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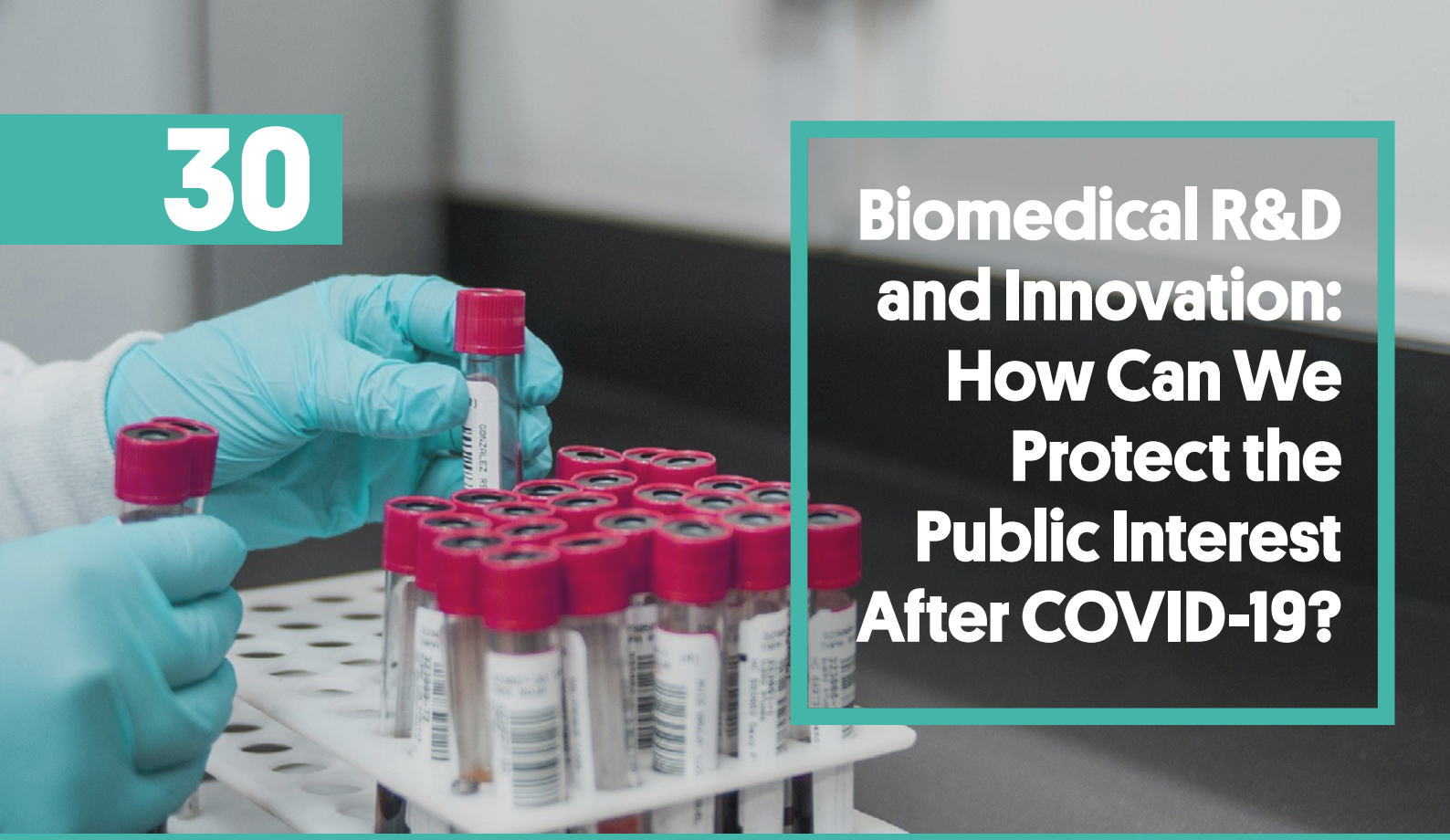

Biomedical R&D and Innovation: How Can We Protect the Public Interest After COVID-19?

Series | COVID-19 & response strategy

ISGlobal Barcelona Institute for Global Health

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[This is the 30th document in a series of discussion notes addressing fundamental questions about the COVID-19 crisis and response strategies. These documents are based on the best scientific information available and may be updated as new information comes to light.]

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Since before the pandemic was officially declared one year ago, the international community has been hard at work on **research and development (R&D)** and **innovation** efforts against COVID-19. According to data compiled by the global health think tank Policy Cures Research, as of 1 October 2020, at least **$9.18 billion** had been invested in basic research and the development of diagnostics, therapeutics and vaccines against SARS-CoV-2 (see *Figure 1*)[1].

The scale of these efforts is **unprecedented**. Investment in R&D against COVID-19 over the past several months is four times the combined annual expenditure against HIV/AIDS, malaria and tuberculosis between 2007 and 2018. Moreover, this figure likely underestimates the actual amount that has been invested. The **lack of transparency** surrounding many contracts between the public sector and private companies makes it difficult to accurately estimate total spending. Under the umbrella of **Operation Warp Speed** alone, the US government advanced $12 billion to the industry, most of it for R&D projects[2]. Also not included in this estimate are the sums invested by **China and Russia**, as well as other investments made by private companies.

These investments paid off quickly. By late 2020, the international scientific community had opened up lines of research for the **development of 1,052 products** related to COVID-19: 469 **diagnostics**, 362 **therapeutics** and 221 **vaccines** (six out of every ten dollars invested went to vaccine research) (see *Figure 2*). Current figures may be even higher. Most of

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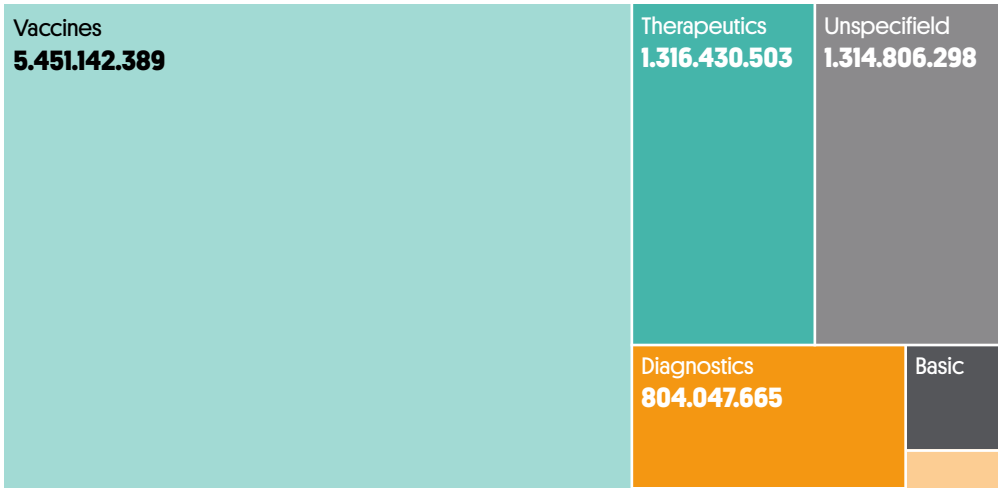
[1] COVID-19 R&D Tracker. Policy Cures Research.

[2] Operation Warp Speed. US Department of Defense.

these projects are being **led by developed countries**: the United States (460), Canada (49), the European Union (149, including **13 in Spain**) and the United Kingdom (34); however, a significant number of research projects are also underway in China (168), South Korea (47) and India (31).

Figure 1. Overall Funding Commitments for COVID-19 R&D from 1 January 2020.

Total: $9,177,159,308



Source: COVID-19 R&D tracker, Policy Cures Research. Updated 20 December 2020.

Figure 2. Global Pipeline of Potential New Vaccines, Therapeutics and Diagnostics Currently under Investigation for COVID-19.

Total: 1,052

Source: COVID-19 R&D tracker, Policy Cures Research. Updated 20 December 2020.

According to information compiled by Policy Cures Research, nearly all (92%) of the resources invested in these efforts came from the **public funds** of the United States (48% of the total amount), Germany (12%), the United Kingdom (8%), Canada (7%) and the European Commission (4%), among other countries. The only **private donor** in the top ten is the Bill & Melinda Gates Foundation, accounting for just under 3% of the total funds invested. These figures do not account for the public funds invested in basic research on messenger RNA (mRNA) biology and its potential applications in immunology over the past few decades at centres of excellence such as the University of Pennsylvania, the University of Oxford and the Salk Institute in San Diego, or the billions invested in advance purchases of vaccines and the expansion of industrial production.

In other words, if not for this **earlier publicly funded basic research**, the rapid response to COVID-19 would not have been possible •

1. Access to Essential Medicines: Dilemmas and Responses

"The conventional model of biomedical innovation has for years been the subject of intense debate regarding its implications for equity and access to essential medicines and treatments for all people."

The **conventional model of biomedical innovation** has for years been the subject of intense **debate** regarding its implications for **equity** and **access** to essential medicines and treatments for all people. The four key elements of this critique are as follows:

1. Unequal distribution of the risks and benefits of the process

Failure to recognise the role of the public sector as risk-bearer and direct investor in biomedical R&D has led to an unequal distribution of the risks and benefits of the innovation process. As a result, the rewards are mainly reaped by the holders of **industrial property rights**, whereas the value generated by the cumulative and multi-stakeholder nature of the research and innovation processes tends to be disregarded.

2. Patents as the main driver of innovation

Although ownership of knowledge is considered a useful tool for fostering innovation, patent **monopolies** can lead to prices that are **unaffordable** for countries' health systems, regardless of income level. **Misuse** of patents can in some cases hamper innovation, particularly during the acute phase of an epidemic, leading to the withholding of knowledge, the blockage of knowledge transfer and, consequently, production capacity shortages. Moreover, patent-based systems can **discourage investment in areas that are not profitable in the short term** but should nevertheless be public health priorities, including epidemic preparedness, antimicrobial resistance and neglected tropical diseases.

3. Lack of a health-oriented vision

As a result of dubious intellectual property management practices and a focus on customers' ability to pay, some players in the pharmaceutical industry have adopted a **business model** oriented towards the management of intangible assets—such as patents—and raising prices on potentially high-profit therapeutics. These objectives take precedence over the efficacy and impact of biomedical R&D in terms of public health.

4. Lack of transparency

The allocation of risks and rewards in the R&D process is also hampered by the difficulty of obtaining **real data on investments** made by public and private institutions, as well as the **real cost of developing and manufacturing** biomedical products. This lack of transparency can make it difficult for public investors to impose conditions in connection to the

provision of funds, including the ability to regulate and negotiate prices.

To circumvent these difficulties, public and private funders of global health have developed a number of **mechanisms and incentives** to promote innovation and facilitate access to medicines. These include **"push"** incentives, i.e. investments or in-kind contributions that cover part of an R&D and innovation investment. The idea is to nudge the research programmes of the company or centre in a **particular direction**, accepting the risk that these efforts ultimately may not bear any fruits.

Another category is known as **"pull"** incentives. These incentives **reward research results**: removal of administrative hurdles (for example, fast-track approval procedures), rewards for the development of certain products, and advance market commitments (AMCs).

Finally, **pooling mechanisms** bring together data, patents, designs and other types of value related to a particular disease or therapy for the purpose of sharing these resources and averting the barriers created by secrecy. The **pooling of assets protected by intellectual property rights** enables researchers and manufacturers to contribute to the R&D and innovation process, thereby increasing production capacity and reducing prices through generic versions of the product. Pooling reduces innovation costs, creates viable markets and facilitates competition, leading to lower prices

2. What Is Happening During the COVID-19 Epidemic?

"The experience of COVID-19 vaccines has starkly demonstrated the limitations of an excessively opaque pharmaceutical innovation system built upon a questionable distribution of risks and benefits."

The international community's response to COVID-19 has incorporated **lessons learned from previous epidemics**—including HIV/AIDS and the Ebola virus—and made use of several of the tools described in the previous section. The **Access to COVID-19 Tools (ACT) Accelerator** is a multi-stakeholder initiative led by the World Health Organisation (WHO) that seeks to guarantee the development of diagnostics, treatments and vaccines against the disease and ensure equitable access to these resources. In addition to diagnostics, treatments and vaccines, the fourth pillar of the ACT Accelerator involves strengthening health systems.

The **vaccine**-specific mechanism of the ACT Accelerator is known as **COVAX**. COVAX is coordinated by three of the field's leading organisations—the Coalition for Epidemic Preparedness Innovations (CEPI); Gavi, the Vaccine Alliance; and the WHO—which have adopted a multi-pronged strategy:

- **CEPI**[3] was created in 2017 to accelerate the R&D and innovation of vaccines for diseases with epidemic potential. With funding from public institutions and private philanthropists, CEPI uses **push mechanisms to encourage research** into new responses, offering conditions that theoretically guarantee the public interest of the results: batches of vaccines at no cost in the event of an epidemic, commercial returns on products in which they have participated, free access to data and samples, and licensure for vaccines to which they have contributed. As the COVID-19 experience has demonstrated, these conditions do not always serve their purpose.

- **GAVI**[4] has made intensive use of **pull mechanisms** on an unprecedented scale. This organisation is tasked with securing resources for the **advance purchase of products** and **ensuring stable and sustained demand over time**, allowing producers to take greater risks in the process and offer lower prices. Gavi must also ensure a fair market segmentation that guarantees access to affordable vaccines for the 92 low- and middle-income countries included in its AMC scheme.

None of these initiatives challenges the fundamentals of the intellectual property protection system; instead, they rely on **direct negotiation with the companies** involved in research, development and production. The mechanism designed to facilitate discoveries using open licences is known as the COVID-19 Technology Access Pool (C-TAP) (see *Box 1*).

[3] CEPI.

[4] GAVI.

Box 1. C-TAP: An Alternative for the Open Development of Pharmaceutical and Technological Responses to COVID-19.

In May 2020, the WHO World Health Assembly passed a resolution to create the COVID-19 Technology Access Pool (C-TAP). The purpose of this initiative is to **pool and ensure open access to technologies** for detecting, preventing and responding to COVID-19. The idea is to eliminate, for the duration of the pandemic, barriers created by legal and business models that raise the price of products or otherwise limit access.

The creation of C-TAP was met with **scepticism** from the **pharmaceutical industry**, which argued that **eliminating property rights** would remove incentives for innovation. This view appears to be shared by virtually all **developed countries**[5], which have opted not to support a proposal put forth by the government of **Costa Rica**. The proposal has received the backing of just 40 countries, mostly low-income ones. The closest precedent for C-TAP is the **Medicines Patent Pool**, a similar initiative launched a decade ago that has already secured agreements with around a dozen patent owners.

Source: WHO and the Medicines Patent Pool.

COVAX has succeeded in coordinating the actions of 183 countries to **ensure global access** to at least 2 billion **vaccine** doses by 2021. However, as explained in greater detail in issue #28 of this series[6], this aspiration has come up against **three main obstacles**: funding, production and distribution. **Funding needs**—around $8 billion to guarantee vaccine purchases in 2021—have largely been resolved in this initial phase, thanks to the return of the United States to the system. Nevertheless, this issue will undoubtedly crop up again in the coming months. Of far greater concern at the moment is "**vaccine nationalism**"—a race to stockpile doses, with the richest countries elbowing each other out of the way—and the objective difficulties of vaccine **distribution** in places where the infrastructure and health systems do not meet minimum standards.

However, the experience of COVID-19 vaccines has also starkly demonstrated the limitations of an excessively opaque pharmaceutical innovation system built upon a questionable distribution of risks and benefits. International pooling mechanisms and bilateral purchases of vaccine doses have both been characterised by a disturbing **lack of transparency**. Private companies have retained considerable negotiating power, stemming in part from the scarcity of alternatives in the midst of a pandemic emergency, and in part from the weakness of states in the negotiations. As the **squabbles** between the European Commission and AstraZeneca have shown, even EU institutions have been unable to impose their conditions and unwilling to release the full details of contracts signed under confidentiality agreements.

The response to this situation has been swift. In October 2020, the governments of **India** and **South Africa** formally called for the World Trade Organisation (WTO) to place a **temporary freeze on patents**, trade secrets and other forms of intellectual property affecting COVID-19 treatments, vaccines and other technologies[7]. The purpose of this **request** was to further the public interest to the greatest extent possible by facilitating mass production with the participation of **generic** drug makers. The proposal hearkened back to the decades-old conflict between rich and poor countries over antiretroviral treatments for HIV, which was at the centre of the debate at the WTO conference in Doha in 2001. History repeats itself: the new proposal by India and South Africa has mostly been supported by African, South Asian, Caribbean and Pacific Island countries, as well as some prominent South American governments such as Bolivia, Venezuela and Argentina. It is opposed by the bloc of richer countries, as

[5] With the exception of Belgium, Luxembourg, Norway, the Netherlands and Portugal.

[6] What Are the Main Challenges That Global COVID-19 Immunisation Efforts Must Now Overcome? ISGlobal. 22 January 2021.

[7] Usher, AD. South Africa and India push for COVID-19 patents ban. *The Lancet*. 5 December 2020.

well as some allies from the developing world such as Brazil and Ecuador.

Despite its recent experience—and the support of a minority of the European Parliament[8]—the **EU will continue to block** in the WTO **any proposal** that weakens the established industrial property model. The European Commission's official response cites a lack of evidence linking this model to the limitations of the COVID-19 response, defends the value of these incentives in the innovation process and advocates voluntary technology transfers as an alternative to more coercive measures. The reality, however, is that the powerful **global pharmaceutical industry** is among the **main beneficiaries of this model**, and the stakes extend well beyond COVID-19. Ceding any ground in this debate would set a dangerous precedent for pharmaceutical corporations

3. Preferred Suppliers: An Alternative Based on the Influence of Public Investment and Procurement

"If the preferred supplier system were applied in the biomedical sector, companies wishing to do business with the public sector would have to compete on the basis of assessable criteria oriented towards the public interest."

At present, the issue of reforming the incentives of the pharmaceutical R&D system—including intellectual property protection—remains **unresolved**. If such reforms were to be enacted, they would solve some of the challenges described in the second section of this document. However, these reforms are not the only path forward, and the response in recent weeks suggests that changes are unlikely in the short or medium term. There are **other possibilities** that would rely on states' **negotiation capacity** and the strength they derive from their **investments** in research and their importance as **major customers** of pharmaceutical companies.

Investments and public procurement mechanisms are used by states in various economic sectors to establish certain guarantees for the public interest[9]. Such guarantees always specify the price and quality of products and services but often go further, incorporating **conditions** relating to the environment, labour, human rights, etc. It seems reasonable, therefore, that this same logic should be extended to a sector as sensitive to the public interest as the biomedical sector. In this field, the **relationship between the public and private sectors** is constant and significant:

- As we have seen in the case of COVID-19, companies receive **multi-million-dollar sums** from states for research and development of their products.
- Pharmaceutical companies' clinical trials often make use of **public infrastructure** and **resources**.
- **Regulatory agencies** assess and verify the safety and efficacy of pharmaceutical products before they are released on national markets.

[8] Chaudhury, DR. European parliament members back India request for patents waiver. *The Economic Times*. 5 February 2021.

[9] OECD Business and Finance Outlook 2020 | READ online. Accessed 15 October 2020.

- **Representatives** of private companies **interact** with **health and health-management professionals** to provide information and promote the sale of their products.

- Pharmaceutical companies participate in **public tenders** and other health system procurement mechanisms.

These avenues clearly add up to a **relationship of mutual interest** that states could use to their advantage. This is also the logic of the European Commission, whose recent statement on its pharmaceutical strategy for Europe included the following:

"Actions in the area of public procurement can foster competition and improve access. Public buyers should design smart and innovative procurement procedures, e.g. by assessing the role of 'winner-takes it all' procedures and improving related aspects (such as price conditionality, timely delivery, 'green production' and security and continuity of supply) […]."

Many public systems have already adopted **responsible sourcing practices**. Specific recommendations on responsible sourcing are set out by the **Sustainable Development Goals** and the **Global Compact**[10], and certification mechanisms such as **B Corp**[11] are available. Moreover, it does not seem necessary to create complicated governance mechanisms or to open up a thorny debate over legislative reforms.

The **first step** is simpler: establish a set of **basic principles** to help guide subsequent decisions at all levels. If the *preferred supplier* system were applied in the biomedical sector, companies wishing to do business with the public sector would have to compete on the basis of assessable criteria oriented towards the public interest. These criteria can be summarised as **four main principles**:

- **Sharing needs.** To ensure that the biomedical research agenda prioritises public health and social needs, suppliers should invest a tangible part of their R&D efforts in meeting these needs. The model should also take into account the regulatory and market-access commitments of new medicines.

- **Sharing risks and rewards**. To ensure a more balanced and transparent sharing of R&D risks and rewards at all stages along the development pipeline, preferred suppliers should declare all of the public resources they receive throughout the R&D cycle, as well as the production costs associated with the new asset. The amount of public funds received should have an impact on the level of intellectual property protection, or at least on the distribution of commercial benefits associated with the final product. Public investors should also have a say in setting the final price of the product. In return, preferred suppliers should have access to higher aggregate demand from public institutions.

- **Sharing results**. If public funds are invested in pharmaceutical R&D and innovation, conditions must be imposed to ensure that the benefits derived from the process—i.e. the knowledge generated as well as the final product—are accessible. A preferred supplier would provide access to clinical trial results as well as complete information on any unsuccessful drug candidates. Because of its enormous scientific value, this information should be construed as a public good.

- **Sharing products and results**. To ensure that the industry is sustainable and focused not only on the bottom line but also on the health impact of its activities, interactions between the public sector and its private suppliers should be subject to different standards. Preferential access to public funds could be granted to companies that demonstrate compliance with best environmental practices in manufacturing and distribution, or on the basis of criteria related to corporate practices, such as strict policies to reduce buybacks and encourage capital reinvestment in the R&D process. Similarly, equitable access practices could be measured and used to determine preferred supplier status.

At first blush, these four principles may seem like a pipe dream. To be sure, they have not been standard practice in the international community's unprecedented response to COVID-19. However, the **introduction of public interest criteria** in public procurement systems is by no means unheard of[12]. In fact, the

[10] United Nations Global Compact.

[11] Certified B Corporation.

[12] O'Brien, C y Martín-Ortega, O. Public procurement in the EU: Eroding or supporting the European social and political model? December 2018.

case of **CEPI** proves that such criteria are well-aligned with the **aspirations** of many stakeholders in the new global health governance regime. The original conception of this novel initiative to promote public-interest research included a series of aspirations quite similar to those defined in the preferred supplier model. Unfortunately, these criteria were modified at an early stage of the process (see *Box 2*).

Box 2. The case of CEPI: Could the Response to COVID-19 Have Been Different?

The Coalition for Epidemic Preparedness Innovations (CEPI) imposes a number of **obligations** on its partners to facilitate transparency and the sharing of clinical trial information. In the earliest stages of its existence, however, CEPI envisaged a much more ambitious set of **public-interest principles and clauses** than it does today[13]:

- Develop plans to manufacture and maintain an investigational vaccine stockpile.
- Publish pricing methodology and strategies to guarantee affordability.
- Place obligations on funding recipients regarding the registration and marketing of vaccines, as well as the volume of doses that must be made available.
- Require transparency regarding the results of clinical trials and open access to publications, data and other relevant research information.
- Impose a risk- and benefit-sharing system, including an accounting of the costs covered by CEPI and the sharing of any commercial benefits arising from the products.

CEPI began its activities in 2017. Under **pressure from the pharmaceutical industry and potential partners**, the organisation reversed course in 2018. Many of the original conditions were scrapped and guarantees are now negotiated on a case-by-case basis.

[13] Coalition for Epidemic Preparedness Innovations. CEPI Policy Documentation. 2017. Accessed 24 July 2020.

4. Conclusions and Recommendations

"From a public-interest standpoint, the coronavirus pandemic is of a piece with the Ebola virus outbreak, the antimicrobial resistance crisis of tomorrow and the HIV/AIDS epidemic of years past. There is an urgent need to align the system with people's real needs."

The COVID-19 pandemic is forcing us to **reconsider some of the economic, political and social fundamentals** that we have long taken for granted. The model of innovation and access to essential medicines is one such area requiring re-examination. The international community has undertaken extraordinary efforts in recent months. However, the impressive results of these efforts could be undermined by the **imperfections of the system** and its **inability to adapt** to the needs of the new context. From a public-interest standpoint, the coronavirus pandemic is of a piece with the Ebola virus outbreak, the antimicrobial resistance crisis of tomorrow and the HIV/AIDS epidemic of years past. There is an **urgent** need to align the system with people's real needs.

The **public sector** is not just any player in this debate. Given the scale of its investments and its status as the main recipient of biomedical innovations, the public sector must play a **leading role** in defining the new model. This role must be translated into **rules and principles** that optimise value for the public interest.

ISGlobal encourages national and international stakeholders to consider the following measures:

On transparency:

- Public, corporate and non-profit entities involved in the research, development or marketing of medicines must provide **reliable data** on their investments, profit margins and any public funds to which they have access.

- **Negotiations** between governments and pharmaceutical companies for the purchase of medicines with public funds must be conducted within a framework of absolute transparency. Countries should provide a prior analysis of cost-effectiveness and health technology to determine whether to include each drug in their national health system and these results should be made publicly available.

- During **trade agreement** negotiations, it is essential to guarantee access to negotiating drafts and public consultations prior to their approval.

On the regulation of intellectual property:

- Countries that are signatories to WTO agreements and other regional and bilateral trade agreements must guarantee consistency between trade rules and access to essential medicines. The first step is to introduce **flexibility and exceptions** to intellectual property rules, but it is equally important that existing rules be enforced without being systematically blocked by one party.

- The **EU** and its member states should facilitate this process whenever necessary, especially when it comes to **neglected diseases** or when there is a market failure that prevents access to essential medicines for **price-related reasons**.

- The amount of public funds received should have an impact on the level of intellectual property protection, or at least on the distribution of commercial benefits associated with the final product. **Public investors should also have a say** in setting the final price of the product. In return, preferred suppliers should have access to higher aggregate demand from public institutions.

On preferred suppliers:

- The public sector should reinforce the public interest in health by using its position to **set conditions for suppliers** with regard to investment, access and affordability of essential medicines. The institutions responsible for setting these conditions should engage in a **process of reflection and public consultation** to determine how best to implement this idea in practice.

- Funders, investors and shareholders in the pharmaceutical industry have an opportunity to become agents of **new social enterprise models**. Their active participation can shift the balance of power in this debate and contribute to the engagement of the pharmaceutical sector

TO LEARN MORE

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