CONTRIBUTION TO THE UNITED NATIONS SECRETARY-GENERAL'S HIGH LEVEL PANEL ON ACCESS TO MEDICINES

INCREASING THE TRANSPARENCY OF MARKETS FOR DRUGS, VACCINES, DIAGNOSTICS AND OTHER MEDICAL TECHNOLOGIES

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The organizations and individuals supporting this submission are listed in alphabetical order:

Organizations:

1. Coalition Plus
2. Commons Network
3. European Public Health Alliance (EPHA)
4. Health Action International (HAI)
5. Health Gap, USA
6. Health Poverty Action (HPA)
7. Incentives for Global Health (IGH)
8. Innovarte, Chile
9. KEI Europe
10. Knowledge Ecology International (KEI)
11. Mission Salud, Colombia
12. People's Health Movement (PHM)
13. Stop AIDS, UK
14. Transparency International (TI)
15. Treatment Action Campaign (TAC), South Africa.
16. Union for Affordable Cancer Treatment (UACT)
17. Young Professionals Chronic Disease Network (YPCDN)

Individuals

18. Aidan Hollis, Professor of Economics, University of Calgary, Calgary, Canada.
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Members of the European Parliament

20. Franziska Maria "Ska" Keller, Member of the European Parliament
21. Julia Reda, Member of the European Parliament
22. Sergio Cofferati, Member of the European Parliament

Section 1. Briefly describe your contribution

The United Nations Secretary-General's High Level Panel on Access to Medicine (HLP) calls for "evidence-informed" submissions on measures that can promote research and development (R&D) and increased access to medicines, vaccines and diagnostics and related health technologies. This submission addresses the need to improve the transparency of such markets, so that policy makers, patients and other stakeholders have access to better evidence, and to reduce the information asymmetries that currently exist between manufacturers of products and everyone else.

Without transparency, there is no public accountability to ensure that states protect human rights, businesses respect human rights, and victims can pursue adequate judicial and non-judicial remedies. Transparency International defines transparency in the following way:

> "Transparency is about shedding light on rules, plans, processes and actions. It is knowing why, how, what, and how much. Transparency ensures that public officials, civil servants, managers, board members and businesspeople act visibly and understandably, and report on their activities. And it means that the general public can hold them to account."[1]

Key components of the business model of the pharmaceutical industry, including research, development and commercialisation, remain shrouded in secrecy, particularly as regards access to information by patients and the general public. This undermines trust in and accountability of the pharmaceutical industry, and leaves patients vulnerable to human rights violations, including the right to the highest attainable level of health and ultimately the fundamental right to life, and makes it unnecessarily more difficult for society to make the appropriate policies regarding the financing and priority setting of R&D, and product purchases. Given the complexity, size and volume of transactions in the pharmaceutical sector, the lack of transparency creates a range of opportunities to exercise power and influence that can have negative health outcomes and can result in corruption.

Section 2: Impact on public health:

The lack of transparency in how the pharmaceutical industry operates has wide-ranging consequences for patients' access to medicines. Moreover it hinders informed public debate about the current policies used to finance R&D and how well they are suited to ensure robust and cost-effective mechanisms to finance of R&D in areas of global public need, and ensure affordable prices and fair and acceptable access to products.

Since R&D is situated at the beginning of the value chain, the impacts of a lack of transparency can increase in magnitude as they descend down to the individual. Thus lack of transparency will impact regulators who decide on whether a product is safe to enter market, those who will purchase the product, or the health-care professionals who will administer the final product to patients.

This proposal first identifies areas where it is important to expand transparency – and second, proposes measures that UN agencies, governments and partnerships can adopt to progressively increase transparency in markets for drugs, vaccines and diagnostics.

The economics of R&D

[1] Transparency International: http://www.transparency.org/what-is-corruption/#define – consulted on 24/2/16.

There is a pervading opaqueness around funding flows for R&D. Publicly traded companies self-report some information about R&D budgets for investors, but with limited detail, depending upon the relevance of the data to the share price.

Of particular interest are the data on the economics of clinical trials used to establish the safety and efficacy of drugs and vaccines. According to PhRMA's 2013 annual industry survey, approximately 67 percent of all member R&D outlays were spent on clinical trials[2].

The companies and organisations involved in undertaking clinical trial have detailed information on the costs of specific trials and rich statistical information on how those costs vary by disease, location, design and size of trials, and on specific products, but this information is not generally available to the public. While smaller companies sometimes report on the costs associated with some specific trials, this is the exception, and much more frequently such outlays are lumped together in aggregate reporting on R&D outlays that are not assigned to a specific drug or vaccine, let alone a specific trial. This allows companies great discretion in making assertions about R&D spending for specific products, and makes it more difficult for anyone but industry insiders to model the risk adjusted costs of R&D, because costs need to be associated with the timing and the phase of development.

The third parties that conduct or help manage trials have been reluctant to share information about trial costs, and governments and many non-profit research organisations have been unwilling or unable to provide the types of information necessary to establish benchmarks that can be used to estimate R&D costs.

Investments in trials and priority setting

Better data on the costs of trials by disease and drug targets are needed to better evaluate and influence the direction of R&D funding, and to ensure there are sufficient resources for areas of priority, including those involving global health needs.

Government funding of R&D

The role of the government in funding or subsidising R&D costs is important, but for the most part, remains very difficult or impossible to assign to specific trials or drugs. For example, the U.S. National Institutes of Health (NIH) has a registry for trials (http://clinicialtrials.gov) and a database for grants (RePORT), but makes no effort to assign the grant money to specific trials. The U.S. Orphan Drug Tax Credit, which provides a subsidy of 50 percent of the costs of qualifying clinical trials, and which was relevant to 80 percent of the new oncology products approved by the U.S. FDA from 2014 to 2015, is only reported by the IRS in highly aggregate numbers that are not assigned to individual companies or individual trials. Cooperative research and development agreements (CRADAs) by government agencies often do not report the value of in-kind research subsidies. Many other governments also provide direct subsidies, regulatory incentives and tax credits for research on specific types of products. Enhanced transparency can enable governments and taxpayers to better coordinate and document the effectiveness of such measures to support research.

Prices and units of goods

[2] Pharmaceutical Research and Manufacturers of America, 2013 Biopharmaceutical Research Industry Profile (Washington, DC: PhRMA, July 2013) p. 65: http://www.phrma.org/sites/default/files/pdf/PhRMA%20Profile%202013.pdf – consulted on 24/2/16.

Companies provide some detail on the sales of goods to their investors, but often only in terms of the sales revenues, and even then, with limited detail as regards product lines and geographic regions. When sales of a product are significant enough to require separate reporting for investors, the geographic regions are normally highly aggregated. Country level data may be limited to The United States market only, and regions can be defined very broadly, such as "Europe, Middle East and Africa" into a single region, or "the Americas" or "Asia Pacific." Sales are normally presented in terms of revenue and not by price or units of sales.

Data on units of sales by country is needed to better understand how access varies across borders. Similarly data on prices by country are needed to better evaluate the impact of policies on affordability of products and the related inducements for investments in R&D.

The companies selling the products have this information, and IMS Global Health also has detailed data on both prices and units disaggregated not only by country but with considerable detail within the channels of sales within countries.[3] Countries fail to require disclosure of such data, and furthermore, the Trans-Pacific Partnership (TPP) has a provision which prohibits countries from requiring such data in connection with the regulatory approval to sell products[4].

Manufacturing costs

The cost of manufacturing drugs, vaccines and diagnostics is often unknown. Companies that claim to sell products at 'no-profit' prices are not required to verify such claims, and often does not comport by independent, third party estimates of per gram costs of formulated products. Even as volumes increase (generating economies of scale) companies do not revise their per unit manufacturing costs downwards. Studies carried out by universities and third party experts have provided useful estimates for manufacturing costs, but still do not provide an authoritative accounting of manufacturing costs.

Marketing costs

Industry costs for marketing are often reported to investors, but typically aggregated across all products, and/or aggregated with other costs. In order to assess the true level of spending on marketing, disaggregated data for drug marketing, broken down by country and product, is required.

In some countries and for some companies, there is reporting of payments to doctors[5], in order to better monitor the risks of conflicts of interest and unwanted distortions of medical decision-making, and such reporting should be expanded.

Times-series data on expenditures on direct-to-consumer advertising should be available, disaggregated by product, in order to better assess the impact of such expenditures on rational use of products and health outcomes, including information on both "ask your doctor" about an unnamed drug, and ads that specifically mention a drug by name.

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[3] Many countries (including LMICs) rely on "external reference pricing" mechanisms to set prices. Unfortunately, this model is completely flawed in a world in which many countries are getting confidential rebates from manufacturers.

[4] Chapter 8, Technical Barriers to Trade, Annex A-C Pharmaceuticals, 7bis, and Annex 8-E Medical Devices, paragraph 8. See a discussion of this in "KEI statement on TPP for the January 13, 2016 hearing of the United States International Trade Commission," Investigation No. TPA105001, TransPacific Partnership Agreement: Likely Impact on the U.S. Economy and on Specific Industry Sectors, December 29, 2015.

[5] See, for example: Open Payments DataOpenPaymentsData.CMS.gov, and Charles Ornstein, Eric Sagara, "How Much Are Drug Companies Paying Your Doctor? New data released today will promote transparency and help patients know when docs receive money from product makers," Scientific American, September 30, 2014.

Many new medicines are duplicative, "me too" products that are minor variations of the original medicine and offer no therapeutic advantage over other medicines that are already available[6]. Gaining market share for these medicines has numerous consequences: healthcare professionals may not be able to keep up to date with relevant/current information on each medicine and to compare alternatives; it can contribute to inconsistency in prescribing within the healthcare system; and – crucially for LMICs – when patients switch to products protected by patents that have higher prices, there is less money to spent on other drugs.

Clinical trial data

A lack of public access to data from all clinical trials, including data on trials that fail, reduces access to knowledge that is critical for advances in science, and hinders appropriate scrutiny of trial design and accuracy of reporting which have direct consequences for our knowledge about the safety and efficacy of medicines that are prescribed to patients.

One element of the right to health concerns the right of access to information about the risks and benefits of treatment options, including by patients and prescribers. The secrecy of trials leads to duplication of research, exposing patients to unnecessary risks of harm, including being asked to use the same failed drug.

Drug prices or rewards for innovation

Debates about drug pricing or the appropriate rewards for successful research outcome should be informed by reliable, transparent and detailed data on the costs of R&D inputs (including information of the role of public funding and subsidies), the medical benefits and added therapeutic value of products[7], and the actual access or lack of access to products by patients.

When prices bear no relationship to costs or benefits from products, or when prices are associated with barriers to access, policy makers have a duty to introduce reforms to improve the efficiency and the fairness of the system.

Patent landscape

At present, the patenting of products is surprisingly non-transparent. Concerns about the transparency of patent landscapes are particularly vexing in the areas of biologic products.

Pharmaceutical companies file numerous patent applications relevant to specific medicines and vaccines. These patent applications are often difficult for third parties, and even patent offices, to link to individual medicines. Generics companies, patient groups and government ministries, including drug regulators are often unable to assess whether there are existing applications or granted patents related to specific medicines, and the uncertainty can present a barrier to entry for affordable generics, a fact recognized in the U.S. Affordable Care Act, in the context of biologic drugs[8].

Some of these concerns can be addressed by requiring patent applicants and patent holders to disclose the international non-proprietary name (INN) of the biopharmaceutical(s) to which the patent relates, and for the WHO or another entity to create public databases of patent filing.

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[6] 72 percent of all medicines put on the European market between Revenue Prescrire, February 2015; 35(376) : 132-136; Revenue Prescrire, February 2015: 25(258) :139-148.

[7] Including possibly through more standardized reporting of the evidence supporting health benefit claims.

[8] The Biologics Price Competition and Innovation Act (BPCIA) limits the availability of injunctions and damages for infringement when patents are not constructively disclosed to biosimilar competitors.

Governments should also create systems to share information about administrative and judicial challenges to patents.

Registration of products

Companies that have invested vast resources developing a medicine will be under considerable pressure to have a product registered for market entry, which is conducive to corruption vulnerabilities. Drug companies' registration strategies are also often non-transparent. In some cases, companies simply do not register their medicines or confine the registration to a limited number of countries regardless of needs and public health considerations. The lack of information concerning companies' registration plans leaves medical providers and governments that await registration of new products, unable to take steps to ensure early availability of new medical tools that can save lives, including such steps as working with WHO or other collaborative registration mechanisms, or directly with other regulatory authorities. There should also be a duty and mechanisms to share changes in regulatory status with other regulators.

Licensing of intellectual property rights

In a limited number of cases, the licenses to use patents and other intellectual property rights are made public by the parties, including, for example, the licenses with the Medicines Patent Pool (MPP), or licenses or licensing terms reported in United States Securities and Exchange Commission (SEC) disclosures to investors. However, such disclosures remain the exception. Having more complete information about actual licensing terms would make it easier to evaluate the reasonableness of terms and conditions of licensing, and to avoid anticompetitive practices.

Of particular interest are the contracts involving intellectual property developed by the public sector or by government grants or research contracts to businesses, university programs or other recipients of public or charitable funds. Rarely are the terms and conditions of such license agreements public.

The licensing of intellectual property from publicly funded research is a critical opportunity for governments to ensure that holders of licenses meet critical milestones to ensure timely development (stewardship), provide fair compensation to taxpayers, and ensure affordable access to products.

Adverse events

There is a need for better reporting and sharing of information on adverse events from the use of drugs and vaccines, both to advance science, and to address the prescribers', patients' and regulators' rights to know.

The Periodic Safety Update Reports that manufacturers are required to provide to regulators should be made available. Many countries put their Adverse Drug Report (ADR) databases online for public access and that could become a norm for all countries.

Know-how and technology transfer

Governments should design and implement obligations to disclose the know-how to make drugs, vaccines and diagnostic tests. This is particularly important for biologic drugs, which often remain de facto monopolies or face limited competition long after patents expire. This is an important issue for drugs used to treat rare diseases, where the cost of obtaining manufacturing know-how limits competition, and is associated with extremely high prices of products.

Implementation

This submission proposes two approaches to expand transparency of the pharmaceutical sector.

i. UN led policies to progressively expand the transparency of markets for drugs, vaccines and diagnostic tests

The various UN agencies and partnerships and global entities that work closely with the UN, such as the World Bank, the TDR, the Medicines Patent Pool (MPP), UNITAID and the Global Fund to Fight AIDS, TB and Malaria, and the many product development partnerships (PDPs), should build upon or establish new, coherent programs to expand transparency across the entire pharmaceutical sector.

Such measures should be done through careful collaboration to avoid duplication, to identify relevant strengths of each institution and to ensure that the entire UN system is working towards this common, critical goal.

Some existing initiatives include the following:

- The V3P price reporting database on vaccines at the WHO, which is supported in part by the publication of prices by UNICEF, PAHO and GAVI for their own respective price negotiations.
- The Price and Quality Reporting Mechanism of the Global Fund to Fight AIDS, TB and Malaria, whose scope may be expanded this year through the introduction of the E-marketplace.
- The licensing agreements of the Medicines Patent Pool, all of which are published after having been signed with pharmaceutical companies (and increasingly with universities and product development partnerships).
- The newly launched WHO R&D Observatory, which has been introduced to track existing R&D funding flows for priority diseases, and to identify critical gaps for essential health needs.
- The multiple efforts of the Medicines Patent Pool, UNITAID, WIPO and WHO to develop and issue patent landscapes for new medicines.

New measures which UN agencies may take include the following:

- Development of model legislation to introduce transparency measures that governments can introduce in specific areas. Such model legislation can then be presented and discussed at the national level by agencies through their programmatic and technical links with governments
- The UN initiate a Heads of State political process to introduce normative measures through one or more new agreements on R&D financing and coordination, including initiatives that may be launched this year via the WHO as one of the ‘remaining issues’ under the Consultative Expert Working Group (CEWG)
- Considering the creation of an annual or biannual forum on transparency of markets for drugs, vaccines and diagnostics, to evaluate progress toward the progressive expansion of transparency

Member State Transparency Initiatives

The UN should work with governments, industry, civil society, shareholders and other third parties to launch a new global transparency initiative for the pharmaceutical sector. In 2001, the UK government, in partnership with industry and civil society, launched an Extractive Industries Transparency Initiative (EITI)[9], which sought to improve transparency across the oil, gas and mining sector, including the payments made by such companies to governments in resource rich countries. The EITI has not only succeeded in encouraging a range of oil, gas and mining companies to voluntarily release such payments, but has led to legal obligations in the United States, Canada and European Union for mandatory disclosure of such information[10].

A similar initiative led by the UN, in partnership with industry, civil society and shareholders, and key governments, can work to slowly accelerate voluntary and mandatory commitments to pharmaceutical sector transparency for the benefit of all – starting first and foremost with millions of patients around the world.

Governments can also avoid measures in trade agreements that limit transparency of information from clinical trials, disclosures of manufacturing know-how, or the reporting of data on drug prices, revenues and other relevant medical or economic information.

Provisions in trade agreements or in national law dealing with trade secrets should provide for robust exceptions to enable sufficient transparency for pharmaceuticals and other medical technologies when the needed disclosures are presumptively in the public interest.

Member states can impose an obligation on manufacturers to reveal information on total antibiotics produced by class.

Governments can link the disclosure of information to the exercise of exclusive rights in patents or data. For example, the United States eliminates injunctions and royalty payments as a remedy for infringement on patents that are not adequately and timely disclosed to biosimilar competitors, and some patent holders who withhold information about potential claims of infringement to standards bodies are likewise not allowed to later enforce such patents against standards[11].

In closing, we note governments should limit overreaching claims that scientific, manufacturing and economic information be withheld from disclosure on the grounds that it represents confidential business information. One objective of the proposed disclosure requirements is to redefine certain information that is now held as confidential so that it becomes public. The standard should not be whether or not the firm wants the information to confidential, but rather whether the disclosure is in the public interest.

PERMISSION TO PUBLISH

We give permission and encouragement for this contribution to be made public on the High-Level Panel's website.

[9] For more information please consult: https://eiti.org/

[10] The United States: The Dodd-Frank Act, 2010; Canada: The Extractive Sector Transparency Measures Act, 2014; The European Union: The Accounting Directive, 2013.

[11] See footnote 8, and United States Department of Justice and the United States Patent and Trademark Office Policy Statement on Remedies for Standards-Essential Patents Subject to Voluntary F/RAND Commitments. January 8, 2013.