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Process is Due: The World Health Organization Prequalification of Medicines

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Process is Due: The World Health Organization Prequalification of Medicines

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Abstract

Process is Due: The World Health Organization Prequalification of Medicines

By: Connor Fuchs

A lack of access to essential medicines is a significant—but largely preventable—contributor to mortality, primarily in low-income countries. The World Health Organization (WHO)—through its Prequalification of Medicines Programme—prequalifies drugs that meet minimum quality standards and are used in the treatment of certain conditions, such as HIV and tuberculosis. To date, nearly all of the drugs that the WHO has prequalified have been produced in middle- and high-income countries.

Many international drug procurement entities and donors require the drugs they purchase from low- and middle-income countries be prequalified. These purchasers represent a sizeable portion of the essential medicines market. This has effectively made the Prequalification Programme a *de facto* drug approval authority for manufacturers in many low-and middle-income countries. However, there is currently no way for manufacturers to challenge a prequalification decision before an independent body.

This Comment argues that the WHO is failing to uphold customary international due process law, specifically the right to a fair trial, because it does not provide manufacturers whose products are denied prequalification or removed from the prequalification list the opportunity to challenge the decision before an independent body. It also argues that providing these manufacturers the opportunity to challenge an adverse decision is important because of the WHO's emphasis on human rights promotion and the great power the Programme holds over many manufacturers. It proposes that the WHO adopt an Independent Review Panel before which manufacturers may challenge the Prequalification Programme's decision to reject or de-list a product.

This Comment also proposes that the WHO— to facilitate the production of essential medicines in low-income countries—give manufacturers in these countries access to an additional approval pathway called "conditional prequalification." Conditional prequalification would likely provide eligible manufacturers—whose products meet a lower defined threshold of compliance with good manufacturing practices than is currently required—access to additional segments of the essential medicines market. Conditional prequalification would be contingent

upon manufacturers' adherence to a plan to achieve full compliance within a specified time period.

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INTRODUCTION

More than a quarter of the world's population lacks access to essential medicines.[1] This lack of access results in ten million preventable deaths per year—four million in Africa and South-East Asia alone.[2] One major factor contributing to this lack of access is the fact that drugs are not produced in the places where they are most needed.[3] Africa, for example, is home to a large share of the global disease burden, including 70% of the world's HIV cases and 90% of malaria deaths.[4] But, an estimated 80% or more of all pharmaceuticals in Africa are imported.[5] This misalignment can increase the cost of the drugs and leave people vulnerable to supply

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[1] Access to Med. Found., *The 2016 Access to Medicine Index: Methodology 2015* 1, 6 (2015), http://apps.who.int/medicinedocs/documents/s22176en/s22176en.pdf; Paul Hunt (Special Rapporteur on the Right to Health), *Rep. of the Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health*, U.N. Doc. A/63/263, annex, at 15 (Aug. 11, 2008).

[2] Hunt, *supra* note 1, at 15.

[3] *See* Jicui Dong & Zafar Mirza, *Supporting the Production of Pharmaceuticals in Africa*, 94 BULL. WORLD HEALTH ORG. 71, 71 (2016).

[4] *Id.*

[5] *Id.* (estimating that imported pharmaceuticals make up 79% of those consumed in Africa); Tefo Pheage, *Dying From a Lack of Medicines*, UNITED NATIONS, AFR. RENEWAL (Dec. 2016–Mar. 2017), http://www.un.org/africarenewal/magazine/december-2016-march-2017/dying-lack-medicines (estimating that 98% of pharmaceuticals consumed in Africa are produced outside of the continent).

interruptions.[6] The finished pharmaceutical products (FPPs) and active pharmaceutical ingredients (APIs) that have been prequalified by the World Health Organization (WHO) reflect this larger trend of geographic production misalignment. As of April 2015, less than 1% of prequalified FPPs[7] and no prequalified APIs were manufactured in low-income countries[8]—the countries in greatest need of these medicines.[9]

Although the goal of the WHO is not to supplant national drug regulatory authorities,[10] its Prequalification of Medicines Programme (Prequalification Program) has become the *de facto* drug approval authority for essential medicine manufacturers operating in many low- and middle-income countries (LMICs). Despite wielding this considerable authority, there is no formal independent review mechanism by which manufacturers can challenge a withdrawal[11] or denial of prequalification of their products. This lack of review raises international due process

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[6] *Id.*

[7] This Comment uses the terms "drugs" and "FPPs" interchangeably.

[8] *See* Dong and Mirza, *supra* note 3, at 71.

[9] Petra Brhlikova et al., *Aid Conditionalities, International Good Manufacturing Practice Standards and Local Production Rights: A Case Study of Local Production in Nepal*, 11 GLOBALIZATION & HEALTH 1, 4 (2015), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4470019/pdf/12992_2015_Article_110.pdf.

[10] *About Who*, WORLD HEALTH ORG. http://www.who.int/about-us (stating that the goal of Who is to "build[] a better, heathier future for people all over the world") (last visited Sept. 21, 2018).

[11] This Comment uses both "withdrawal" and "de-listing" to refer to situations in which a product's prequalification is withdrawn or cancelled.

concerns,[12] particularly a manufacturer's right to a fair trial. In addition, essential medicines[13] are overwhelmingly needed in low-income countries, but prequalified essential medicines are almost exclusively produced in middle- and high-income countries.[14] In order to remedy this misalignment, which is resulting in negative health and economic consequences, the WHO should add another prequalification pathway for manufacturers of drugs produced in low-income countries.

Prequalification is a process through which the WHO assesses and approves the product quality and manufacturing processes of (1) FPPs and (2) APIs that are used to combat priority diseases, including HIV, tuberculosis, and malaria.[15] Many international drug procurement

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[12] This Comment uses "due process" to refer specifically to procedural due process.

[13] The WHO defines essential medicines as "those that satisfy the priority health care needs of the population." *Essential Medicines,* WORLD HEALTH ORG. http://www.who.int/medicines/services/essmedicines_def/en/ (last visited Sept. 21, 2018). This definition encompasses more medicines than the ones WHO currently prequalifies. However, there is significant overlap between the two categories.

[14] Dong and Mirza, *supra* note 3, at 71.

[15] WORLD HEALTH ORG., FORTY-SEVENTH REPORT OF THE WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS: WHO TECHNICAL REPORT SERIES NO.981, at 28 (2013) [hereinafter WHO EXPERT COMMITTEE REPORT NO. 981]. The Prequalification of Medicines Program also involves the review and approval of "quality control laboratories." *Id.* at 30. Although the quality control laboratories are important, this Comment will focus only on the prequalification of FPPs and APIs.

entities and donors, including U.N. agencies, only purchase medicines for priority diseases that have been prequalified by the WHO or another "stringent regulatory authority."[16] These procurement agencies do not currently consider any drug regulatory authorities in LMICs to be "stringent."[17] Thus, gaining the WHO prequalification stamp of approval is effectively the only

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[16] SKHUMBUZO NGOZWANA ET AL., AFRICAN UNION, PHARMACEUTICAL MANUFACTURING PLAN FOR AFRICA: BUSINESS PLAN 1, 32 (2012) ("Without exception, [international donor entities and non-governmental organizations] require that products be prequalified by WHO or approved by a stringent regulatory authority.").

[17] Generally, the definition of "stringent regulatory authority" only includes authorities that participate in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), as well as special regulatory schemes found in Canada, the European Union, or the United States; members of the ICH currently include the United States, the European Union, some European countries, Japan, and Australia. *See, e.g.* THE GLOBAL FUND TO FIGHT AIDS, TUBERCULOSIS, AND MALARIA, GUIDE TO GLOBAL FUND POLICIES ON PROCUREMENT AND SUPPLY MANAGEMENT OF HEALTH PRODUCTS 15 (2017); UNITAID, QUALITY ASSURANCE OF HEALTH PRODUCTS 2 n.6 (2017). The WHO uses a nearly identical definition of stringent regulatory authority. *See Clarification with Respect to a Stringent Regulatory Organization as Applicable to the Stringent Regulatory Authority (SRA) Guideline*, WORLD HEALTH ORG., 1 (Feb. 15, 2017), https://extranet.who.int/prequal/sites/default/files/documents/75%20SRA%20clarification_February2017_0.pdf.

way for manufacturers in LMICs to sell their products to international drug procurement entities and donors—a large and profitable share of the essential medicines market in these countries.[18]

The evidence indicates that compliance with the WHO's Good Manufacturing Practices (GMPs)—a pre-requisite for prequalification—is particularly challenging for manufacturers based in low-income countries because of financial constraints, a lack of technical expertise, and inconsistent or non-existent enforcement of GMP standards by national regulatory authorities.[19] This lack of enforcement allows manufacturers who do not comply with stringent GMPs to continue to operate, but results in an exclusion from the international donor market.[20]

The lack of access to quality-assured essential medicines is responsible for the deaths of millions of people each year.[21] Individuals in low-income countries disproportionately succumb to diseases that can be easily treated with timely access to quality medicines.[22] In 2015, an estimated 1.6 million people in Africa alone died from malaria, tuberculosis, and HIV-related

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[18] *See, e.g.*, NGOZWANA ET AL. *supra* note 16, at 32 ("The majority of the market for [anti-retrovirals] is controlled by the international donor entities and Non Governmental Organisations (NGOs).").

[19] *See* WORLD HEALTH ORG., ASSESSMENT OF MEDICINES REGULATORY SYSTEMS IN SUB-SAHARAN AFRICAN COUNTRIES: AN OVERVIEW OF FINDINGS FROM 26 ASSESSMENT REPORTS 16 (2010); Brhilkova et al., *supra* note 9, at 9.

[20] Brhilkova et al., *supra* note 9, at 9.

[21] Hunt, *supra* note 1, at 15; Pheage, *supra* note 5.

[22] *See* Pheage, *supra* note 5.

illnesses.[23] This lack of access has been driven by a host of factors, including unaffordable drug prices and an inadequate supply of medicines.[24] Strategies to address these challenges include the proliferation of low-cost generic medicines, as well as a strengthening of the domestic pharmaceutical manufacturing industries in countries with the highest disease burdens.[25]

Given the Prequalification Program's approval authority, the WHO possesses great power over both consumers and drug manufacturers in low-income countries. On the one hand, the WHO performs an essential role in countries with weak regulatory authorities, protecting consumers from the dangers of substandard medicines.[26] But, on the other hand, the WHO is failing to uphold customary international due process principles, specifically the right to a fair trial, because it does not allow manufacturers whose products are denied prequalification or de-listed an opportunity to challenge these decisions. Similarly, by failing to give manufacturers a

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[23] *Id.*

[24] MARGARET CHAN, TEN YEARS IN PUBLIC HEALTH: 2007–2017, at 14–15 (2017).

[25] *See, e.g.*, NGOZWANA ET AL., *supra* note 16*,* at 6; Frederick M. Abbott & Jerome H. Reichman, *The Doha Round's Public Health Legacy: Strategies for the Production and Diffusion of Patented Medicines Under the Amended TRIPS Provisions*, 10 J. INT'L ECON. L. 921, 977–79 (2007); Kinsley Rose Wilson et al., *The Make or Buy Debate: Considering the Limitations of Domestic Production in Tanzania*, 8 GLOBAL HEALTH 1, 1–2, (June 29, 2012).

[26] Ellen F.M. 't Hoen et al., *A Quiet Revolution in Global Public Health: The World Health Organization's Prequalification of Medicines Programme*, 35 J. PUB. HEALTH POL'Y 137, 154 (2014).

way of challenging a denial or de-listing, the WHO is ignoring its immense power and deviating from its role as a promoter of human rights.[27]

Customary international law refers to rules that emanate from the "general and consistent practice of states", which are followed out of "a sense of legal obligation."[28] Customary international law is binding on international organizations, such as the WHO, as well as states.[29] Specifically, customary international law obligates international organizations that are performing a governmental or quasi-governmental function to provide persons whose rights and freedoms may be infringed an opportunity to be heard before an independent and impartial tribunal.[30] Here, the WHO—through the Prequalification Program—is performing a governmental function in deciding to grant, deny, or withdraw a product's prequalification. Additionally, an adverse decision implicates manufacturers' cognizable right to engage in commercial activity, particularly because of these decisions' large economic implications. [31]

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[27] *See supra* note 10 and accompanying text.

[28] RESTATEMENT (THIRD) OF THE FOREIGN RELATIONS LAW OF THE UNITED STATES § 102(2) (AM. LAW INST. 1987).

[29] *See* Lisa Clarke, *Responsibility of International Organizations Under International Law for the Acts of Global Health Public-Private Partnerships*, 12 CHI. J. INT'L L. 55, 73 (2011); *infra* Section II.A.

[30] *See* Bardo Fassbender, *Targeted Sanctions Imposed by the UN Security Council and and Due Process Rights*, 3 INT'L ORGS. L. REV. 437, 445–46 (2006).

[31] *Infra* Section II.B.

This Comment argues that the WHO should implement a two-part solution to protect and advance international due process principles and to spur the production of pharmaceuticals in low-income countries. First, the WHO should introduce an Independent Review Panel, comprised of independent subject matter experts from geographically and economically diverse regions. Giving manufacturers whose products are either denied prequalification or de-listed the opportunity to contest such a ruling before this panel would bring the Prequalification Program into compliance with international procedural due process principles. This Comment argues that the introduction of this review mechanism would also comport with WHO's emphasis on human rights promotion and the Prequalification Program's immense authority. The introduction of an Independent Review Panel would bring practical benefits, such as improving the accuracy of a prequalification decision, increasing the accountability of the Prequalification team, and increasing manufacturer confidence in, and respect for, prequalification decisions.

Second, this Comment argues that the WHO should institute a procedure that enables manufacturers in lower-income countries[32] to have their drugs "conditionally" prequalified, based on a lower defined threshold of compliance with WHO GMPs than is currently required. The still relatively high level of compliance, coupled with additional oversight, would be a practical way to increase the supply of quality-assured drugs produced in low-income countries.

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[32] This Comment uses "lower-income countries" to refer to those countries whose gross national income per capita is below or equal to $1,580 in 2017. Manufacturers in these lower-income countries would be eligible for "conditional prequalification." As will be discussed, *infra* Section III.B., "lower-income countries" encompasses all low-income countries and the poorest middle-income countries, as defined by the World Bank.

The prequalification would be "conditional" because manufacturers' approval for a drug would be contingent upon their adherence to a WHO-approved plan that leads to full GMP compliance within a specified time period. Conditional prequalification has the potential to increase the supply of—and subsequent access to—essential medicines, help develop the pharmaceutical industries in lower-income countries, bring economic benefits to these countries, and incentivize manufacturers in lower-income countries to fully comply with WHO GMPs.

This Comment begins with an overview of the Prequalification Program's procedures and the important role the Program plays in providing people in LMICs access to high-quality essential medicines. Part I also lays out the challenges, including GMP compliance, that manufacturers in low-income countries face when attempting to have their products prequalified. Part II discusses procedural due process under international law and concludes that the WHO should allow its decisions to be reviewed by an independent and impartial body. Part III examines the review mechanism of another international organization—the World Bank's Inspection Panel, which offers lessons on how to structure the proposed Prequalification Independent Review Panel. Part IV sets forth the suggested Prequalification Independent Review Panel, as well as the conditional prequalification proposal for manufacturers in lower-income countries. This Comment concludes by suggesting that these proposed changes would lead to substantial health, economic, and institutional gains.

I. ACCESS TO ESSENTIAL MEDICINES AND PREQUALIFICATION

Improving access to high-quality essential medicines has occupied a central role on the international development agenda for at least the last roughly two decades.[33] Despite significant progress over the last forty years,[34] far too many lives are still lost due to a lack of timely access to effective and affordable drugs for preventable or treatable diseases.[35] In response to concerns about the quality of essential medicines that international donors and drug procurement entities

[33] *See* G.A. Res. 55/2, United Nations Millennium Declaration, ¶ 20 (Sept. 8, 2000) ("We also resolve . . . [t]o encourage the pharmaceutical industry to make essential drugs more widely available and affordable by all who need them in developing countries."); G.A. Res. 70/1, Transforming our World: The 2030 Agenda for Sustainable Development, at 16 (Oct. 21, 2015) (Goal 3.8: "Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all."); *Id.* at 16–17 (Goal 3.b: [P]rovide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the TRIPS Agreement and Public Health . . . .").

[34] It is estimated that the fraction of people globally without access to life-saving medicines decreased from "less than one-half of the world's population" in 1975 to about one-third in 1999. WORLD HEALTH ORG., THE WORLD MEDICINES SITUATION 61 (2004).

[35] *See* Hunt, *supra* note 1, at 15; Pheage, *supra* note 5.

were purchasing, U.N. partners created the Prequalification of Medicines Programme in 2001.[36] Since that time, the Prequalification Program's role and influence has increased dramatically.

A. *Strategies for Increasing Access to Quality Essential Medicines*

Two of the most prominent strategies to increase access to quality essential medicines are ensuring greater supply of generic medicines and increasing the production of drugs—typically generics—in the countries where they are most needed. Affordability is a critical component of access.[37] The WHO has recognized that generic medicines play an important role in making medicines more affordable.[38] The manifestation of this strategy can be seen in the WHO's Essential Medicines List, which serves as the basis for many national essential medicines lists.[39] About ninety-five percent of the medicines on the latest WHO list are generic products.[40]

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[36] A.J. van Zyl, *WHO Prequalification of Medicines Programme*, 25 WHO DRUG INFO. 231, 231 (2011).

[37] U.N. MDG GAP TASK FORCE, DELIVERING ON THE GLOBAL PARTNERSHIP FOR ACHIEVING THE MILLENNIUM DEVELOPMENT GOALS 35 (2008).

[38] *Id.* at 41.

[39] REED F. BEALL, PATENTS AND THE WHO MODEL LIST OF ESSENTIAL MEDICINES (18th ed.): CLARIFYING THE DEBATE ON IP AND ACCESS 1 fig.1 (2016).

[40] *Id.* at 2.

Generic drugs are "identical—or bioequivalent—to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use."[41] Generics are legally marketed and sold after the expiry of any patent and market exclusivities on the pioneer drug, or under a voluntary or compulsory license from the manufacturer of the pioneer product.[42]

Generics are almost always cheaper than their brand-name equivalents because of the lower upfront research and development costs borne by manufacturers, as well as the greater market competition that normally follows the introduction of generic medicines.[43] To gain approval in many regulatory systems, including the WHO's Prequalification Program, generic drug manufacturers are not required to replicate the costly and time-consuming animal and human clinical studies required of pioneer drugs.[44] They must simply demonstrate that the

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[41] Rafael Alfonso-Cristancho et al., *Definition and Classification of Generic Drugs Across the World*, 13 (Supp. 1) APPLIED HEALTH & ECON. HEALTH POL'Y 5, 6 (2015) (citing the United States Food & Drug Administration's definition).

[42] *See* WORLD TRADE ORG., TRIPS AND PHARMACEUTICAL PATENTS 7 (2006), https://www.wto.org/english/tratop_e/trips_e/tripsfactsheet_pharma_2006_e.pdf.

[43] U.N. MDG GAP TASK FORCE, *supra* note 37 at 41; *Generic Drug Facts*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/GenericDrugs/ucm167991.htm (last updated June 4, 2018).

[44] *See, e.g.*, World Health Org., *Generic Medicines*, 30 WHO DRUG INFO. 370, 370–71 (2016); *Generic Drug Facts*, *supra* note 43.

generic product provides the same clinical benefits to humans as an already approved drug.[45] In addition, once applicable patent and market exclusivities on a brand-name drug expires, multiple generic drugs are often introduced into the marketplace within a short time frame, typically resulting in increased competition and lower costs.[46] One notable exception to the entry of multiple generics is for drugs intended to treat rare conditions, for which there is a small market.[47]

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[45] *Generic Drug Facts*, *supra* note 43. Demonstrating bioequivalence typically requires human trials, but only in about twenty-four to thirty-six individuals, compared to the hundreds or thousands of human subjects required in the clinical trials of pioneer drugs. *FDA Ensures Equivalence of Generic Drugs,* U.S. FOOD & DRUG ADMIN., https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm134444.htm (last updated Dec. 4, 2017).

[46] *Generic Drug Facts*, *supra* note 43.

[47] *See, e.g.*, Andrew Pollack, *Drug Goes From $13.50 a Tablet to $750, Overnight*, N.Y. TIMES (Sep. 20, 2015), https://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html (describing the lack of competition (and large price increases) surrounding a 62-year old drug, Daraprim—for which there were no effective patents or exclusivities—used to treat a rare condition, toxoplasmosis).

Another strategy to increase access to essential medicines is through the expansion of the domestic pharmaceutical manufacturing capacity in countries with the highest disease burden.[48] The African Union[49] has strongly endorsed this strategy:

> [T]he development of the sector will provide a basis for sustainable treatment programmes as the contribution that donors can make plateaus or even begins to diminish. The sector can also make a contribution to economic growth through enhanced exports, increased intra-African trade, emergence of supportive industries and the reduced reliance on imports that use up precious hard currency and for which only limited regulatory oversight by our national regulatory authorities is possible.[50]

However, for the benefits of affordable essential medicines to be realized, the drugs produced domestically must be of an acceptable quality. Ensuring adequate quality has proven to be incredibly challenging, with some experts labeling the problem of substandard medicines a potential "public-health crisis."[51] Substandard medicines "are authorized medical products that

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[48] *See, e.g.*, NGOZWANA ET AL., *supra* note 16, at 6; Abbott & Reichman, *supra* note 25, at 977–79; Wilson et al., *supra* note 25, at 2.

[49] The African Union is an intergovernmental organization comprised of 55 member states. *Member State Profiles*, AFR. UNION, https://au.int/memberstates (last visited Sept. 22, 2018). Its vision is "[a]n integrated, prosperous and peaceful Africa, driven by its own citizens and representing a dynamic force in global arena." *Vision and Mission*, AFR. UNION, https://au.int/en/about/vision (last visited Sept. 22, 2018).

[50] NGOZWANA ET AL., *supra* note 16, at 6.

[51] Atholl Johnston & David W. Holt, *Substandard Drugs: A Potential Crisis for Public Health*, 78 BRITISH J. CLINICAL PHARMACOLOGY 218, 218 (2014).

fail to meet either the quality standards or their specifications, or both."[52] Substandard medicines do not include deliberately counterfeit drugs.

People living in LMICs are particularly vulnerable to being supplied substandard drugs.[53] The drug regulatory authorities in many LMICs lack the necessary resources and capacity to vigilantly monitor the quality of drugs within their territory.[54] For example, it is estimated that 34% of drugs in Sub-Saharan African are substandard or counterfeit.[55] The conditional prequalification proposal, as well as the Independent Review Panel to a lesser extent, would help alleviate these dual concerns of supply and quality by stimulating the production of quality-assured essential medicines in lower-income countries. Increasing access to quality-assured essential medicines continues to be a challenging, but critically important, task.

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[52] World Health Org. Res. 70/23, annex, at 34 (Mar. 20, 2017).

[53] Johnston & Holt, *supra* note 51, at 229 (noting that patients may also be supplied substandard medicines in developed countries, but at a very low rate).

[54] Raffaella Ravinetto et al., Commentary, *Fighting Poor-Quality Medicines in Low- and Middle-Income Countries: The Importance of Advocacy and Pedagogy*, 9 J. PHARMACEUTICAL POL'Y & PRAC. 1, 2 (2016).

[55] Tariq Almuzaini et al., *Substandard and Counterfeit Medicines: A Systematic Review of the Literature*, 3 BMJ OPEN 1, 4 (2013).

B. *Prequalification Process*

Recognizing the significant risk that substandard medicines pose, U.N. partners established the Prequalification Program as a pilot project in 2001.[56] At the time (and still to this day), most generic drugs used in LMICs were manufactured in India.[57] However, international procurement entities had reservations about whether the Indian drug regulatory authorities were able to adequately assess the quality of these generic drugs.[58] These concerns were further elevated by the recognition that low-cost, quality-assured generic drugs were needed to combat the HIV/AIDS epidemic.[59] Largely in response to these developments, WHO Member States asked the organization to assess the quality of medicines, so that international procurement

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[56] van Zyl, *supra* note 36, at 231. The Program was initiated by the Interagency Pharmaceutical Coordination Group, a group of senior pharmaceutical advisors from U.N. agencies including the WHO and other international organizations (such as the African Development Bank and the Global Fund to Fight AIDS, Tuberculosis, and Malaria), who meet every six months to better coordinate their pharmaceutical policies and the technical advice they give. *The Interagency Pharmaceutical Coordination Group*, WORLD HEALTH ORG., https://www.who.int/medicines/areas/policy/ipc/en/ (last visited Sept. 22, 2018).

[57] 't Hoen, et al., *supra* note 26, at 138.

[58] *Id.*

[59] *Id.* at 142; *see also* WORLD HEALTH ORG., WHO PREQUALIFICATION: PROGRESS REPORT 1 (2013).

entities could ensure the drugs they purchased met recognized standards of quality.[60] In March 2001, the Prequalification of Medicines Programme was launched, initially as a pilot project.[61]

The Prequalification Program is technically a U.N. program that the WHO administers.[62] The purpose of the Prequalification Program has remained the same during its relatively brief history: "to assess the quality, safety, and efficacy of medicinal products."[63] However, the types of medicines it prequalifies has expanded. Initially, the WHO only prequalified FPPs used to treat HIV/AIDS, tuberculosis, and malaria. Now, hepatitis C medications, zinc, and products used for reproductive health are also eligible for prequalification.[64] A FPP—as the name implies—is the "finished dosage form of a pharmaceutical product, which has undergone all

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[60] 't Hoen, et al., *supra* note 26, at 138.

[61] The Interagency Pharmaceutical Coordination Group, *Ten Years of IPC: Report on Achievements 1996–2006*, WHO 1, 3 (2007), www.who.int/medicines/publications/IPC_En.pdf.

[62] WHO EXPERT COMMITTEE REPORT NO. 981, *supra* note 15, at 28.

[63] *Prequalification of Medicines by WHO*, WORLD HEALTH ORG., (Jan. 31, 2013) http://www.who.int/news-room/fact-sheets/detail/prequalification-of-medicines-by-who.

[64] *Id.*; *In the Lead-Up to Paris AIDS Conference, WHO Prequalifies First Generic Hepatitis C Medicine and First HIV Self-Test*, WORLD HEALTH ORG., http://www.who.int/medicines/news/2017/1st_generic-hepC_1stHIVself-test-prequalified/en/ (last visited Sept. 24, 2018). Zinc is used in the treatment of children with acute diarrhea. *Prequalification of Medicines by WHO*, supra note 63.

stages of manufacture, including packaging in its final container and labelling."[65] In October 2010, the WHO began prequalifying APIs.[66] An API is the biologically active ingredient in a drug that is intended to have a "direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to have direct effect in restoring, correcting or modifying physiological functions in human beings."[67]

There are five general components of the Prequalification process: (1) invitation, (2) dossier submission, (3) assessment, (4) site inspection, and (5) decision.[68] First, the WHO, Joint United Nations Programme on HIV and AIDS, United Nations Children's Fund, and UNITAID[69] invite all interested manufacturers to submit an expression of interest for specified medications.[70] Second, interested manufacturers may submit comprehensive data—called the dossier—on the

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[65] WORLD HEALTH ORG., FORTY-FIFTH REPORT OF THE WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS: WHO TECHNICAL REPORT SERIES NO.961, at 375 (2011) [hereinafter WHO EXPERT COMMITTEE REPORT NO. 961].

[66] WHO EXPERT COMMITTEE REPORT NO. 981, *supra* note 15, at 28.

[67] WHO EXPERT COMMITTEE REPORT NO. 961, *supra* note 65, at 374–75.

[68] *Prequalification of Medicines by WHO*, *supra* note 63.

[69] "Unitaid is an international organisation that invests in innovations to prevent, diagnose and treat HIV/AIDS, tuberculosis and malaria more quickly, affordably and effectively . . . . Unitaid is a hosted partnership of the World Health Organization." *About Us*, UNITAID, (last visited Sept. 24, 2018), https://unitaid.eu/about-us/#en.

[70] *Prequalification of Medicines by WHO*, *supra* note 63.

specified pharmaceutical product.[71] The dossier includes data on the purity of ingredients in the product, the stability of the product, clinical data, and product samples that allow for chemical and pharmaceutical analysis.[72] Third, the submitted dossier is evaluated by a group of experts from the WHO and national regulatory authorities that the WHO appoints.[73] Fourth, following the review of submitted data, inspectors visit manufacturing sites to check compliance with WHO GMPs.[74] The inspection team is made up of experts appointed by the WHO, preferably from national regulatory authorities, and coordinated and led by a WHO staff member.[75] Compliance with the GMPs is a particularly challenging step of the Prequalification process for manufacturers and will be discussed in more detail below.[76] Finally, the Prequalification Program renders a decision on whether to include the FPP or API on its respective prequalified list.[77] Marketing approval from the national regulatory authority in the country of manufacture is

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[71] *Id.*

[72] WHO EXPERT COMMITTEE REPORT NO. 961, *supra* note 65, at 380; *Prequalification of Medicines by WHO*, *supra* note 63.

[73] WHO EXPERT COMMITTEE REPORT NO. 961, *supra* note 65, at 381; *Prequalification of Medicines by WHO*, *supra* note 63.

[74] *Id.*

[75] WHO EXPERT COMMITTEE REPORT NO. 961, *supra* note 65, at 382.

[76] *Infra* Section I.E.

[77] *Prequalification of Medicines by WHO*, *supra* note 63.

a pre-condition for WHO Prequalification.[78] However, national regulatory authorities in many LMICs are underfunded and lack the technical capacity to enforce stringent standards.[79]

Manufacturers whose drugs achieve prequalification must submit data and information for re-qualification every five years or as requested by the Prequalification Program.[80] The WHO also inspects manufacturers' facilities "at least once every three years."[81] If a prequalified product is found to be non-compliant with prequalification standards, the WHO may suspend or remove the product (and manufacturing sites) from the list of prequalified products.[82] A manufacturer may also voluntarily withdraw its product from the WHO Prequalification list.[83]

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[78] UNITED NATIONS CONFERENCE ON TRADE & DEVELOPMENT, LOCAL PRODUCTION OF PHARMACEUTICAL AND RELATED TECHNOLOGY TRANSFER IN DEVELOPING COUNTRIES: A SERIES OF CASE STUDIES BY THE UNCTAD SECRETARIAT 250 (2011).

[79] Sten Olsson et al., *Pharmacovigilance Activities in 55 Low- and Middle-Income Countries: A Questionnaire-Based Analysis*, 33 DRUG SAFETY 689, 691 (2010) (finding that only 47% of countries surveyed reported having "a budget for pharmacovigilance activities"); *Infra* Section I.E.

[80] WHO EXPERT COMMITTEE REPORT NO. 961, *supra* note 65, at 386.

[81] *Id.*

[82] *Id.* at 386–87.

[83] *See*, *e.g.*, Fiona Fleck, *Ranbaxy Withdraws All of Its AIDS Drugs From WHO List*, 329 BRITISH MED. J. 1205, 1205 (2004) ("Ranbaxy, an Indian generic drug company, has withdrawn all of its AIDS medicines from the World Health Organization's list of recommended drugs, not

If a manufacturer's drug is de-listed from the prequalified list or denied prequalification, there is no formal way to challenge that decision before an independent and impartial review body. As will be discussed in Part II, this lack of an independent review body raises serious concerns about whether the WHO is adhering to international procedural due process principles. The proposed Independent Review Panel would bring the WHO into compliance with these principles. However, there are currently two stages of the prequalification process that involve some kind of informal review. The first opportunity is after the applicant's dossier has been assessed. The applicant may "request a hearing or meeting" with the team that reviewed its dossier in order to clarify any identified issues.[84] The other opportunity is following the site visit after the WHO issues an inspection report to the manufacturer that details the findings from its visit.[85] WHO guidance states that any disagreements between the applicant manufacturer and the WHO are resolved according to a standard operating procedure.[86] However, this standard operating procedure is not publicly available.[87]

A 2010 survey conducted by the WHO Prequalification team revealed that manufacturers who had previously had at least one product prequalified were generally not satisfied with the

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because they are unsafe or of poor quality, but because they may not be as effective as they should be, a spokeswoman for WHO said.").

[84] WHO EXPERT COMMITTEE REPORT NO. 961, *supra* note 65, at 381.

[85] *Id.* at 383.

[86] *Id.*

[87] The fact that the standard operating procedures are not publicly available raises its own set of concerns that are beyond the purview of this Comment.

Program's problem resolution mechanisms.[88] Overall, the Prequalification assessors and inspectors were meeting or exceeding these manufacturers' expectations for service delivery.[89] But, manufacturers identified several areas in which they felt the Prequalification Program was coming up short, including "[q]uestion/problem resolution during assessment, . . . [o]pportunities for in-person communication during the assessment process, . . . [c]onsistency of membership in the team of assessors throughout the process, . . . [and l]ocal/national representation in on-site inspection teams."[90] It should be emphasized that respondents in this survey were limited to those who had at least one product prequalified.[91] To gain a more complete view of manufacturers' opinions of the Prequalification Program, it would be necessary to survey manufacturers who have applied for, but never prevailed in, having a drug prequalified; unfortunately, this information is currently unavailable. The WHO states that the results of this survey would be used to improve the current Program, an important goal given the great influence the Program has in many LMICs.[92]

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[88] *See* World Health Org., *WHO Prequalification Programmes*, 24 WHO DRUG INFORMATION 293, 296 (2010).

[89] *Id.*

[90] *Id.*

[91] *Id.*

[92] *Id.* at 293.

C. *Prequalification Program: The Developing World's Drug Approval Agency*

The WHO—through its Prequalification Program—has in many ways become the *de facto* drug approval authority in many LMICs. The governments of LMICs often use the WHO's list of prequalified medicines to guide their decisions on which medicines to purchase.[93] Some African drug authorities, in particular, have used WHO prequalification as a proxy in their own drug assessment and approval processes.[94] Similarly, large drug procurement entities—including U.N. agencies and the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund)—require the drugs they purchase from LMIC-based manufacturers to be prequalified, except in very limited circumstances.[95]

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[93] *WHO Prequalification Financing Model-Questions and Answers*, WORLD HEALTH ORG., http://who.int/medicines/news/prequal_finance_model_q-a/en/ (last visited Sept. 25, 2018).

[94] Mary Moran et al., *Registering New Drugs for Low-Income Countries: The African Challenge*, 8 PLOS MED. 1, 3 (2011).

[95] *See Procurement Agencies*, WORLD HEALTH ORG., https://extranet.who.int/prequal/information/medicines-purchasing-organizations (last visited Sept. 25, 2018); *Sourcing and Management of Health Products, Medicines*, THE GLOBAL FUND, https://www.theglobalfund.org/en/sourcing-management/quality-assurance/medicines/ (last visited Sept. 25, 2018) ("[I]mplementing Principal Recipients have three options when selecting which antiretrovirals, antituberculosis medicines and antimalarial medicines to purchase. They can choose medicines that have been either: 1. Prequalified by the World Health Organization Prequalification Programme; 2. Authorized for use by a Stringent Drug Regulatory Authority; 3.

These actors—LMIC governments, international donors, and international drug procurement agencies—represent a substantial portion of the market for medicines, particularly essential medicines, in LMICs.[96] Unfortunately, pinpointing the precise share of the essential medicines market that these actors occupy is not currently possible "due to a lack of comparable data on pharmaceutical expenditures" in many LMICs.[97] Data from 2006 indicated that public expenditures represented 23.1% of total pharmaceutical spending in low-income countries and 33.5% in LMICs.[98] The report, however, cautions that the low-income numbers do not capture the spending of international donors and drug procurement entities, such as U.N. agencies, the Global Fund, or the United States President's Emergency Plan for AIDS Relief (often referred to

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Recommended for use by the Expert Review Panel."). The Global Fund Expert Review Panel is only an option in the rare circumstance when "only one or no product is available on the global market . . . ." *Id.* Additionally, no drug authorities in LMICs currently qualify as "stringent." *See* discussion, *supra* note 17.

[96] *See* NGOZWANA ET AL., *supra* note 16, at 32.

[97] YE LU ET AL., WORLD HEALTH ORG., THE WORLD MEDICINES SITUATION 2011: MEDICINE EXPENDITURES 2 (2011); *see also* MANJIRI BHAWALKAR & ABEBA TADDESE, GUIDE TO TRACKING PHARMACEUTICAL EXPENDITURES IN A HEALTH SYSTEM 1 (2014) (noting that a lack of uniform methodology for collecting detailed pharmaceutical expenditure data in LMICs inhibits comparisons of pharmaceutical expenditures between countries).

[98] LU ET AL., *supra* note 97, at 7 tbl.1.2.

by its acronym: PEPFAR).[99] International donors and procurement entities, alone, purchase billions of dollars' worth of medication annually for distribution in low-income countries.[100] The Prequalification Program stamp of approval is therefore critical for many LMIC-based drug manufacturers' profitability and sustainability.

D. *Left Out: Drug Manufacturers in Low-Income Countries*

Although critically important, it has been nearly impossible for drug manufacturers in low-income countries to get their products prequalified. In April 2015, only three out of 419 WHO prequalified FPPs, and none of the prequalified APIs were produced by a manufacturer in a low-income country.[101] The results of a 2012 study examining all of the generic FPP and API dossiers—from both low-income and non-low-income countries—that had been submitted for

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[99] *See id.* at 7 n.1. The amount of money these donors and procurement entities spend on pharmaceuticals increased significantly after 2006. *Id.* Between fiscal years 2005 to 2011, the congressionally-funded PEPFAR program purchased more than $1.2 billion in antiretroviral drugs to treat those infected with with HIV. U.S. GOV'T ACCOUNTABILITY OFF., GAO-13-483, PRESIDENT'S EMERGENCY PLAN FOR AIDS RELIEF: DRUG SUPPLY CHAINS ARE STRONGER, BUT MORE STEPS ARE NEEDED TO REDUCE RISKS 1 (2013).

[100] *Prequalification of Medicines by WHO*, *supra* note 63.

[101] Brhlikova et al., *supra* note 9, at 4. Of the 419 FPPs, 119 were produced in high-income country manufacturers while 297 were produced by middle-income country manufacturers. *Id.* Of the prequalified APIs, three were produced by high-income country manufacturers and 75 were produced by middle-income manufacturers. *Id.*

Prequalification between 2007 and 2010 provides an interesting contrast.[102] The authors—primarily WHO Prequalification officials—found that of the 178 dossiers accepted for review,[103] 60 (33.7%) had been prequalified as of December 2011, while 54 (30.33%) had been cancelled or withdrawn.[104] The remaining 64 dossiers were presumably still under assessment at the time of the study.

Although the data from these two studies do not reveal whether manufacturers from low-income countries are applying for prequalification and getting rejected or simply not applying, they do reveal three important trends. First, the numbers unequivocally demonstrate that the medicines being prequalified are not being produced in the low-income countries they are often destined for. Second, they show that the large international donor and national LMIC market is out of reach for current and potential manufacturers of essential medicines who are based in low-income countries. Finally, they suggest that the WHO's strategy of increasing the manufacturing capacity in countries with the highest disease burden is largely failing.

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[102] Wondiyfraw Z. Worku et al., *Deficiencies in Generic Product Dossiers as Submitted to the WHO Prequalification of Medicines Programme*, 9 J. GENERIC MEDS. 63, 64 (2012).

[103] *Id.* at 63, 65. 245 dossiers had been submitted, but 45 (18%) were rejected either because "the product was not invited to the programme or later due to the applicant's failure to respond to the PQP queries in a timely fashion (maximum 1 year)." *Id.* at 67.

[104] *Id.* at 72. One notable finding is that HIV dossiers contained substantially less deficiencies than did tuberculosis, malaria, and reproductive health dossiers for both FPPs and APIs. *Id.* at 73.

E. *Good Manufacturing Practices Pose a Particular Challenge for Manufacturers in Low-Income Countries*

The limited available evidence indicates that compliance with GMPs poses a particular challenge for drug manufacturers in low-income countries.[105] GMPs are used by the Prequalification Program, as well as national regulatory agencies,[106] "to ensure the quality, safety and efficacy" of medicines.[107] GMPs prescribe minimum standards with which manufacturers must comply throughout every stage of the manufacturing process.[108] At the national and Prequalification levels, GMPs are enforced by making compliance a precondition to market entry and prequalification, respectively.[109] If detected and enforced, failure to comply with GMPs may

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[105] Brhlikova et al., *supra* note 9, at 9.

[106] WORLD HEALTH ORG., *WHO Prequalification of Medicines Programme: WHO launches the PQD Collaborative Registration Procedure*, 27 WHO DRUG INFO., 325, 325 (2013).

[107] *See e.g.,* WORLD HEALTH ORG., FORTY-EIGHTH REPORT OF THE WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS: WHO TECHNICAL REPORT SER. NO.986, at 90 (2014) [hereinafter WHO EXPERT COMMITTEE REPORT NO. 986].

[108] *Id.*

[109] *See, e.g.,* U.S. Dep't of Health and Human Services, *Current Good Manufacturing Practice (CGMP) Regulations*, U.S. FOOD & DRUG ADMIN. (last updated Mar. 30, 2018), https://www.fda.gov/Drugs/ DevelopmentApprovalProcess/Manufacturing/ucm090016.htm; *Prequalification of Medicines by WHO*, *supra* note 63.

result in the denial or withdrawal of a drug's marketing authorization.[110] GMPs are aimed at ensuring "products are consistently produced and controlled according to the quality standards appropriate to their intended use and . . . managing and minimizing the risks inherent in pharmaceutical manufacture. . . ."[111]

Pharmaceutical regulators and industry groups in more than 100 countries—primarily LMICs—use the WHO's GMPs.[112] However, manufacturers in low-income countries generally do not comply with GMPs at a level that would allow the drugs they produce to be prequalified.[113] This is due in part to manufacturers lacking the requisite financial resources and technical expertise, as well as operating in countries with weak national medical regulatory

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[110] *See, e.g., Current Good Manufacturing Practice (CGMP) Regulations*, *supra* note 109; *Prequalification of Medicines by WHO*, *supra* note 63.

[111] *Id.*

[112] JOSEPH D. NALLY, *Worldwide Good Manufacturing Practices*, *in* GOOD MANUFACTURING PRACTICES FOR PHARMACEUTICALS, 335, 339 (Joseph D. Nally, ed., 6th ed. 2007).

[113] *See, e.g.,* WORLD HEALTH ORG., *supra* note 19, at 16, 21; Brhlikova et al., *supra* note 9, at 8 ("Domestic producers report that compliance with the stringent standards of GMP is a major obstacle for domestic production of affordable pharmaceutical products."). The WHO conducted an assessment of the regulatory systems in twenty-six Sub-Saharan African countries and found that nine of the countries did not require that manufacturers have any GMP certification; "only five . . . had published GMP guidelines meeting WHO standards;" and of the countries that did require compliance, they were generally poorly enforced. WORLD HEALTH ORG., *supra* note 19, at 16.

authorities.[114] The drug regulatory authorities of many low-income countries do not require GMP compliance, poorly enforce compliance, or publish standards that do not fully adhere to the minimum requirements of WHO's GMPs.[115] This allows manufacturers to continue to operate regardless of adherence to stringent GMPs.[116] These factors contribute to make compliance with WHO's GMPs particularly challenging for manufacturers in lower-income countries who seek to have their drugs prequalified.

This Comment has made some conclusions about access to essential medicines and the WHO's Prequalification Program, with particular focus on GMPs. First, far too many people—especially in low-income countries—do not have access to quality-assured essential medicines. Second, the Prequalification Program has performed a critical role in helping to ensure essential medicines meet minimum quality, safety, and effectiveness standards. Third, by adopting this gatekeeper role, the WHO—through the Prequalification Program—has become the *de facto* drug approval authority in many low-income countries that currently lack the capacity to verify the quality of many of the drugs in their territory. However, manufacturers whose products are denied prequalification or de-listed have no formal way to challenge the WHO's decision before an independent body, which raises substantial international due process concerns.

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[114] *See* WORLD HEALTH ORG., *supra* note 19, at 6, 8, 12, 21; Brhlikova et al., *supra* note 9, at 9.

[115] WORLD HEALTH ORG., *supra* note 19, at 16.

[116] Brhlikova et al., *supra* note 9, at 9.

II. DUE PROCESS IN INTERNATIONAL LAW

Historically, international law exclusively governed the relationships between states.[117] However, this view that sovereigns are the sole actors in international law is now obsolete.[118] It is now generally accepted that international organizations are also bound by at least some aspects of international law.[119] Customary international law requires international organizations to provide individuals and companies the opportunity to be heard before an independent and impartial tribunal when the organization is performing a governmental or quasi-governmental function that determines the rights and obligations of these individuals and companies.[120] The WHO is performing a governmental function in administering the Prequalification Program, specifically in its decision to grant, deny, or revoke a product's prequalification. Further, under European Court of Human Rights' jurisprudence, entities have a cognizable right to engage in commercial activity, particularly when the economic consequences of an adverse decision are

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[117] Paul B. Stephan, *Privatizing International Law*, 97 VA. L. REV. 1573, 1574 n.1 (2011) (citing Jeremy Bentham, *Principles of International Law*, *in* 2 THE WORKS OF JEREMY BENTHAM 550 (John Bowring ed., Edinburgh, Simpkin, Marshall & Co. 1843)).

[118] *Id.* at 1574.

[119] *See* Clarke, *supra* note 29, at 73.

[120] Fassbender, *supra* note 30, at 473–74; *see also* International Covenant on Civil and Political Rights, art. 14, Dec. 19, 1966, 999 U.N.T.S. 171; Convention for the Protection of Human Rights and Fundamental Freedoms, art. 6, Nov. 4, 1950, 213 U.N.T.S. 222 [hereinafter European Convention on Human Rights]; G.A. Res. 217 A (III), Universal Declaration of Human Rights art. 10 (Dec. 10, 1948) [hereinafter Universal Declaration of Human Rights].

significant.[121] Therefore, this Comment argues that by failing to provide manufacturers whose drugs are denied prequalification or de-listed the opportunity to challenge the WHO's decision before an impartial tribunal, the WHO is failing to uphold international due process principles. It also argues that the WHO should provide these manufacturers the opportunity to challenge a denial or de-listing because of the WHO's emphasis on human rights promotion and the Prequalification Program's great power over many manufacturers.

A. *Customary International Law Applies to International Organizations*

International organizations are bound by at least some aspects of international law, in particular customary international law. The major sources of international law include international agreements or treaties, customary international law, and "the general principles of law recognized by civilized nations."[122] Customary international law has been defined as the "general and consistent practice of states followed by them from a sense of legal obligation."[123] States must follow customary international law, except when they have consistently objected to a

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[121] *See infra* note 166 and accompanying text.

[122] Statute of the International Court of Justice art. 38, ¶ 1. Additionally, "[j]udicial decisions and the teachings of the most highly qualified publicists of the various nations, as subsidiary means for the determination of rules of law." *Id.*

[123] RESTATEMENT (THIRD) OF THE FOREIGN RELATIONS LAW OF THE UNITED STATES § 102(2) (AM. LAW INST. 1987).

particular law each time the opportunity has arisen or they expressly contract around it.[124] States, however, are always bound by customs that are considered *jus cogens*.[125] Literally meaning "compelling law," *jus cogens* are "peremptory norm[s] of general international law."[126] *Jus cogens* are rules that are so widely "accepted and recognized by the international community of States as a whole" that derogation is not permitted.[127] Examples of *jus cogens* include the prohibitions against genocide, slavery, and the use of force principles found in the U.N. Charter.[128]

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[124] RESTATEMENT (THIRD) OF THE FOREIGN RELATIONS LAW OF THE UNITED STATES § 102 cmt. j (AM. LAW INST. 1987); Roozbeh (Rudy) B. Baker, *Customary International Law in the 21st Century: Old Challenges and New Debates*, 21 EUR. J. INT'L L. 173, 176 (2010).

[125] Vienna Convention on the Law of Treaties art. 53, *opened for signature* May 23, 1969, 1155 U.N.T.S. 331.

[126] *Id.*; RESTATEMENT (THIRD) OF THE FOREIGN RELATIONS LAW OF THE UNITED STATES § 102 cmt. k (AM. LAW INST. 1987); Kamrul Hossain, *The Concept of Jus Cogens and the Obligation under the UN Charter*, 3 SANTA CLARA J. INT'L L. 72, 73 (2005).

[127] Vienna Convention on the Law of Treaties, *supra* note 125, art. 53.

[128] RESTATEMENT (THIRD) OF THE FOREIGN RELATIONS LAW OF THE UNITED STATES § 102 n. 6 (AM. LAW INST. 1987).

International organizations are obligated to respect international law, including *jus cogens*[129] and customary international law.[130] In an advisory opinion, the International Court of Justice found that "[i]nternational organizations are subjects of international law and, as such, are bound by any obligations incumbent upon them under general rules of international law, under their constitutions or under international agreements to which they are parties."[131] Further, to contract around customary international law, parties to an agreement must do so expressly.[132] This has led to the conclusion that international organizations are bound by customary

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[129] Kristina Daugirdas, *How and Why International Law Binds International Organizations*, 57 HARV. INT'L L.J. 325, 346 (2016) ("*Jus cogens* norms bind IOs [(international organizations)] because states cannot, by treaty, establish IOs that are authorized to violate *jus cogens* norms.") (citations omitted).

[130] Clarke, *supra* note 29, at 73. *But see* Daugirdas, *supra* note 129, at 331–35 ("In short, the answers that scholars have given to the question of whether general international law binds IOs include: maybe, sometimes, and always.").

[131] Interpretation of the Agreement of 25 March 1951 Between the WHO and Egypt, Advisory Opinion, 1980 I.C.J. Rep. 73, 89–90 (Dec. 20). Although the International Court of Justice has not always used the term "general international law" consistently, it generally includes at least customary international law. *See* Clarke, *supra* note 29, at 73; Daugirdas, *supra* note 129, at 333. *But* see Daugirdas, *supra* note 129, at 331–34, for an argument that the International Court of Justice's *WHO-Egypt* opinion does not shed much light on international organizations' obligations.

[132] Daugirdas, *supra* note 129, at 348.

international law unless the member states of that organization have expressly conveyed their intent to deviate from it..[133]

Although at least one commentator has argued that procedural due process in civil cases should constitute *jus cogens*,[134] the European Court of Human Rights—an influential court with a rich body of case law—has previously stopped short of such a recognition.[135] It has, however, observed that the right to bring a civil claim before an independent tribunal is "one of the universally recognised fundamental principles of law . . . ."[136] Even if the right to bring a civil claim before an independent tribunal is not considered a rule of *jus cogens*, the WHO should still respect this principle because it is a part of customary international law.[137]

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[133] *Id*.

[134] S.I. Strong, *General Principles of Procedural Law and Procedural Jus Cogens*, 122 PENN ST. L. REV. 357 (2018).

[135] Al-Dulimi. v. Switzerland, App. No. 5809/08 at 65–66 (Eur. Ct. H.R. June 21, 2016), https://hudoc.echr.coe.int/eng/#{"fulltext":["al-dulimi"],"itemid":["001-164515"]}.

[136] Golder v. United Kingdom, 18 Eur. Ct. H.R. (ser. A) at 17 (1975) (internal quotations omitted).

[137] Fassbender, *supra* note 30, at 444 ("On the basis of constitutional and statutory rules and practices common to a great number of States of all regions of the world, and as guaranteed by universal and regional human rights instruments, rights of due process, or "fair trial rights", have been generally recognized in international law protecting individuals from arbitrary or unfair treatment by State organs.").

Although due process is nearly always discussed in terms of obligations that a state owes individuals, the United Nations and its organs are now bound by these principles because they are increasingly asked to perform "tasks of global governance that go beyond its traditional purposes and functions."[138] The evolving authority of the United Nations (and its organs) is part of a larger shift in global governance, including in the area of regulatory decision-making.[139] Global actors, including international organizations, now perform regulatory functions once reserved almost exclusively for states.[140]

It is often said that the Universal Declaration of Human Rights (UDHR) and International Covenant on Civil and Political Rights (ICCPR) form two-thirds of the International Bill of Human Rights.[141] Unlike the ICCPR, the UDHR is not a binding treaty.[142] However, many of the

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[138] *Id.* at 467.

[139] Richard B. Stewart, *The Global Regulatory Challenge to U.S. Administrative Law*, 37 N.Y.U. J. INT'L L. & POL. 695, 695 (2005).

[140] *Id.*

[141] *See e.g*. Hurst Hannum, *The Status of the Universal Declaration of Human Rights in National and International Law*, 25 GA. J. INT'L & COMP. L. 287, 340–41 & n.221 (1995–96). The other document forming this Bill of Rights is the International Covenant on Economic, Social, and Cultural Rights. *Id* at 341 n.221.

[142] Mary Ann Glendon, *The Rule of Law in the Universal Declaration of Human Rights*, 2 NW. U.J. INT'L HUM. RTS. 1, 4 (2004); Anne Lowe, Note, *Customary International Law and International Human Rights Law: A Proposal for the Expansion of the Alien Tort Statute*, 23 IND. INT'L & COMP. L. REV. 523, 537 (2013).

provisions found in both of these documents, including the right to a fair trial, are now widely considered customary law, which generally binds even non-parties.[143] These two seminal documents contain provisions expressly guaranteeing procedural due process, specifically the right to a fair trial. Article 10 of the UDHR states: "[e]veryone is entitled in full equality to a fair and public hearing by an independent and impartial tribunal, in the determination of his rights and obligations and of any criminal charge against him."[144] Using similar language, article 14 of the ICCPR provides: "[i]n the determination of any criminal charge against him, or of his rights and obligations in a suit at law, everyone shall be entitled to a fair and public hearing by a competent, independent and impartial tribunal established by law."[145] The bifurcation of these provisions into "rights and obligations" and "criminal charges" makes clear that the right to a fair trial provided by these documents—and now customary law—applies to both civil and criminal cases. Article 6(1) of the European Convention on Human Rights (ECHR),[146] closely tracks the language of article 14 of the ICCPR. It states that "[i]n the determination of his civil rights and obligations or of any criminal charge against him, everyone is entitled to a fair and public

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[143] *See, e.g.,* Abdullahi v. Pfizer, Inc., 562 F.3d 163, 176 (2d. Cir. 2009) (recognizing the ICCPR as customary international law); Lowe, *supra* note 142, at 537 ("[E]ven though the UDHR is not a binding treaty, it is considered to be a source of customary international law, and, therefore, imposes binding international legal obligations.").

[144] Universal Declaration of Human Rights, *supra* note 120, art. 10.

[145] International Covenant on Civil and Political Rights, *supra* note 120, art. 14.

[146] Formally, it is called the Convention for the Protection of Human Rights and Fundamental Freedoms.

hearing within a reasonable time by an independent and impartial tribunal established by law."[147] The ECHR explicitly applies in both the civil and criminal context.

Although entities can contract around customary international law, there is no evidence that the WHO Constitution or the Expert Committee Report that formally endorsed the Prequalification Program even contemplated—much less expressed a desire to deviate from—procedural due process. Therefore, the WHO is obligated to respect procedural due process rights, specifically the right to a fair trial.

B. *Companies May Avail Themselves of Human Rights Protections*

The theory that international organizations exercising governmental authority over an individual are obligated to respect due process standards is rooted in human rights law.[148] Since applicants to the Prequalification Program are companies, including corporations, an important question becomes whether human rights apply to companies or if this body of law is reserved only for natural persons. In other words, do companies have legal personality under human rights law that would grant them rights similar to those afforded to individuals?

Looking at the language of these international human rights agreements, as well as the practice of regional human rights bodies, companies often do in fact enjoy basic human rights, including the right to be heard before an independent tribunal.[149] The broad language found in

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[147] European Convention on Human Rights, *supra* note 120, art. 6.

[148] Fassbender, *supra* note 30, at 445–46.

[149] *See, e.g.*, Lucien J. Dhooge, *Human Rights for Transnational Corporations*, 16 J. TRANSNAT'L L. & POL'Y 197, 211–13 (2007). There are, however, limits on corporations' human

the right to a fair trial provisions of these international human rights agreements lends credence to the argument that companies enjoy this right.[150] The drafters of these documents used intentionally broad language, rather than limiting it to simply "natural persons."[151] Article 10 of the UDHR, article 14 of the ICCPR, and article 6 of the ECHR state that "everyone" or "all persons" shall be entitled to a fair hearing before an independent and impartial tribunal.[152] Additionally, companies have long been able to bring claims in the European Court of Human Rights.[153] A prime justification for extending human rights, particularly due process protections,

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rights. For a discussion of these limits, see Julian G. Ku, *The Limits of Corporate Rights Under International Law*, 12 CHI. J. INT'L L. 729, 751–753 (2012).

[150] Dhooge, *supra* note 149, at 211–13.

[151] *Id.*

[152] International Covenant on Civil and Political Rights, *supra* note 120, art. 14; European Convention on Human Rights, *supra* note 120, art. 6; Universal Declaration of Human Rights, *supra* note 120, art. 10.

[153] European Convention on Human Rights, *supra* note 120, art. 34 ("The Court may receive applications from any person, non-governmental organization or group of individuals . . . ."); *see* Winfried H.A.M. van den Muijsenbergh & Sam Rezai, *Corporations and the European Convention on Human Rights*, 25 GLOBAL BUS. & DEV. L.J. 43, 49 (2012) ("Among the Convention rights always and easily deemed applicable to corporations are the right to a fair trial . . . .").

to companies is that companies, including corporations, are "merely associations of individuals united for a special purpose."[154] Therefore, companies do enjoy human rights protections.

C. *Process is Due*

Having established that the WHO is generally bound by international procedural due process rules and that companies have legal personality under international human rights law, this Comment now turns to whether the Prequalification Program, in particular, must provide participants access to an independent and impartial tribunal. The United Nations has previously grappled with a similar question in a different context.[155] In 2005, the U.N. General Assembly commissioned Professor Bardo Fassbender to conduct a study on the due process concerns involved in the U.N. Security Council's (UNSC) targeted sanctions regime, specifically UNSC Resolution 1267— which sanctions individuals and entities belonging to or associated with Al-Qaeda or the Taliban.[156] The listing and de-listing of these individuals, in particular, raised significant due process concerns.[157]

Fassbender concluded that, under customary international law, the United Nations and its organs must provide procedural due process if two conditions are met.[158] First, the United Nations or its organs must be exercising "governmental or quasi-governmental authority" over

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[154] Pembina Consol. Silver Mining & Milling Co. v. Pennsylvania, 125 U.S. 181, 189 (1888) (holding that the Fourteenth Amendment extends to corporations).

[155] Fassbender, *supra* note 30, at 441.

[156] *Id.* at 440–42.

[157] *Id.* at 442–43.

[158] *Id.* at 467, 474.

individuals or entities.[159] Second, the United Nations or its organs must be "taking action that *adversely affects, or has the potential of adversely affecting, the rights and freedoms* of individuals."[160] In the civil context the three human rights documents discussed above—the UDHR, ICCPR, and ECHR—phrase this second condition as an action that determines an individual's "rights and obligations."[161] As discussed, companies may assert this right to due process, specifically the right to a hearing before an independent tribunal.[162]

The Prequalification Program's decision to list and de-list medicines satisfies both criteria. First, the WHO, which is an organ of the United Nations, is exercising a governmental or quasi-governmental function—through its Prequalification Program—when it decides to grant, deny, or withdraw prequalification approval. The approval and removal (or de-listing) of pharmaceutical products is a function primarily carried out by national governments.[163] The

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[159] *Id.* at 467 (quoting KAREL WELLENS, REMEDIES AGAINST INTERNATIONAL ORGANISATIONS 89 (2002)).

[160] *Id.* at 474 (emphasis added).

[161] *See supra* note 152 and accompanying text.

[162] *See supra* note 148–154 and accompanying text.

[163] Warren A. Kaplan and Richard Laing, *Paying for Pharmaceutical Registration in Developing Countries*, 18 HEALTH POL'Y & PLAN. 237, 237 (2003). One exception is the European Union's centralized procedure, which allows a company to obtain a single market authorization for all of the member states in the European Union. Ines M. Vilas-Boas & C. Patrick Tharp, *The Drug Approval Process in the U.S., Europe, and Japan* 3 J. MANAGED CARE & SPECIALTY PHARMACY 459, 461 (1997).

WHO itself states that "[m]edicines regulation is essentially a public function."[164] Additionally, the ultimate purpose of the Prequalification Program—the protection of public health[165]—has historically been a government function. Therefore, the WHO is exercising a governmental or, at the very least quasi-governmental, function in the administration of its Prequalification Program.

Second, the Prequalification Program is determining (or taking an action that has a potentially adverse effect on) an entity's cognizable right when it makes the decision to deny prequalification or de-list an already prequalified product. The European Court of Human Rights has held that the right to a fair trial covers the right to engage in commercial activity, particularly when an adverse decision would carry significant economic consequences.[166]

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[164] World Health Org., *Building Quality-Assured Manufacturing Capacity in Nigeria*, 28 WHO DRUG INFO. 425, 429 (2014).

[165] *See supra* note 63 and accompanying text.

[166] *See* Tre Traktörer AB v. Sweden, 159 Eur. Ct. H.R. (ser. A) at 19 (1989); Benthem v. Netherlands, 97 Eur. Ct. H.R. (ser. A) at 16 (1985); Nuala Mole & Catharina Harby, *The Right to a Fair Trial: A Guide to the Implementation of Article 6 of the European Convention on Human Rights*, *in* HUMAN RIGHTS HANDBOOKS, NO. 3 at 13 (2d ed. 2006), https://rm.coe.int/168007ff49. *Compare* I.T.C. Ltd. v. Malta, App. No. 2629/06 Eur. Ct. H.R. at 11 (2007), http://hudoc.echr.coe.int/app/conversion/pdf/?library=ECHR&id=001-84144&filename=001-84144.pdf (holding that one of the losing bidders for a public contract had no civil right to the award of the contract for the purposes of a right to a fair trial), *with* Araç v. Turquie [Araç v. Turkey], App. No. 69037/01 Eur. Court. H.R. at 4 (2006), https://hudoc.echr.coe.int/eng"{"item"d""["001-769"4"]}, *translated by* Google Translate

The European Court of Human Rights has held that the denial as well as revocation of a license interferes with a legal person's "civil" right[167] for the purposes of receiving a fair trial.[168] In *Benthem v. Netherlands*, the court held that a person possesses a civil right when his/her application for a business license is denied.[169] The applicant in *Benthem* sought a license to establish and operate a gas station.[170] Municipal authorities initially granted the license, but on appeal, determined that the license should be refused.[171] The European Court of Human Rights held that the dispute over the license denial implicated a civil right within the purview of the right to a fair trial.[172] Additionally, the court specifically rejected the government's argument that this dispute did not concern a substantive right because Mr. Benthem could obtain a license for a

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(finding that a civil right was at issue for person who was excluded from all future public tenders because of the serious economic consequences of the exclusion).

[167] European Convention on Human Rights, *supra* note 120, art. 6. The European Court of Human Rights uses the term "civil right" to refer to non-criminal (i.e. civil) rights covered by the right to a fair trial provision. European Convention on Human Rights, *supra* note 120, art. 6.

[168] *Tre Traktörer AB*, 159 Eur. Ct. H.R. (ser. A) at 19; *Benthem*, 97 Eur. Ct. H.R. (ser. A) at 16; *See also* Mola & Harby, *supra* note 166, at 13 (citing cases involving licenses that the court held were covered by the right to a fair trial).

[169] *Benthem*, 97 Eur. Ct. H.R. (ser. A) at 16.

[170] *Id.* at 9–10.

[171] *Id.* at 10–11.

[172] *Id.* at 16.

different location.[173] "[A] change of this kind—which anyway would have involved an element of chance since it would have required a fresh application whose success was in no way guaranteed in advance—might have had adverse effects on the *value of the business and of the goodwill*. . . ."[174] Thus, Mr. Benthem was entitled to a fair trial before an independent tribunal following the denial of his license application.[175]

The European Court of Human Rights came to the same conclusion—namely that a civil right is at issue—when a license is revoked. In *Tre Traktörer AB v. Sweden*, a restaurant that had previously been licensed to serve alcohol had its license revoked by a local administrative board.[176] After a rather long procedural journey, the County Administrative Board—following an order by the National Board of Health and Welfare—revoked the restaurant's alcohol license.[177] The restaurant then appealed this decision back to the National Board of Health and Welfare, which declined to review the County Administrative Board's decision.[178] The European Court of Human Rights found that the revocation of the license "adversely affected the goodwill and value of the restaurant." [179] The court therefore held that the alcohol license conferred a right on

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[173] *Id.*

[174] *Id.* (emphasis added).

[175] *Id.* at 16–17.

[176] *Tre Traktörer AB v. Sweden*, 159 Eur. Ct. H.R (ser. A) at 13 (1989).

[177] *Id.* at 12–13.

[178] *Id.* at 13.

[179] *Id.* at 19.

the restaurant and thus, the former licensee was entitled to a fair trial before an independent tribunal.[180]

In contrast to the earlier licensing cases, the European Court of Human Rights has more recently considered the right to engage in commercial activity in the context of bids for a public tender.[181] These recent decisions—*I.T.C. Ltd. v. Malta* and *Araç v. Turkey*—indicate that the court is more likely to find that a party possesses a right to engage in commercial activity when an adverse decision would result in significant economic consequences, such as being excluded from multiple—rather than just one—contract.[182]

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[180] *Id.* The court also held that neither the County Administrative Board nor the National Board of Health and Welfare constituted an independent tribunal. *Id.* at 20.

[181] *See* I.T.C. Ltd v. Malta, App. No. 2629/06 Eur. Ct. H.R. at 11 (2007), http://hudoc.echr.coe.int/app/conversion/pdf/?library=ECHR&id=001-84144&filename=001-84144.pdf; Araç v. Turkey, App. No. 69037/01 Eur. Ct. H.R. at 5 (2006), https://hudoc.echr.coe.int/eng#{"itemid":["001-76944"]}.

[182] *See* I.T.C. Ltd. v. Malta, App. No. 2629/06 Eur. Ct. H.R. at 11 (2007), http://hudoc.echr.coe.int/app/conversion/pdf/?library=ECHR&id=001-84144&filename=001-84144.pdf; Araç v. Turkey, App. No. 69037/01 Eur. Ct. H.R. at 5 (2006), https://hudoc.echr.coe.int/eng#{"itemid":["001-76944"]}.

In *I.T.C. Ltd. v. Malta*, the Maltese Ministry for Youth and Arts issued a public call for tenders related to a national event, for which three companies submitted bids.[183] Following the announcement of the winning bid, one of the companies that was not awarded the contract attempted to challenge the Ministry's decision in the judicial system.[184] The European Court of Human Rights held that "[t]he issuance of a call for tenders did not give any tenderer any enforceable civil right against the issuer."[185] The court distinguished *I.T.C.* from the case decided a year earlier, *Araç v. Turkey*, in which the court held that an applicant for a public tender did possess an enforceable civil right.[186] In *Araç*, the applicant was excluded not only from the tender at issue, but also all future tendering processes.[187] "The [*Ara*ç] decision thus entailed very [different] significant economic consequences for him."[188] Therefore, it appears that the court takes account of the economic consequences at stake in determining whether a legal person possesses a cognizable right for the purposes of a fair trial.

Here, the Prequalification Program's decision to deny or withdraw a drug's prequalification is interfering with a manufacturer's civil right to engage in commercial activity

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[183] I.T.C. Ltd. v. Malta, App. No. 2629/06 Eur. Ct. H.R. at 2 (2007), http://hudoc.echr.coe.int/app/conversion/pdf/?library=ECHR&id=001-84144&filename=001-84144.pdf.

[184] *Id.* at 3–5.

[185] *Id.* at 8.

[186] *Araç*, App. No. 69037/01 Eur. Ct. H.R. at 5.

[187] *Id.* at 4–5.

[188] *I.T.C.*, App. No. 2629/06 at 11.

under both the licensing and more recent public tender lines of cases. Under both lines, manufacturers enjoy this right because an adverse decision by the Prequalification Program substantially restricts their ability to engage in commercial activity—now and in the future—and carries significant economic consequences for the manufacturers.

Similar to the denial of a license application in *Benthem*, and the revocation of a license in *Tre Traktörer AB*, the denial or revocation of a product's prequalification status affects the "value and goodwill" of the manufacturer's operation. As the court made clear in *Benthem*, the fact that a manufacturer can re-apply for approval does not make the right to engage in commercial activity unenforceable.[189] The WHO's decision to grant, deny, or withdraw a product's prequalification has a significant impact on manufacturers' profitability and sustainability.[190] In other words, there are "direct links between the grant of the license and the entirety of the applicant's commercial activities."[191]

Under the public tender cases, manufacturers under the Prequalification Program are more similar to the applicant in *Araç* than the one in *I.T.C. Ltd.* Like the applicant in *Araç*,[192] a manufacturer whose product is denied prequalification or de-listed is excluded not from one contract, but from all contracts with drug procurement entities that require the drugs they purchase to be prequalified. As discussed, this category of purchasers constitutes a sizeable and

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[189] Benthem v. Netherlands, 97 Eur. Ct. H.R. (ser. A) at 16 (1985).

[190] *See supra* Section I.D.

[191] *Benthem*, 97 Eur. Ct. H.R. (ser. A) at 16; *See also supra* Section I.C.

[192] Araç v. Turkey, App. No. 69037/01 Eur. Ct. H.R. at 5 (2006), https://hudoc.echr.coe.int/eng#{"itemid":["001-76944"]}.

profitable portion of the essential medicines market.[193] Therefore, an adverse decision by the Prequalification Program carries significant economic consequences. Under customary international law, manufacturers whose drugs are denied prequalification or de-listed are entitled to a fair hearing before an independent tribunal.

D. *WHO: Human Rights Promotion and Power*

In addition to alleviating due process concerns, the WHO should allow manufacturers whose products are de-listed or denied prequalification the opportunity to challenge such a decision due to its role as a promoter of human rights and the immense power it exerts over many drug manufacturers. Just prior to his 2017 selection as WHO Director-General, Dr. Tedros Adhanom Ghebreyesus stated that he was "committed to transforming the way that WHO operates. A more effective and efficient WHO will strengthen the entire UN system . . . . Too often, human rights and gender equity are secondary considerations when UN organizations develop programming. This is outdated and must change."[194] Although Dr. Tedros was mainly referring to an individual's right to health,[195] his statement underscores the important role that international organizations, including the WHO, play in not only the protection, but promotion, of human rights.

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[193] *See supra* Section I.C.

[194] Benjamin Mason Meier, *Human Rights in the World Health Organization: Views of the Director-General Candidates*, 19 HEALTH & HUM. RTS. J. 293, 294 (2017).

[195] *Id.*

The WHO was created as a norm-setting agency, with human rights at the organization's core.[196] The WHO Constitution begins with the proclamation that "[t]he enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being . . . ."[197] Although historically the WHO's human rights focus has been on the right to health, there is a need for it to expand the rights it protects and promotes in a way that is commensurate with its growing authority. By failing to provide Prequalification applicants the ability to challenge an adverse decision, the WHO has not only missed an opportunity to advance human rights principles, but is actually lagging behind some countries.

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[196] *See generally* L. O. Gostin et al., *The Normative Authority of the World Health Organization*, 129 PUB. HEALTH 854, 855 (2015) (discussing the mission, authority, and functions of the WHO).

[197] CONSTITUTION OF THE WORLD HEALTH ORGANIZATION, preamble, *opened for signature* July 22, 1946, 62 Stat. 2679.

For example, a manufacturer who applies to have its drug approved by the European Medicines Agency[198] may have a denial reviewed by the European Court of Justice.[199] Similarly,

[198] This is specifically referring to the Centralized Procedure. Similar to the Prequalification Program, approval through the Centralized Procedure enables entities to effectively gain authorization to distribute (or market) their product in multiple countries. Regulation 726/2004 of the European Parliament and of the Council of 31 March 2004 Laying Down Community Procedures for the Authorisation and Supervision of Medicinal Products for Human and Veterinary Use and Establishing a European Medicines Agency, 2004 O.J. (L 136) 1 (EC); Directive 2001/83/EC, of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use, 2001 O.J. (L 311) 67 (EC); Vilas-Boas & Tharp, *supra* note 163, at 461.

[199] Case T-74/00, Artegodan GmbH v. Comm'n of the European Communities, 2002 E.C.R. II-4948, II-4952, II-5019–21; *See* Levan Makhashvili & Paul Stephenson, *Differentiating Agency Independence: Perceptions from Inside the European Medicines Agency*, 9 J. CONTEMP. EUR. RES. 4, 9–10 (2013) (citing R. Daniel Kelemen, *The Politics of 'Eurocratic' Structure and the New European Agencies*, 25 W. EUROPEAN POLITICS 93, 99 (2002) ("In addition, the European Court of Justice (ECJ) monitors the actions and decisions of the EMA ([European Medicines Agency]) and, at the request of EU institutions or citizens can further scrutinise its functioning.")); Johannes Saurer, *The Accountability of Supranational Administration: The Case of European Union Agencies*, 24 AM. U. INT'L L. REV. 429, 461–62 (2009) (providing an overview of the EMA-specific jurisprudence on when an action may be challenged in court).

in the United States, manufacturers whose applications for generic drug approval[200] are denied or withdrawn may either request a hearing with the Food and Drug Administration (FDA) or seek judicial review in a U.S. court of appeals.[201] If an applicant opts for a hearing with the FDA and is still displeased with the agency's decision, it retains the ability to appeal that decision to a U.S. court of appeals[202] It should be noted, however, that courts accord FDA decisions substantial deference.[203] Courts also do not perform their own fact-finding, but rather review only the information that the agency possessed at the time it made its decision.[204] These examples

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[200] The discussion of the FDA approval process will focus exclusively on the FDA review of generic drug applications. This is done for two reasons: (1) the review procedure at this stage of the process is substantially similar for brand name and generic manufacturers that an examination of one will suffice; and (2) most of the drugs that are prequalified by the WHO are generic products. Worku et al., *supra* note 102, at 63–64.

[201] 21 C.F.R. § 314.200(c)(1) (2018); 21 C.F.R. § 314.235(b) (2018).

[202] 21 C.F.R. § 314.235(b) (2018).

[203] Fed. Power Comm'n v. Fla. Power & Light Co., 404 U.S. 453, 463 (1972) ("[W]hen resolution of that question depends on 'engineering and scientific' considerations, we recognize the relevant agency's technical expertise and experience, and defer to its analysis unless it is without substantial basis in fact.").

[204] Citizens to Preserve Overton Park, Inc. v. Volpe, 401 U.S. 402, 420 (1971); Bristol-Myers Squibb Co. v. Shalala, 923 F.Supp. 212, 216 (D.D.C. 1996) (citing Camp v. Pitts, 411 U.S. 138, 142 (1973)).

demonstrate that the WHO has thus far missed an opportunity to promote robust due process protections.

The WHO should allow manufacturers whose drugs are denied prequalification or de-listed the opportunity to challenge such a decision due also to the great power the Prequalification Program holds over many manufacturers. In 1928, Clyde Eagleton wrote that "power breeds responsibility" to describe states' responsibilities under international law.[205] Scholars began to apply this idea to international organizations, as their roles and powers expanded.[206] As international organizations increasingly act in ways that affect the "social, political, economic and legal status of individuals," their responsibility to be accountable for their decision increases as well.[207] The WHO—in deciding to award prequalification to a manufacturer—consistently makes decisions that have a significant impact on an applicant's profitability and sustainability.[208] Due to this power, the WHO's Prequalification Program should have structural mechanisms in place to make it more accountable for its decisions.

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[205] CLYDE EAGLETON, THE RESPONSIBILITY OF STATES IN INTERNATIONAL LAW 206 (1928); *see also* Clarke, *supra* note 29, at 65.

[206] Clarke, *supra* note 29, at 65 (citing E. Paasivirta & P.J. Kujjper, *Does One Size Fit All?: The European Community and the Responsibility of International Organizations*, 36 NETH. YRBK OF INT'L L. 169, 173 (2005)).

[207] *Id.* (quoting Gerhard Hafner, *Accountability of International Organizations—A Critical View*, *in* TOWARDS WORLD CONSTITUTIONALISM 585, 592–93, 629 (Ronald St. John MacDonald & Douglas M. Johnston, eds., 2005)).

[208] *See supra*, Section I.C.

Allowing manufacturers whose drugs are denied prequalification or de-listed the opportunity to challenge such a decision would ensure the WHO is promoting human rights and help alleviate concerns that it is unaccountable.

III. WORLD BANK INSPECTION PANEL: A MODEL FOR INDEPENDENT REVIEW

The WHO is not the only international organization to face calls for the introduction of a review body.[209] In 1993, the World Bank's Board of Executive Directors[210] created an Inspection Panel in response to charges—both internal and external—that the Bank was not considering the sometimes negative social and environmental effects of the loans it was administering.[211] This Comment will look to the World Bank Inspection Panel to offer lessons on how to structure the proposed WHO Prequalification Independent Review Panel.

The Inspection Panel is made up of a diverse group of appointed individuals. The President of the World Bank nominates three people from different states, and then the panelists are appointed by the Executive Directors to serve non-renewable five year terms.[212] The Panel is

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[209] Granted, at least some of those calls to the WHO are coming from this Comment.

[210] The World Bank is a global partnership with 189 member countries dedicated to reducing poverty by providing zero or low interest loans, credits, grants, and technical assistance to developing countries. *Who We Are*, The WORLD BANK, http://www.worldbank.org/en/who-we-are (last visited Sept. 30, 2018).

[211] Yvonne Wong & Benoit Mayer, *The World Bank's Inspectional Panel: A Tool for Accountability?*, *in* 6 THE WORLD BANK LEGAL REVIEW 495, 496 (Jan Wouters et al. eds., 2015).

[212] Int'l Bank for Reconstruction and Development [IBRD], Res. No. IBRD 93-10 (Sep. 22, 1993),

tasked with receiving and investigating allegations that the World Bank has not complied with "its operational policies and procedures."[213] The Inspection Panel can consider claims brought by (1) at least two individuals affected by the project, (2) an entity representing affected individuals, or (3) the Executive Director or Board of Executive Directors, which can order the Panel to investigate a certain loan.[214] Prior to bringing a claim, there is an exhaustion of remedies requirement: individuals or representative claimants must assert that they have brought their concerns to Bank Management, and—in the complainant's view—the Management's response was inadequate.[215] The Panel is an investigatory body, whose ultimate goal is to bring World Bank projects into conformity with its own operational policies and procedures.[216] Therefore, the Panel does not compensate individuals who have been negatively affected by a loan.[217] Rather, it presents its findings to the World Bank's Board, which then decides how to proceed.[218] Panel

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http://siteresources.worldbank.org/EXTINSPECTIONPANEL/Resources/ResolutionMarch2005.pdf; IBRD, THE INSPECTION PANEL ANNUAL REPORT: JULY 1, 2017–JUNE 30, 2018 5 (2018).

[213] Wong & Mayer, *supra* note 211, at 501.

[214] *Id.* at 502.

[215] *Id.* at 503 (citing World Bank, *1999 Clarification of the Board's Second Review of the Inspection Panel* (1999)).

[216] *Id.* at 514–15.

[217] *Id.* at 515.

[218] *Id.*

proceedings typically lead to an action plan, which on occasion has included the cancellation or revocation of funding for the project in question..[219]

While not perfect, the Inspection Panel has been credited with bringing about more careful decision-making and encouraging the Bank to take corrective actions. First, the mere presence of the Panel encourages staff to be more cognizant of the Bank's policies and to more diligently monitor their projects.[220] Second, the Panel's findings can prompt the Board of Executive Directors to take corrective action when a project is not in full compliance.[221]

The Inspection Panel, however, has also faced criticism that its practices both limit utilization and participation and raise questions about the Panel members' independence. According to some, there are linguistic and cultural barriers that impede people from filing claims, which may ultimately result in underutilization of the Panel.[222] Additionally, some claimants have stated that they are largely sidelined during the Panel's investigation and deliberation processes.[223] Finally, there have been doubts about the true independence of the Panel since Panelists are appointed by the Executive Director and claims must be approved by the Board of Executive Directors in order to proceed..[224] The experience of the Inspection Panel

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[219] *Id.*

[220] *Id.* at 516–17.

[221] *Id.* at 516.

[222] *Id.* at 507–08 (noting that the World Bank's working language is English, and filing a claim against an authority may run counter to the norms and values of some cultures).

[223] *Id.* at 511–12.

[224] *Id.* at 510–12.

can provide guidance on how to structure the proposed Prequalification Independent Review Panel.

IV. A TWO-PART SOLUTION TO THE PREQUALIFICATION CHALLENGES

This Comment proposes a two-part solution to address both the international due process concerns and the lack of pharmaceutical production in low-income countries. First, as discussed above, the WHO should allow drug manufacturers whose drugs are denied prequalification or de-listed the opportunity to be heard in front of an independent panel. Second, the WHO should institute a procedure that enables manufacturers in lower-income countries to have their drugs "conditionally" prequalified. Conditional prequalification would require manufacturers to meet a lower defined threshold of GMP compliance that ensures manufacturers' facilities have basic quality control mechanisms. The prequalification is "conditional" because manufacturers' approval for a drug is contingent upon their adherence to a plan, approved by the WHO, that leads to full GMP compliance within a defined time period. This Comment will now address these two parts in turn.

A. *Prequalification Independent Review Panel*

The WHO should create a review panel comprised of an odd number of independent experts that—upon request from manufacturers—will review decisions to withdraw or deny prequalification. As explained below, an independent review panel would not only provide manufacturers with robust due process protections, but also ensure the accuracy of prequalification decisions, increase the accountability of Prequalification staff members, and instill more confidence in the decisions of the Prequalification team.

Beginning with the composition of the Panel, the WHO Prequalification Independent Review Panel should adopt the approach of the World Bank Inspection Panel, with respect to

diversity of representation and term limits.[225] It is important that the Prequalification Review Panel represent a geographically and economically diverse group of countries to encourage the greatest level of actual and perceived independence, fairness, and credibility. The following example could be one way to achieve such a Panel.

The panel could consist of seven people, each serving a term of five years. The panelists' terms would be staggered to ensure panel continuity. The staggering of terms would, of course, require some of the initial panelists to serve less than five year terms (*e.g.* two initial panelists serve three-year terms, two serve four-year terms, and the other three serve for the full five-years). Individuals would be allowed to serve more than once, but not in successive terms. One panelist would come from each of the six WHO regions: the African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region, and Western Pacific Region (collectively regional panelists).[226] The seventh and final panelist would be appointed by the U.N. agencies that procure prequalified drugs. The seventh panelist could—but would not be required to—be an employee of a U.N. agency. All of the panelists should have expertise in the area of pharmaceuticals. Similar to criticisms of the World Bank Inspection Panel[227], questions may be raised about the independence of the panelists. To assuage some of these concerns, there could be a cooling-off rule for regional panelists: individuals are not eligible to be a regional panelist for some specified period of time (for example, five years) after

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[225] *See supra* note 212 and accompanying text.

[226] *WHO Regional Offices*, WORLD HEALTH ORG., http://www.who.int/about/regions/en/ (last visited Sept. 30, 2018).

[227] *See supra* notes 224 and accompanying text.

they have been directly employed by the WHO or served on a Prequalification assessment or inspection team. These measures would satisfy the international law requirement of providing applicants a hearing before an independent, and impartial tribunal.[228]

Applicant manufacturers would be able to bring before the Panel challenges based on a rejection of their dossier or a finding of non-compliance with the GMPs. There would however be an exhaustion of remedies requirement, similar to the World Bank Inspection Panel.[229] The manufacturer would be required to raise its concerns with the Prequalification team and make a good faith effort to resolve any disputes before filing a claim with the Independent Panel. For the Panel to overturn a prequalification decision, at least 60% of the panelists would need to vote in favor of such a measure.[230] Requiring a 60% threshold for reversals is intended to guard from an overly active Panel and build in limited deference to the Prequalification team.

For products that are de-listed, the Panel could either uphold or reverse the WHO's decision. The Panel would uphold the de-listing of a product when it agrees with the Prequalification team that there are immediate deficiencies in the safety or effectiveness of a

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[228] *See supra* Section II.A.

[229] *Supra* Part III. The U.S. FDA and the European Court of Human Rights appeal procedures contain a similar requirement. European Convention on Human Rights, *supra* note 120, art. 26 ("The Commission may only deal with the matter after all domestic remedies have been exhausted . . . ."); *supra* Section II.D.

[230] For a full panel of seven individuals, five of the seven panelists would need to vote in favor of overturning the prequalification decision. However, if one or more panelist were absent, the required number of votes would change accordingly.

product. The Panel would reverse the WHO's de-listing of a product—and restore its prequalification status—when the evidence indicates that the product remains both safe and effective, and is manufactured in compliance with GMPs.

For manufacturers who are applying to have their product(s) prequalified, the Panel could (1) uphold the Prequalification team's decision, (2) reverse a denial and grant prequalification, (3) grant the proposed "conditional" approval that will be discussed in section B of this Part, or (4) change the Prequalification team's grant of conditional prequalification to "full" prequalification.[231] First, the Panel would uphold a WHO denial of prequalification when there are material deficiencies in the applicant's dossier submission or non-compliance with GMPs. Second, the Panel would reverse a WHO denial of Prequalification if it determines the facts clearly show that an applicant's dossier submission and manufacturing facilities comply with the Prequalification requirements. Third, the Panel could grant conditional approval if the manufacturer's dossier submission is satisfactory, the manufacturer is from an eligible country,[232] and its compliance with the GMPs is not fully satisfied but meets the minimum standards discussed in section B of this Part. Finally, the Panel would change a conditional prequalification result to full prequalification if it determines there is clear evidence demonstrating that the applicant's dossier submission and compliance with GMPs warrant such a change.

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[231] "Full" prequalification refers to the current prequalification granted by the WHO. It is used to distinguish between the proposed "conditional prequalification" and the current system.

[232] *See infra* Section IV.B.

In deciding what information to review, the Panel should adopt the approach of U.S. courts[233] and review only the information that the Prequalification team possessed at the time it made its decision.[234] Limiting the reviewable information to only what is contained in the administrative record safeguards against lengthy and costly discovery and litigation.[235] A lack of financial and human resources is already a concern for both the WHO[236] and many manufacturers.[237] Therefore, a procedure that is efficient, in terms of cost and time, is in the best interests of all parties.

The Panel, however, should depart from U.S. courts' high level of agency deference,[238] and review the case de novo. A primary justification for U.S. courts' deference to agency decisions is that judges do not possess the same expertise as agency officials.[239] Here, the

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[233] *See supra* Section II.D.

[234] Accordingly, the Panel would not make a site or inspection visit to the facility, but would rely on the report of the inspection team.

[235] *See generally* Paula Hannaford-Agor & Nicole L. Waters, *Estimating the Cost of Civil Litigation*, 20 CASELOAD HIGHLIGHTS 1, 7 (2013) (discussing the costs and inefficiencies of litigation).

[236] Eigil Sørensen, *Challenges for the World Health Organization*, J. OF THE NOR. MED. ASS'N (Jan. 2018), https://tidsskriftet.no/en/2018/01/kronikk/challenges-world-health-organization.

[237] *See, e.g.*, Brhilikova et al., supra note 9, at 8 (discussing the problems encountered in the authors' Nepali study, including "financial constraints").

[238] *See, e.g.*, Chevron v. Nat. Res. 467 U.S. 837, 844 (1984).

[239] *See, e.g.*, *id.* at 865.

Prequalification Panel would be comprised of subject-matter experts. Thus, the justification of deferring to the agency—in this case the WHO Prequalification team—is absent.

As discussed in Part III, international law principles require the WHO to provide manufacturers whose products have been denied prequalification or de-listed an opportunity for a hearing before a competent, independent, and impartial body. The Independent Review Panel would satisfy this obligation. Such a Panel would also bring practical benefits. First, the Panel would ensure that prequalification decisions are accurate. It logically follows that having a group of seven widely-respected subject matter experts review a decision would increase its accuracy. Second, similar to the World Bank Inspection Panel, the mere existence of the Prequalification Panel puts additional pressure on the Prequalification team to take care in its decisions to prequalify drugs or not. The possibility of bad publicity and loss of credibility associated with prequalifying an unsafe drug is likely to safeguard from the Prequalification team over-approving applications in an effort to avoid having decisions overturned by the Panel. Finally, stemming from these first two benefits, manufacturers would likely have more confidence in, and respect for, the decisions of the Prequalification team, if they had the opportunity to appeal negative decisions. It is possible that this confidence would increase the number of manufacturers from across the world—including lower-income countries—that apply for prequalification. However, more than simply an appeals process is likely necessary to facilitate the production of quality drugs in lower-income countries. A modified prequalification process available to manufacturers based in these countries, such as the proposed condition prequalification, has the potential to do just that: increase the supply of quality-assured medicines produced in lower-income countries.

B. *Conditional Prequalification*

Conditional prequalification would be an approval pathway available only to manufacturers producing FPPs and APIs in lower-income countries. For their drugs to be conditionally prequalified, manufacturers in these countries would be required to meet a defined threshold of GMP compliance that is below what is required for full prequalification, but one that ensures the drugs are safe and effective, and that the facilities in which they are produced have basic quality control mechanisms in place. The prequalification would be conditioned upon manufacturers adhering to a WHO-approved plan that leads to full compliance within a specified time period.

The criteria used to determine the countries in which manufacturers would be eligible for conditional prequalification would mirror the economic standards used by Gavi, the Vaccine Alliance.[240] The Gavi eligibility criteria generally capture countries that have the highest disease

[240] "Gavi is an international organisation - a global Vaccine Alliance, bringing together public and private sectors with the shared goal of creating equal access to new and underused vaccines for children living in the world's poorest countries." *About Gavi, the Vaccine Alliance*, GAVI, THE VACCINE ALLIANCE, http://www.gavi.org/about/ (last visited Oct. 1, 2018). In addition to having a certain 3-year gross national income per capita, countries applying for Gavi support must also satisfy other criteria, as dictated by the specific vaccine they are applying for. *See Transition Process*, GAVI, THE VACCINE ALLIANCE, https://www.gavi.org/support/sustainability/transition-process/ (last visited Oct. 9, 2018).

burdens and lowest drug production rates.[241] To be eligible for conditional prequalification, the manufacturer's drugs would have to be produced in a country with an average gross national income per capita of US$1,580 or less over the past three years.[242] The $1,580 figure would be the 2018 level, subsequently adjusted annually for inflation. Currently, manufacturers in forty-seven countries would be eligible for conditional prequalification.[243] The Gavi level of $1,580 is desirable for conditional prequalification because it includes not only "low-income" countries[244] but also a limited number of poorer "middle-income" countries, as classified by the World Bank.[245] Making manufacturers in all middle-income countries eligible for conditional prequalification would be overly inclusive as the economic conditions in these countries varies significantly: middle-income countries are defined as having a gross national income per capita

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[241] *See Gavi's Mission*, GAVI, THE VACCINE ALLIANCE, https://www.gavi.org/about/mission/ (last visited Aug. 31, 2018).

[242] *Countries Eligible for Support*, GAVI, THE VACCINE ALLIANCE, http://www.gavi.org/support/sustainability/countries-eligible-for-support/ (last visited Oct. 1, 2018).

[243] *Id.*

[244] Under 2019 fiscal year classifications, countries with a gross national income per capita below $995 are classified as low-income. *World Bank Country and Lending Groups*, THE WORLD BANK, https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups (last visited Oct. 9, 2018).

[245] *Id.*

between $996 to $12,055.[246] Manufacturers in a country such as India (a middle-income country) clearly do not need the conditional prequalification approval pathway.[247] If a country's gross national income per capita increases above the threshold level, that country will "graduate," and no new manufacturers based in these countries will be eligible for conditional prequalification. If a manufacturer has multiple facilities, only some of which are in eligible countries, only the drugs produced in the eligible countries may be conditionally prequalified.

For a manufacturer to take advantage of conditional prequalification, both the FPP and its API must be produced in an eligible country. It is not necessary that the same manufacturer produce both the API and FPP; just that both are produced in eligible countries. If both are produced in eligible countries but by different manufacturers, both the API and the FPP would be eligible for conditional prequalification. This requirement ensures that the benefits of local production of medicines are fully captured. If conditional prequalification only required that the FPP be produced in an eligible country, it is conceivable that much of the actual production of the drug would occur outside an eligible country, then shipped into an eligible country for the final step of production. In this scenario, the economic benefits of local production would be reduced and the populations in lower-income countries would still be susceptible to supply interruptions because the ingredients would have to be imported. Alternatively, allowing an API to be conditionally prequalified and then shipped out of an eligible country for final assembly is no different—from the consumer's perspective—from a drug that was produced entirely outside

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[246] *Id.*

[247] *See* Worku et al., *supra* note 102, at 65, 72.

of an eligible country. Therefore, to be eligible for conditional prequalification, both the FPP and its API must be produced in eligible countries.

The other requirements manufacturers would have to meet for their drugs to gain conditional prequalification would be identical to those for full prequalification *except* in regard to GMP standards.[248] The GMP standards would be the only difference between conditional and full prequalification for two primary reasons: (1) it does not appear that all deviations from full GMP compliance represent a safety risk[249] and (2) GMP compliance is a particularly difficult step in the prequalification process for many manufacturers based in lower-income countries.[250]

The GMP standards for conditional prequalification would not be as stringent as current WHO GMP standards, but would be strong enough to provide acceptable assurances that conditionally prequalified drugs are safe. This Comment will not propose specifics regarding the minimum standards that manufacturers would have to meet to be conditionally prequalified. That is a determination undoubtedly best left to experts, such as the WHO Expert Committee on

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[248] Thus, for example, the requirements a manufacturer's product dossier would need to meet would be identical regardless of whether the manufacturer was granted full or conditional prequalification.

[249] *See* KAY WEYER ET AL., UNITED NATIONS INDUSTRIAL DEVELOPMENT ORGANIZATION, KENYA GMP ROADMAP: A STEPWISE APPROACH FOR THE PHARMACEUTICAL INDUSTRY TO ATTAIN WHO GMP STANDARDS 12 (2014).

[250] Chimezie Anyakora et al., *Cost Benefit of Investment on Quality in Pharmaceutical Manufacturing: WHO GMP Pre- and Post-Certification of a Nigerian Pharmaceutical Manufacturer*, 17 BMC HEALTH SERV. RES. 665 (2017); *supra* Section I.E.

Specifications for Pharmaceutical Preparations. But one way in which quality could be ensured is through the more frequent submission—compared to that required for full prequalification—of product samples to allow for consistent testing of a product's safety.

It appears that not all facilities which fail to comply with the full WHO GMPs are in danger of producing unsafe drugs, as demonstrated by a study conducted in Kenya.[251] In an effort to bring drug manufacturers in the country into compliance with WHO GMPs, the research team in the Kenya study initially examined the current manufacturing practices of seven Kenyan pharmaceutical companies and assessed each company's compliance with WHO GMP standards.[252] As part of the study, the team divided GMP compliance into two broad categories: "site" compliance and "quality management system" compliance.[253] Site refers primarily to the "physical . . . premises, utilities and equipment used for pharmaceutical manufacturing."[254] It includes aspects ranging from whether the facility has designated, self-contained areas where hazardous products are produced to whether there is sufficient space at the site.[255] The quality management system, on the other hand, refers to "all documentation systems and procedures

[251] WEYER ET AL., *supra* note 249, at 12.

[252] *Id.* at 5, 13.

[253] *Id.* at 10.

[254] *Id.*

[255] *Id.* at 27.

used by a company to ensure GMP compliance,"[256] including things such as the establishment of product sampling procedures and frequencies.[257]

The team assigned a score of one, two, or three for both site and quality management system compliance, with a one corresponding to general compliance with WHO GMPs for that indicator, and a three representing inadequate compliance.[258] Companies tended to score better on the quality management system variable than the site variable.[259] A company that had "[a] systematic approach in line with WHO GMP[s] in place and implemented" (a score of one on quality management system) and a "[s]ite [that] shows significant deficiencies from WHO GMP, but does not impair production safety" (a score of two on site) would not be fully compliant with WHO GMPs.[260] Thus, their drugs would not be prequalified.[261] Manufacturers that fall into this category would be prime candidates for conditional prequalification because production safety would not be impaired.

A manufacturer whose product meets the conditional prequalification minimum standards would be required to adhere to a WHO-approved plan that would bring its facilities and operations into compliance with the full GMPs within a specified time period. Repeated failures to meet the goals in the approved plan could result in the WHO cancelling or withdrawing its

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[256] *Id.* at 10.

[257] *Id.* at 37.

[258] *Id.* at 10–12.

[259] *Id.* at 16.

[260] *Id.* at 12.

[261] *Id.* at 7, 12.

conditional prequalification until the manufacturer makes the necessary changes. The WHO's decision to withdraw a product's conditional prequalification would, at the manufacturer's request, be subject to review by the Prequalification Independent Review Panel.

Conditional prequalification has the potential to increase the supply of—and subsequent access to—essential medicines, help develop the pharmaceutical industries in lower-income countries, bring economic benefits to these countries, and incentivize manufacturers in lower-income countries to fully comply with WHO GMPs. Because of the potential of conditional prequalification, drug purchasers, pharmaceutical manufacturers in lower-income countries, and the general population in these countries—particularly individuals in need of essential medicines—would all likely benefit from such a system. The benefits to each of these three stakeholders will be analyzed in turn.

Drug purchasers stand to gain from a system like conditional prequalification. As discussed in Part I, there is a shortage of high-quality essential medicines. This inevitably leads to drug procurement entities and LMIC governments either not purchasing enough drugs or purchasing drugs of a questionable quality.[262] Conditionally prequalified drugs would signal to potential purchasers that a drug has been produced under regulatory oversight, but that the GMPs followed are not quite as rigorous as those followed by fully prequalified drugs. This represents a significant improvement over the status quo, in which people in need either go without essential medicines because of a shortage or only have access to medicines of an unknown quality.

Current and potential pharmaceutical manufacturers in lower-income countries would also benefit from conditional prequalification because they would gain immediate and long-term

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[262] *See supra* Section I.A.

access to additional segments of the essential medicines market. Manufacturers would likely have immediate access to a greater share of the market because they could demonstrate that their drugs were produced under some level of regulatory oversight. At the same time, manufacturers whose drugs are conditionally prequalified would be incentivized to have their products achieve full prequalification. These incentives are procurement entities' likely preference to purchase fully prequalified drugs over conditional ones and the fact that non-compliance with the WHO-approved plan to achieve full prequalification would be grounds for revoking a product's conditional status. Once these manufacturers achieve full prequalification, they would then gain access to the important international drug procurement entities market. Access to these additional segments of the market could lead to a significant expansion of the pharmaceutical industry in lower-income countries. This expansion would bring with it attendant economic benefits, namely "enhanced exports, . . . emergence of supportive industries and the reduced reliance on imports that use up precious hard currency."[263]

Finally, and most importantly, the general population in lower-income countries, including those currently without access to quality-assured essential medicines, would likely benefit the most from conditional prequalification. Conditional prequalification has the potential to both increase access to essential medicines and bring benefits associated with a more developed pharmaceutical industry to persons living in these countries. First, supply is a key component of access, and conditional prequalification has the potential to increase the supply of—and subsequent access to—drugs in lower-income countries. Second, a more developed domestic pharmaceutical industry would likely provide additional economic opportunities for

[263] NGOZWANA ET AL., *supra* note 16, at 6.

persons living in lower-income countries. Higher income is associated with better health: both at the individual and population levels.[264] Wealthier people are generally healthier than their poorer counterparts;[265] and people living in higher-income countries generally enjoy greater overall health than those living in lower-income countries.[266] Additionally, the overall economic benefits attached to the growth of a domestic pharmaceutical industry has the potential to lead to greater individual purchasing power and increased government subsidization of essential medicines. Therefore, the introduction of a conditional prequalification pathway has the potential to benefit drug purchasers, pharmaceutical manufacturers in lower-income countries, and the general population in these countries particularly those in need of essential medicines.

CONCLUSION

WHO's Prequalification Program has contributed greatly to improving the quality of essential medicines purchased by international donors and drug procurement entities. Due to the market share these donors and procurers occupy, as well as the fact that many of them require the

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[264] *See infra* notes 265–266 and accompanying text.

[265] Fiona Imlach Gunasekara et al., *Change in Income and Change in Self-Rated Health: Systematic Review of Studies Using Repeated Measures to Control for Confounding Bias*, 72 SOC. SCI. & MED. 193, 201 (2011) (finding "a small positive association" between individual income increase and self-rated health, based on thirteen studies conducted in four different countries).

[266] Michael Marmot, *The Influence of Income on Health: Views of an Epidemiologist*, HEALTH AFF. 31, 37 (2002) (citing WORLD BANK, WORLD DEVELOPMENT REPORT (1993)).

drugs they purchase to be prequalified, the Prequalification Program has become akin to a drug approval authority in many LMICs.

Stemming from this authority to take actions that adversely affect applicants, the Prequalification Program is obligated to respect international due process principles, including the guarantee of a fair trial. Instituting an Independent Review Panel before which manufacturers whose products are denied prequalification or de-listed could appeal their cases would ensure the program is respecting these principles. Creating an Independent Review Panel would also align with the WHO's role as a promoter of human rights and be commensurate with the great power it exerts over many manufacturers.

Although important from a human rights perspective, it is unclear whether the Independent Panel alone would increase access to essential medicines. One way to improve access to essential medicines is by strengthening the domestic manufacturing capacity in countries with the highest disease burden. Unfortunately, nearly all the FPPs and APIs that have been prequalified have been produced by manufacturers in middle- and high-income countries. By adopting a procedure like conditional prequalification, the WHO would increase the likelihood that a pharmaceutical industry capable of producing quality-assured medicines develops in these lower-income countries. Conditional prequalification could also help ensure that individuals living in these countries enjoy greater access to essential medicines and the economic benefits that come with a developed pharmaceutical industry.