	Yes	HIV/AIDS	Yes	
Benin	2009	Par7	ARVs	Yes	HIV/AIDS	Yes	
Burkina Faso	2005	Par7	ARVs +	Yes	HIV/AIDS	Yes	
Burundi	2005	Par7	ARVs +	Yes	HIV/AIDS	Yes	
Cameroon	2005	Art 31	NVP, 3TC, 3TC/AZT	Yes	HIV/AIDS	No	No response
Cape Verde	2004	Par7	All medicines	Unknown	All	Yes	
CAR	2004	Par7	ARVs +	Yes	HIV/AIDS	Yes	
CAR	2005	Par7	ARVs +	Yes	HIV/AIDS	Yes	
Chad	2005	Par7	ARVs	Yes	HIV/AIDS	Yes	
Chad	2007	Par7	All medicines	Yes	All	Yes	
Comoros	2007	Par7	ARVs +	Unknown	HIV/AIDS	Yes	
Congo	2007	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Congo	2014	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Congo	2005	Art 31	ARVs +	Yes	HIV/AIDS	Yes	
DRC	2005	Par7	ARVs	No	HIV/AIDS	Yes	
Eritrea	2005	Par7	ARVs	No	HIV/AIDS	Yes	
Ethiopia	2004	Art 31	ARVs	No	HIV/AIDS	Yes	
Gabon	2005	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Gabon	2006	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Gabon	2013	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Gambia	2004	Par7	ARVs	Yes	HIV/AIDS	Yes	
Gambia	2007	Par7	All medicines	Yes	All	Yes	
Ghana	2005	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Guinea	2004	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Guinea	2005	Par7	ARVs	Yes	HIV/AIDS	Yes	
Guinea Bissau	2005	Par7	ARVs	Yes	HIV/AIDS	Yes	
Guinea Equatorial	2009	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Ivory Coast	2004	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Ivory Coast	2007	Art 31	3TC, 3TC/AZT, 3TC/AZT/NVP, 3TC/D4T, 3TC/D4T/NVP, DDI, EFV, IDV	Yes	HIV/AIDS	Yes	
Ivory Coast	2007	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Kenya	2002	Par5d	Generics	Yes	All	Yes	
Kenya	2004	Art 31	3TC	Yes	HIV/AIDS	No	Voluntary licence
Kenya	2004	Art 31	3TC/AZT	Yes	HIV/AIDS	No	Voluntary licence
Kenya	2004	Art 31	AZT	Yes	HIV/AIDS	No	Voluntary licence
Kenya	2004	Art 31	NVP	Yes	HIV/AIDS	No	Voluntary licence
Lesotho	2004	Par7	ARVs	Yes	HIV/AIDS	Yes	
Lesotho	2006	Par7	All medicines	Yes	All	Yes	

Country	Date	Flexibility	Product	Patent filed/granted	Disease	Executed	Reason if not executed
Liberia	2005	Art 31	ARVs	No	HIV/AIDS	Yes	
Malawi	2004	Par7	All medicines	Yes	All	Yes	
Malawi	2005	Par7	ARVs	Yes	HIV/AIDS	Yes	
Mauritania	2004	Par7	ARVs	Yes	HIV/AIDS	Yes	
Mozambique	2004	Art 31	3TC/D4T/NVP	No	HIV/AIDS	Yes	
Mozambique	2005	Art 31	EFV	No	HIV/AIDS	Yes	
Mozambique	2005	Par7	ARVs	Yes	HIV/AIDS	Yes	
Niger	2004	Par7	All medicines	Yes	All	Yes	
Niger	2008	Par7	ARVs	Yes	HIV/AIDS +	Yes	
Rwanda	2007	Par7	3TC/AZT/NVP	No	HIV/AIDS	Yes	
Rwanda	2007	Par7	All medicines	Yes	All	Yes	
Senegal	2006	Par7	ARVs +	Yes	HIV/AIDS +	Yes	
Sierra Leone	2009	Par7	IDV, LPV/r, NVP, TDF	No	HIV/AIDS	Yes	
Sierra Leone	2009	Par7	DDI, IDV, LPV/r	No	HIV/AIDS	Yes	
South Africa	2003	Art 31	AZT, 3TC, AZT/3TC, NVP	Yes	HIV/AIDS	No	Voluntary licence
South Sudan	2007	Par7	All medicines	Yes	HIV/AIDS	Yes	
Swaziland	2005	Art 31	NVP, AZT	Yes	HIV/AIDS	Yes	
São Tomé and Príncipe	2006	Art 31	ARVs	No	HIV/AIDS	Yes	
Tanzania	2008	Par7	All medicines	Yes	All	Yes	
Togo	2004	Par7	All medicines	Yes	All	Yes	
Togo	2008	Par7	TDF/3TC	Yes	HIV/AIDS	Yes	
Togo	2009	Par7	EFV, NVP, 3TC/AZT	Yes	HIV/AIDS	Yes	
Uganda	2006	Par7	3TC/D4T/NVP	Yes	HIV/AIDS	Yes	
Zambia	2004	Art 31	3TC/D4T/NVP	Yes	HIV/AIDS	Yes	
Zambia	2004	Par7	ARVs +	Yes	HIV/AIDS +	Yes	
Zambia	2006	Par7	ARVs +	Yes	HIV/AIDS +	Yes	
Zimbabwe	2002	Art 31	ARVs +	Yes	HIV/AIDS +	Yes	
Zimbabwe	2003	Art 31	ARVs +	Yes	HIV/AIDS +	Yes	
Zimbabwe	2004	Art 31	ARVs	Yes	HIV/AIDS	Yes	
Zimbabwe	2005	Art 31	ARVs +	Yes	HIV/AIDS	Yes	

Table 5 below provides a snapshot of flexibilities that have been enacted into law by African Region countries. Our analysis did not find any country that had legislated on research exception, regulatory review exception and patent term extension.

Table 5: Summary of flexibilities enacted into law by African Region countries

Flexibility provision	Country
Patentability criteria	Namibia, Rwanda and Zambia have legislated against new or second use of already patented pharmaceutical products to stop "evergreening" of patents
Compulsory Licensing	Botswana, The Gambia, Ghana, Kenya, Lesotho, Liberia, Malawi, Mozambique, Namibia, Rwanda, Sierra Leone, Swaziland, South Africa, Tanzania, Uganda, Zambia, Zimbabwe, and OAPI countries
Exhaustion of rights and parallel importation	International exhaustion – Botswana, Ghana, Kenya, Liberia, Rwanda, Namibia, Sierra Leone, South Africa Uganda, Zambia Regional Exhaustion – Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Congo Republic, Cote d'Ivoire, Gabon, Guinea, Guinea-Bissau, Mali, Mauritania, Niger, Senegal, Togo – essentially all OAPI countries within the framework of the Bangui Agreement). National exhaustion – The Gambia, Lesotho, Mozambique, Swaziland, and Tanzania, Nigeria
Limits on test data protection	Uganda
Transition periods for LDC	Liberia, Rwanda & Uganda allow for pharmaceutical product exemption from patentability.

Discussion

From the patenting trends analysis, we observe an increase in the number of patent applications at ARIPO and OAPI which, coincide with the adoption of the TRIPS Agreement in 1994 and goes on for a couple of years. Another important observation in the patent application trends is the decreasing number in applications after 2015 at both offices, which coincides with the TRIPS Council and WTO General Council decisions IP/C/73 and WT/L/971 respectively of 2015, which accorded Least Developed Countries (LDCs) waivers on obligations under Articles 70.8 of the TRIPS Agreement which requires states to provide means by which patent applications can be filed for pharmaceutical and agricultural chemical products and 70.9 with respect to provision of exclusive marketing rights of these products up to 2033. These waivers affect the implementation of the non-discriminatory requirement in Article 27.1, which extends patentability to inventions in all technological fields including pharmaceutical products and processes. 22 countries in the African Region, namely Benin, Burkina Faso, Central African Republic, Chad, Gambia, Guinea, Guinea-Bissau, Lesotho, Liberia, Malawi, Mali, Mauritania, Mozambique, Niger, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Togo, Uganda, Tanzania and Zambia are classified by the United Nations as LDCs and, with the exception of Sao Tome and Principe which is not signatory to the TRIPS Agreement, are entitled to waivers under Articles 66.1, 70.8 and 70.9. Additionally, in 2013 LDCs got a transition period extension in accordance with Article 66.1[1] of the TRIPS Agreement to fully comply with the TRIPS Agreement by 2021. Unfortunately, these LDC countries in the Region are unlikely to benefit from these waivers since they are signatories to Regional frameworks such as the Harare Protocol on Patents and Industrial Designs (1982) or the Bangui Agreement (1977), which require them to attain a TRIPS – plus standard, where patentability criteria extends to pharmaceutical products and process, hence more onerous than the one required under TRIPS.

The findings of this study show that there is very low health-patenting activity at ARIPO and OAPI by African countries. Should this finding be taken to mean that African countries are not engaging in pharmaceutical R&D and innovation? It has been argued[2] that patent numbers are not sufficient indicators of innovation but rather, a better indicator would be how often a patent gets cited. We suggest that it is necessary to further interrogate this finding through further research in order to fully understand reasons for low patenting activity by African countries.

In the years following the adoption of the TRIPS Agreement, developing countries experienced challenges in applying TRIPS flexibilities such as compulsory licensing (Article 31) and parallel importation (Article 6) of drugs in their bid to address the HIV/AIDS crisis that was facing most developing countries towards the end of the 20th century. One such example in the African Region was South Africa, which enacted the Medicines and Related Substances Control Amendment Act 1997 that allowed for parallel importation and compulsory licensing of pharmaceuticals in the country. These amendments to the law led to a backlash from pharmaceutical companies and culminated into legal action against the South African government, which was later withdrawn. Over time and with a lot of public pressure on the pharmaceutical industry African countries exploited some available TRIPS flexibilities to address the HIV/AIDS challenge.

Compulsory licensing was a commonly applied flexibility by countries, which was most often not executed, hence the conclusion that these may have served to encourage pharmaceutical companies to enter into voluntary licensing arrangements.

We observe that exhaustion of rights and parallel importation is not commonly applied in the Region. This could be due to the fact that some countries have adopted a national exhaustion approach such, while those governed by the Bangui Agreement have precluded international exhaustion and restricts parallel importation to the regional exhaustion regime within OAPI countries. We found that no country in the Region has put in place legislation that allows for research exception and regulatory review exception.

Conclusions

The experiences of the HIV/AIDS pandemic in the nineties, and most recently, the search for an effective treatment and vaccine for COVID-19 highlight the tensions between intellectual property rights and public health interests. There is evidence that learning has taken place from the lessons of the HIV/AIDS pandemic. Some of these lessons include the willingness by pharmaceutical companies such as Gilead Sciences to enter into voluntary licensing agreements with manufacturing companies in developing countries to serve less developed markets. The speed with which countries such as Canada, Germany, Chile and Ecuador have amended their respective patent laws to prohibit market exclusivities and to allow for compulsory licensing, should it become necessary, of COVID-19 medicinal products are examples of how TRIPS flexibilities can be deployed to address health needs.

The low levels of patenting activity by African Region countries calls for the need to develop and strengthen health innovation systems in the Region. This can be done through policies that support health research systems and a local incentive structure that focuses research on local health challenges. Other aspects of developing health innovation systems would include developing local scientific and biomedical research capacities and local manufacturing capabilities.

The findings of this study provide an opportunity for the WHO Regional Office for Africa to work closely with ARIPO and OAPI to develop and promote a Regional IP framework that is responsive to public health challenges of the Region; and to support countries in reviewing national IP laws taking into account available flexibilities such as research exception, regulatory review exception and patent term extension.

Abbreviations

3TC	Lamivudine
AIDS	Acquired Immune Deficiency Syndrome
ARIPO	African Regional Intellectual Property Organization
ARV	Antiretrovirals
AZT	Azidothymidine
COVID-19	Corona Virus Disease of 2019
D4T	Stavudine
DG	Director General
DNA	Deoxyribonucleic Acid
DNDi	Drugs for Neglected Diseases Initiative
EFV	Efavirenz
EMRO	Eastern Mediterranean Region
EVD	Ebola Disease Virus
GSK	GlaxoSmithKline
GSPOA-PHI	Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property
HIV	Human Immuno Deficiency Syndrome
IP	Intellectual Property
IPC	International Patent Classification
IPP	Intellectual Property Protection
IPR	Intellectual Property Rights
LDC	Least Developed Countries
MS	Microsoft
NVP	Nevirapine
OAPI	Organisation Africaine de la Propriete Intellectuelle
PDP	Product Development Partnership
R&D	Research and Development
RNA	Ribonucleic Acid
TDF	Tenofovir Disoproxil Fumarate
TRIPS	Agreement on Trade-Related Aspects of Intellectual Property
USA	United States of America
US FDA	United States Food and Drug Administration

WHA World Health Assembly

WHO World Health Organization

WIPO World Intellectual Property Organization

WTO World Trade Organization

Declarations

Ethics approval and consent to participate

Since this research does not include human participants, no permission was needed from the WHO African Region Ethics Review Committee.

Consent to publish

Not applicable as manuscript does not include details, images or videos relating to individual persons.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to the fact that they are held by ARIPO and OAPI patent depositories but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MM contributed to conception and design, data collection, analysis and writing of the manuscript. JBN and OMJK contributed by providing inputs to the study conception and design and in data collection. SK, AL, AS and PT provided inputs in the analysis of the manuscript. All authors read and approved the final manuscript.

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