Forum Discussion Paper

Aligning incentives for pharmaceutical innovation to achieve fair pricing

WHO/MHP/HPS/MIA/2021.03

© World Health Organization 2021. All rights reserved.

This discussion paper does not represent an official position of WHO. It is a tool to explore the views of participants on the subject matter. References cited in this document do not constitute or imply any endorsement or recommended preference to others of a similar nature that are not mentioned.

All reasonable precautions have been taken by WHO to verify the information contained in this discussion paper. However, this discussion paper is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the discussion paper lies with the reader. In no event shall WHO be liable for damages arising from its use.

Acknowledgements

With many thanks to the Fair Pricing Forum preparatory working group on aligning incentives for pharmaceutical innovation to achieve fair pricing:

Chairs Suerie Moon and Anthony So, members Deena Alasfoor, Biswajit Dhar, Helga Festøy, Komal Kalha, Mariana Mazzucato, Mirna Metni, Daudi Msasi, Maja Sercic, Santiago Torales, and Jaume Vidal. Additional support provided by Henry Li, Adrían Alonso Ruiz, and Prateek Sharma.

Thank you also to the additional experts who provided resources and perspectives throughout the term of the preparatory working group.
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTENTS</td>
<td>2</td>
</tr>
<tr>
<td>BACKGROUND</td>
<td>3</td>
</tr>
<tr>
<td>About this discussion paper</td>
<td>6</td>
</tr>
<tr>
<td><strong>TOPIC I: PROMOTING TRANSPARENCY FOR ACCOUNTABLE MEDICAL INNOVATION</strong></td>
<td>6</td>
</tr>
<tr>
<td>Types of data that merit greater transparency</td>
<td>7</td>
</tr>
<tr>
<td>Concrete measures to improve transparency: a menu of options</td>
<td>8</td>
</tr>
<tr>
<td>Degree of disclosure</td>
<td>9</td>
</tr>
<tr>
<td>Challenges and opportunities for transparency</td>
<td>10</td>
</tr>
<tr>
<td>Questions for discussion during the Forum</td>
<td>10</td>
</tr>
<tr>
<td><strong>TOPIC II: PLACING ACCESS CONDITIONS ON INCENTIVES FOR INNOVATION</strong></td>
<td>10</td>
</tr>
<tr>
<td>Conditionality options along the pharmaceutical value chain</td>
<td>11</td>
</tr>
<tr>
<td>Challenges to implementing access conditions</td>
<td>12</td>
</tr>
<tr>
<td>Questions for discussion during the Forum</td>
<td>13</td>
</tr>
<tr>
<td><strong>TOPIC III: MAKING THE PUBLIC SECTOR MORE EFFECTIVE STEWARDS OF INNOVATION AND ACCESS</strong></td>
<td>13</td>
</tr>
<tr>
<td>Innovation platforms</td>
<td>14</td>
</tr>
<tr>
<td>Public sector-supported manufacturing</td>
<td>15</td>
</tr>
<tr>
<td>Procurement</td>
<td>16</td>
</tr>
<tr>
<td>Challenges and opportunities for further public sector stewardship</td>
<td>17</td>
</tr>
<tr>
<td>Questions for discussion during the Forum</td>
<td>17</td>
</tr>
<tr>
<td><strong>DIRECTIONS FOR FURTHER RESEARCH AND COLLABORATION</strong></td>
<td>18</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>19</td>
</tr>
</tbody>
</table>
Background

How fair are the prices of medicines? Questions have been raised regarding the appropriate relationship between a medicine’s price and several factors, including:

- The costs to research, develop and/or manufacture the product;
- The immediate and long-term affordability for health systems and households, as well as its therapeutic or health system value; and
- The parties bearing the costs and risks of R&D and manufacturing, and the fairness of profits accruing to sellers.1,2,3

Understanding medicines pricing requires examining not only the price transacted when a product reaches the market, but also a number of other factors, including the innovation system that underlies those prices.4 The focus of this discussion paper is the system of actors, incentives, rules and financial flows that shape which medicines are developed and how they are priced.

Pharmaceutical innovation is a hybrid public and private effort. Public laws and regulations at national, regional and global levels establish the ground rules of the system, for example, governing intellectual property, regulatory standards for product safety and efficacy, tax policy, regulatory incentives, conditions for procurement or reimbursement, import and export, and marketing. Public funds generally pay for the basic scientific research that lays the foundation for product development, and in many countries, the public sector is a major -- if not the main -- purchaser of medicines. In general, earlier stage research has been carried out by public and academic labs, and private firms invest in and carry out the later stages of product development, applying for regulatory approval, manufacturing, marketing, pricing, selling, distributing and conducting post-marketing surveillance of the medicine.5

Overall, the public sector accounts for about 30% of the upfront total investment in pharmaceutical R&D and takes on the earlier higher-risk stages, and the private sector accounts for about 60% of upfront investment and takes on the later relatively lower-risk stages (with the remaining 10% coming from other sources such as philanthropic organizations).6 However, these estimates are based on data largely from high-income countries; information on public and private investment in other countries is limited. The incentive for firms to invest in R&D -- which entails significant risks, costs and time -- is the prospect of market returns. The size of market returns is enhanced by time-limited monopoly protections, often secured through intellectual property rights and/or regulatory barriers to market entry by competitors.

This innovation system promotes R&D investment in lucrative areas where product development risk is manageable. It has resulted in the development of products offering significant benefits for individual and public health, such as those to treat HIV/AIDS, hepatitis C, some cancers and rare diseases, and vaccines to prevent diseases such as HPV and COVID-19. However, profit-maximizing prices are built into the system by design, without guarantees of affordability. And this system does not generate adequate innovation where the risk is too high and/or the expected profits are too small, such as for the neglected diseases of poverty, antibiotics, many rare and/or pediatric diseases, or pathogens of pandemic potential. In these areas, there is generally an even higher degree of public investment, incentives and/or direct involvement in the R&D process.

For example, the majority of neglected disease R&D is paid for by public and philanthropic funds;7 rare (“orphan”) disease R&D is eligible for additional regulatory and tax incentives; the public sector
has created new initiatives to reduce the risk and further subsidize the development of antibiotics; and the public sector has de-risked and subsidized the R&D and manufacturing costs of many COVID-19 vaccines through different incentives with various impacts, including grants, loans, technical assistance, coordination and advanced purchase agreements.\(^8\) \(^9\) \(^{10}\) (See Topic III below on public sector stewardship for further discussion.) The question has arisen as to whether the division of public and private investment, risk-taking and reward is appropriately reflected in the prices of final products.\(^{11}\) Assessing this division of labor requires greater transparency on the innovation process (see Topic I below on transparency for further discussion.)

What might “fair pricing” mean in principle and in practice? This was a key question debated at the Fair Pricing Forums 2017 and 2019. While a precise consensus definition did not emerge from those debates, some overarching principles have emerged. “Central to the concept of fair pricing is striking a balance between the public health needs for innovation and affordability, while recognizing that quality health products are imperative, and that sustainable production comes at a cost.”\(^{12}\) (see Figure 1).

**Figure 1: Innovation is central to the concept of fair pricing**

Assessing the fairness of prices also implies considering both sides of the transaction, that is, both sellers and buyers of medicines. For sellers, one could reasonably account for the risk-adjusted costs (e.g. R&D, production, distribution, business operating cost, including the cost of capital and the cost of failures) that have been borne by the seller and a fair profit. For buyers, short- and long-term affordability, the therapeutic and health system value of the medicine, and supply security are key considerations.

In this conceptualization, a fair price is one that falls within the zone above the price floor represented by the sellers’ costs and fair \(^{13}\) \(^{06}\) See Figure 2, and further discussion in the companion Fair Pricing Forum discussion paper exploring pricing approaches sensitive to health systems’ ability to pay and to the need for achieving universal coverage of pharmaceutical products.
In practice, there can be direct tradeoffs between profit levels for sellers and affordability for consumers. How far a price should be allowed to rise above costs (even while remaining below the affordability threshold) relates directly to what level of profit to the seller is considered fair or normal (vs supra-normal). Assessing fairness of profit relates directly to the question of what level of profit is required as an adequate incentive to pay for innovation. However, assessing costs, profits and affordability requires a significant increase in the transparency of information disclosed about the pharmaceutical market (see Topic I below on transparency for further discussion.)

The mainstream R&D model has not adequately aligned incentives to achieve fair pricing, suggesting that the model should be revisited to help ensure equitable access. Governments and multilateral institutions, working with stakeholders, have implemented a range of policies to support medicines R&D. These include patents and other forms of intellectual property rights, research grants and subsidies, R&D tax credits, flexibility for regulatory and reimbursement approval, and longer monopoly periods (e.g. through patent term extensions, data exclusivity, or other regulatory exclusivities). Other measures include technical assistance and matching firms with complementary capacities, guiding development towards priority public health needs and innovations with desired characteristics by defining targeted product profiles, and guaranteeing viable markets for a product upon successful development through advance market commitments.

However, such incentives rarely include guarantees of affordability of the resulting product to the payer or the end user. While price signals can stimulate innovation, unaffordable prices are an important factor restricting access and prevent society from realizing the full benefits of scientific progress. From the perspective of economic efficiency, excessive prices can also encourage wasteful spending, increase total societal deadweight loss, distort investment, and eventually stifle innovation. Prices (and market size) should not be the main drivers of innovation. What measures would be most effective in encouraging fair pricing of end-products while ensuring innovation?
About this discussion paper

This discussion paper presents the discussions by one of the two working groups convened in preparation for the Fair Pricing Forum 2021. This working group focused on aligning incentives for pharmaceutical innovation. Three broad topics were discussed where potential reforms could more adequately align incentives to achieve fair pricing:

1. Promoting transparency for accountable medical innovation;
2. Placing access conditions on incentives for innovation; and
3. Making the public sector more effective stewards of innovation and access.

Several limitations should be noted from the outset. This discussion paper, in its brevity, only intends to describe the main issues for discussion and does not represent a consensus on the part of the working group. Any proposed approaches presented are only preliminary drafts intended for stimulating discussions during the Fair Pricing Forum 2021, with a view to advancing discussions and identifying potential solutions and further areas of work to find feasible and sustainable approaches to affordable pricing. The contents are a work-in-progress, not intended to be comprehensive, and do not necessarily represent the World Health Organization’s position or policy.

Topic I: Promoting transparency for accountable medical innovation

A major challenge in better understanding the pharmaceutical R&D system has been a shortage of reliable data on key aspects of its functioning. The lack of transparency on many aspects of the pharmaceutical sector has attracted increased concern in recent years. The lack of reliable, sufficiently detailed, timely information also undermines the objective of a well-informed public debate on medicines prices, and makes it far more difficult to agree on policies that can yield better results for the public interest. The lack of transparency regarding R&D costs, inputs and outcomes is of concern to patients and payers, as it can contribute to higher prices, less medical knowledge being made publicly available when all research results are not published in a timely manner, and difficulties regulating the R&D system appropriately.

While confidentiality is the widespread norm in the pharmaceutical industry, the lack of transparency also has negative implications for firms and investors. Firms may engage in costly and wasteful duplication of research when the results of other firms’ research are not quickly published, for example. For investors, lack of transparency on the contractual obligations surrounding a technology, its key features, and its potential market (including a transparent pricing & reimbursement framework) can all make it difficult to make well-informed decisions about where and how to invest. While there are legitimate reasons to keep some information private, there are also legitimate reasons to require disclosure of a far broader set of information than is currently available in the public domain about the R&D system.

These transparency challenges have received growing recognition. At the 2019 World Health Assembly, an important step was taken to begin addressing these concerns when Member States passed by consensus Resolution 72.8 calling for increased transparency in pharmaceutical markets. In 2020, the European Union’s new Pharmaceutical Strategy flagged that “there is a lack of transparency (particularly of R&D costs) and consensus on costing principles. Better understanding and greater clarity are fundamental as a basis for policy debates on the pricing of niche medicines and ‘fair return’ on research contributions.”
The Wellcome Trust’s inaugural Access to Healthcare Interventions report in 2020 highlighted as “Challenge 1: a lack of transparency makes it hard for funding agencies to implement best practice on access.” Some important steps have been taken towards improving transparency along various dimensions, by different actors and at national, regional and global levels, as detailed further below.

Key questions have arisen regarding the types of data where greater transparency would be useful, the potential benefits and risks, and the means by which increased transparency could be secured.

Types of data that merit greater transparency

For what kinds of information is greater transparency potentially needed, and what are the underlying rationales and/or concerns that have been expressed? The overall rationale is to improve equitable and comprehensive access to medicines. The following table summarizes the main categories for which information transparency along the value chain remains challenging, including but not limited to those listed in WHA Resolution 72.8, as well as rationales expressed for greater transparency, concerns expressed regarding greater transparency, and comments that emerged from the working group discussions:

<table>
<thead>
<tr>
<th>Type of information:</th>
<th>Rationale expressed for greater transparency</th>
<th>Concerns expressed re greater transparency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Net/real) Prices</td>
<td>Increase buyer’s negotiating leverage by reducing information asymmetry</td>
<td>May undermine price discrimination (tiered pricing)</td>
<td>Many factors shape outcome of a price negotiation</td>
</tr>
<tr>
<td></td>
<td>Reduce prices</td>
<td></td>
<td>-Global price transparency is high in a few areas (e.g., HIV drugs, childhood vaccines) where there is also significant tiered pricing</td>
</tr>
<tr>
<td></td>
<td>Assess fairness of prices</td>
<td></td>
<td>-Trade secret</td>
</tr>
<tr>
<td></td>
<td>Public accountability &amp; trust</td>
<td></td>
<td>-Technical feasibility</td>
</tr>
<tr>
<td></td>
<td>Understand market</td>
<td></td>
<td>-Debate on what should qualify as an R&amp;D cost, for example, whether IP acquisitions or all clinical trials should be included</td>
</tr>
<tr>
<td>(Net/real) R&amp;D and manufacturing costs:</td>
<td>Assess fairness of prices (e.g., costs, risks, profits)</td>
<td>-Trade secret</td>
<td>-Debate on what should qualify as a marketing cost</td>
</tr>
<tr>
<td>-Public/philanthropic investment</td>
<td>-Understand innovation system</td>
<td>-Build public trust in product</td>
<td>-Earlier regulatory approval with less safety &amp; efficacy data for some products raises challenges</td>
</tr>
<tr>
<td>-Private investment</td>
<td>-Calibrate R&amp;D incentives</td>
<td>-Health system effects difficult to quantify early</td>
<td>-Some implementation re patents (MPP, WAPO)</td>
</tr>
<tr>
<td>-Cost of clinical trials</td>
<td>-Understand manufacturing challenges and possibilities</td>
<td></td>
<td>-Limited information regarding licensing and various market exclusivities</td>
</tr>
<tr>
<td>-Tax benefits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revenues, units sold, marketing costs</td>
<td>Assess fairness of prices (e.g., costs, risks, profits)</td>
<td>-Trade secret</td>
<td>-Debate on what should qualify as a marketing cost</td>
</tr>
<tr>
<td>Clinical trial protocols and outcomes (e.g., safety, efficacy)</td>
<td>Patient safety, health and ethical treatment</td>
<td>-Health system effects difficult to quantify early</td>
<td>-Earlier regulatory approval with less safety &amp; efficacy data for some products raises challenges</td>
</tr>
<tr>
<td></td>
<td>Assess fairness of prices</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calibrate prices to value for patients and health system</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Build public trust in product</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patent, licensing and other market exclusivities</td>
<td>Understand where, for how long, and how strong a monopoly is in effect</td>
<td>-Licensing may contain confidential and competitive data and therefore may not be easy to collate</td>
<td>-Some implementation re patents (MPP, WAPO)</td>
</tr>
<tr>
<td></td>
<td>Understand innovation system</td>
<td></td>
<td>-Limited information regarding licensing and various market exclusivities</td>
</tr>
<tr>
<td>Registration</td>
<td>Understand challenges and possibilities for availability</td>
<td></td>
<td>Limited information globally on registration status of products in all Member States</td>
</tr>
<tr>
<td></td>
<td>Understand varying rational assessments of safety and efficacy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Understand market exclusivities linked to regulatory system (e.g., data exclusivity)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In order to better align innovation incentives to achieve fair pricing, there is need for greater transparency and understanding of how those incentives operate, including the sources and magnitude of incentives (e.g. public, philanthropic and private funding), strength and duration of incentives (e.g. patent landscapes, regulatory exclusivities), innovation outcomes (e.g. clinical trial protocols and data, registration status), costs (e.g. R&D, production, marketing, profits) and pricing
outcomes (e.g. real transacted prices). Trying to align innovation incentives without such information is like conducting surgery blindfolded.

**Concrete measures to improve transparency: a menu of options**

There is a range of concrete measures that different actors could take to improve transparency:

**Improving the collection and analysis of data in the public domain:** Some data is available in the public domain, but is not necessarily gathered, analyzed, nor easy to find. Analysts can increase efforts to collate, analyze and make publicly accessible existing data. Indeed, academic research over the past decade has made considerable advances in estimating the costs, timeframes and success/attrition rates for pharmaceutical R&D with much larger datasets and a variety of methodological approaches, for example. There have also been valuable efforts to increase understanding of innovation incentives, for example, by collecting R&D funding data, contract clauses from model and executed R&D and procurement agreements, and price information for specific products.

**Persuasion, voluntary initiatives and political pressure:** Advocacy, political pressure or other means of persuading research funders, labs and companies to increase voluntary sharing of previously undisclosed information can also increase transparency. For example, the past decade has witnessed increased disclosure of patent information on medicines through initiatives of the Medicines Patent Pool and Pat-INFORMED. Companies developing and producing COVID-19 vaccines took the unusual step of publishing their clinical trial protocols in September 2020 (and later the trial results) to build public trust, for example, and some procurement contracts between vaccine producers and government purchasers have been published in redacted form upon the agreement of both parties. Two important challenges arise with relying on voluntary self-reporting, however. First, information may not be disclosed as thoroughly or as regularly as if such disclosure were mandated. Second, in the absence of clear standards or methods of calculating allowable costs (e.g. for R&D or marketing costs), the numbers may be difficult to interpret, compare and use to inform decision-making.

**Ad hoc disclosure:** Some information has entered the public domain without the explicit agreement of all parties. Information has been leaked to journalists or NGOs, for example, or accidentally published, as when the prices the EU negotiated for COVID-19 vaccines was tweeted by a government official. Valuable information has entered the public domain through these channels, but it should be emphasized that this is no substitute for systematic approaches to improving transparency.

**Freedom of information laws:** Some information can be obtained through freedom of information laws (or “sunshine” laws), particularly information directly involving government entities such as contracts for R&D subsidies or purchases. However, the speed and thoroughness of the data obtained varies widely, as documents can be heavily redacted or only provided months or years after a time-sensitive policy process has passed.

**Economic levers:** Economic levers can also increase transparency. For example and as described further under Topic II, a number of public and philanthropic research funders require as a condition of funding that the recipient put all data resulting from the research into the public domain within a particular time period. Such policies require careful follow-up to ensure compliance, however, as a number of studies have found that compliance has remained incomplete and slow. Government regulatory approval and procurement (or reimbursement) of medicines are two other key moments when information disclosure (e.g. on prices, R&D investments, patent status) could be more broadly required as a condition of market-entry or sales.
**Regulatory, legislative or judicial levers:** Public rulemaking and adjudication is another means to increase transparency. For example, the Italian Medicines Agency (AIFA), which regulates market entry and reimbursement in the country, issued a Pricing and Reimbursement Decree in 2019 that requires increased disclosure by industry on prices, public contributions to R&D, patent status, and sales/revenue/marketing data. Legislatures can require increased transparency of both public and private actors as a measure to protect the public interest, as the French Parliament did in 2020 when it passed new requirements that public contributions to medicines R&D be disclosed. Finally, increased information disclosure can be linked to judicial proceedings; for example, competition authorities have required companies to provide cost and other information in cases examining potential excessive pricing of medicines (for additional discussion around regulating excessive pricing, please see the accompanying Fair Pricing Forum discussion paper on pricing approaches sensitive to health systems’ ability to pay and to the need for achieving universal coverage of pharmaceutical products).

**Degree of disclosure**

The availability of information is not necessarily binary, but rather, may more usefully be depicted as falling along three dimensions: degree of disclosure, degree of specificity, and timeliness and reliability of disclosure (see Figure 3). Full, detailed, immediate public disclosure of information lies at one end, while total non-disclosure outside of an organization or group lies at the other. In between lies a broad range of possible arrangements in which some parties may have access to some information at some times with varying degrees of reliability.35

Different degrees of transparency may be appropriate, depending on the type of data, public purpose, potential benefits and risks, and contextual factors. For example, if the purpose of increased transparency is to strengthen public accountability and trust, full, detailed and public information disclosure may be necessary. In contrast, if the purpose of increased transparency is to strengthen negotiating leverage of a buyer or to determine an appropriate judicial remedy, disclosure to the relevant public authorities may be appropriate. It is beyond the scope of this discussion paper to analyze all the scenarios falling within these three dimensions for all types of data.

**Figure 3: dimensions of transparency framework**
Challenges and opportunities for transparency

Tracing the effects of increased transparency directly to changes in pricing or innovation is challenging, as information is only one of multiple variables that shape the final prices agreed in any particular transaction. Other relevant factors, such as degree of competition, volume of the purchase, and terms of payment also affect the negotiating leverage of sellers and buyers. Nevertheless, the strategic value of information is widely recognized in economic theory, and amply reflected in the regular use of price and patent databases by procurement professionals. Increased understanding of the utility of such information sources would be valuable.

Information can be used in combination with other policy levers to assess and achieve fairer prices of medicines. Public debate on the fairness of medicines prices, such as those taking place in legislative hearings, conferences or in the media, often make reference to key datapoints such as real transacted prices, net R&D costs, market information, clinical trial results, patents and registration status. It is reasonable to conclude that such information is likely to shape price negotiations, and judgments on whether a given price is fair. Given that measures to systematically increase the transparency of pharmaceutical markets are relatively recent, it will be important to conduct further research and analysis to understand better its effects across different health systems, including on the affordability and availability of medicines.

Questions for discussion during the Forum

1. What are concrete measures that could be taken by your country or organization to improve information transparency, and in which specific areas?
2. For which kinds of information would greater transparency most assist you to achieve a fair price, or to assess whether a given price is fair?
3. How can legitimate concerns about increased information transparency be addressed and potential negative impacts be mitigated?

Topic II: Placing access conditions on incentives for innovation

Traditional development models offer incentives to innovators to reward investing at risk, usually in the form of protections and too often with no stipulations on the price or equitable distribution of the resulting product. In a study of the top twenty medicines on the global market, the premium earned in the U.S. above the list prices in Canada, Denmark, United Kingdom and Ireland yielded $116 billion for the 15 companies involved—far more than the $76 billion spent by the same companies on their R&D globally. Unchecked, there is no clear relationship between input costs like R&D expenses and output prices.
Across the pharmaceutical value chain, access conditions may be placed on incentives for innovation to achieve fairer pricing of health products. Such conditions may help ensure fair returns on public investments by requiring disclosure of clinical trial data, open access publication of findings, or non-exclusive licensing of research tools. In other cases, conditions placed on public or philanthropic financing can provide guarantees of pricing or volume of the product delivered for particular target markets. Health products might need to meet specified performance characteristics, including a unit price, to receive incentive payments.

Such conditions have come into play with varying success to enable fairer pricing, with notable examples including product development partnerships for neglected diseases and CEPI. The COVID-19 pandemic has also encouraged efforts to improve public health and research data sharing during public health emergencies through the GloPID-R Data Sharing Principles. The Global Health Innovation Alliance Accelerator has recently launched the Master Alliance Provisions Guide (MAPGuide) project, an online database of template contractual provisions in global health, searchable by issues such as equitable access to medicines and affordable or reasonable pricing. At WHO, related initiatives include the SDG3 Global Action Plan Accelerator on R&D Innovation and Access including the Global Good Access Practices, Global Late Stage Innovators Coordination Forum and Elevating Country Priorities recommendations.

By analyzing learnings from experiences with conditional innovation incentives and key elements of success, this discussion aims to identify potential applications of conditionality to other contexts and how to successfully engage stakeholders in the process to enable its success.

**Conditionality options along the pharmaceutical value chain**

Access conditions placed on innovation incentives can help ensure fairer pricing in various ways:

**Target product profiles** specify the optimal characteristics of a product. Several initiatives underway, including one at the WHO, seek to guide the development of new health products by publishing key characteristics of needed health products. This can help shape market innovation, including the pricing of the product and its adaptation to resource-limited settings. While such target product profiles are not necessarily binding, product development partnerships such as the Drugs for Neglected Diseases Initiative and the Medicines for Malaria Venture have incorporated affordable pricing into target profiles and R&D decision-making for neglected disease treatments.

**Conditioning push or pull financing incentives** for innovation can play an important role in helping achieve fairer pricing. Public funding of research provided the knowledge base for all 210 new chemical entities approved by the US FDA from 2010-2016. Public-sector research institutions (PSRIs) already contribute disproportionately to therapeutic innovation. Between 1990 and 2007, PSRIs contributed to the discovery of roughly 10-20% of all medicines in new drug applications. Nearly half of these received priority review by comparison to only 20% of applications based solely on private-sector research. PSRIs also had a role in nearly all the key, innovative vaccines over the past 25 years. This positions the public sector to be more strategic in its financing of R&D.

**Open-access publication and data-sharing requirements** can ensure the public dissemination of clinical trial findings, the open availability of results, and the sharing of data. These requirements have increasingly come from medical journals that have required data sharing plans for clinical trials and their registration, major research funders from the Wellcome Trust, Howard Hughes Medical Institute and Bill and Melinda Gates Foundation to cOAlition S that require open access publication, governments and public-private partnerships that have public access and data sharing policies, and research institutions. COVID-19 has only accelerated preprints and at least temporarily, the opening
of closed access journals, an acknowledgement that the open sharing of knowledge is critical to speeding innovation during a pandemic.

**Licensing of patented inventions** can shape how such knowledge is used. Public sector funders have provided extensive rules over the reporting of new inventions, including acknowledging public funding in patent filings, and providing a license to the government to practice the invention. Non-exclusive licensing, the government authority to march in or grant additional licenses, and government use rights are all important safeguards to ensuring broad access to publicly funded inventions, even if not sufficiently exercised by governments. Like pricing, tiered royalty arrangements can be used to calibrate incentives to affordability, including royalty-free options for lower-income countries.

**Cost-effectiveness criteria:** While payers applying cost-effectiveness criteria in the post-marketing evaluation of innovations is not new, making such criteria more explicit earlier in the innovation process has proven difficult. Product development is a risky investment, with long lead times, uncertain scientific outcomes, and changing political environments, which all affect future sales forecasts. When payers have expressed a willingness to pay threshold, either explicitly or implicitly via case-law, industry is in turn perceived as gaming the system by pricing directly at such a price ceiling. Certain regulators and payers have begun offering “early advice” programs to support industry to undertake research that would meet their requirements. For further discussion around price and value of health products, please see the accompanying Fair Pricing Forum discussion paper on pricing approaches sensitive to health systems’ ability to pay and to the need for achieving universal coverage of pharmaceutical products.

**Conditions on reinvestment:** The public sector is increasingly recognizing that they are “paying twice” - once for the research and again for the resulting medicine. There is also increasing scrutiny on the role of financing in the pharmaceutical space: the cost of acquisitions, claims of reinvestment in future innovation versus share buybacks and shareholder dividends. Transparency around development costs (see Topic 1) will also shed light on the substantial role of the public sector in funding research and development.

**Challenges to implementing access conditions**

Risks and rewards should be fairly shared between private industry, public funders and the populations they serve. Increasingly patients are also demanding a voice in the decision on willingness to pay for therapies in which they have participated in clinical trials. Further advancements in the progress we have seen toward public health-oriented access conditions are needed to ensure sustained support and enable payers to be more strategic investors in innovation and access, guaranteeing a public return on public investment. Crucial to such discussion is ensuring that such conditions still incentivize innovators and manufacturers to participate, and that additional actors are encouraged to innovate as well.

An ongoing area of debate, both within the Fair Pricing Working Group on aligning incentives for pharmaceutical innovation but also more broadly, is regarding the role of intellectual property rights as an incentive for innovation. While much innovative pharmaceutical R&D relies on securing private sector capital by holding intellectual property rights, monopoly pricing can work against ensuring equitable access. Ensuring innovation, yet mitigating the barriers to knowledge sharing and affordable access, requires rethinking how the public sector can be a more effective steward of the intellectual property system. While such proposals were beyond the scope of this discussion, they will be taken up during the Fair Pricing Forum during the session on intellectual property and new initiatives for more affordable prices.
The urgency to respond to the COVID-19 pandemic has prompted rapid large-scale public funding of R&D, unprecedented sharing of research results through preprints and freely available publication, speed in developing new vaccines, and support in public financing and procurement of these health products. Though the aspiration is to treat these health products as global public goods, their consumption is indeed rivalrous, and access has been highly unequal globally. While there is a global call to make the knowledge behind these products openly available (i.e. non-excludable), concrete steps to do so have been limited and insufficient to date. Yet efforts from COVAX to C-TAP present an opportunity to examine closely how public sector financing can most strategically apply access conditions to achieve fairer pricing.

Questions for discussion during the Forum

1. In what ways should governments, public funders and buyers, and research groups ensure that incentives for innovation better achieve fair pricing?

2. What lessons might be learned from best practice examples? Where in the pharmaceutical value chain might such access conditions be best applied to achieve the aim of fairer pricing?

3. Do these access conditions work better for specific types of health technologies or markets? How can shortcomings of these approaches be mitigated?

4. Has the COVID-19 pandemic presented opportunities for the public sector to be a better steward of its financing of health products?

Topic III: Making the public sector more effective stewards of innovation and access

From bench to bedside, the public sector can play a key role in ensuring not only innovation of health products that meet public health priorities, but also access by those in need. When there is a mismatch between what is supplied and what is demanded, some call this a market failure. Effective stewardship involves shaping and creating the markets, not just patching its failures. However, there is no reason to believe that even with perfectly working markets, the distribution of life-saving health products would bend towards equity.

The public sector can also advantage some innovators over others by awarding push or pull financing, intellectual property rights, or timely regulatory approval. However, the rationale for such policies may be motivated as much by industrial policy as the goal of universal healthcare access. The public sector must do more and commit to “mission-oriented” policies—tilting the playing field towards the public objective, in this case, of achieving fairer pricing as integral to shaping incentives for innovation.
Now there are many ways in which the public sector can serve as an effective steward in ensuring that incentives for innovation serve this objective. With public sector investment, it is fair to ask how government policies might enable the sharing of resources, risks and rewards (the 3Rs) on these health products. Applied to antibiotic innovation, it has been proposed that the 3Rs might suggest operating principles against which to benchmark potential policies. How might the public sector steward its inputs into the innovation of health products, such that it reaps fair returns from its investments to share resources, risks and rewards in developing these products? What new institutional approaches might unleash this potential?

At each point in the supply chain, the public sector has strategic opportunities to shape innovation incentives to achieve fair pricing. As discussed, access conditions placed on push or pull financing of health products can help ensure fairer pricing. Reimbursement also serves as an important signal to innovators as to whether a market would take up introduction of a novel health technology. An important consideration is ensuring that such measures contribute to and do not deter access and the introduction of health products across markets.

Unpacking several examples across the supply chain might help illustrate where public sector stewardship might play an important role. In the R&D pipeline, publicly supported innovation platforms can not only make accessible the building blocks of knowledge for adapting technologies for resource-limited settings at an affordable price point, but also ensure transparency of R&D costs. Bringing essential health commodities to market, public sector support of manufacturing can bring economies of scale, security of supply, and alignment of supply and demand in ways that prices are closer to marginal cost rather than the high prices seen with shortages and stockouts. Finally, public sector stewardship must include responsibility over the financing of the purchase of health products. Stewardship over pooled procurement fosters not only incentives for pharmaceutical innovation, but also support efforts to ensure fair pricing for health products by coordinating volume buys.

**Innovation platforms**

Public sector investment in innovation platforms can help ensure that key research tools contribute to follow-on innovation or that technologies receive contracted services that help them successfully cross the valley of death. Innovation platforms can also build upon medicine repurposing, where new uses for already approved medicines are discovered. This approach can take advantage of preclinical data and clinical insights from an existing medicine, repositioned for another indication. Such approaches can help de-risk R&D that addresses public health priorities, provide transparency of R&D inputs, and reduce the investment needed. For antibiotic innovation, the valley of death may first be encountered in the preclinical stages, where the probability of success in generating leads to novel classes of antibiotics via high-throughput screening is low, especially compared to other therapeutic classes of medicines. For other health products, like COVID-19 vaccines, products may face this valley of death in moving from preclinical to clinical testing.

The U.S. National Institutes of Health (NIH) supports multiple innovation platforms. For antibacterial drug development, the National Institute of Allergy and Infectious Diseases offers preclinical services, from hit-to-lead to early lead optimization; resources in genomics, bioinformatics and structural biology; and support for clinical trials through phase 2. Similarly, the National Center for Advancing Translational Sciences offers similar services for bringing early stage research to first-in-human clinical trials, but is precluded from supporting clinical trials beyond phase IIb, unless no public or private organization has credible plans for doing so.
Federal funding to the U.S. Patient-Centered Outcomes Research Institute is restricted from support of research carrying out a formal cost-effectiveness analysis: "research studies also may not directly compare the costs of care between two or more alternative approaches to providing care, or rely on modeling to develop estimates of ‘total costs of care’ designed to enable such comparisons." So by statute, several key programs in the United States government have been precluded in taking these products the last mile to market, or evaluating these products through cost-effectiveness studies, even though this can make a significant difference in achieving a fair price upon market entry.

However, the potential value in sharing knowledge, information, data, and resources can be key to enabling availability and affordability to health products. This also has certainly been an important motivation behind the Pandemic Influenza Preparedness Framework and the proposed COVID-19 Technology Access Pool (C-TAP). Real-world data can also speed the evaluation of treatments and contribute to collaborative research. The need for responding rapidly to the unfolding COVID-19 pandemic has tested the value of real-world data through the COVID-19 International Collaborative Research Project. The Health Insurance Review and Assessment Service of Korea provides an example of how such data collection could be managed through the country’s universal health insurance program and how it can be shared in response to researcher requests. As a complement to clinical trial data, findings from real-world data can accelerate the identification of promising treatments, as well as avert the unnecessary costs of providing ineffective ones. Real-world data, of course, face limitations, from confounding bias to missing data, so studies based on such findings must be viewed with these limitations in mind. However, such evidence has helped to determine that hydroxychloroquine, azithromycin or their combination did not affect the survival time of hospitalized COVID-19 patients.

Public sector-supported manufacturing

Public sector support of manufacturing can help achieve fairer pricing, both by ensuring security of supply and by averting price shocks from shortages and stockouts. Stewardship of such efforts can also provide the public sector a transparent window into the actual costs inputs in bringing a health technology to market. This can provide another way of benchmarking what is fair when pricing products. These arrangements have taken various forms, from private sector manufacturing as part of a product development partnership to non-profit or government-owned manufacturing.

Adapting health products for resource-limited settings, including at an affordable price, is a key reason for public sector stewardship over manufacture of a product. The meningococcal conjugate vaccine, adapted to the disease strains endemic in Africa, is an excellent example of a manufacturer working with a product development partnership. With the support of the Bill and Melinda Gates Foundation, the Meningitis Vaccine Project engaged PATH, the World Health Organization and the Serum Institute of India in an effort to bring to market MenAfriVac, a conjugate vaccine focused on meningitis strains endemic to Africa at a price point of US$0.50 per dose. Public sector partners were instrumental in facilitating the transfer of conjugate vaccine technology, laying the groundwork for in-country vaccine introduction, and absorbing the risks of clinical trial costs. Unlike a traditional manufacturing arrangement, the publicly supported Meningitis Vaccine Project selected multiple partners for this project with the Serum Institute of India. The vaccine’s introduction has had a significant impact in reducing group A meningitis in Africa.

The Fixed-Dose Artesunate-based Combination Therapies (FACT) Project offers another example where a product development partnership positioned a much-needed health technology for manufacturing. Together with Sanofi-aventis, the Drugs for Neglected Diseases Initiative and a host of academic and public sector partners brought forward a bilayer formulation of a fixed-dose
combination of artesunate and amodiaquine for treating malaria. Sanofi-aventis played a key role in building the registration file and regulatory filing in endemic countries, securing WHO prequalification of the product, and also scaling its initial manufacture. This dispersible, fixed-dose, antimalarial combination was developed with no patents as a public good. Since 2007, over a half billion treatments have been distributed in 35 countries and territories where it has been registered at a cost of US$0.50 for children and US$1.00 for adults. The technology transferred to a Tanzanian firm, Zenufa, and ASAQ products from five different manufacturers have been prequalified by WHO.

The public sector’s role in manufacturing medicines has also been attributed as a factor critical to the success of Brazil and Thailand in achieving steps towards universal access to antiretroviral therapy for HIV/AIDS. Left behind by tiered pricing arrangements, Brazil and Thailand as middle-income countries had to rely on state-owned and domestic pharmaceutical manufacturers to ensure affordably priced medicines for HIV/AIDS. While this worked for generic, first-line regimens, keeping pace with newer, patented, second-line HIV/AIDS medicines has presented further challenges. More recently, U.S. health care organizations and several philanthropies have created their own not-for-profit generic drug company, CivicaRx, to contract and eventually manufacture products that have undergone significant price hikes or shortages. Thus far, CivicaRx’s members include over 1200 hospitals and have benefited from CivicaRx bringing over 20 generic medicines to market, resulting in millions of dollars in savings.

**Procurement**

Another example of where public sector stewardship can make a difference is procurement. Pooled procurement models range from information sharing to joint purchasing:

- **Informed buying** – defined as information sharing, in which purchasers or countries share information on prices and suppliers but procurement is done individually.
- **Coordinated informed buying** – is also defined as information sharing, whereby purchasers or countries conduct joint market research, share information on supplier performance and prices, but procurement is done individually.
- **Group contracting** – member countries negotiate prices collectively and select suppliers based on the agreement that procurement will be from the selected suppliers, while the actual purchase can be conducted individually.
- **Central contracting and procurement** – this generally involves a central buying unit established by the member countries to act as their procurement agent in the tendering and award of contracts.

A pooled procurement facility affords the public sector a vantage point from which prices for a product can be made transparent, thereby bolstering the ability to negotiate for fairer pricing. Pooled procurement also enables the use of volume buys to negotiate and shape the market. This leverages monopsony power and delivers to the supplier predictable volume, both useful in keeping prices lower. Pooled procurement facilities also are well positioned to conduct horizon scanning to identify and prioritize emerging health products that might have public health value and that might affect healthcare costs. By making such information available, country-level decision-makers are better equipped to facilitate affordable access to these health products.

Country-level markets may be too small, and pooled procurement efforts at the country level, too fragmented to exercise this leverage. However, at the global and regional level, pooled procurement facilities, from UNICEF to PAHO’s Revolving Fund for Vaccine Access, deliver quality-assured health products at lower prices. For example, UNICEF reported that in 2019, “through its strategic procurement and influencing market approach,” the organization had exceeded its cost saving target by 25 per cent, amounting to $363.3 million for donors and governments. Pooled procurement facilities can also work to help manufacturers efficiently meet regulatory requirements across countries and reduce delays to market in countries, where companies may otherwise not have significant economic incentive. Through its prequalification program, WHO evaluates vaccines for UN supply, including for UNICEF’s pooled procurement efforts.
More directly though, pooled procurement can also shape markets for the introduction of new treatments. To communicate its priority needs, UNICEF also has created target product profiles as a guide to industry. These target product profiles share how UNICEF envisions the product might be used along with both minimum and ideal criteria for its performance. In an evaluation of UNICEF’s procurement efforts, however, suppliers indicated that they wanted advance market commitments before investing in developing products according to the target product profiles. In another example of how the public sector can encourage innovation and fair pricing, the Stop TB Partnership’s Global Drug Facility enabled the scale-up of Johnson & Johnson’s bedaquiline at US$340—a price discount of 32%—for the six-month treatment in more than 135 countries.

In 2020, the PAHO Strategic Fund rapidly responded to supply chain disruptions caused by the COVID-19 pandemic carrying out emergency purchases, analyses of stockouts, and horizontal lending schemes as well as optimizing treatment protocols. These efforts enabled Member States to procure over US$237 million in medicines, supplies, and diagnostic tests, supporting the treatment and diagnosis of over 27.4 million people in the region in therapeutic areas such as HIV, TB, Malaria and NCDs. Likewise, the PAHO Strategic Fund offered its first similar biotherapeutic for breast cancer – trastuzumab – with potential savings ranging between 50% to 90% to some countries in Latin America and the Caribbean. This has made an expensive, life-saving treatment more affordable in the region.

**Challenges and opportunities for further public sector stewardship**

The examples documenting successful ways of ensuring innovation and fairer pricing suggest exciting opportunities to build upon and pilot new approaches. Some of these successes, however, may have only been demonstrated in specific contexts or geographies, and more work will need to be done to assess how the ingredients of success might be more widely generalizable to other therapeutic areas or markets. In the ongoing COVID-19 pandemic, regulatory agencies have set a minimum threshold for vaccine effectiveness, and both publicly funded procurement by the COVAX Facility and bilateral agreements between countries and manufacturers have shaped the market for innovation of these vaccines. The bilateral agreements for COVID-19 vaccines are a sober reminder that public sector stewardship at the national level sometimes may serve narrower national interests at the risk of disregarding larger issues of global health equity. So, frameworks for global governance may be required to ensure that public sector stewardship works for the broader public interest across the community of nations.

**Questions for discussion during the Forum**

1. In what ways can public sector involvement in the supply chain, from pooled procurement to public sector manufacturing, help achieve fair pricing?
2. Are there non-profit alternatives to public sector ownership that may achieve the same ends?
3. What are the strengths and shortcomings from implementing such models? Where are the most strategic opportunities for applying such an approach?
4. In what ways has the COVID-19 pandemic provided early lessons and potential opportunities to exercise stronger public sector stewardship to achieve more enduring approaches to incentivize innovation and achieve fair pricing?
Directions for further research and collaboration

As discussed in prior Fair Pricing Fora, “Central to the concept of fair pricing is striking a balance between the public health needs for innovation and affordability, while recognising that quality health products are imperative and that sustainable production comes at a cost.”85 Balancing these imperatives has proven challenging in the traditional R&D model, since there are often limited markets and incentives to develop medicines for significant unmet health needs, and the pressure for return on such investments often makes ensuring access to the resulting innovations a seemingly insurmountable hurdle.

To achieve fair pricing, the pharmaceutical innovation system must balance the risk and returns to those bringing the health technology to market and the availability and affordability of the end-product as well as the role of public and private sectors in enabling and sustaining such outputs. The public sector makes significant investments upfront in R&D and foots the bill for products that successfully make it to market. However, the mismatch between what markets and public health prioritize demands a greater role for public sector stewardship.

This discussion paper provides a starting point for considering how transparency can support more accountable medical innovation. As recognized in WHA Resolution 72.8, transparency is a critical tool for aligning innovation incentives to achieve fair pricing. It can help shed light over the inputs and outputs to R&D and how governments afford protections over intellectual property, prices and data, thereby allowing the public, policymakers and procurers to assess the fairness of returns to innovators and the affordability to those who might benefit from these products. Funders, payers, and government regulators all have roles to play in ensuring that a more complete picture comes together, so that the prices paid for health products are fair.

The public sector actively finances pharmaceutical innovation through push and pull mechanisms. This financing shapes the market, signals priorities for R&D, and can also place access conditions that can help ensure fairer pricing. With varying reach, these access conditions can influence decisions across the value chain, from target product profiles and licensing of patented inventions upstream to sharing of publications, data, IP and know-how downstream. The response to the ongoing global pandemic underscores the importance of not only bringing therapeutics, diagnostics and vaccines to market, but also ensuring globally-equitable access and finding new solutions to doing so.

Effective public sector stewardship will require going further than patching market failure with access conditions on its financing. The public sector may need to ensure the security of supply, both against shortage and pricing beyond the reach of those in need. Such public sector stewardship involves investing and sharing resources, risks and rewards in bringing these innovations forward. Innovation platforms, public sector support of manufacturing, and pooled procurement are among the approaches that might be applied to align better innovation incentives to achieve fairer pricing.

The Working Group discussions that explored these topics suggested other areas, in turn, for developing further. Coordinating the needed transparency from across the pharmaceutical value chain prompted the idea of exploring the feasibility of a global policy unit for access and fair pricing. The response to COVID-19 has required reengineering the pharmaceutical value chain, speeding the R&D process and compressing the regulatory review of potentially life-saving products. The challenge of addressing the pandemic has provided an opportunity to rethink how and where access conditions are placed on public financing as well as what is the public sector’s role in ensuring that manufacturing can be scaled and products can be procured and equitably accessed.
While the working group on aligning incentives for pharmaceutical innovation at fair prices represented a broad set of stakeholders and geographies, another key element discussed was the need for broadening collaboration. The Fair Pricing Forum traditionally targets Member State participation from Ministries of Health, but deepening collaborative discussions with Ministries of Science, Technology, and Innovation might help bridge the divide between innovation and access. The COVID-19 pandemic has also highlighted the need for diversifying the locations of research, development, and production of pharmaceuticals to ensure broad access and affordability.

Making fair pricing a reality in practice will require continued collaboration on the part of all stakeholders, while ensuring innovation to address our greatest public health needs.

References


2 Morgan SG, Bathula HS, Moon S. Pricing of pharmaceuticals is becoming a major challenge for health systems. BMJ. 2020 Jan 13;368:l4627.


4 Suleman F, Low M, Moon S, Morgan SG. New business models for research and development with affordability requirements are needed to achieve fair pricing of medicines. BMJ. 2020 Jan 13;368:l4408.


9 Novavax closes in on Covid triumph after 33 years of failure. Financial Times 1 March 2021, available at https://www.ft.com/content/22d3805e-c304-4d95-ae32-f559ff34886a


14 The other working group seeks to explore pricing approaches sensitive to health systems’ ability to pay and to the need for achieving universal coverage of pharmaceutical products.


16 Mancini DP. Vaccine contracts shrouded in secrecy despite massive public funding. Financial Times, 23 November 2020. https://www.ft.com/content/95c49b5a-f2c7-49a3-9ac5-3e7a66e3ad6b


18 G-FINDER. Policy Cures Research, available at https://www.policycuresresearch.org/g-finder

19 The Global Health Innovation Alliance Accelerator, available at https://ghiaa.org/ghiaa/


29 International Committee of Medical Journal Editors. Clinical Trials Registration. Available at: http://www.icmje.org/about/icmje/faqs clinical-trials-registration/


35 “Partial accessibility” as Vogler et al. have described it in an ongoing study commissioned by WHO EURO on transparency of pharmaceutical markets: Vogler S, Habimana K; Haasis AM (2021): Mapping European region countries’ access to information on medicines outlined in the WHO Transparency Resolution. Study Protocol. Gesundheit Österreich, Vienna.


38 Cernuschi T, Gilchrist S, Hajsa A, Malhame M, Mariat S, Widmyer G. Price transparency is a step towards sustainable access in middle income countries. BMJ 2020;368:i5375 https://www.bmj.com/content/368/bmj.i5375


45 Target product profiles,” Drugs for Neglected Diseases initiative. Available at: https://dndi.org/research-and-development/target-product-profiles/


58 Cockburn, Lanjouw and Shankerman “Patents and the global diffusion of new drugs” (2014)


69 World Health Organization. Pandemic influenza preparedness Framework for the sharing of influenza viruses and access to vaccines and other benefits, 2011. Available at: https://apps.who.int/iris/bitstream/handle/10665/44796/9789241503082_eng.pdf?sequence=1


74 Kulkarni PS, Socquet M, Jadhav SS, Kapre SV, LaForce FM, and Poonawalla CS. Challenges and opportunities while developing a group A meningococcal conjugate vaccine within a product development partnership: a manufacturer’s perspective from the Serum Institute of India. Clinical Infectious Diseases 2015; 61(suppl_5): S483-S488. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4639485/


77 Ford N, Wilson D, Chaves GC, LotROWSka M, Kjitwatchakul K. Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand. AIDS 2007; 21 (suppl 4):S21-S29. Available at: https://fieldresearch.msf.org/bitstream/handle/10144/19975/Sustaining%20access%20to%20antiretroviral%20therapy%20in%20the%20less-developed%20world.pdf?sequence=1&isAllowed=y


