**Key highlights in the USITC Report: Supports Extension of the 17th June Ministerial Decision on the TRIPS Agreement to COVID 19 Diagnostics and Therapeutics**

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- In the Executive summary, the USITC report highlights its finding on the "disparity among countries of different income groups is wide in terms of access and availability to COVID-19 diagnostics and therapeutics". It adds that while many factors impact availability and demand **"high prices and the lack of price transparency appear detrimental to many countries seeking access"** and that patent protection is generally found to be less beneficial to innovation in the health sector for developing countries, and leads to high prices. It also **finds that compulsory licenses "is linked to increased generics and lower prices, and increased access to pharmaceuticals"**.

- In the Executive Summary, the USITC report factually states that WHO has declared that COVID-19 would no longer be classified as a public health emergency of international concern, adding that market demand has waned. **However, the Report does not sufficiently emphasize that COVID-19 is a pathogen with continuing pandemic potential, and as new variants emerge, there is a strong likelihood of rise in infections, morbidity, and mortality, with national and global social and economic consequences, and hence the need for developing countries to be ready with policy tools to address future risks and their needs.** The Report also fails to mention the continuing need for therapeutics that prevent, shorten, or ameliorate long covid, which could greatly expand needed supplies to cover all at risk of developing long covid. **It is apparent from the report that mechanisms such as VLs, donations, tier-pricing have severe shortcomings and are inadequate to address access needs in developing countries.**

- In Chapter 2, the USITC recognizes that there are patents on COVID-19 diagnostics and therapeutics. In this Chapter, USITC also finds there are patent protection has little to no positive effect for innovation in developing countries and negative effects for access and affordability (see below quotes from Chapter 2).

- Responding to the question on how to define COVID-19 diagnostics and therapeutics, in Chapter 3 USITC points out that generally "COVID-19 diagnostic is a good used to diagnose COVID-19 or identify how patients respond to a treatment for COVID-19, and a COVID-19 therapeutic is a good used to treat COVID-19" adding that "the universe of products that fall within these expansive definitions is broad and varied" and that "as the virus mutates, the efficacy of a given diagnostic or therapeutic for COVID-19 can also change."(pg 92-93). **Regrettably, the Report fails to acknowledge that therapeutics can also be used as pre-exposure to prevent COVID-19 infection for both people who are immune-compromised and who should not be vaccinated.**[1] Given the dynamic nature of the virus, the Report notes that as of 2023, there have been hundreds of tests produced and hundreds of therapeutics studied, all specific to COVID-19, and there are new clinical trials for therapeutics being added to the pipeline every week around the world. This Chapter discusses the difficulties in further

[1] For example Tixagevimab and cilgavimab are long-acting monoclonal antibodies that are specifically directed against the spike protein of SARS-CoV-2, designed to block the virus' attachment and entry into human cells." https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-new-long-acting-monoclonal-antibodies-pre-exposure#:~:text=Tixagevimab%20and%20cilgavimab%20are%20long,and%20entry%20into%20human%20cells. See:https://www.ncbi.nlm.nih.gov/books/NBK574507/#:~:text=Monoclonal%20antibodies%20to%20treat%20COVID,factors%20for%20severe%20disease%20progression.

defining COVID-19 diagnostics and therapeutics, highlighting in particular the danger of excluding critical COVID-19 diagnostics and therapeutics. (see below quotes from Chapter 3).

- Chapter 4 exposes high concentration in the manufacturing of COVID-19 diagnostics, most of which is focused in developed countries. They are also the main importers of these products. The chapter also points to some manufacturing capacity in developing countries but stresses on the need for economies of scale. With respect to COVID-19 therapeutics, chapter 4 also recognizes manufacturing capacity in developing countries, although most exports have been to developed countries. (see below quotes from Chapter 4).

- In Chapter 5, the USITC report stresses on the role the U.S. government and universities have played an important role in funding R&D of certain COVID-19 diagnostics and therapeutics, adding that "substantial levels of U.S. government support also have raised concerns that the government has not received sufficient returns on its investments", referring to commentators stating that "companies should be required to make their products more widely available and at lower prices, and that contract terms should be more transparent". (see below quotes from Chapter 5)

- Chapter 5 discussion also makes clear that **bilateral and MPP licenses are insufficient to facilitate timely equitable access to COVID-19 diagnostics and therapeutics** and "that the substantial control maintained by the licensor can give rise to disadvantages in terms of access to medicine in LICs, LMICs, and UMICs". (pg 178)

- **In particular, the Report raises the issue of exclusion of supply to many developing countries.** Referring to one analysis in fall 2022, only 10 percent of global diagnoses of COVID-19 occurred in LICs, LMICs, and UMICs included in the Pfizer-MPP deal but 29 percent of diagnoses came from LMICs and UMICs not included in the agreement. It adds that substantial number of UMIC countries are excluded under MPP licenses for molnupiravir (28 of 54 UMICs), nirmatrelvir (+ ritonavir) (41 of 54 UMICs), and ensitrelvir (19 of 54 UMICs), as well as countries outside the scope of the remdesivir BLAs (22 of 54 UMICs). (pg 183)

- On availability of tier-pricing, USITC refers to concerns by public health and non-profit organizations that it generally results in much higher prices compared to licensed or generic products. (pg 186)

- The report also points to the VL requirement of regulatory approval by a stringent regulatory approval or the WHO to be an advantage—because they support the distribution of safe therapeutics **as well as a challenge—because of the difficulties and delays that may be associated with regulatory review.** (pg 187). WHO prequalification, which is also required for certain MPP sublicensing agreements, requires significant effort by manufacturers in order to complete the application requirements and address data standards, which may be challenging for some manufacturers. **It can also be costly**. As noted in chapter 2, a one-time application fee of $25,000 is required in addition to a $20,000 annual fee for a full product assessment. Industry representatives have noted that these fees may be **too expensive for smaller manufacturers in many LMICs.** (pg 255)

- With respect to compulsory license, the USITC in its Chapter 5 notes **"The primary, commonly cited benefit for countries utilizing CLs is the reduced cost of the pharmaceutical product or products at issue and improved access" (pg 188) adding that "When prices of the patented product are unaffordable and VLs are not granted, CLs can provide an avenue of developing a local solution and then increasing access" (pg 189).** The report points out that countries often encounter political and economic pressure when granting a CL or attempting to issue a CL. USITC adds that "**The implementation of the 2022 Ministerial Decision has been highlighted as a potential means of reducing both this political pressure and potentially limiting retaliation from the pharmaceutical**

**sector, as it reaffirms the right to issue a CL in a similar way to the 2001 Doha Declaration on the TRIPS Agreement and Public Health" (pg 189-190)**

- It finds that "requirement of Article 31(f) that a CL issued under that provision be used predominantly for the domestic market **limits t**he extent to which countries without a capable domestic manufacturing base can **benefit from the flexibility**".(see pg 191)

- The report notes that academic research on the effects of compulsory licensing is limited but "In the available literature on the impact of CLs on pharmaceutical products, researchers have generally found that **CLs are associated with decreased pharmaceutical prices in the countries that used CLs**. The available research also **associates CLs with increases in the number of people with access to patented products**. There is **some evidence that CLs encouraged innovation**, where the literature has generally focused on the broader chemical industry" (pg 192)

- In Chapter 6, the USITC points to the different factors involved in estimating needs: "**Estimates depend on many specific factors**, including timely testing and tracking of COVID-19 caseloads; assumptions about the number of confirmed COVID-19 infections in high-risk patients; the health-seeking behavior of individuals; and other considerations such as regulatory guidance, country priorities, and test availability and turnaround. Estimating future need also depends on the trajectory of the virus in terms of infection rates and emergence of new variants" (pg 228). As stated previously, the Report should at least acknowledge that estimated need could expand dramatically for therapeutics addressing long-covid. Also as previously discussed, Chapter 6, pursuant to its overly restricted definition of "therapeutics" fails to directly recognize that some therapeutics, especially monoclonal antibodies, have been used as pre-exposure prophylaxis for severely immune-compromised people and people who should not be administer COVID-19 vaccines for medical reasons.

- Chapter 6 of the Report erroneously over-estimated the percentage of COVID-19 antivirals actually made commercially available to LMICs by counting the UNICEF and Global Fund option agreements as fully-funded pre-purchase agreements. UNICEF and Global Fund did not pay for 4 and 6 million courses of treatment. Global Fund purchased a very small quantity, but the bulk was for reserved sale to LMICs either on a no-profit basis to LICs and L-MICs (still a high price estimated at a minimum of 80-90 per course of treatment) or unaffordable tiered prices to U-MICs ($250 per course of treatment or higher).

- It notes that prices of COVID-19 diagnostics and therapeutics vary dramatically between and within countries. In particular it points to the lack of price transparency as pharmaceutical companies insist on "confidential supply agreements that prevent public disclosure of pricing details".

- USITC finds that **"The affordability of COVID-19 therapeutics has been noted as a significant barrier to access for many LICs and MICs" adding that "Even though the middle and lowest "best access" prices are well below the highest price points paid by HICs, they may still be untenably high for LICs, LMICs, and UMICs.** Indeed, for many countries, the "best access price" exceeds the average annual health care expenditure for LICs ($39 per capita) and is more than half the price of the average annual per capita health care expenditure of LMICs ($137)" (pg 251).

- "for many drugs, but especially for nirmatrelvir (+ ritonavir), generics have been slow to become available... Several sources stated that, without more manufacturers coming on board with generic versions of nirmatrelvir (+ ritonavir) and further lowering the price, the pricing for LICs and LMICs may be untenable." (pg 253)

- **In Chap 6, the USITC reiterates concerns around tier-pricing: "**The tiered price for these UMICs is about $250 per treatment course for nirmatrelvir (+ ritonavir), which is about half of the average per capita annual health care expenditure ($524) (figure 6.5). Many UMICs excluded from certain MPP agreements have average annual per capita health expenditures that are even less than that. For example, a $250 treatment course price would comprise almost 70 percent of the $354 annual per capita health expenditure in the Dominican Republic."

- USITC also addresses the argument about funds provided by international organizations: "countries must prioritize what to purchase with these funds. At $80–90 per course (the "best access price" for nirmatrelvir (+ ritonavir)), many courses may not be affordable, given the total amount of funding dollars, and other priorities for limited national healthcare budgets may be competing".(pg 253)

- Chapter 7 presents views of interested persons including those opposing extension of the TRIPS Decision (e.g. Big Pharma) who stress on the importance of IP for innovation, while suggesting an extension will have an impact in developed countries. However, such assertions are flawed. The TRIPS Decision text is narrow in scope and it does not waive IP. The Decision only waives the limitation on exports, a condition in Article 31(f) of the TRIPS Agreement attached to the use of compulsory license to address patent barriers. Further **the Decision is only applicable for use by developing countries.** On this point, the USITC report refers to Prof Brook Baker's testimony "that more than 87 percent of branded pharmaceutical sales are made in developed-country markets where the extension of the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would not apply. Baker stated that pharmaceutical companies would continue to have the same incentives to develop therapeutics to sell in their primary markets in developed countries" (see pg 285), adding "that extending the 2022 Ministerial Decision to COVID-19 diagnostics and therapeutics would not have a negative effect on the development and marketing of products in high-income countries. Baker asserted that profits are made in high-income, developed countries, which would not be affected by an extension of the 2022 Ministerial Decision" (see pg. 291)

  **Note:** See also TWN's Submissions to the USITC Investigation rebutting concerns and arguments raised by those opposing extension of the TRIPS Decision to diagnostics and therapeutics. https://www.twn.my/title2/intellectual_property/TWNSubmissionstoUSITC.htm

## Selected Quotes from Chapters 2-6 of the USITC Report.

### Chapter 2: Background on Intellectual Property and Regulations

A difference between the 2022 Ministerial Decision and existing TRIPS flexibilities, in particular under Article 31bis, is that, while both provide for waiver of the requirement of Article 31(f), the Decision does not require that export be in accordance with the terms set forth in the Annex to Article 31bis. (pg 57)

The 2022 Ministerial Decision also includes an understanding that Article 39.3 of the TRIPS Agreement does not prevent an eligible member from enabling the rapid approval of a COVID-19 vaccine produced under the decision. Article 39.3 requires members—when requiring submission of undisclosed test data for the approval of a pharmaceutical product using new chemical entities—to protect that undisclosed data against unfair commercial use. It also requires members to protect such data from disclosure, except where necessary to protect the public or unless steps are taken to ensure protection of the data from unfair commercial use. (pg 57)

Patenting of COVID-19 Diagnostics: Landscape and Examples

The foundational patent for PCR tests—the "gold standard" of COVID-19 tests—reportedly was originally filed in 1987 and expired 20 years later (over 15 years ago). Foundational patents for antigen tests also have expired, according to industry and nonprofit sources. Reportedly, the best evidence that patents did not act as a primary barrier to the production of COVID-19 diagnostic tests is substantial global manufacturing of COVID-19 diagnostic tests—900 producers in 53 countries have produced over 2,000 different COVID-19 diagnostic testing products, as of June 2023. **This does not mean that patents are irrelevant; for example, they may be used to protect testing platforms and associated inputs used in automated testing processes for COVID-19 and other diseases. There are also emerging diagnostic technologies, including those identified in the U.S. Patent and Trademark Office (USPTO) patent landscape report, that may be subject to patent protections.** (pg 59-60)

**The USPTO patent landscape report identifies 824 COVID-19 diagnostic-specific published patent filings at the USPTO between December 2019 and the end of March 2023. [….] Published patent filings for COVID-19 diagnostics represented a small share of overall diagnostic patent filings during the same period—2.6 percent at its peak in the fourth quarter of 2021 and tapering to 1.4 percent in the most recent data (2023 Q1).** (pg 60)

**IP protections associated with COVID-19 diagnostic testing platforms reportedly have given rise to access challenges.** [pg 62)

In 2021, GeneXpert accounted for 44 percent of the automatic PCR tests procured by the Diagnostics Supply Consortium. **The cartridges needed to perform a GeneXpert test are reported to be under patent until 2037.** Patent and trade secret barriers to generic replication of cartridges are reported to have constrained testing capacity for laboratories dependent on GeneXpert devices for automated PCR testing.[pg. 62]

Patenting of COVID-19 Therapeutics: Landscape and Examples

**According to WIPO's patent landscape report, 4,787 patent applications for COVID-19 therapeutics were filed between January 2020 and the end of September 2022**. (pg 63)

**Virtually all COVID-19 therapeutics have many primary and secondary patent applications pending, as well as granted patents in multiple jurisdictions**. This substantial patenting is documented in the voluntary license agreements for ensitrelvir fumaric acid (originated by Shionogi), nirmatrelvir (+ ritonavir) (Pfizer), molnupiravir (Merck), and remdesivir (Gilead). In these agreements, the originator companies identify numerous product and process patents filed in multiple jurisdictions, including HICs, UMICs, and LMICs. (pg 64)

Model-based analyses often find mixed results on the relationship between patent protection and innovation in the pharmaceutical industry. Some cross-country studies **have provided evidence that patent protection supports innovation in the health sector in more developed countries but has little to no positive effect for innovation in developing countries and negative effects for access and affordability.** (pg 64-65)

## Chapter 3: Definitions and the Universe of COVID-19 Diagnostics and Therapeutics

"the definitions of diagnostics and therapeutics generally coalesce around the explanation that diagnostics are tools used to identify or diagnose a disease or health condition, including how the body is responding to a treatment, and therapeutics are products or remedies used to treat or cure a disease. **By that rationale,**

**a COVID-19 diagnostic is a good used to diagnose COVID-19 or identify how patients respond to a treatment for COVID-19, and a COVID-19 therapeutic is a good used to treat COVID-19.** The Trade Representative's request letter specifically requested that the Commission identify the universe of COVID-19 diagnostics and therapeutics covered by patents as well as those in development. **The universe of products that fall within these expansive definitions is broad and varied.** It is difficult to catalogue in its entirety the full scope of products that fall within the vast universe of COVID-19 diagnostics and therapeutics, both for existing products under patent and those in development. Public awareness of the SARS-CoV-2 virus has only existed for a short time, **and the virus regularly mutates to a new variant. Therefore, the full epidemiology of COVID-19 in humans is still being discovered and understood, as are the means that can be used to treat it. Further, as the virus mutates, the efficacy of a given diagnostic or therapeutic for COVID-19 can also change."** (pg 92-93)

"Looking at emerging COVID-19 therapeutics and diagnostics is important, owing to the dynamic nature of the virus, the changing efficacy of drugs, and uncertainty over the eradication of SARS-CoV-2. Since the early days of the pandemic, the push to develop new, effective COVID-19 diagnostics and therapeutics has been ongoing. **As of 2023, there have been hundreds of tests produced and hundreds of therapeutics studied, all specific to COVID-19, and there are new clinical trials for therapeutics being added to the pipeline every week around the world."** (pg 98)

A search of the NLM database for studies outside clinical trials for COVID-19 **diagnostics yielded 202 results; these results are not exhaustive of the research and development occurring with respect to COVID-19 diagnostics around the world.** Rather, they provide a snapshot of research and innovation that are occurring for COVID-19 diagnostics. As of July 2023, the database includes a total of 1,762 clinical trials of COVID-19 drugs in all phases worldwide, with 30 percent (530) of them occurring in the United States. During that same period, of the total number of clinical trials in phase III status (407), more than one quarter were occurring in the United States (103). (pg 98 -99)

**Compiling a list of COVID-19 diagnostics and therapeutics that have been approved by a regulatory body is challenging.** One element of this challenge is that lists of products approved to diagnose or treat COVID-19 change over time, meaning the lists are different depending on when during the pandemic the list was created or updated. (pg. 102)

## Chapter 4: COVID-19 Diagnostics and Therapeutics Manufacturing Supply Chain and Trade

Comment: **In the case of COVID-19 diagnostics**, this chapter reveals a high concentration in the manufacturing of diagnostics, most of which is focused in developed countries. They are also the main importers of these products. The chapter also points to manufacturing capacity in developing countries, stressing the need for economies of scale.

HICs contributed 95 percent of world exports of diagnostics, including COVID-19 diagnostics, in 2022 and accounted for 86 percent of world imports (pg 137)

The country [India] accounts for 21 of the 30 manufacturers in LMICs. (pg. 135)

Because of their small production volumes, local manufacturers often fail to attract private investors interested in larger operations with profit-generating products. (pg 136)

Comment: **In the case of COVID-19 therapeutics,** this chapter shows that most supply of COVID-19 products including therapeutics are to developed countries. It also reveals that developing countries have manufacturing capacity for COVID-19 therapeutics.

As of July 2023, UMICs had 46 manufacturers of COVID-19 virus-directed therapeutics. (pg 150)

Historically, pharmaceutical manufacturing capacity in LMICs like India, Bangladesh, Pakistan, and Vietnam has been substantial. (pg 151)

Major exporters of products classified under HS subheadings that include COVID-19 therapeutics exported most of these goods to HICs, 81.9 percent in 2022 (figure 4.11).Most of these exports from HICs went to other HICs, as did most of the exports from UMICs and LMICs. (pg 153)

**Chapter 5: Approaches to Access the IP Associated with COVID-19 Diagnostics and Therapeutics**

R&D Collaboration Agreements for COVID-19 Therapeutics and Diagnostics

the R&D of molnupiravir involved multiple collaborations with academic researchers, SMEs, the U.S. government, and Merck & Co., Inc. (Merck). Initial research was carried out at Emory University (Emory), with **funding from various government agencies**. (pg 159)

The **U.S. government also played a substantial role in the R&D associated with remdesivir**. […] According to the U.S. Government Accountability Office (GAO), federal funding for remdesivir preclinical studies and clinical trials totaled $161.5 million from 2013 through 2020. (pg 159)

**Public-private collaborations also supported the development of diagnostic tests and testing platforms**. For example, **total U.S. government, nonprofit, and donor agency investment in the development** of the GeneXpert diagnostic platform—a rapid, automated device for analyzing polymerase chain reaction (PCR) tests that is widely used in developing countries—**has been estimated at $252 million.** The GeneXpert platform reportedly is based on technology initially developed by the U.S. government's Lawrence Livermore National Laboratory (LLNL). A researcher involved in the initial technologies formed the U.S. company Cepheid in 1996. In exchange for a fee and royalties, the LLNL technologies formed the basis of Cepheid's commercial products. Cepheid's GeneXpert products were first approved for clinical use in 2006, with new assays for diseases approved thereafter, including SARS-CoV-2 in 2020. In addition to the LLNL patents, government-supported inventions from the University of Utah, Baylor College of Medicine, and the California Institute of Technology also were licensed to Cepheid. (pg 170)

the U.S. government and universities have played an important role in some of the R&D underlying diagnostic and therapeutic discoveries. (pg 170)

Substantial levels of U.S. government support also have raised concerns that the government has not received sufficient returns on its investments. U.S. government funding and participation in the development of molnupiravir, remdesivir, and the GeneXpert diagnostic platform have led some commentators to state that **companies should be required to make their products more widely available and at lower prices, and that contract terms should be more transparent.** (pg 172)

Advantages and Challenges of Bilateral License Agreements for COVID-19 Therapeutics

**the substantial control maintained by the licensor can give rise to disadvantages in terms of access to medicine in LICs, LMICs, and UMICs.** First, the licensor determines what IP rights and products are made available to licensees. There is no assurance that the most successful or most needed treatments will be made available for licensing. Second, licensors control the countries to which licensees may export their products and the countries that may obtain access through imports from licensees. With respect to COVID-19, this option may exclude countries for which access to licensed products would be valuable from a public health perspective, as discussed in further detail below. Third, BLAs generally are not published; this means complete information about the terms and conditions of the agreements is not available. This lack of transparency makes it difficult for the public to assess competing claims about the advantages and limitations of the agreements' terms and conditions. (pg 178)

**The geographical scope of MPP licenses is a challenging aspect of the program,** with many calling for licensors to increase the scope and authorize sales in more UMICs, given high rates of infection that occurred in those countries and high prices for medicines in those countries (as compared to countries within the geographical scope). According to **one analysis in fall 2022, only 10 percent of global diagnoses of COVID-19 occurred in LICs, LMICs, and UMICs included in the Pfizer-MPP deal but 29 percent of diagnoses came from LMICs and UMICs not included in the agreement.** (pg (183)

Figure 5.1 identifies UMICs, LMICs, and LICs where products licensed under MPP licenses or BLAs cannot be offered for sale under the terms of MPP licenses or BLAs. It illustrates the **substantial number of UMIC countries excluded under MPP licenses for molnupiravir (28 of 54 UMICs), nirmatrelvir (+ ritonavir) (41 of 54 UMICs), and ensitrelvir (19 of 54 UMICs), as well as countries outside the scope of the remdesivir BLAs (22 of 54 UMICs). (pg 183)**

**Public health and nonprofit organizations raise concerns about differential pricing for branded products, stating that it generally results in much higher prices compared to licensed or generic products**. In the case of COVID-19 therapeutics, tiered prices reportedly were multiples higher than the price negotiated by the Clinton Health Access Initiative. Concerns also have been raised about the exclusion of UMICs from the coverage territory of VLs because the exclusion may limit necessary economies of scale to make production of licensed products financially viable. According to advocacy organizations, the markets covered by VLs may not be valuable enough to support the multiple competitors they believe are needed for adequate supplies and lower prices for developing countries. (pg 186)

**Regulatory approval requirements, particularly at SRAs and the WHO, may be considered both an advantage—because they support the distribution of safe therapeutics—and a challenge—because of the difficulties and delays that may be associated with regulatory review**. (pg 187)

Advantages and Challenges Associated with the Use of Compulsory Licenses

**The primary, commonly cited benefit for countries utilizing CLs is the reduced cost of the pharmaceutical product or products at issue and improved access.** (pg 188)

**When prices of the patented product are unaffordable and VLs are not granted, CLs can provide an avenue of developing a local solution and then increasing access** (pg 189)

**Countries that use CLs often encounter political and economic pressure when granting a CL or attempting to issue a CL.** According to witness testimony and submissions, countries utilizing a CL have faced this pressure in various forms, including the threat of sanctions, claims of expropriation under investment law, and withdrawal of financial support on unrelated matters. In addition to the detrimental effects of these actions after CL implementation, commentators also note a chilling effect on the use of CLs

by developing countries in the first place. Furthermore, the pharmaceutical sector reportedly has publicly retaliated against countries for utilizing CLs by withdrawing investment or withholding pharmaceutical products from the relevant market. **The implementation of the 2022 Ministerial Decision has been highlighted as a potential means of reducing both this political pressure and potentially limiting retaliation from the pharmaceutical sector, as it reaffirms the right to issue a CL in a similar way to the 2001 Doha Declaration on the TRIPS Agreement and Public Health.** (pg 189-190)

**Legal and procedural hurdles in various forms present another substantial challenge for countries to utilize CLs.** On the multilateral front, the requirement of Article 31(f) that a CL issued under that provision be used predominantly for the domestic market limits the extent to which countries without a capable domestic manufacturing base can benefit from the flexibility. (pg 191)

However, the conditions imposed by Article 31*bis* on the CL grantor and the CL beneficiary (i.e., importer) are considered particularly burdensome and prevent utilization of that flexibility, according to various commentators. (pg 191)

Academic research on the effects of compulsory licensing is limited. **In the available literature on the impact of CLs on pharmaceutical products, researchers have generally found that CLs are associated with decreased pharmaceutical prices in the countries that used CLs. The available research also associates CLs with increases in the number of people with access to patented products. There is some evidence that CLs encouraged innovation, where the literature has generally focused on the broader chemical industry.** (pg 192)

Since 2001, there have been approximately 121 attempts to issue a public health CL, including four by the United States. The majority of these attempts were ultimately executed and resulted in a CL, but about a quarter of the attempts never came to fruition (pg 192)

## Chapter 6: Availability and Consumption of COVID-19 Diagnostics and Therapeutics

Estimating Need

**Estimates depend on many specific factors, including timely testing and tracking of COVID-19 caseloads; assumptions about the number of confirmed COVID-19 infections in high-risk patients; the health-seeking behavior of individuals; and other considerations such as regulatory guidance, country priorities, and test availability and turnaround. Estimating future need also depends on the trajectory of the virus in terms of infection rates and emergence of new variants.** (pg 228)

A central question regarding access to COVID-19 diagnostics and therapeutics is whether, under existing IP rules, supplies are currently sufficient at affordable prices and available to anyone who could benefit from them**. Answering this question is challenging owing to a lack of data**. (pg 232)

Diagnostics

The pricing of COVID-19 diagnostics diverges significantly across regions and countries because of different healthcare systems, economic conditions, and domestic regulations. Pricing also differs depending on the technology used, such as polymerase chain reaction (PCR) tests or rapid antigen tests (also known as rapid tests). The pricing and affordability of COVID-19 diagnostics vary dramatically by country, and even within country where prices differ by manufacturer, or if a test was acquired through a healthcare provider or purchased in the marketplace. (pg 233)

Therapeutics

**Price transparency for COVID-19 therapeutics is lacking.** Pharmaceutical companies often negotiate prices with governments, health systems, insurance providers, and multilateral organizations. These negotiations are typically conducted in private, resulting in **confidential supply agreements that prevent public disclosure of pricing details**. This lack of transparency is challenging when trying to evaluate cross-country comparisons of prices for COVID-19 drugs. Additionally, pricing can vary significantly between countries as a result of differences in healthcare systems, economies, and purchasing power. (pg 238)

**COVID-19 therapeutics are potentially accessible to countries of all income categories, but the avenues through which countries can obtain access differ significantly among HICs, UMICs, LMICs, and LICs.** Broadly, the six potential access avenues are: (1) direct purchase of branded product from originator, (2) purchase of licensed versions of product from a manufacturer operating under a bilateral license agreement with an originator, as discussed in chapter 5, (3) purchase of licensed versions of product from manufacturer operating under a sublicense agreement with the MPP, as discussed in chapter 5, (4) procurement of branded product through a multilateral organization, such as UNICEF and the Global Fund, (5) purchase of generic versions of product from manufacturers operating under a Least Developed Country exemption (for example, Bangladesh) or under a compulsory license (for example, Hungary), as discussed in chapter 5, and (6) donations. The price of drugs in a particular country depends upon the avenues of access that are available to it. Although pricing is not very transparent, countries able to access drugs via multilateral organizations and donations are likely to pay significantly less than countries with sole access through direct purchase from the originator. Prices under bilateral and MPP licenses and LDC exemption are generally lower than branded prices. Therefore, the avenues of access available to a particular country are important in determining its purchases and consumption.

As noted earlier, concern has been raised about certain countries having limited access through voluntary licenses (VL) and multilateral programs. In particular, some stakeholders view UMICs as countries with limited or unaffordable access to products, or only via direct procurement from originator firms. (pg 241)

Contract negotiations for the agreements between multilateral organizations and originators were prolonged and at times reportedly difficult, leading to delays in delivery. Agreement was particularly difficult to reach on contract clauses dealing with disclosure and confidentiality, as well as liability and indemnity. Confidentiality of pricing information was of particular concern to many eligible countries in making the funding requests to donors necessary to pay for the treatments procured (see box 6.1). Ultimately confidentiality clauses resulted in few financial details of the procurement agreements, including prices, being made available to the public.

Negotiations over liability and indemnification issues were also protracted. (Pg 247)

Data on COVID-19 therapeutics consumption, as defined as the number of full treatment courses administered (i.e., number of patients treated), are limited to a few HICs and only for nirmatrelvir (+ ritonavir) and molnupiravir, according to Airfinity. No data are available for any MICs and LICs, representing a significant data gap for analyzing global trends in consumption. (pg 250)

Factors Affecting Demand and Availability of Diagnostics and Therapeutics

**The affordability of COVID-19 therapeutics has been noted as a significant barrier to access for many LICs and MICs**, especially where generic manufacturers for a given product are not authorized under VLs, CLs, or the LDC exception to the TRIPS Agreement. [...]**Even though the middle and lowest "best access" prices are well below the highest price points paid by HICs, they may still be untenably**

**high for LICs, LMICs, and UMICs. Indeed, for many countries, the "best access price" exceeds the average annual health care expenditure for LICs ($39 per capita) and is more than half the price of the average annual per capita health care expenditure of LMICs ($137)** (figure 6.5).(pg 251)

As of publication, however, no licensed manufacturers party to the CHAI arrangement are producing nirmatrelvir (+ ritonavir). First, **for many drugs, but especially for nirmatrelvir (+ ritonavir), generics have been slow to become available**. Only one licensed manufacturer, who is not part of the CHAI arrangement, has received WHO prequalification for nirmatrelvir(+ ritonavir)— a pre-condition of the MPP sublicensing agreement—and the firm has had little demand for its products priced at $60 per treatment course. Additionally, the potential $25 per treatment course price under the CHAI agreement would only be available once a minimum purchase threshold is reached, which may be difficult given declining demand. **Several sources stated that, without more manufacturers coming on board with generic versions of nirmatrelvir (+ ritonavir) and further lowering the price, the pricing for LICs and LMICs may be untenable. (pg 253)**

**One of the main concerns expressed by several stakeholders about affordability and access is centered on the tiered prices for many MICs and UMICs that are offered high per treatment prices and are generally excluded from the MPP and CHAI agreements**. This includes countries like Brazil, Panama, and Thailand. The tiered price for these UMICs is about $250 per treatment course for nirmatrelvir (+ ritonavir), which is about half of the average per capita annual health care expenditure ($524) (figure 6.5). Many UMICs excluded from certain MPP agreements have average annual per capita health expenditures that are even less than that. For example, a $250 treatment course price would comprise almost 70 percent of the $354 annual per capita health expenditure in the Dominican Republic.(pg 253)

While products are available through international organizations using each country's allocated funds, uptake has been minimal. ...These products are essentially "free" because the allocated funds are donated, but the countries must prioritize what to purchase with these funds. At $80–90 per course (the "best access price" for nirmatrelvir (+ ritonavir)), many courses may not be affordable, given the total amount of funding dollars, and other priorities for limited national healthcare budgets may be competing.(pg 253)

In the case of some therapeutics, such as remdesivir, WHO recommendation and prequalification came a full two years after U.S. authorization and the first VLs were signed. This means that although treatments were available, many countries were not immediately able to access them. **WHO prequalification, which is also required for certain MPP sublicensing agreements, requires significant effort by manufacturers in order to complete the application requirements and address data standards, which may be challenging for some manufacturers. It can also be costly. As noted in chapter 2, a one-time application fee of $25,000 is required in addition to a $20,000 annual fee for a full product assessment. Industry representatives have noted that these fees may be too expensive for smaller manufacturers in many LMICs. (pg 255).**