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March 20, 2023

Katherine M. Hiner
Acting Secretary to the Commission
U.S. International Trade Commission
500 E. Street, SW
Washington, D.C., 20436

RE: Prehearing Brief for Investigation No. 332-596: *COVID-19 Diagnostics and Therapeutics and Flexibilities Under the TRIPS Agreement*

Dear Acting Secretary Hiner,

Public Citizen submits the following prehearing comments regarding the U.S. International Trade Commission's March 29-30, 2023, public hearing in connection with Investigation No. 332-596: *COVID-19 Diagnostics and Therapeutics and Flexibilities Under the TRIPS Agreement*. This submission does not contain CBI. Public Citizen is a nonprofit consumer advocacy organization with 500,000 members and supporters. Public Citizen's Access to Medicines Program works with partners across the United States and around the world to make medicines available for all through tools in policy and law.

Sincerely,

Peter Maybarduk
Public Citizen Access to Medicines Director

Summary

The intellectual property provisions of the TRIPS Agreement constrain generic competition and rapid, widespread production of therapeutics and diagnostics. This contributes to inequitable global access to COVID-19 medical tools. Extending the June 17, 2022 World Trade Organization Ministerial Decision on the TRIPS Agreement (the 'TRIPS Decision') to therapeutics and diagnostics would simplify efforts to ensure adequate, affordable supply of these medical tools in the years ahead.

There is massive unmet global health need for Covid-19 therapeutics and diagnostics. The world's failure to quickly scale test-to-treat programming has cost many lives. Yet country orders for these medical tools, and other signals of market demand, were distressingly anemic in 2022. For example, the estimated health need for Paxlovid in low- and middle-income countries (LMICs) exceeded market demand by 8,330,833 courses. It is important to understand why.

At least four factors contribute to the artificial suppression of global demand for COVID-19 diagnostics and therapeutics. First, many patented tools are unaffordable for LMICs. The secrecy of supply agreements complicates country procurement decisions. Second, it is challenging for budget constrained LMICs to compete with high-income countries to purchase products in initially limited and/or unreliable supply. Third, competing health priorities and strained resources limit the ability of governments to prioritize their country's COVID-19 response. Lastly, there are knowledge gaps regarding the available health technologies and the value of testing and therapeutics. In other words, supply challenges – high prices, opacity and delayed and unpredictable availability – constrain demand.

Without diverse, affordable, and reliable supply, demand for diagnostics and therapeutics will continue to be far lower than health need. Flexibilities within the TRIPS Agreement and patent holders' licensing and contract manufacturing arrangements can mitigate the problems of monopoly supply, but they fall short of overcoming IP barriers to global access of generics or unleashing the world's full pandemic tool manufacturing capabilities. Voluntary licenses contain geographic restrictions, resulting in market fragmentation and gaps in access, particularly for upper middle-income countries. Compulsory licensing options are critical to fill these gaps and are much more easily applied to therapeutics and diagnostics than to vaccines. But TRIPS rules still needlessly complicate compulsory licensing, making it harder to clear paths to expansive, affordable, global supply. Simplifying TRIPS rules, including through the proposed extension, would help clear paths to generic entry, and make it a little easier for health agencies to meet the extreme, ongoing health needs of the Covid-19 pandemic.

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COVID-19 diagnostics and therapeutics are critical to preventing hospitalizations and deaths and ending the pandemic. However, there are extreme disparities in access to these tools across the world. According to the purchase data collected by the Duke Global Health Innovation Center, 74.1% of COVID-19 therapeutics have been purchased directly by high-income countries.[1] Additionally, while low- and lower-middle income countries comprise 76.3% of the world population, only 36.9% administered worldwide have been used in these countries.[2] Despite the lack of robust access to diagnostics and therapeutics in non-HICs, the COVID death toll has been estimated to be four times higher in poorer nations than in rich countries.[3] Based on this data, there is clearly great need in LMICs for COVID-19 technologies.

We will first discuss the gaps between market demand and population-based need for COVID-19 diagnostics and therapeutics, the factors that have resulted in a suppressed demand for these COVID-19 technologies in LMICs, and why the Commission should use population-based need as the global demand indicator. Then, the discrepancy between demand and need within non-HICs will be quantified through a retrospective case study of Paxlovid in 2022. Finally, we will comment on the challenges of relying on voluntary measures to ensure global access and the attempted use of compulsory licensing to increase access to Paxlovid in upper middle-income countries.

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[1] Duke Global Health Innovation Center Launch and Scale Speedometer, available at https://launchandscalefaster.org/covid-19/therapeutics [accessed February 17, 2023]

[2] FIND COVID-19 Test Tracker, available at https://www.finddx.org/tools-and-resources/dxconnect/test-directories/covid-19-test-tracker/ (2/21/23)

[3] Oxfam. Pandemic of Greed: A Wake-Up Call for Vaccine Equity at a Grim Milestone. 3 March 2022, available at https://oi-files-d8-prod.s3.eu-west-2.amazonaws.com/s3fs-public/2022-03/Pandemic%20of%20greed-Oxfam%20media%20briefing-March2022.pdf

Market Demand vs. Population-Based Need

As the USITC considers key demand factors and unmet demand for COVID-19 diagnostics and therapeutics, it is important that the Commission bases the report's definition of demand on population need rather than market demand. Population-based need is the theoretical maximum demand in a population that is determined by the number of infections that would require treatment to maximize the prevention of hospitalizations and deaths.[4] If therapeutic courses and tests were available, population-based need would indicate the maximum level at which they would benefit the population. As the future of the pandemic remains uncertain, it is essential that the health needs of populations are prioritized. However, the number of COVID-19 therapeutic courses and tests being delivered or requested by countries, particularly non-HICs, is significantly fewer than the health need. There are a number of factors contributing to the discrepancy between population-based need and market demand that should be explored by the Commission. We describe four of these factors below.

1. Unaffordable and Confidential Pricing Agreements

The lack of a robust generics market for diagnostics and therapeutics, in part due to patents, has resulted in prices that are unaffordable for many governments. When diagnostics and therapeutics are unaffordable, demand will be suppressed. For instance, a South African senior health official cited the "extremely expensive" price of Paxlovid as a reason that the South African government is not intending to buy the treatment for public sector patients.[5] The Medical Director at Socios en Salud (Partners in Health – Perú) also commented that the organization does not plan to use Paxlovid in the COVID-19 treatment regime if it is too expensive.[6] Additionally, according to a People's Vaccine Alliance report, tensions arose between procurers and manufacturers of antigen RDTs during the early stages of the pandemic because constrained budgets and challenges forecasting procurement resulted in the initially agreed upon volumes exceeding funding amounts.[7]

In 2019, per capita health spending averaged US$36 in low-income countries, US$125 in lower middle-income countries, US$516 in upper middle-income countries, and US$3,243 in high-income countries.[8] For low- and middle-income countries, the prices for diagnostics and therapeutics purchased from the manufacturer would exceed or consume a significant portion of their per capita health spending. Panama, whose classification has shifted from high-income to middle-income and back to high-income in recent years, reportedly obtained Paxlovid for US$250, the lowest reported price in a bilateral deal with Pfizer. While this price is significantly reduced from the prices paid by some high-income countries, it is nearly

[4] Airfinity. 'Paxlovid/TRIPS Analysis'
[5] S. Africa not planning to buy Pfizer's COVID pill for public sector, available at https://finance.yahoo.com/news/africa-not-planning-buy-pfizers-073311851.html
[6] Matahari Global Solutions. Mapping COVID-19 Access Gaps: Results from 14 Countries and Territories, available at https://app.box.com/s/ewdjytgt0tk0fdgmqnlm4l30hmdyevxw
[7] People's Vaccine Alliance, 'Study on the Availability and Affordability of Diagnostics for COVID-19 and MPOX in Low and Middle-Income Countries' (2022), available at https://peoplesvaccine.org/wp-content/uploads/2023/02/Study-on-the-Availability-and-Affordability-of-Diagnostics.pdf
[8] World Health Organization. Global Health Expenditure Database, available at https://apps.who.int/nha/database/Select/Indicators/en

50 percent of the average per capita health spending in upper middle-income countries and 200 percent of the average per capita health spending in lower middle-income countries.

In addition to exorbitant pricing, the lack of transparency in supply agreements prohibits countries from having a sense of the full pricing landscape and complicates the decision-making environment for purchasers. It was reported that Pfizer has offered Paxlovid to the Global Fund and some low-income countries at a not-for-profit price.[9] Pfizer also has described a tiered pricing scheme whereby prices are negotiated based on a country's income level. But specifics on these prices have not been disclosed.

Without this disclosure, prices paid for COVID-19 diagnostics and therapeutics are largely unknown and are reported for only a subset of purchase agreements made. The reported prices are staggering and unaffordable for most countries. For low- and middle-income countries that are particularly price sensitive, understanding the full pricing landscape would be a key decision-making factor. These countries are left waiting for a more affordable price, lowering the number of orders placed (i.e., market demand) below the level of public health need. For example, test-to-treat programs launched by ACT-A partners in early 2021 cited the "complex and evolving landscape of treatments and costs" as a barrier that hindered the introduction of oral antivirals in LMICs. These pilot programs demonstrated that full price transparency and affordable treatments are instrumental factors in generating demand and uptake of therapeutics.[10]

Additionally, the price to the consumer can suppress demand even when country-level procurement costs are non-prohibitive. Recent economic challenges, such as rising inflation, have made it even more difficult for individuals to afford getting tested for COVID-19. In addition to the cost of the test itself, related costs, such as paying for transportation to the hospital or laboratory, are unaffordable for many people in LMICs and have lowered the demand for diagnostics at the community level.[11] As of early 2022 in Zimbabwe, when free tests ran out at the poorly supplied walk-in testing centers, individuals were left to purchase rapid tests in pharmacies for up to US$15 – an unaffordable price for a majority of the population in the country.[12] It is essential that countries are able to procure COVID-19 technologies at a price that allows for public health needs to be met, without exorbitant prices being passed along to individuals.

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[9] Pfizer to Supply Global Fund Up to 6 Million PAXLOVID™ Treatment Courses for Low-and-Middle-Income Countries, available at https://www.pfizer.com/news/press-release/press-release-detail/pfizer-supply-global-fund-6-million-paxlovidtm-treatment; Pfizer Expands 'An Accord for a Healthier World' Product Offering to Include Full Portfolio for Greater Benefit to 1.2 Billion People in 45 Lower-Income Countries, available at https://www.pfizer.com/news/press-release/press-release-detail/pfizer-expands-accord-healthier-world-product-offering

[10] Report of the Access to COVID-19 Tools Accelerator Facilitation Council Working Group on Therapeutics and Diagnostics, available at https://www.who.int/publications/m/item/act-accelerator-facilitation-council-working-group-report-on-diagnostics-and-therapeutics

[11] UNICEF. Access to COVID-19 Tools Accelerator, Humanitarian Situation Report No. 4, End of Year Report 2022

[12] In Africa At-home COVID Tests are Scare and Expensive, Help May Not Come Until Next Year, available at https://www.pbs.org/newshour/world/in-africa-at-home-covid-tests-are-scarce-and-expensive-help-may-not-come-until-next-year

As rising inflation and increasing levels of public debt in 2022 have put pressure on countries' health spending capacities,[13] diverse and affordable supply is key to bring prices down and generate robust global demand for COVID-19 health technologies.

2. Lack of Available and Reliable Supply

Low- and middle-income countries have continually fallen to the bottom of the supply chain for COVID-19 technologies. The vaccine apartheid has been widely documented throughout the pandemic, with high-income countries quickly purchasing and stockpiling enough supply to vaccinate their populations multiple times over while low- and middle-income countries received only a fraction of the doses needed.[14] These same challenges have been seen in diagnostic and therapeutic supply to LMICs.

For example, soon after clinical studies showed promising results for Paxlovid at the end of 2021, high-income countries began entering into advance purchase agreements with Pfizer for millions of courses. Before any low- and middle-income countries were able to secure supply agreements, nearly 30 million courses – the amount that Pfizer could produce in the first half of 2022 – had already been purchased by HICs.[15] By early September of 2022, it was reported that many LMICs still had no access to the drug.[16] Similarly, HICs were able to outbuy LMICs in diagnostics, resulting in restricted supply of diagnostic tools such as PCR machines, test reagents, and consumables before manufacturers could scale up production.[17]

Supply of COVID-19 diagnostics and therapeutics to LMICs has been largely unreliable throughout the pandemic. This unreliable supply has exacerbated the effects of the pandemic in LMICs while also hindering the demand for these technologies. When advance purchase agreements consume the supply for six months and more, as with Paxlovid, LMICs are left to purchase therapeutics that will be unavailable for months. With the unpredictability of COVID-19 case surges and entry of variants, it is challenging for countries with constrained spending capacities to enter into a supply agreement for products with unreliable supply.

Additionally, the effectiveness of current COVID-19 therapeutics is reliant on well-developed test-to-treat strategies, including diagnostic capacity and the immediate availability of therapeutics.[18] An unreliable

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[13] The World Bank. From Double Shock to Double Recovery – Implications and Options for Health Financing in the Time of COVID-19, available at https://openknowledge.worldbank.org/bitstream/handle/10986/35298/September%202022.pdf?sequence=12&isAllowed=y

[14] Prasad S et al. Vaccine apartheid: the separation of the world's poorest and most vulnerable and the birth of Omicron. Ther Adv Vaccines Immunother. 2022 Jul 5, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9272166/

[15] The Looming COVID-19 Treatment Equity Gap, available at https://www.devex.com/news/the-looming-covid-19-treatment-equity-gap-102816

[16] Why Paxlovid is still not available in many LMICs, available at https://www.devex.com/news/why-paxlovid-is-still-not-available-in-many-lmics-103904

[17] Boro E, Stoll B. Barriers to COVID-19 Health Products in Low-and Middle-Income Countries During the COVID-19 Pandemic: A Rapid Systematic Review and Evidence Synthesis. Front Public Health. 2022 Jul 22, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9354133/

[18] COVID Gap. Pills to People: Accelerating Equitable Global Access to Oral Therapeutics for COVID-19, available at https://www.covidcollaborative.us/assets/uploads/pdf/Covid-Gap-Oral-therapeutics-v8.pdf

supply of diagnostics and therapeutics prevents countries from scaling-up the implementation of test-to-treat strategies. Robust test-to-treat programs are critical in generating demand for COVID-19 diagnostics and therapeutics. Without these programs in place, countries will not have the program capacity to rapidly deploy tests and treatments so demand will appear lower than public health need, even when supply of products become available.

3. Strained Health System Capacity

Strained health system resources and capacity in LMICs also has limited the demand for COVID-19 diagnostic and therapeutic tools. For example, competing health priorities in ACT-A countries, such as new disease outbreaks of cholera and mpox, limited community interest in ACT-A's efforts to promote trust in COVID-19 tools.[19] Additionally, humanitarian crises such as conflicts and natural disasters impacting regions including Eastern and Southern Africa, the Middle East, and North Africa have exacerbated the challenge for many countries to implement a robust COVID-19 response.[20] During procurement of the vaccine, it was reported that gaps in cold chain and service delivery and insufficient workforce capacity in low- and lower-middle income countries contributed to the discrepancy between the number of available vaccine doses and the amount that ended up in low-income countries.[21] For diagnostics and therapeutics, strained health system capacity limits the prioritization LMICs can place on procuring and distributing COVID-19 tools.

Additionally, many LMICs were unprepared to quantify and forecast national needs for diagnostics.[22] It is challenging for countries to make the decision to disburse significant funds for diagnostic tools when there is not a system in place to forecast the amount that is needed. Similarly, when diagnostics are unavailable or underutilized, infections will go unreported. For example, in October of 2021, the WHO reported that only one in seven COVID-19 infections are detected in Africa.[23] Without an accurate estimate of infection-level in a population, the demand for therapeutics will be lower than the true population-based need.

A People's Vaccine Alliance report also highlighted that the demand for COVID-19 diagnostics in low- and middle-income settings is impacted by individuals' demand factors, such as the challenges associated with receiving a positive test.[24] LMICs often do not have the resources or capacity to operate social safety net programs that will address these challenges, such as issues with forgoing wages for many days to isolate due to a positive test. This suppressed demand at the community level will make it challenging for countries to request products at the level needed to meet true public health need.

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[19] UNICEF. Access to COVID-19 Tools Accelerator, Humanitarian Situation Report No. 4, End of Year Report 2022
[20] UNICEF. Access to COVID-19 Tools Accelerator, Humanitarian Situation Report No. 4, End of Year Report 2022
[21] Usher AD. The global COVID-19 treatment divide. Lancet. 2022 Feb 26
[22] People's Vaccine Alliance, 'Study on the Availability and Affordability of Diagnostics for COVID-19 and MPOX in Low and Middle-Income Countries' (2022), available at https://peoplesvaccine.org/wp-content/uploads/2023/02/Study-on-the-Availability-and-Affordability-of-Diagnostics.pdf
[23] WHO. Six in Seven COVID-19 Infections Go Undetected in Africa, available at https://www.afro.who.int/news/six-seven-covid-19-infections-go-undetected-africa
[24] People's Vaccine Alliance, 'Study on the Availability and Affordability of Diagnostics for COVID-19 and MPOX in Low and Middle-Income Countries' (2022), available at https://peoplesvaccine.org/wp-content/uploads/2023/02/Study-on-the-Availability-and-Affordability-of-Diagnostics.pdf

4. Knowledge Gaps in LMICs

Market demand also cannot reach the levels of population health need when there are gaps in knowledge that hinder the use of diagnostics and therapeutics. Matahari Global Solutions, a global health consultancy firm, conducted interviews in 14 countries and reported instances in countries such as Haiti, Madagascar, and Nigeria where health care workers did not have any knowledge of the existence of Paxlovid.[25]

Additionally, when health care workers and communities are aware of the existence of diagnostics and therapeutics, the demand for these products can still be artificially suppressed by gaps in knowledge of the importance of these tools in combatting the pandemic. According to a 2022 situation report by UNICEF, the level of awareness of the value of diagnostics constrained the provision of diagnostics globally.[26] In September 2022, the ACT-A Working Group on Diagnostics and Therapeutics reported that government officials, health workers, and communities in many LMICs are unaware of the importance of test-to-treat strategies and COVID-19 therapeutics.[27] Without knowledge of the value of these tools, they will be underutilized and there will be limited community buy-in for initiatives such as test-to-treat.

It is critical that population-based need is prioritized and demand is generated through robust supply of generics. Using a case study of Paxlovid, we will quantify the number of need-based doses that exceeded market demand in 2022 to illustrate the disparity.

Quantifying Market Demand vs. Population-Based Need: Paxlovid in 2022

Pfizer's oral antiviral Paxlovid (nirmatrelvir-ritonavir) has been deemed by the WHO as the best therapeutic choice for high-risk patients with non-severe disease.[28] Despite the potential of Paxlovid to be a game-changer in the pandemic and prevent significant numbers of hospitalizations and deaths, there has been limited supply of the branded product in LMICs.[29] Based on the principles described in the previous section, the market demand for Paxlovid is likely suppressed below the level of population-based need, particularly in low- and middle-income countries. To further illustrate this disparity, we quantified the number of need-based doses that exceeded demand for Paxlovid in LMICs in 2022.

The Duke Global Health Innovation Center's Launch and Scale Speedometer tracks purchases of COVID-19 therapeutics and maintains a dashboard that details data on these purchases.[30] This dashboard reports that 48,186,517 courses of Paxlovid have been purchased worldwide, with over 70% of the courses having

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[25] Matahari Global Solutions. Mapping COVID-19 Access Gaps: Results from 14 Countries and Territories, available at https://app.box.com/s/ewdjytgt0tk0fdgmqnlm4l30hmdyevxw

[26] UNICEF, Access to COVID-19 Tools Accelerator, Humanitarian Situation Report No. 4, End of Year Report 2022

[27] Report of the Access to COVID-19 Tools Accelerator Facilitation Council Working Group on Therapeutics and Diagnostics, available at https://www.who.int/publications/m/item/act-accelerator-facilitation-council-working-group-report-on-diagnostics-and-therapeutics

[28] WHO. Therapeutics and COVID-19: Living Guideline, 13 January 2023, available at https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.1

[29] Just a Quarter of Pfizer's COVID-19 Treatment Orders Will Go to Developing Countries, available at https://www.oxfam.org/en/press-releases/just-quarter-pfizers-covid-19-treatment-orders-will-go-developing-countries

[30] Duke Global Health Innovation Center Launch and Scale Speedometer, available at https://launchandscalefaster.org/covid-19/therapeutics [accessed February 17, 2023]

been purchased directly by high-income countries. Lower-middle income countries (Egypt and Ukraine) purchased a total of 320,000 courses and upper middle-income countries (Mexico and Thailand) purchased a total of 350,000 courses. Two ACT-A partners have entered into an agreement with Pfizer for an additional 10 million courses for LMICs.[31]

The courses available to ACT-A partners are offered to eligible countries and countries then confirm the number of courses that they want to receive. With this model, the market demand would be considered the number of courses that were confirmed by countries, rather than the total amount procured by ACT-A partners. Using the WHO Therapeutics Dashboard, we determined that 2,132,304 courses of Paxlovid have been offered to LMICs by ACT-A, but only 135,120 courses were confirmed.[32]

Our analysis was limited to data that is publicly available. Due to the lack of transparency in supply agreements, there are potentially purchases made by non-HICs that have not been captured. For future analyses of the supply and demand dynamics in the COVID-19 diagnostic and therapeutic markets, supply agreement transparency is critical.

Based on the available data, market demand in non-HICs, or the number of treatments that were being ordered or requested, could be defined as the number of courses that were confirmed by ACT-A countries combined with identified non-HIC originator supply deals. To date, LMICs have ordered or requested 805,120 courses of Paxlovid (Table 1).

Table 1: Market demand for Paxlovid in non-HICs

Courses confirmed from ACT-A	135,120
Ukraine	300,000
Egypt	20,000
Mexico	300,000
Thailand	50,000
Total	**805,120**

Source: Duke Global Health Innovation Center Launch and Scale Speedometer; WHO Therapeutics Dashboard

To determine the population-based need for Paxlovid, we consider the total number of infections in LMICs that would have benefitted from the use of Paxlovid had it been available. Paxlovid is indicated for patients with non-severe COVID-19 at the highest risk of hospitalization. While reliably identifying those at the highest risk is challenging, the WHO has determined that patients with older age, immunosuppression, and/or chronic diseases are the typical characteristics of high-risk patients.[33] The lack of COVID-19 vaccination is an additional risk factor that is particularly significant in the non-HIC setting due to the low vaccination rates. Airfinity, a health analytics company, estimated the population need for

[31] 6 million courses were purchased by the Global Fund and 4 million courses were purchased by UNICEF
[32] World Health Organization Therapeutics Dashboard, available at https://partnersplatform.who.int/en/therapeutics-dashboard [accessed February 27, 2023]
[33] Therapeutics and COVID-19: Living Guideline, 13 January 2023, available at https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.1 [accessed February 27, 2023]

Paxlovid using the total infections in populations over 65 years old as the measure for high-risk infections.[34] This estimation does not capture key population groups that would benefit from Paxlovid, such as those with chronic diseases under the age of 65. Additionally, due to data constraints, the estimation only spans from the beginning of 2022 through Nov. 22, 2022. Both of these factors make this figure an underestimate of population need.

From the beginning of 2022 through Nov. 22, 2022, the population need in non-HICs surpassed nine million doses of Paxlovid. When compared to the previous calculation of market demand, we estimate that population-based need exceeded market demand by over eight million courses of Paxlovid (Table 2). This is more than eight million individuals that could have benefitted from a course of Paxlovid, potentially avoiding hospitalization or loss of life.

Table 2: Difference between market demand and population-based need for Paxlovid in LMICs (2022)

Market Demand	Population-Based Need	Need-based courses in excess of demand
805,120	9,135,953	**(8,330,833)**

Source: Airfinity; Launch and Scale Speedometer; WHO Therapeutics Dashboard

It has also been estimated by the ACT-A Council Working Group on Diagnostics and Therapeutics that across ACT-A eligible LMICs, there will be an unconstrained need for 223 million antiviral treatments in 2023, compared to demand for 31 million treatment courses.[35] This would result in 192 million COVID-19 infections in LMICs that would benefit from antivirals, but will ultimately not have access.

Given the significant disparity between market demand and population-based need, the Commission has a responsibility to fully consider population need, rather than market demand, when exploring key demand factors, unmet demand, and the market segmentation of global demand.

Generics Markets and Demand for COVID-19 Diagnostics and Therapeutics: Voluntary Measures and Compulsory Licensing

Intellectual property protections have contributed to challenges in developing timely, robust generics markets for diagnostics and therapeutics. Without diverse, affordable, and reliable supply, demand for diagnostics and therapeutics will continue to be suppressed globally. An extension of the TRIPS Decision to diagnostics and therapeutics would promote the entry of generic manufacturers to the market for COVID-19 health technologies, inducing demand and increasing access to supply at more affordable prices.

While the relationship between IPRs within trade agreements and access to medicines is complicated and difficult to demonstrate empirically due to the short time periods and small markets, the issue of TRIPS and access to medicines is really one of generic competition. It has been widely demonstrated that

[34] Airfinity. 'Paxlovid/TRIPS Analysis'

[35] Report of the Access to COVID-19 Tools Accelerator Facilitation Council Working Group on Therapeutics and Diagnostics. "Unconstrained need is the total number of cases in LMICs in the next 12 months, regardless of a country's testing capacity, interest in the product, or capacity to roll it out"

increasing generic competition puts downward pressure on price and effectively increases access. If countries could purchase reliable supply of COVID-19 therapeutics and diagnostics at an affordable price, global demand for these technologies would rise. The IP protections within the TRIPS Agreement have the chief function of blocking competition, hindering generic manufacturing of the COVID-19 technologies that are essential to controlling and ending the pandemic. The current tools deployed to overcome IP barriers to generic competition are inadequate in increasing global access and generating market demand that meets population health need.

Voluntary Measures

Licensing is one mechanism to increase access to generic COVID-19 therapeutics and diagnostics within LMICs. While voluntary licensing measures are successful in accelerating affordable and reliable supply of generic products to certain markets, the agreements typically exclude many upper middle-income countries.

Patent holders have signed agreements through the Medicines Patent Pool (MPP) for 15 COVID-19 technologies, including licenses for three oral antiviral treatments and four diagnostics.[36] Using the MPP license for Paxlovid, the Clinton Health Access Initiative (CHAI) has announced that generic Paxlovid will be available to LMICs for US$25 per course.[37] Considering the prices that have been reportedly paid for the brand-name drug, this agreement between CHAI and generic manufacturers is significant and will play a large role in ensuring affordable access to Paxlovid for LMICs. However, countries not included in the MPP licensing agreement will not be able to benefit from the generic pricing. This results in a fragmented market where low-income and lower-middle income countries can access the generic drug at an affordable price, increasing market demand towards the level of population health need, while many upper middle-income countries continue to lack access to reliable and affordable supply.

The restricted geographical reach of the voluntary licenses also limits the markets available for generics, resulting in a less attractive opportunity for generic manufacturers. For example, in the Paxlovid agreement between CHAI and generic manufacturers, the price of US$25 will only apply if volume requirements are met – any single order must be for a quantity of at least 50,000-treatment courses and the aggregate of all orders must meet or exceed one million treatment courses.[38] If larger markets were available to generic manufacturers, increasing the global demand for the drug, the market opportunity may be sufficiently enticing and these stipulations would not be necessary for generic manufacturers to enter the market. An extension of the TRIPS Decision would play an important role in expanding the market for generic products, increasing both the supply of and demand for generic diagnostics and therapeutics.

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[36] MPP Products Licensed, available at https://medicinespatentpool.org/progress-achievements/licences

[37] Press Release: CHAI Announces Agreements with Leading Generic Manufacturers to Make Affordable COVID-19 Treatment Available in Low- and Middle-Income Countries, available at https://www.clintonhealthaccess.org/news/chai-announces-agreements-with-leading-generic-manufacturers-to-make-affordable-covid-19-treatment-available-in-low-and-middle-income-countries/

[38] FAQ: What you need to know about CHAI's generic Paxlovid deal, available at https://www.clintonhealthaccess.org/news/frequently-asked-questions-for-nir-r-agreement-announcement/

Furthermore, timely access to generics is critical and could be better achieved with a waiver of the TRIPS IP provisions. For instance, the MPP and Pfizer signed a licensing agreement in November 2021 for nirmatrelvir, and the MPP then signed agreements with 35 companies to manufacture nirmatrelvir in March 2022.[39] One of these companies, Hetero in India, received WHO prequalification for their generic Paxlovid in late December 2022.[40] Pfizer declined to include China in the MPP license territory. Instead, Pfizer concluded a separate licensing deal for supply of China many months later -- too late to mitigate the extreme supply shortfall during China's deadly COVID-19 outbreak at the end of 2022. Other upper middle-income countries excluded from the MPP license may face challenges accessing generic Paxlovid until 2041.[41] Without the intellectual property barriers of the TRIPS Agreement, global access to generic products could be achieved quicker. The delayed access of diagnostics and therapeutics will continue to cost lives and put additional strain on health systems.

Tiered pricing is another voluntary mechanism that theoretically provides access to affordable technologies for countries that are left out of voluntary licensing agreements. The Pfizer CEO commended their tiered pricing system as a "critical step that will boost equitable access for high-risk patients in low-and-middle income countries."[42] However, relying on tiered pricing systems to ensure equitable access for countries that are not covered by voluntary licensing agreements, and thus do not have access to generics, is flawed. Tiered pricing does not ensure that therapeutics and diagnostics are affordable for the purchaser, but rather charges a price that is developed by and acceptable to the manufacturer, ensuring a fair profit.[43] In a study of price reduction strategies for antiretroviral drugs, researchers found that for 15 of 18 ARVs, differential pricing schemes were 23-498% more expensive than generic products.[44] Panama paid US$250 for Paxlovid, presumably under the tiered pricing scheme. This differential price is ten times higher than the generic price negotiated by CHAI ($25). Tiered pricing is not aligned with public

[39] 35 generic manufacturers sign agreements with MPP to produce low-cost, generic versions of Pfizer's oral COVID-19 treatment nirmatrelvir in combination with ritonavir for supply in 95 low- and middle-income countries, available at https://medicinespatentpool.org/news-publications-post/35-generic-manufacturers-sign-agreements-with-mpp-to-produce-low-cost-generic-versions-of-pfizers-oral-covid-19-treatment-nirmatrelvir-in-combination-with-ritonavir-for-supply-in-95-low-and

[40] India-based Hetero's Paxlovid generic gets WHO backing, available at https://www.reuters.com/business/healthcare-pharmaceuticals/india-based-heteros-paxlovid-generic-gets-who-backing-2022-12-27/

[41] Latin America: How Patents and Licensing Hinder Access to COVID-19 Treatments, available at https://msfaccess.org/latin-america-how-patents-and-licensing-hinder-access-covid-19-treatments

[42] Pfizer to Supply Global Fund Up to 6 Million PAXLOVID Treatment Courses for Low-and-Middle-Income Countries, available at https://www.pfizer.com/news/press-release/press-release-detail/pfizer-supply-global-fund-6-million-paxlovidtm-treatment

[43] Moon S, Jambert E, Childs M, von Schoen-Angerer T. A win-win solution?: A critical analysis of tiered pricing to improve access to medicines in developing countries. Global Health. 2011 Oct 12, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3214768/

[44] Waning, Brenda, et al. "Global strategies to reduce the price of antiretroviral medicines: evidence from transactional databases." Bulletin of the World Health Organization 87.7 (2009)

interests and is not correlated with population need or a country's ability to pay, which is unsurprising as the decision making is in the hands of private firms.[45]

While there are some routes for low- and lower middle-income countries to access COVID-19 products at an affordable price, upper middle-income countries are left without access to tools that will meet population needs during the pandemic. These countries are largely excluded from voluntary licensing agreements and are left with unaffordable prices through tiered pricing schemes, resulting in a fragmented market for generic diagnostic and therapeutic suppliers to operate within. As many UMICs have been highly devastated by the pandemic and exhibit extreme income disparities, the lack of access to affordable COVID-19 diagnostics and therapeutics is consequential. When voluntary mechanisms fail to achieve global access, there is a need for compulsory solutions that will enable countries to address the health needs of their populations.

Compulsory Licensing

Compulsory licensing is a flexibility under the TRIPS Agreement that can expand generic markets and provide access to COVID-19 therapeutics and diagnostics. Developing countries are discouraged from using this mechanism by pharmaceutical companies and some high-income countries. An MSF Access Campaign briefing describes the challenges that developing countries have faced when using compulsory licensing, including lawsuits from pharmaceutical companies, threatened trade sanctions through the USTR Special 301 Reports, and warnings from the European Commission.[46] Compulsory licensing actions relating to Latin American countries, compiled by Knowledge Ecology International, further demonstrates pressure and threats from HICs and pharmaceutical companies to discourage the use of compulsory licensing by LMICs.[47] The extension of the TRIPS Decision to diagnostics and therapeutics could be instrumental in allowing compulsory licensing to be more freely used. If developing countries are able to effectively grant compulsory licenses, both supply and demand for affordable products would be induced.

Pfizer's licensing agreement with the MPP for Paxlovid, signed in November 2021, covers 95 countries.[48] However, many upper middle-income countries, including China, Thailand, Turkey, and most Latin American and Caribbean countries, were excluded from the deal.[49] As seven of these excluded countries have case-fatality rates that are among the top 20 highest case-fatality rates worldwide,[50] there is significant public health need for Paxlovid in upper middle-income countries. We previously discussed the

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[45] Moon S, Jambert E, Childs M, von Schoen-Angerer T. A win-win solution?: A critical analysis of tiered pricing to improve access to medicines in developing countries. Global Health. 2011 Oct 12, available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3214768/

[46] Medecins Sans Frontieres. Compulsory Licenses, the TRIPS Waiver and Access to COVID-19 Medical Technologies, available at https://msfaccess.org/sites/default/files/2021-05/COVID_TechBrief_MSF_AC_IP_CompulsoryLicensesTRIPSWaiver_ENG_21May2021_0.pdf

[47] KEI. 'Latin America, Compulsory Licensing,' available at https://www.keionline.org/cl/latin-america-compulsory-licensing

[48] MPP Nirmatrelvir License, available at https://medicinespatentpool.org/licence-post/pf-07321332

[49] Latin America: How Patents and Licensing Hinder Access to COVID-19 Treatments, available at https://msfaccess.org/latin-america-how-patents-and-licensing-hinder-access-covid-19-treatments

[50] Paraguay, North Macedonia, Bulgaria, Ecuador, Bosnia and Herzegovina, Mexico and Peru; Johns Hopkins University Mortality Analyses, available at https://coronavirus.jhu.edu/data/mortality

market fragmentation and gaps in access for upper middle-income countries that result in part from voluntary licensing agreements and tiered pricing schemes. Compulsory licensing is a mechanism that could be used to expand the market for generic diagnostics and therapeutics to countries that are not covered by voluntary licenses, increasing global demand for the products. According to the Global Humanitarian Progress Corporation (GHP Corp), five compulsory license actions are in progress in LAC for Paxlovid – Chile, the Dominican Republic, Colombia, Perú, and Costa Rica.[51] Pfizer has filed a patent application for nirmatrelvir in all five of these countries.[52]

Luz Marina Umbasia Bernal, Legal Advisor at GHP Corp in Colombia and Legal Fellow at Public Citizen's Access to Medicines Program, has been working to ensure that the Colombian population can benefit from the COVID-19 technologies that are on the market and available in most high-income countries. However, due to the high prices of the technologies and competing health priorities in the country, market demand is low, and the public continues to lack access to both diagnostics and therapeutics. GHP Corp, alongside other civil society organizations, submitted a request for government use of Paxlovid on March 14, 2022, but did not receive a response.[53] After the presidential election in 2022, the civil society organizations filed another application for government use to the new Colombian government. There have been reports of previous instances in which the Colombian government received pressure from the U.S. government not to issue compulsory licenses.[54]

Similarly, on Dec. 3, 2021, Knowledge Ecology International submitted a request to the government of the Dominican Republic for an open compulsory license relating to Paxlovid.[55] Pfizer responded to this request with opposition, putting pressure on the government of the Dominican Republic to reject the request.[56]

Given the challenges that countries have faced in granting compulsory licenses, extending the TRIPS Decision could contribute to increasing the use of this flexibility. Compulsory licensing is a key flexibility in the TRIPS Agreement that could develop generic markets in countries that are excluded from voluntary licenses. These expanded markets would induce greater supply of affordable generics, generating market demand that could better address population heath need in LMICs.

Future Considerations

The COVID-19 products that are currently on the market represent a small subset of the future tools that will be developed to combat the pandemic. According to the BIO COVID-19 Therapeutic Development

[51] Global Humanitarian Progress Corporation, Acceso a tratamientos COVID 19 en LAC, available at https://www.ghpcorporation.co/accesoatratamientoscovid-19
[52] Latin America: How Patents and Licensing Hinder Access to COVID-19 Treatments, available at https://msfaccess.org/latin-america-how-patents-and-licensing-hinder-access-covid-19-treatments
[53] Global Humanitarian Progress Corporation, Acciones en Colombia, available at https://www.ghpcorporation.co/blank
[54] KEI. 'Latin America, Compulsory Licensing,' available at https://www.keionline.org/cl/latin-america-compulsory-licensing
[55] KEI Requests an Open Compulsory License Relating to Paxlovid in the Dominican Republic, available at https://www.keionline.org/37066
[56] https://keionline.org/misc-docs/1/Translation-Pfizer-opposition-KEI-CL-Paxlovid-18march2022.pdf

Tracker, 76 therapeutics are in late-stage clinical development.[57] Shionogi's new therapeutic, Xocova (ensitrelvir fumaric acid), has been approved in Japan and began clinical trials in the US.[58] The drug is a promising treatment for COVID-19 and has shown some preliminary strengths over Pfizer's Paxlovid. For example, Xocova treats patients irrespective of their risk status, is the first drug that has been shown to shorten the number of day people test positive and has the potential to treat long COVID (based on unverified claims by the manufacturer).[59]

In October 2022, Shionogi signed a licensing agreement for ensitrelvir fumaric acid with the MPP that covers 117 countries.[60] While the license covers more countries than the molnupiravir and nirmatrelvir licenses, there continues to be upper middle-income countries that are excluded. The inequitable rollout of Paxlovid, hindered by the intellectual property provisions of the TRIPS Agreement, should serve as a lesson for the upcoming global distribution of Xocova.

Conclusion

Each time a patented product comes to market, LMICs will be left with unreliable supply at high prices due in part to a lack of diverse, affordable supply that comes from a robust generics market. We will also see a continuation of suppressed demand that is a symptom of the intellectual property barriers of the TRIPS Agreement. The continued overreliance on voluntary action by patent holders will hinder global access to COVID-19 diagnostics and therapeutics. It is important that the TRIPS Decision is extended to diagnostics and therapeutics, contributing to creating an environment that makes it straightforward for countries to address the health needs of their population.

We appreciate the opportunity to comment. Thank you.

[57] BIO COVID-19 Therapeutic Development Tracker, available at https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker

[58] U.S. NIH Starts Trial for Shionogi's COVID-19 Pill, available at https://www.reuters.com/business/healthcare-pharmaceuticals/us-nih-starts-trial-shionogis-covid-19-pill-2023-02-15/

[59] COVID Pill is First to Cut Short Positive-Test Time After Infection, available at https://www.nature.com/articles/d41586-023-00548-6

[60] Ensitrelvir Fumaric Acid License, available at https://medicinespatentpool.org/licence-post/ensitrelvir