WORKING PAPER

ESSENTIAL MEDICINES AND PATENTS ON THE WORLD HEALTH ORGANIZATION ESSENTIAL MEDICINES LIST 22ND EDITION (2022)

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Key Takeaways

- The latest edition of the World Health Organization's Essential Medicines List, the 22nd Edition (2021), has seen a decline in the percentage of patented medicines for the first time since researchers have been tracking the number. As of January 2022, 35 out of the 477 total items (7.3%) listed on the 22nd edition of the EML are patented in a middle or low income country.
- 19% of lower income countries surveyed do not have any active patents listed for the 35 patented medicines on the 22nd EML. 83% of lower income countries have 50 or fewer active EML medicine patents.
- Approximately 25% of all active EML patents in lower income countries are subject to an MPP license, bilateral license, and/or commitment to not enforce.

1. Introduction

Every two years the World Health Organization (WHO) publishes its Model List of Essential Medicines (EML), which identifies medicines "deemed essential for addressing the most important public health needs globally." Innovation in the life sciences is constant and public health needs evolve, so new medicines are added to each edition of the EML while others are removed.

The EML occupies an important role in public health practice and policy. First, it is a source of guidance and a measuring stick for public health systems as to the drugs and other treatments they should have available for patients. Second, it is a focus for public health policy discussions about which treatments should be prioritized and how well public health systems are meeting the goal to make them available.

Since the EML plays this important role, the availability and accessibility of medicines on the EML is a frequent topic of policy discussion. The access to these medicines in lower- and middle-income countries is a particular concern. This policy discussion often addresses the patent status of medicines on the EML. Of course, nearly all the medicines on the EML started out as patented; all of them eventually come off patent, either before or after being listed on the EML. Patent status is sometimes viewed as a proxy for affordability, but, things are not that simple, as many patented medicines on the EML are subject to institutionalized access programs to ensure availability and affordability in developing countries.

Trends regarding the EML are thus of great interest and relevance to public health policy discussions. This paper measures and addresses two trends in recent editions of the EMLs:

- The percentage of medicines on the most recent publication of the EML (22nd edition, 2022) currently under patent in lower income countries.
- The availability of institutionalized access programs, such as the Medicines Patent Pool and other initiatives to make medicines broadly available in low-income countries.

The number of patented medicines in the 22nd edition of the EML is down significantly from the previous edition, reversing trends from the past decade. Of the 477 medicines listed on the 22nd edition EML, 35 (7.3%) may be considered under patent in a lower or middle income as of January 2022. Our earlier review of the 21st edition EML found that 46 out of 457 items (10.1%) listed on the 2019 EML were under patent in at least one lower- or middle-income country. Therefore, the 2021 EML is down a net 11 patented medicines from the 2019 EML. (We say "net" due to patent expirations and removals from the list.)

The WHO made a significant change to the latest edition of the EML by consistently naming therapeutic alternatives to EML medicines for the first time. We explain this change further in our paper and the notable impact it had on the patent status of EML medicines.

Our methodology builds upon the one we previously used in our study of the 2019 Edition of the EML[2] and, ultimately, the one employed by Reed Beall and Amir Attaran's 2016 study for the World Intellectual Property Organization, *Patent-based Analysis of the World Health Organization's 2013 Model List*

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of Essential Medicines. Our methodology differs, however, in that we were able to make use of several public databases that have become available since Beall and Attaran did their study.[3] We explain our methodology in detail in Appendix A.

2. Understanding the Patent Status of Medicines on the EML

Determining "the number of medicines on the EML that are patented" is a more complex task than one might think. Each part of the statement embodying that concept poses certain complications, some of which have policy implications. We explain the relevant considerations here, particularly the most significant change to the EML's nature in years – the explicit listing of therapeutic equivalents.

2.1 Which Items on the EML are "Medicines"?

First, there is the question of which items on the EML count as "medicines," as the list defines them more broadly than the conventional understanding of a compound or preparation used to treat or prevent disease. Although almost all of items on the list fit this conventional understanding, the list also includes things that do not, such as oxygen, condoms and diaphragms, vitamins and minerals, and glass ionomer cement for dentistry.

It would be unproductive to quibble as to whether these items are "medicines" for EML purposes, as such fine distinctions have little public health or policy relevance in this context. The preface to the latest edition of the EML states that "Essential medicines are those that satisfy the priority health care needs of a population. . . . They are intended to be available in functioning health systems at all times."[4] The focus in the EML is thus on what items need to be available to address public health needs, rather than how they might be categorized.

For this reason, we take an inclusive, comprehensive approach simply counting each item on the EML as a "medicine." Thus, if it is an item on the EML, it contributes to the total number of items on the list – 477 this year.[5]

2.2 Which Medicines are "Listed" on the Essential Medicines List?

The Essential Medicines List is not just simply list of medicines, and changes to the latest edition have made it more complex. There are several ways in which EML medicines are further specified, some of which are relevant to patent status. The latest edition of the EML, the 22nd, made a major change, consistently providing an explicit list of therapeutic alternatives for the first time for certain groups of medicines. The significance of this change is discussed below.

1. Indications.

The indication or indications for which a medicine is used are listed on the EML. Not every potential or approved indication for a medicine is listed on the EML. The EML-specified indication can be relevant to patent status, as there are occasionally later-expiring patents that apply only to a particular indication (typically method of treatment patents) not specified on the EML.

2. Dosage Forms.
For each medicine, the EML lists one or more form of administration such as tablet, capsule, oral liquid, or injection as well as the size of the dose. In some instances, the dosage form may be relevant to patent status.

3. Core vs. Complementary Lists.
The EML breaks medicines into two categories: First, a "core list," which "presents a list of minimum medicine needs for a basic health-care system."[6] Second, the "complementary list presents essential medicines for priority diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed."[7] While the distinction between the two categories matters for treatment and public health purposes, for purposes of this analysis, all medicines in both categories are EML medicines.

4. Therapeutic Equivalents.
In many instances, the entry for a medicine listed on the EML is intended to be merely representative of a group of medicines that are therapeutic equivalents. Since 1983, WHO has placed a square box symbol next to such an entry to indicate that a therapeutic equivalent can be used. However, in most instances,[8] the EML did not specify therapeutic equivalents to the listed medicine, leaving that determination up to physicians and public health systems. The importance of the representative medicine explicitly listed was arguably magnified by the lack of explicit information as to alternatives.

The latest edition of the EML began to provide an explicit list of recommended therapeutic alternatives for each square box listing. The WHO Expert Committee on the Selection and Use of Essential Medicines recommended this change to provide greater clarity and better information to decisionmakers at the national level.[9] The recommendation cited a paper that reviewed problems with the square box designation such as potential confusion and uncertainty as to the suitability of potential alternatives caused by an "overflow of information" from many drug studies of varying quality and reliability.[10]

With this change, therapeutic alternatives are more clearly and certainly part of the EML. While the use of therapeutic alternatives for square box listings was always a possibility, the change to specifically listing them makes their use more likely. Making it easier for users to identify and purchase or prescribe them was essentially the purpose of the change. Incidentally, the certainty afforded by this change allowed the inclusion of therapeutic alternatives in this paper's analysis.

Previous analyses of the patent status of medicines on the EML did not address the patent status of unlisted therapeutic alternatives to square box listings. The reasoning was essentially the same as what motivated WHO to begin explicitly listing therapeutic alternatives: Identifying therapeutic alternatives is challenging. It requires knowledge of what is available, understanding of the specific disease condition, and the appropriateness of the alternative. The determination is demanding for public health authorities and physicians and simply outside the scope of an analysis such as this.

> *This study does not look at the patent status of EML medicines in every country in the world but focuses on 150 lower income countries – specifically those countries classified as low or middle income by the World Bank.*

Now that therapeutic alternatives are specifically documented in the EML, they can be considered in the analysis of the patent status of EML medicines. For this latest analysis of the 22nd Edition, we have reviewed the patent status of both the "primary" medicine listed for all square box entries and the newly specified alternatives. If at least one of the medicines among the group is off patent, we count the entire group as off patent. The reason for this determination is the premise of this paper, as well as longstanding policy discussions, is that the patent status of an EML medicine matters in some sense. The usual assumption is that patented medicines cost more, and while this isn't always true due to various targeted programs (discussed in this paper) or competition from substitutes, it is a starting point for discussions. If patent status does indeed matter, then the existence of an unpatented therapeutic alternative clearly identified on the EML should also be consequential for prescribers, public health systems, and producers of competing patented medicines.

Later in the paper, we note instances where the specific listing of therapeutic alternatives has changed an EML listing from patented to off patent since the prior edition of the EML. The change to the square box listing has made that difference in several instances. It also may matter in the future, where currently patented therapeutic alternatives have earlier-expiring patents. We now list such alternatives and the relevant patents in our analysis in the Annex to this paper.

2.3 Which Listed EML Medicines are "Patented"?

Determining the patent status of medicines on the EML is open to some interpretation. While we explain our methodology in detail in Appendix A, a few caveats and explanations here are useful.

1. The Analysis Applies to 150 Lower Income Countries Only

This study does not look at the patent status of EML medicines in every country in the world but focuses on 150 lower income countries – specifically those countries classified as low or middle income by the World Bank. The list is provided in Appendix A. These countries have been the focus of EML patent studies ever since the first such study by Attaran (2004). These are also the countries examined in the MedsPal database, managed by the Medicines Patent Pool, which provides freely available and public patent information for a large majority of EML medicines.

The motivation for this focus among researchers and policy experts has been, and continues to be, the ongoing policy discussion as to whether patents significantly affect affordability of essential medicines in developing countries. In this regard, it is helpful to note that the choice of countries examined is comprehensive and objective, based solely on low and middle-income status as defined by the World Bank, all of which are included. The list includes countries with significant generic manufacturing capacity such as India and China.

2. Many Patents are Relevant for the Purposes of EML Analysis, But Not Every One of Them Counts

Determining the patent status of an EML medicine is more demanding than simply checking the expiration date on a particular patent. Many patents may be potentially applicable to an EML medicine, but not all of them are relevant for purposes of this analysis. A patent "counts" here only if it provides exclusive rights to an innovator for the indication listed on the

EML. The reason is that the ultimate point of interest is the possibility of generic competition for that EML medicine and indication, so only patents that might prevent such competition are relevant.

One reason that many patents may be relevant to a single medicine is that drug innovation does not stop with discovery of a new compound. During the development of a drug, the first chemical entity developed and patented may differ from the medicine that is eventually developed and approved for marketing to patients. Creating a useful, safe, and reliable medicine might require further innovation – for example a specific formulation or a form of administration -- and those innovations may also be patented. Later innovations often include new formulations that provide for extended release, longer shelf life, or better absorption. Innovators may also invent new methods of treatment, dosing regimens, delivery devices, or manufacturing methods for a particular medicine.

Whether patents relevant to an EML medicine might affect generic competition is often uncertain and open to interpretation. This determination requires significant expertise on both the technical subject matter and national laws. For these reasons, generic drug manufacturers and the experts they consult devote significant time and resources to freedom to operate analyses to determine the applicability of patents. And even if a manufacturer determines that existing patents are not an obstacle to making a generic version, that conclusion is often contested in litigation by patent owners.

For these reasons, this paper, and the data sources from which it draws, err on the side of inclusion when identifying unexpired patents that potentially cover an EML medicine. Annex B identifies many patents relevant to EML medicines set to the expire over the next decade or so. Some of these patents likely will not impede generic competition, but for now they are listed until their applicability becomes more certain. As part of this inclusive approach, we include a patent or patent application, even if it is contested in litigation, until it expires, or is abandoned, finally rejected, finally adjudicated invalid, or generic competition proves it irrelevant for EML purposes.

However, there are instances in which a patent relevant to an EML medicine clearly should not "count" for purposes of this analysis, even allowing for our conservative approach. Instances where this paper finds patents clearly not applicable to EML applications include:

- Medical device patents (e.g., inhalers) where the EML indication is for another dosage form;
- Later-expiring method of treatment patents that differ from the EML indication; and
- Instances where early patents expire, followed by widespread generic entry.

For an example of how later-filed patents on a medicine do not impede generic competition or count for EML purposes, consider the EML medicine ibuprofen. It is widely available globally, produced by many different generic manufacturers. The earliest relevant patents, first filed in 1962, are long since expired but various patents relevant to ibuprofen are still being filed -- for example a 2021 method of treatment patent application specifies the use of ibuprofen in one of its claims.[11] Given the widespread availability

> *In this latest 22nd Edition of the EML, 7.3% of the medicines were under patent in lower income countries, compared to 10.1% in the previous edition.*

of generic versions of ibuprofen and the nature of such later-filed patents, it is safe to say that ibuprofen is not patented for EML purposes, where it is indicated for use in cases of pain relief and migraines.

3. Recent Trends in Patent Status for EML Medicines

Every other year, the WHO revises its Model List of Essential Medicines (EML) adding some medicines and removing others as standards of care advance. In recent editions of the EML, the length of the list has grown significantly, from 373 in 2013 to 477 in 2021 as additions have outpaced removals.

Some of each new EML's additions have been under patent when added, although never the majority of additions. In this latest 22nd edition, just 3 of the 23 additions are under patent, the lowest number in the years for which we have tracked trends.

This Section provides a look at the trends regarding patent status on the EML, then takes a more in-depth look at where those patents are filed in lower income countries and finishes with an overview of some available information regarding institutionalized access programs for these medicines, including low-cost licenses and commitments not to enforce.

3.1 Trends Regarding Patented Medicines on the EML

Here we examine the basic numerical trends and additions and removals in the EML, changes in patent status, and the net effect of those changes on the percentage of patented medicines on the EML.

1. The EML and Patents by the Numbers

The percentage of the EML composed of medicines under patent in lower income countries fell in 2021 after rising for several previous editions. In this latest 22nd Edition of the EML, 7.3% of the medicines were under patent in lower income countries. In our study of the 21st Edition of the EML two years ago, published in early 2020, we found that patented medicines accounted for about 10.1%, having risen from 5.4% in the 18th Edition of the EML in 2013.

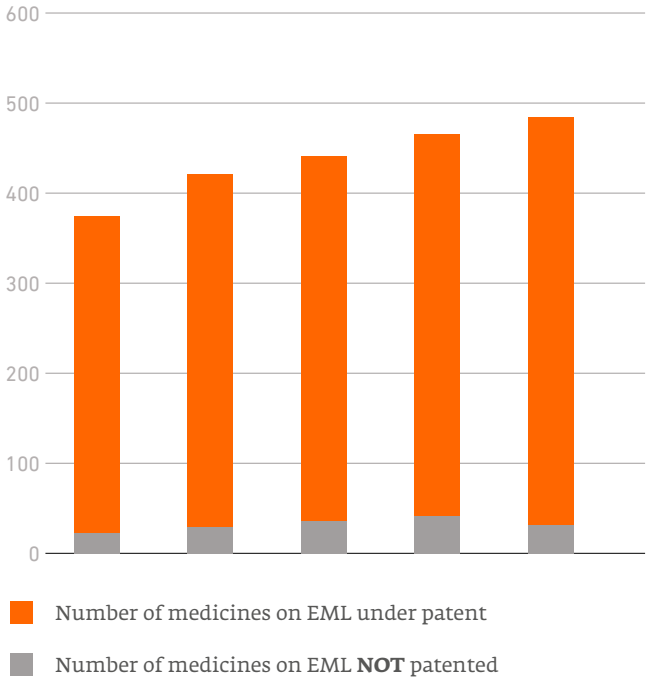
The number of medicines on the EML under patent in lower income countries is down in absolute terms as well. There are now 35 medicines under patent, the lowest number since 2015, when 34 medicines were patented, and the lowest percentage since 2013, when 5.4% were patented.

Table 1 and **Figures 1 and 2** illustrate these trends.

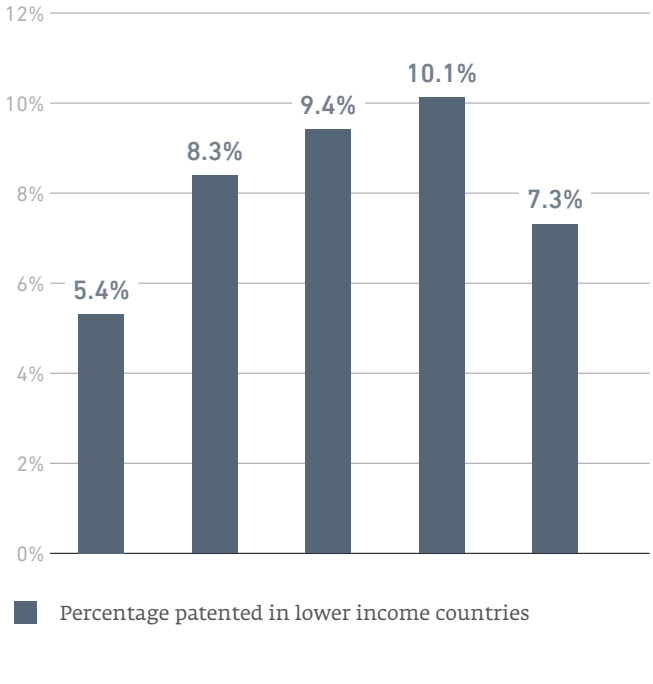
▸ **Table 1:** *Medicines on EML Under Patent in Lower Income Countries, 2013 - 2021*

	Number of Medicines on EML Under Patent	Number of Medicines on EML Not Patented	Total Number of Medicines on EML	Percentage Patented in Lower Income Countries
18th Edition, 2013	20	353	373	5.4%
19th Edition, 2015	34	375	409	8.3%
20th Edition, 2017	41	395	436	9.4%
21st Edition, 2019	46	411	457	10.1%
22nd Edition, 2021	35	442	477	7.3%

▸ **Figure 1:** *Number of Medicines Patented in Lower Income Countries as a Proportion of All EML Medicines, 2013 - 2021*



▸ **Figure 2:** *Percentage of EML Medicines Patented in Lower Income Countries 2013 - 2021*



2. Additions and Removals from the EML & Changes in Patent Status

The listing of medicines on the EML changes significantly between editions and over time, as does the patent status of medicines. With each new edition, some medicines are added but others are removed. Moreover, patents have a limited term, so the number of patented medicines on the EML is not simply cumulative. Although new, patented medicines are added with each edition, at least some earlier patents expire (or are abandoned, rejected, or invalidated) between editions of the EML. But for the addition of new, more-recently patented medicines in successive editions of the EML, the percentage of medicines under patent on the EML would decline over time until eventually reaching zero.

The following **Table 2** details the changing nature of the EML for the last 5 editions of the EML, going back to 2013.

▸ **Table 2:** *Changes to Listings and Patent Status in Recent Editions of the EML*

EML Edition	Type of Change to EML Status	Numerical Result
22nd Edition, 2021	Total number of medicines added to EML	23
	Total number of medicines removed from EML	3
	Net change in size of EML	+20
	Patented medicines added to EML	4
	EML medicines no longer patented plus patented medicines removed from EML	15
	Net change in patented EML medicines	-11
	Proportion of medicines under patent as of EML publication	35/477
	Percentage of medicines under patent as of EML publication	7.3%
21st Edition, 2019	Total number of medicines added to EML	33
	Total number of medicines removed from EML	12
	Net change in size of EML	+21
	Patented medicines added to EML	17
	EML medicines no longer patented plus patented medicines removed from EML	12
	Net change in patented EML medicines	+5
	Proportion of medicines under patent as of EML publication	46/457
	Percentage of medicines under patent as of EML publication	10.1%
20st Edition, 2017	Total number of medicines added to EML	34
	Total number of medicines removed from EML	7
	Net change in size of EML	+27
	Patented medicines added to EML	11
	EML medicines no longer patented plus patented medicines removed from EML	4
	Net change in patented EML medicines	+7
	Proportion of medicines under patent as of EML publication	41/436
	Percentage of medicines under patent as of EML publication	9.4%
19th Edition, 2015	Total number of medicines added to EML	39
	Total number of medicines removed from EML	3
	Net change in size of EML	+36
	Patented medicines added to EML	16
	EML medicines no longer patented plus patented medicines removed from EML	2
	Net change in patented EML medicines	+14
	Proportion of medicines under patent as of EML publication	34/409
	Percentage of medicines under patent as of EML publication	8.3%
18th Edition, 2013	Proportion of medicines under patent as of EML publication	20/373
	Percentage of medicines under patent as of EML publication	5.4%

3. Patents and the EML: A Dynamic Relationship

The number of patented medicines on the EML is not simply cumulative, because patents have a limited term. Although new, patented medicines are added with each edition, at least some earlier patents expire between editions of the EML (and some applications are finally rejected and other patents are invalidated). But for the addition of new, more-recently patented medicines in successive editions of the EML, the percentage of medicines under patent on the EML would decline over time until reaching zero.

Moreover, patents for EML medicines are sometimes abandoned by innovators. For example, in 2020, Sanofi abandoned its patents on fexinidazole in lower income countries to facilitate access to this newly approved treatment for sleeping sickness.[12] Sanofi had worked with the Drugs for Neglected Diseases Initiative for 10 years to repurpose this drug to treat sleeping sickness and secure regulatory approval.[13] Similarly, Sanofi abandoned patents on a particular formulation and tablet coating for a rifapentine and isoniazid combination in 2020,[14] shortly before the rifapentine + isoniazid combination treatment was added to the EML with this latest 22nd Edition.

The turnover in patent status for this latest 22nd edition was relatively large, partly due to several expirations, but also due to the change to explicitly listing therapeutic alternatives. In all, 15 medicines that were patented in the 21st edition no longer count as such in the 22nd. Of these, 1 medicine was removed from the EML, 10 had patents that expired, and 4 had therapeutic alternatives listed, at least one of which was no longer under patent in lower- and middle-income countries. **Table 3** lists these changes.

▸ **Table 3:** *Medicines Counted as Patented on 21st EML That Changed Status for 22nd EML and Reason for Status Change*

Medicines Counted as Patented on 21st EML	Reason No Longer Counted as Patented on 22nd EML
Abacavir	Removed from EML
Adalimumab	At least one newly listed therapeutic alternative off patent
Bortezomib	Relevant patents expired
Budesonide + Formoterol	At least one newly listed therapeutic alternative off patent
Dabigatran	Relevant patents expired
Dasatinib	Relevant patents expired
Efavirenz	Relevant patents expired
Efavirenz + Emtricitabine + Tenofovir	At least one newly listed therapeutic alternative off patent
Emtricitabine + Tenofovir	At least one newly listed therapeutic alternative off patent
Erlotinib	Relevant patents expired
Fexinidazole	Relevant patents expired or abandoned

Medicines Counted as Patented on 21st EML	Reason No Longer Counted as Patented on 22nd EML
Lenalidomide	Relevant patents expired or abandoned
Moxifloxacin	Relevant patents expired
Telmisartan + Hydrochlorothiazide	Relevant patents expired
Trastuzumab	Relevant patents expired

Another way to illustrate the ever-changing nature of patent status on the EML is to consider the cumulative number of patented medicines added to the list versus the current number of patented medicines still on the 21st Edition of the EML. Since the 18th Edition of the EML studied by Beall and Attaran (which serves as our baseline), included 20 patented medicines, 48 patented medicines have been added to the list. However, the current number of medicines on the list is 35 due both to patents expiring and to some medicines being removed from the list.

▸ **Table 4:** *Changes in Patent Status on EML Between 18th and 22nd Editions*

Number of Patented Medicines on 18th Ed. EML 2013	Cumulative Number of Patented Medicines Added to EML Since 2013	Number of Patented Medicines on 21st Ed. EML 2019 (as of May 2020)	"Attrition" Due to Patent Expirations and List Removals
20	48	35	33

What these examples illustrate is the dynamic nature of the EML and patent status. Almost all medicines on the EML were under patent for a time when first marketed. Those patents may have expired before or after placement on the EML (or have yet to expire). Any item on the EML is subject to replacement as the standard of care advances, and a replacement may or may not still be under patent for a time.

Inevitably and eventually, today's patented EML medicines will no longer be tomorrow's patented EML medicines either due to patent expiration or replacement with another medicine as standards of care advance.

4. What Kinds of New Treatments on the EML are Patented?

The evolution of standards of care is why patented medicines are placed on the EML. Each new medicine represents an opportunity to provide a better treatment or one where none existed before, or a chance to address a new or growing public health problem. As scientific research advances, new treatments are added to the existing, wide-ranging arsenal used to combat constant health concerns such as cancer, MDRs, NCDs, and HIV/AIDS. The newest ones are still under patent.

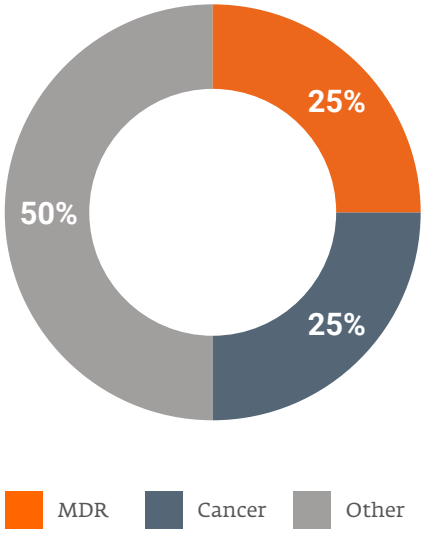
Examined in this light, it is useful to consider what the 4 newly added patented medicines on the 22nd Edition of the EML in 2021 are used to treat.

▸ **Table 5:** *Patented Additions to the 22nd EML, By Treatment Area*

Treatment	Number
Cancer	1
Dental	0
Multi-drug resistant organisms (MDRs)	1
Non-communicable diseases (NCDs) affecting the heart.	0
Hepatitis C	0
HIV/AIDS	0
Other, including parasitic infection, respiratory infection, other autoimmune diseases, or in conjunction with birth or other cancer and chemotherapy-related issues.	2*
Vaccine	0
Vitamin or mineral supplements	0

** The two medicines in this category were anti-rabies virus monoclonal antibodies; and empagliflozin (and its therapeutic equivalents), which is used to treat diabetes.*

▸ **Figure 3:** *Patented Additions to the 22nd EML, By Treatment Area*



The basic trends discussed so far only tell part of the story. Just because a medicine is subject to a patent somewhere in the world does not necessarily mean that it is patented everywhere. For some of these medicines, there are relatively few patent filings worldwide, especially in lower income countries. Moreover, there are a number of institutionalized solutions to promote greater access to these medicines. We discuss these trends in the next two sections.

3.2 EML Patent Status in Lower Income Countries

While the takeaway for policy discussions from previous studies of the patent status of medicines on the EML (Attaran 2004; Cavicchi & Kowalski 2011; Beall & Attaran 2016) has been the percentage of medicines on the EML under patent somewhere in the world, the picture is much more complex than that simple number. (As those previous studies discuss).

Just because a medicine is under patent somewhere, does not mean it is under patent everywhere. Of course, patents in some countries matter more than others – when a country does not have capacity to produce a medicine, then patent status in potential supplier countries may be of greater consequence.

We therefore consider in greater detail which medicines are patented in which countries and when those patents expire. We focused on 150 lower income countries and obtained most of our data from the Medspal online database supplemented by data from DrugPatentWatch as further explained in our methodology discussion in Appendix A.

Here are some statistics that give a view of the nature of less-than complete patent coverage of EML medicines that are under patent in at least one low- or middle-income country. Of the 150 lower income countries we examined:

▸ **Table 6:** *Volume of Active EML Patent Filings in Lower Income Countries, 22nd EML*

Volume of EML Patent Filings	Number of Countries	Percentage
None	28	19%
1 – 10	41	27%
11 – 25	46	31%
26 – 50	10	7%
51 – 100	15	10%
101 – 200	10	7%

Here are a few key facts about EML patent filings in lower income countries:

» There are about 4000 total active filings within the reviewed jurisdictions for the medicines surveyed

» A significant majority of lower income countries have 50 or fewer total active patent filings. Overall, 125 (83%) of the 150 lower income countries reviewed during this study have 50 or fewer total active patent filings.

» The five countries with the most active patent listings in order from greatest to least are China, Mexico, Turkey, the Russian Federation, and South Africa with 182, 177, 177, 161, and 148 total active patents, respectively.

Before drawing conclusions about these statistics, one arguably might also consider MPP and bilateral licenses or commitments not to enforce, which we discuss later.

Table 7 provides a more detailed summary, listed by medicine. Further details, with country-by-country breakdowns are provided in Appendix B, which is available online on the Geneva Network website[15] as well as in the version of this paper posted on scholarly databases.

The number of medicines on the EML under patent in lower income countries is down in absolute terms as well. There are now 35 medicines under patent, the lowest number since 2015.

Table 7: *Active EML Patent Filings in Lower Income Countries, Listed By Medicine, EML 22nd Edition*

Medicine	Jurisdictions with active filings	Active filings in Lower Income Countries	First expiration	Last expiration
Abacavir	2	2	2009	2023
Anti-rabies Virus Monoclonal Antibodies: 17C7 ARV Mab	6	6	2026	2026
Anti-rabies Virus Monoclonal Antibodies: Docaravimab + Miromavimab ARV Mab Cocktail	4	4	2039	2039
Aprepitant	27	29	2013	2022
Atazanavir + Ritonavir	26	49	2012	2029
Azithromycin - ophthalmologic solution	62	71	2019	2023
Bedaquiline	79	352	2023	2028
Bendamustine	22	29	2026	2029
Carbetocin	13	30	2031	2031
Cefiderocol	22	51	2028	2034
Ceftazidime + Avibactam	60	96	1999	2033
Daclatasvir	16	34	2027	2030
Dasabuvir	6	8	2028	2030
Delamanid	17	38	2023	2031
Dolutegravir	27	56	2026	2031
Dolutegravir + Lamivudine + Tenofovir	34	92	2017	2038
Empagliflozin	63	223	2025	2034
Empagliflozin Therapeutic Equivalent: Canagliflozin	44	158	2027	2031
Empagliflozin Therapeutic Equivalent: Dapagliflozin	36	100	2022	2032
Etonogestrel-Releasing Implant	10	28	2024	2026
Glecaprevir + Pibrentasvir	44	303	2030	2040
HPV Vaccine	55	75	2023	2025

Medicine	Jurisdictions with active filings	Active filings in Lower Income Countries	First expiration	Last expiration
Ibrutinib	26	169	2026	2035
Ledipasvir + Sofosbuvir	87	554	2028	2036
Levonorgestrel-Releasing Intrauterine System	6	13	2028	2028
Lopinavir + Ritonavir	14	14	2012	2029
Meropenem + Vaborbactam	17	25	2023	2031
Nilotinib	47	148	2023	2032
Nivolumab	7	15	2017	2037
Nivolumab Therapeutic Alternative: Pembrolizumab	25	41	2028	2028
Ombitasvir + Paritaprevir + Ritonavir	44	152	2012	2037
Plazomicin	14	16	2028	2028
Raltegravir	52	81	2022	2030
Ritonavir	14	24	2012	2029
Rituximab	2	2	2023	2023
Sofosbuvir	80	264	2024	2036
Sofosbuvir + Velpatasvir	83	406	2024	2037
Thalidomide	4	8	2020	2022
Tiotropium	29	74	2010	2026
Tiotropium Therapeutic Alternative: Aclidinium	25	54	2020	2030
Tiotropium Therapeutic Alternative: Glycopyrronium	7	8	2016	2028
Tiotropium Therapeutic Alternative: Umeclidinium	64	89	2025	2030

3.3 Institutionalized Access Programs and Commitments

When considering the role that patents might play with respect to access to medicines, one concern voiced by some is that the existence of a patent gives the owner pricing power. While pricing power is dependent on many factors, including the availability of therapeutic alternatives, patents can have such an effect.

In the case of patented medicines on the EML, however, patent owners often make commitments to limit their pricing power voluntarily. Medicines Patent Pool (MPP) and bilateral licenses are two ways manufacturers and NGOs are working to ensure access to already developed essential medicines in lower income and underserved countries. Likewise, endeavors such as Medicines for Malaria Venture (MMV) oversee the research and development of affordable, essential medicines. Some manufacturers even choose to sign a commitment to not enforce their IPRs for certain medicines in specific regions. These are just some of the methods used to increase access to essential medicines.

The extent of such commitments is not always well documented, but thanks largely to the MedsPal online database we were able to determine that an MPP license, bilateral license, and/or commitment to not enforce is known to exist for at least 12 of the 35 medicines currently on the EML and subject to a patent:

- Atazanavir + Ritonavir
- Bedaquiline
- Daclatasvir
- Delamanid
- Dolutegravir
- Dolutegravir + Lamivudine + Tenofovir
- Glecaprevir + Pibrentasvir
- Ledipasvir + Sofosbuvir
- Lopinavir + Ritonavir
- Ritonavir
- Sofosbuvir
- Sofosbuvir + Velpatasvir

MPP and bilateral licenses allow for the manufacture of generics to better accommodate regional medicinal needs. Approximately 25% of the nearly 4000 active filings in lower income countries are subject to an MPP license, bilateral license, and/or commitment to not enforce. In fact, all active patent filings in the surveyed jurisdictions for lopinavir+ritonavir and ritonavir are subject the commitments to not enforce.

> *A significant majority of lower income countries have 50 or fewer total active patent filings.*

Conclusion

The number of patented medicines on the EML in lower income countries fell in the most recent, 22nd edition to 35, the lowest number after steady increases across several editions of the EML. The percentage of patented medicines on the EML now stands at 7.3%.

The nature of both the EML and patent status is dynamic. With every new edition, medicines are added and removed. Meanwhile, patents expire and some may be abandoned or invalidated. This edition, the EML saw a significant drop in the number of patents, part of which can be attributed to the WHO's decision to consistently list therapeutic alternatives for the first time. Doctors and public health authorities have a clearer picture of their options for alternatives, and this paper was able to determine whether unpatented alternatives existed – which was the case in 4 instances.

A deeper dive into the data shows that many medicines are only patented in a fraction of lower income countries. Thus, 83% of lower income countries have 50 or fewer active patent filings on that ten percent. Moreover, 1/3 of these patented medicines are subject to institutionalized programs to provide access at lower cost. This paper provides an update to previous efforts to understand the nature of the EML, while expanding previous information thanks in part to the existence of new freely accessible online databases showing patent status and participation in programs to provide access.

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Endnotes

1 Mark Schultz is the Goodyear Endowed Chair in Intellectual Property Law at the University of Akron School of Law. This paper owes much to the co-authorship and research of Jaci McDole in our study of the 21st Edition of the EML. We are also grateful for the research assistance of Adam Claussen.

2 Mark Schultz & Jaci McDole, "Essential Medicines and Patents" (Geneva Network 2020) available at https://geneva-network.com/research/essential-medicines-and-patents-recent-trends-in-the-latest-editions-of-the-world-health-organization-essential-medicines-list/

3 In the interest of making a timely contribution, we forego Beal & Attaran's step of verifying patent status through contacting pharmaceutical companies. However, we were able to use the PatInformed database, which was developed by WIPO with the input of a large portion of the innovative pharmaceutical industry to perform a similar check.

4 Executive summary, The Selection and Use of Essential Medicines 2021, Report of the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines 17 (WHO 2021).

5 The WHO stated that the total number of medicines in the EML as 479, rather than 477. Executive summary, *The Selection and Use of Essential Medicines 2021, Report of the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines* 1 (WHO 2021). We very carefully compiled, reviewed, and verified every EML listing to arrive at our number. This is not the first time our count has differed from the WHO's count – it counted 460 medicines in the 2019 edition, whereas we found 457. *Ibid*. We are confident in our count and can only speculate as to the reason for the difference. It likely stems from simple differences, such as the fact that we count the entry for "sodium stibogluconate or meglumine antimoniate" as one entry, but it could be counted as two. However, it is worth noting that the WHO's executive summary of the latest, 22nd Edition mistakenly states that it added 20 drugs to the EML this year, when it in fact added 23. *Ibid*. Its listing in the executive summary clearly misses three entries: daclatasvir + sofosbuvir (as a combination therapy); isoniazid + rifapentine (as a combination therapy); and the ethinylestradiol + etonogestrel vaginal ring. *See ibid at 19*.

6 Executive summary, The Selection and Use of Essential Medicines 2021, Report of the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines 17 (WHO 2021).

7 Ibid.

8 This usage was not entirely consistent. Sometimes, instead of a square box, previous editions of the EML also used a "*" symbol to indicate therapeutic alternatives. In other instances, the EML included a "qualified" or "restricted" square box, that relied on text in the description or the original technical report recommending inclusion to specify alternatives. See Albert Figueras, on behalf of the EML Secretariat, "Review of the square box symbol uses in the 2019 WHO Model List of Essential Medicines" (WHO 2020) available at https://cdn.who.int/media/docs/default-source/essential-medicines/2021-eml-expert-committee/reviews/r.2_square-box-review-attach1.pdf

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