This is part of a Global Trade Watch series on the TRIPS Waiver.

Existing TRIPS "Flexibilities" Unworkable for Necessary Scale Up of COVID-19 Medicines Production

Key Takeaways

- Existing TRIPS flexibilities have helped to promote access in cases where only patent barriers were in play and supply chains were relatively simple. But these flexibilities rely on "product-by-product" and "country-by-country" compulsory licensing. This process is cumbersome and slow, as spotlighted by the dead ends hit by Canadian firm Biolyse as it tried to use the Canada Access to Medicines Regime to get a license to produce COVID-19 vaccines for export to developing nations. But more broadly, this regime was not designed for, nor does it function effectively in, a global pandemic where vaccines and other technologies are protected by multiple forms of IP and where production relies on complex global supply chains involving inputs from multiple countries.
    - Pharmaceutical firms have made it harder to effectively use compulsory licensing *in any context* by creating broader intellectual property "thickets" of numerous patents, copyrights, trade secrets and industrial designs. Each type of these protections on COVID-19 technologies would require a license.
    - Existing WTO flexibilities may not even encompass elements of IP critical to COVID-19 vaccines and biologic medicines – most especially trade secrets, but also industrial designs and copyright.
    - Restrictive WTO production-for-export rules make compulsory licensing in a global pandemic even more complex and unworkable. This WTO flexibility has only successfully been used once in 20 years.
- Nations attempting to use the TRIPS flexibilities in the past have been subject to fierce U.S. and European attacks and trade pressures to stop doing so. Pharma's 2021 Special 301 filings are filled with demands for the U.S. government to act against countries that have used or plan to use existing flexibilities to fight COVID-19.
- The real issue is not developing nations' inability to make quality vaccines or treatments, but whether a few pharmaceutical corporations should retain complete control over whether and where production occurs, and thus control supply, price, and distribution.

Introduction

Most countries in the World Trade Organization (WTO) support a temporary, emergency waiver of certain WTO rules during the COVID-19 crisis to boost worldwide production of COVID-19 vaccines, treatments and diagnostic tests. The waiver would empower nations to adjust domestic policies and practices to effectively battle COVID-19 by suspending some exclusivities otherwise required by the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) with respect to patents, copyrights, industrial designs and undisclosed information in so far as they hinder access

to products and technologies for prevention, containment and treatment of the COVID-19 pandemic.

In the late 1990s, millions of people in developing countries were dying from AIDS because pharmaceutical firms refused to provide affordable access to the medicines that made AIDS a treatable chronic disease for those who could afford lifesaving drugs. After the U.S. and other wealthy countries blocked reforms and needless millions died, a global campaign demanding WTO changes finally forced the 2001 "Doha Declaration" that clarified flexibilities for governments to mitigate some negative impacts that intellectual property (IP) rules have on public health. Lifesaving antiretrovirals were eventually made available thanks to these flexibilities, especially compulsory licenses, which allow production and/or sale of generics without permission of the patent-holder, who usually receives royalty compensation.

However, **existing TRIPS flexibilities are not workable in the COVID-19 pandemic context**, particularly with respect to vaccines. The early HIV/AIDS experience and many examples since make clear that supplies adequate to meet global need will not be produced by relying on IP-monopoly-holding firms' internal capacity or the arrangements they choose to make with other firms to manufacture for them via contract manufacturing deals and bilateral voluntary licenses. This is especially the case given these are not likely to be one-time vaccines like childhood immunizations. Capacity must be built to produce the 10-15 billion doses annually needed to maintain herd immunity worldwide. But the IP-holding firms do not focus on global coverage, but on sales in profitable markets. They admit this openly: In mid-March a Pfizer VP of investor relations presented Pfizer's profitable plans to sell boosters annually to rich countries that can pay and at substantially higher prices ($150-$175 per dose), while many in poor nations have no access to a first vaccine.

In every region, there are existing firms that could gear up production and governments willing to change domestic policies and practices and invest in expanding supply – if they had freedom to do so. Overcoming exclusive IP rights would boost manufacturing of many small molecule medicines and also create IP-barrier-free space for vaccines. That such capacity exists is evidenced by the world-class pharmaceutical firms in developing countries already making biosimilar versions of biologic hepatitis vaccines and cancer treatments as well as producing new cutting-edge HIV/AIDS medicines. Developing countries' firms also already are pumping out vaccines based on the platforms that, for instance, the Johnson & Johnson (J&J) and Oxford-Astrazeneca and Novavax vaccines use. But these governments face significant challenges, starting with the IP barriers that their TRIPS commitments oblige them to enforce. The governments seek certainty, as do potential investors, that if they adjust domestic laws and practices to provide access to the necessary technology to support expanded manufacture of vaccines, treatment and tests, they will not get dragged into WTO litigation or face sanctions. They also seek greater leverage: Attempts to persuade originator firms with humanitarian arguments have largely failed. The waiver will make clear that not sharing COVID-related medical technology is not an option. Rather, the firms can choose to share technologies to expeditiously expand production via prompt negotiations with governments, alternative suppliers, and global initiatives like the COVID-19 Technology Access Pool (C-TAP), or they risk governments simply going around them. Finally, many nations view the waiver as a worldwide buffer against the withering political pressure and legal harassment to which Big Pharma has subjected countries that sought to use existing WTO flexibilities.

Existing TRIPS flexibilities are largely premised on countries with a public health emergency issuing compulsory licenses to override patents so more companies can produce equivalent medicines. There are three fundamental reasons why the traditional compulsory licenses at the heart of existing TRIPS flexibilities are not workable in the COVID-19 context.

Pharmaceutical Firms Have Made It Harder to Effectively Use Compulsory Licensing by Creating Broader Intellectual Property "Thickets" of Numerous Patents, Copyrights, Industrial Design, Undisclosed Data and Trade Secrets Protections for COVID-19 Technologies – Each of Which Would Require a License

Successfully obtaining a compulsory license over any element of intellectual property requires a time-consuming and administratively burdensome process, as described below. However, in certain circumstances, it can work – as the world saw in the early 2000s with patents on the antiretrovirals that had made AIDS a treatable chronic disease in the developed world and a painful death sentence in developing countries. However, today many key COVID-19 vaccines and medicines are protected by thorny thickets of intertwined IP protection, not just a patent or two.

Pharma's strategy of constructing fortress-like IP monopoly thickets led to warnings in a 2017 Doctors Without Borders report on pneumococcal conjugate and human papillomavirus vaccines: "*Patent activity in the field of vaccine development and manufacturing has been increasingly recognised as problematic over the past 15 years… International organisations with vaccines expertise such as WHO and Gavi, the Vaccine Alliance, have similarly noted that patent thickets are an increasing concern for vaccines. For medical products such as PCV [Pneumococcal conjugate vaccine] and HPV [human papillomavirus] vaccines, patent barriers can slow the development process, increase costs, increase uncertainty and deter or even block other manufacturers considering entering the market. A recent analysis by Chandrasekharan et al. found 106 Patent Cooperation Treaty (PCT) applications 'potentially relevant to the manufacturing of pneumococcal vaccines' and 93 patents applications 'relevant to the manufacturing of HPV vaccines.'*"

The mRNA COVID-19 vaccines include 100-plus key components manufactured in over a dozen countries that may be subject to patents and other IP protections. Pfizer/BioNTech and Moderna have respectively at least 13 and 12 patent claims related to their COVID-19 mRNA vaccines. And this does not account for potential patents over key inputs of these vaccines, such as the lipid nanoparticles that Pfizer/BioNTech source from a small Austrian pharmaceutical firm called Polymun. Additionally, copyright protections on software, algorithms and training materials used to make the drugs and on storage and use guidelines, as well as undisclosed data protections covering some trade secrets, plus perhaps industrial design protections for key machinery used to mix lipids and genetic materials for mRNA vaccines are among the innumerable IP barriers thwarting production by non-originator firms.

While prospective developing country producers might well select to produce non-mRNA vaccines, daunting IP thickets protect these as well. For example, non-mRNA vaccines that rely on biologic technologies to produce the active vaccine ingredient rely on secret, proprietary cell-lines. Production of treatments also faces tickets of IP barriers: Monoclonal antibodies (mAbs), widely used in the United States, are designed to mimic the body's natural immune response and have been a COVID-19 treatment gamechanger. They are unavailable in many parts of the world. Monoclonal antibodies are laboratory-produced molecules that are much more chemically complex than small molecule drugs, which typically rely on one or perhaps two patents per molecule. In contrast, biologic medicines IP often includes not only dozens of patents, but also trade secrets on development techniques and tools for production. To develop markets attractive to new producers, multiple countries would face the impossible complexity of coordinating national compulsory licensing strategies to allow prospective producers to import needed components, machinery and more. In contrast, a TRIPS waiver would simply clear the thorny IP thickets and related investment-chilling liabilities.

TRIPS Flexibilities Weren't Designed for, Nor Do They Function Effectively in, a Global Pandemic Where Vaccines Face Multiple Forms of IP Barrier and Production Relies on Complex Global Supply Chains

Existing WTO flexibilities that require "product-by-product" and "country-by-country" compulsory licensing are not suited to products relying on complex supply chains. mRNA vaccines have 100 key components, many of which are IP protected, and produced in multiple jurisdictions. Thus, in order to manufacture a "generic" COVID-19 mRNA vaccine using TRIPS flexibilities, the relevant producer would have to seek compulsory licenses for each IP-protected commodity in its country of manufacturer and export, which would require the compulsory licensing cooperation of the exporting

country and input producer. It would likewise have to seek a compulsory license allowing for import of each such component and allowing for production of the vaccine. Finally, if a producer wished to export in order to create a viable market, it would have to coordinate further and follow intractable WTO procedures to seek additional compulsory licenses in other countries to allow import and use of the vaccine. These multiple cases of component-by-component and country-by-country licenses result in timing and coordination complexities that are virtually insurmountable.

Existing WTO flexibilities may not even encompass elements of IP critical to COVID-19 vaccines and biologic medicines, including most especially trade secrets, but also industrial designs, and copyright. The most directly relevant flexibility under the TRIPS agreement is Article 31, which allows countries broad discretion to override patent rights so as to allow "generic" production. However, the TRIPS Agreement and Doha Declaration on the TRIPS Agreement and Public Health do not describe explicit mechanisms for easily overcoming trade secrets and undisclosed confidential information with respect to complex manufacturing processes, formulas, bespoke equipment, and biologic resources. Similarly TRIPS copyright protections – which apply to software embedded in instrument-based diagnostics and other medical devices, in e-health technologies, and in production manuals and industrial blueprints – do not allow for easy override, nor are there such provisions for industrial designs. Although such rights might ultimately be clarified under Articles 39, 7, and 8 of the TRIPS Agreement, in the meantime countries are left without a clear pathway to override these non-patent IP barriers in place with respect to COVID-19 vaccines and treatments.

Restrictive WTO production-for-export rules make compulsory licensing in a global pandemic context even more complex and unworkable. Per TRIPS Article 31(f), even in cases of national emergency or cases of non-commercial public use (government use), compulsory licenses are to be issued predominately for the supply of the domestic market, meaning only limited export is allowed without an additional cumbersome process described below. WTO rules covering export of compulsory-licensed products to a country lacking its own production capacity are so complex that this flexibility has only been used once. This paper by Northeastern University Law School Professor Brook Baker reviews this problem. In sum, under Art. 31bis, the importing country must notify the TRIPS Council of the name and expected quantity of the product in need and prove there is not sufficient manufacturing capacity in its territory; the exporting country has to agree with the quantity and notify the duration of the license; products must have special packaging and labelling specific to each country seeking to import; and more. The limitations and additional obstacles for countries seeking to import medicines made under compulsory license not only thwart the economies of scale necessary to achieve commercial viability to produce certain treatments, vaccines or their inputs, as well as to lower prices. But, on the most fundamental level, the mismatch of the existing TRIPS flexibilities relative to the COVID-19 context is that the *whole world* needs large supplies of vaccines, treatments and tests at affordable prices, and while there are producers able to supply every region, there are not producers in every country even if that otherwise made sense.

The production-for-export compulsory licensing process is cumbersome and slow. Consider the dead ends hit by Canadian firm Biolyse as it tries to use Canada's Access to Medicines Regime (CAMR). The Ontario-based firm Biolyse seeks to produce and export a generic version of the J&J adenovirus vaccine to developing countries. As required in Canadian law, to apply for a compulsory license Biolyse had to request a license from J&J first. After J&J rejected that request, Biolyse tried to apply for the compulsory license. People who work in access to medicines know allies in developing countries must spend months literally chasing scores of officials across capitals to gather required compulsory license signatures. The administrative mess and repeated dead ends described in this review of the Biolyse situation show that whether in rich or poor countries, getting a compulsory license for a medicine is not a predictable process, nor one on which essential medicines in a pandemic can rely. (Among the problems: in Canada to get a license intended for export use, a medicine has to be on a list of approved exports, except there is no clear process to get on that list nor is the list published; key forms to apply for the compulsory license are not available; phone numbers listed for assistance were disconnected or general switchboard numbers to large agencies; etc.) This is not a COVID-19 fluke. In 2006, during the avian flu epidemic, Biolyse attempted to get a compulsory license to manufacture and export oseltamivir phosphate, a life-saving therapeutic patented by Roche and sold under the brand name Tamiflu. After seven months the Canadian government finally included the drug in the aforementioned list – too late, as the flu had largely run its course. Sadly, COVID-19 is not going to recede any time soon, however we cannot afford the hatching and global

spread of dangerous variants and millions of lives that would be needlessly lost if we have to depend upon existing TRIPS flexibilities to defeat the pandemic.

Countries Attempting Use Existing TRIPS Flexibilities in the Past Have Been Subject to U.S. and European Government and Corporate Attacks and Trade Pressures to Stop Them Doing So

For instance, the U.S. government 2020 Special 301 List explicitly targets countries seeking compulsory licenses with possible investigations and sanctions: "*…actions by trading partners to unfairly issue, threaten to issue, or encourage others to issue compulsory licenses raise serious concerns… The United States will continue to monitor developments and to engage, as appropriate, with trading partners, including Chile, Colombia, Egypt, El Salvador, India, Indonesia, Malaysia, Russia, Turkey, and Ukraine.*"

The 2021 Special 301 submissions from industry include explicit attacks on compulsory licensing in the context of the COVID-19 pandemic while also explicitly opposing the TRIPS waiver. In Democratic and Republican administrations alike, this government pressure has been fueled by the pharmaceutical industry and allied trade associations, which deploy armies of lobbyists to directly pressure the U.S. Trade Representative and other executive agencies while recruiting members of Congress to also do so, and work to ensure former industry staff are serving in key government positions to maximize inside and outside pressure.

The U.S. Chamber of Commerce 2021 Special 301 submission notes: *"Already, legislative bodies in Chile, Canada, Germany, and Thailand have tabled compulsory license proposals. This is even though other options—such as working alongside industry to ensure broad access—exist. Meanwhile, other countries have also introduced emergency regulations that call for the indiscriminate use of compulsory licenses for COVID-19 products or those implemented under vague national security grounds. For instance, the Hungarian government used its compulsory licensing mechanism for remdesivir, a treatment for COVID-19, following a request by a local company…."*

The Biotechnology Innovation Organization (BIO), which includes Pfizer, Moderna, J&J, and Merck, notes: *"BIO has also been concerned about the ongoing CL [compulsory license] threats during the COVID-19 pandemic. While our members have been dedicating resources to develop treatments and vaccines, threats to undermine IP have done nothing to advance R&D efforts and have only served as a distraction. BIO recognizes lawful, proportionate, and temporary exercise of government emergency powers is available to respond to genuine emergencies or other extraordinary circumstances that cannot be addressed collaboratively between a government and an IP rightsholder; however, new drugs and vaccines are being developed and brought to patients to address the COVID-19 pandemic with unprecedented speed driven by a collaborative approach that respects IP rights and leverages their positive impact on innovation rather than a coercive approach suggested by some policymakers. We are, therefore, concerned that the European Commission, for instance, in their proposed IP Action Plan seeks to 'ensure the availability of critical IP in times of crisis, including via new licensing tools and a system to co-ordinate compulsory licensing.' The misguided claim by the European Commission to ensure that effective systems for issuing CLs are in place and, thereby, suggesting that IP in and of itself poses a barrier to manufacturing and delivery of treatments and vaccines during the COVID-19 pandemic constitutes an unreasonable and regretful mischaracterization by a key U.S. ally."* The submission goes on to attack various countries for issuing compulsory licenses for remdesivir after the IP-holding firm's contract manufacturing deals denied access to the drug for half the world.

The Pharmaceutical Research and Manufacturers of America (PhRMA) submission notes: *"Some countries like Hungary, Colombia and Indonesia, have adopted emergency regulations that allow the grant or blanket use of CLs for COVID-19 products without due process or basic engagement with the patent holder… PhRMA and its members are concerned about the Indonesian Government's implementation of government-use licensing for COVID-19 medicines such as remdesivir… The Indonesian Government should focus on accelerating the necessary regulatory approvals and streamlining procurement processes for COVID-19 medicines, rather than assuming intellectual property as a barrier to access medicines."*

The Real Issue Is Not Lack of Manufacturing Capacity or Potential Developing Country Producers, But Whether Big Pharma Should Retain Complete Control Over Supply, Price, and Distribution

The organizations and academics with the most knowledge about and commitment to access to medicines are unified that at issue is not whether developing country producers have the capacity or skills to manufacture high quality vaccines and medicines, but rather control. Big Pharma has a monopoly over vaccine knowledge and technology platforms and treatments that will determine life and death for millions of people in rich and poor countries alike and decide the fate of the global economy. These corporations stand to make a lot of money. Pfizer and Moderna recently revealed COVID-19 vaccine expected revenues of $15 billion and $18.4 billion respectively in 2021 alone. These firms have no interest in sharing. Given that an honest explanation for why the vaccine originators are ignoring requests to be paid for voluntary licensing or contract manufacturing deals in developing countries would be a PR disaster for them, the industry has been pushing a Big Lie. The claim is that a lack of skills and manufacturing capacity, not monopoly intellectual property protections, are thwarting greater production of COVID-19 vaccines and treatments. A related argument, with decidedly racist overtones, is that COVID-19 vaccines are too complicated for producers in developing countries to make.

The reality is that in every region of the world, there are multiple producers that could be greatly increasing global vaccine supplies if the technology and know-how were shared. The Coalition for Epidemic Preparedness Innovations (CEPI) surveyed companies that could manufacture vaccines (including fill-finish) and found 260+ companies that could add on capacity. And the list is always being expanded. Just in Africa, "Biovac and Aspen in South Africa, Institute Pasteur in Senegal, and Vacsera in Egypt could rapidly retool factories to make mRNA vaccines," notes a group of medicine-production experts in a recent Foreign Policy article. Dr. John Nkengasong, the head of the Africa Centres for Disease Control and Prevention, testified to House Foreign Affairs Committee that six institutions across Africa have the capacity to manufacture these vaccines. Indeed, a former Moderna director of chemistry revealed that with enough technology transfer and know-how-sharing, a modern factory should be able to get mRNA vaccine production online in, at most, three to four months. The Serum Institute in India already is slated to produce the Astrazeneca and Novavax vaccines, while Moderna declined to partner with a qualified Bangladeshi vaccine maker, Incepta, claiming its engineers were too busy to focus beyond U.S. and EU production. Pakistani firm Getz Pharma also got the silent treatment on its vaccine inquiries. In Latin America, existing facilities in Brazil, Argentina and Mexico under contract to monopoly holders are already pumping out vials, and in countries like Chile and Colombia, the pharmaceutical industry has expressed willingness to kickstart vaccine production. In the context of its WTO submission related to the waiver, the South African government provided numerous examples in support of its oft-repeated statement that: *"developing countries have advanced scientific and technical capacities…and that the shortage of production and supply [of vaccines] is caused by the rights holders themselves who enter into restrictive agreements that serve their own narrow monopolistic purposes putting profits before life."*

And, to the extent that decades of research in developed and developing countries on mRNA technology translated into successful but difficult-to-make COVID-19 vaccines, this platform is not the only one on which successful COVID-19 vaccines have been built. A recent presentation by scientists at the Brazilian Butantan Institute described how over-reliance on new technologies could undercut global production of COVID-19 vaccines based on older technology, such as the inactivated virus and protein subunit platforms.

The existing TRIPS flexibilities, while well adapted to overcome patent barriers affecting small molecule medicines that are easily produced, are not workable in the COVID-19 pandemic. U.S. policymakers should not be misled by claims that the flexibilities that industry has long decried, including compulsory licenses, are now somehow adequate to a much more urgent and complex task. Supporting the TRIPS waiver will bring a new urgency and, if need be, a new set of compulsory tools to mandate the technology transfer that is so desperately needed to expand the global supply of diagnostics, vaccines, and medicines so as to overcome the horrendous disparities in access that threaten to prolong the pandemic with all its attendant health, economic, and social costs.