TESS
TECHNICAL EXPERTS FOR SUSTAINABLE SOLUTIONS

Submission to the Consultation on the UN Secretary-General's
High-Level Panel on Access to Medicines

Reducing Information Asymmetry: The role of market data as a contributor to focusing R&D, reducing investment risk and expanding access to medicines

Submitted by TESS Development Advisors
Geneva, 26th February 2016

Abstract

This High-Level Panel on Access to Medicines focuses on law and rights. We argue that innovation of, and access to, new technologies hinges not only on trade rights and IPR but also on another factor which levels the playing field in decision making: reducing information asymmetry, notably in market data required for investments.

In 2000, the EU recognised 'orphan' medicinal products: medicines for rare diseases where there is little commercial incentive to develop a drug. This period also saw several product development partnerships come into being to address gaps in R&D for diseases of low-income countries. Such developments highlight the interplay between innovation, R&D and the existence of markets: ultimately leading to better access to medicines.

Development of new molecules or technologies requires several factors to be aligned: the identification or acknowledgement of medical need; scientific ability to address that need through successful R&D; the right to use or replicate technologies through appropriate trade and intellectual property legislation; willingness of investors to support the development and manufacture of new products.

One question will commonly be asked: "what is demand for this product"? Demand depends on many variables including availability, affordability and appropriateness for the targeted population. IPR and trade law clearly influence several aspects of access to medicines, including local production. But more is needed.

Gaps in market data can undermine willingness to innovate. Without answering the fundamental question of "what is the likely demand?", the domino of other factors promoting R&D and subsequent access to medicines may never come into play.

Such data are not available in many low-income countries or for diseases such as malaria or paediatric TB. The terms of reference of this Panel recognize that "***new solutions are needed to incentivise innovation and increase access to treatment***". Addressing market data gaps is one new solution to achieve that.

Introduction

The HLP indicates that "the Panel looks to receive contributions that will enhance and strengthen the promotion of innovation and access to medicines, vaccines and diagnostics." (1). The Panel clearly has a central focus on addressing and balancing the rights of inventors, international human rights law, trade rules, and public health objectives (2). However, the terms of reference, background materials, and indeed the title of the Panel itself, also indicate a recognition that access to medicines and innovation are influenced by a large number of factors.

Development of new molecules or technologies requires several factors to be aligned: the identification or acknowledgement of medical need; scientific ability to address that need through successful R&D; the right to use or replicate technologies through appropriate trade and intellectual property legislation; willingness of investors to support the development and manufacture of new products.

This submission argues that there is major gap with respect to measuring demand for new products, which contributes to disincentives for investment in innovation, particularly for essential medicines or medicines for rare diseases and diseases with a heavier burden in middle- and low-income countries. This reduces commercial willingness to invest in R&D and product launch. Such data gaps also limit opportunities to optimise public sector investment and health impact, as public health players including Ministries of Health are unable to measure the total uptake and impact of these new products. Thus, access gaps remain but are not measured. Finally, gaps in data create an asymmetry of information between countries, between diseases and between populations: those countries or diseases with better data have lower investment risks, and therefore are more likely to attract investment.

"Information is power". This is a well-recognised call among civil society advocates, notably those working to reduce inequalities. It is also an acknowledged truth among company executives, and decision makers. However, information is also **powerful**. And market data are a key factor which influence decisions around innovation, access to medicines, trade and even patient safety.

Our proposal argues that by investing in better information systems for pharmaceutical market data, the global health community could address many of those factors which reduce information asymmetry, reduce investment risks, remove disincentives to innovation and ultimately improve access to medicines.

This proposal is not about health systems strengthening or supply chain information. It is about reducing information asymmetry and providing data which serve as the foundation for many decisions, which cut across diseases and national income status, influence decisions on R&D investments, innovation and access to medicines.

What are market data?

We define market data here as the core set of variables relating to the structure, size and segmentation of a pharmaceutical market, notably at national level. This includes information about what products are available, which classes of medicines, in what proportions, total volumes and price points, and how they are made available.
For example, in the malaria field, we know that there are three major classes of medicines currently available for the treatment of uncomplicated malaria – a disease which can kill a child within 3 days if left untreated.

Artemisinin-based treatments are the gold standard, recommended by WHO. These are broadly available through the public sector, i.e. government health facilities. Due to the cost of the active ingredient and the production cost, these are significantly more expensive than older classes of drugs such as Sulfadoxine-Pyramethamine (SP) and Chloroquine. These older drugs are not recommended by WHO or many health authorities due to their lower efficacy rates (i.e. over 95% efficacy for artemisin-based treatments, 75% efficacy for SP and 20% efficacy rates for chloroquine (3).

We also know that access to treatment varies significantly between African countries – with up to 74% of children under age 5 with suspected malaria in Zambia being treated in government facilities (4), while inversely, around 57% of similar children with suspected malaria in Uganda were taken to a private facility (5).

Full market data will tell us, for example, what proportion of all antimalarial medicines available in a country (i.e. the market share) which fall into each of these three categories of drugs. Are the same types of medicines available in different facility types? What are the price differences between drugs, and how does this reflect affordability? What are the total volumes of medicines provided relative to estimated health burden – are sufficient volumes of medicines available? Are they the right kind of medicines, with sufficient efficacy levels to treat the disease? And how does this relate to equity in access to treatment? What does the current market tell us about the need for continued R&D for new drugs?

Impact on Policy Coherence - Why are market data important?

Market data are used in a number of different ways. Such data are most widely used by the pharmaceutical industry in high-income countries to target marketing activities. However, the potential uses of such data in middle and low-income countries goes well beyond this, and have significant implications across a broad number of areas including finance, investment, innovation and local manufacturing, access to medicines and patient safety. Some examples of the uses of such data include:

- ***Access***: is there sufficient supply of medicines for those who need them? If not, why not: are there equity issues at stake?

- ***Equity and Affordability***: are there significant differences in the type of treatment received, and if so, what is this based on? Are there availability or affordability issues in access to key medicines?

- ***Equity and Patient Safety***: Are people getting the right kinds of drugs which will treat them effectively? Do policies need to be changed to ensure that different medicines are prioritized?

- ***Patient Safety***: which are the priorities for post-marketing surveillance, i.e. those products which should be prioritized to trace potential substandard or falisified medicines?

- ***Innovation***: are there suitable preventive or treatment options available for the main health risks in a specific country or community?

- ***Innovation and R&D***: If efficacy of existing medicines is decreasing, are there new products in the development pipeline to replace the current generation of drugs in time?

- ***Innovation, Local Manufacture and Finance***: what is the cost and the potential return in developing new medicines or producing medicines locally?

- ***Finance***: what is the budget required to ensure equitable access to medicines?

These different uses all address at least one – or more – of the various medicines-related aspects of Sustainable Development Goal 3. They support essential information for eventual eradication of malaria, access to treatment and essential medicines, and promotion of R&D. In addition, by providing a systematic evidence based, such structured information also supports SDGs 9, 10 and 17 as shown below.

Impact for Public Health

The TOR of the HLP expresses concern that “Failure to reduce the costs of patented medicines is resulting in millions of people being denied access to lifesaving treatments for communicable diseases like HIV, TB, Malaria, and viral hepatitis, non-communicable diseases (NCDs), NTDs and rare diseases” (1).

Policies for new drug development and access are taken on the best data available to the decision maker at that point in time. Unfortunately, with major data gaps such as these, decisions may be reinforcing certain equity gaps or may be failing to make the case for new investments.

The TB community have faced this issue for many years. There have been significant efforts made, notably through one of the above-mentioned product-development

partnerships (the Global Alliance for TB Drug Development) which has successfully increased the pipeline for new TB medicines and in 2015 released a new paediatric TB treatment.

TB was widely assumed to be treated mainly through the public sector. This has led to assumptions that treatment requirements in the public sector will be sufficient. However, more recent studies have indicated that in many middle- and low-income countries, a large number of people seek treatment for TB in the private sector also, leading to a private sector market for TB medicines (6). What is more, paediatric TB is difficult to diagnose. This has led to WHO recognizing that childhood TB cases are significantly under-reported (7). Further studies have indicated that using epidemiological data, or reported cases, does not accurately reflect the true existing or potential market for paediatric TB treatments or treatment needs (8).

The TB example, and notably the paediatric TB case, provides a case study example of the interaction between public health and markets. As a communicable disease transmitted through close contact and thus with a higher burden among poor and vulnerable populations, TB is serious public health challenge. As indicated above, innovation requires several factors to be aligned: scientific and medical knowledge, market information and investment.

In this case, the medical community face challenges in diagnosing childhood TB. This combines with the assumption of limited market demand creates a classic case of market failure, where companies see little benefit in investing in new product development. This combination of scientific challenges, information gaps and limited market incentive led to a long-term stagnation in the development of new TB medicines. This indeed required the intervention of public-health focused donors creating public-private-partnerships and other special initiatives to boost the R&D and drug access programmes for TB.

But addressing one major public health burden is not enough: the Ebola outbreak in West Africa show how such market failures re-occur. Similarly, the public health community has just taken specific steps to address the gap in R&D for basic antibiotics. Thus, the global community must think of cross-cutting, systems-wide solutions whenever possible to minimize disincentives for investment. A market data which cuts across all therapeutic areas and all drugs is one such cross-cutting solution.

Impact on Innovation and the International Trade Context

Continual investment in research and development is essential for the development of new products, whether these be new generations of products to treat existing diseases, or products to treat previously unmet medical needs such as Ebola.

Research and development for new products is generally initiated in academic or other non-commercial environments, and then may be taken up by commercial organisations if companies judge there to be sufficient potential gain (9). However, medicines and technologies which are not expected to be sufficiently profitable are likely to face market failure, and will not be taken forward for development. Products which may have very large gains, on the other hand, main gain intellectual property protection thus delaying the development of generic versions of the medicine.

Several initiatives have been taken in order to address these market failures. In 2000, the EU recognised 'orphan' medicinal products: medicines for rare diseases where there is little commercial incentive to develop a drug (10). This period also saw several product development partnerships come into being to address gaps in R&D for diseases of low-income countries. More recently, middle- and increasingly low-income countries have initiated their own strategies for pharmaceutical development, with successful industries already developed in a number of middle-income countries such as Brazil, India, Ghana, Indonesia, Egypt, South Africa to name but a few. Low-income countries such as Ethiopia are also actively exploring the development of local manufacturing capacity.

Investing in local production capacity requires investments across infrastructure, technology and human resources and information systems. Indeed, the Pharmaceutical Manufacturing Plan for Africa notes the following issues as potential bottlenecks to developing local industry: "***lack of market data***", with implications for strategic planning, access to capital and as a key challenge to achieving good manufacturing practice standards, and the "***lack of accurate, comprehensive market data, analysis and forecasts***", which is cited as one of the main industry concern (11). Similarly, the Ethiopian national strategy for pharmaceutical manufacturing raises the same points, noting that a national Institute, FBPIDI, "needs to…establish market intelligence" (12).

The WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual property notes that "Intellectual property rights are an important incentive for the development of new health care products. This incentive alone does not meet the need for the development of new products to fight diseases where the potential paying market is small or uncertain" (13). The Strategy goes on to call on stakeholders to "identify incentives and barriers, including intellectual property-related provisions, at different levels – national, regional and international – that might affect increased research on public health, and ***suggest ways to facilitate access to research results and research tools*** (emphasis added) (13). In addition, the Strategy explicitly calls for countries and the global community to:

- increase collaboration between public and private partners
- strengthen health surveillance and information system
- support the production and introduction of generic medicines especially essential medicines

- increase information among policy makers…regarding generic products

The provision of systematic information about the pharmaceutical market is an essential component to completing this evidence base, and reducing costs of investment for both national and international investors alike.

Regulatory capacity and drug safety

Public health goals require strong, coordinated measures to ensure quality and safety of products through the establishment and implementation of global standards, strengthening regulatory systems and reducing substandard and falsified medicines. As such, the WHO Global Strategy for Innovation also recognizes the importance of developing national regulatory capacities, calling on stakeholders to "establish and strengthen regulatory capacity in developing countries" (13).

Medicines and health technologies are important tools in the global health arsenal. As such, they must be developed and manufactured to standards which ensure a positive risk-benefit ratio, must be administered correctly and must be followed up in cases of possible adverse event. However, the levels of information and reporting on adverse events in many middle- and low-income countries remains limited, particularly in Africa (14).

More widely than the risk of adverse events, WHO recognizes the "existence of substandard, spurious, falsely labelled, falsified and counterfeit (SSFFC) medical products is an unacceptable risk to public health. They affect every region of the world, and medicines from all major therapeutic categories have been reported, including vaccines and diagnostics. They harm patients and undermine confidence in medical products, healthcare professionals and health systems" (15).

WHO recommends "targeted post-market surveillance of medical products on a systematic basis focused on products known to represent a high risk, and regular surveying of essential and high demand products leads to early detection and early interventions (15). Monitoring systems which provide information about the entire market are a key source of information to help identify, sample and then track such products. A system already established in Zambia, providing regular insights into the entire pharmaceutical supply in that country, has been identified by the Zambian Medicines Regulatory Authority as a key tool to help the resource constrained authority carry out its duties with regard to post-marketing surveillance of medicines.

Implementation

The concept of providing such data as a public good was recognized by the Center for Global Development in 2007, noting that "*The shortcomings in the systems to collect, share and assure data quality are clear. In large measure they can be traced to the current allocation of risk in the market for critical medical technologies… This suggests*

the need for an information intermediary, or infomediary, for global health to effectively gather and analyze data to forecast demand across a variety of diseases and products and to make information available to all stakeholders" (16).

This independent work noted that ideally, the data would be gathered, analysed and provided by a neutral party, thus working to the benefit of the many different interested stakeholders who are involved in both innovation and access to medicines.

A pilot initiative to develop national pharmaceutical market monitoring systems has been developed in a couple of African countries, sponsored by Medicines for Malaria Venture, as a collaboration between different partners and the relevant national authorities. This has shown that such systems can be successfully developed.

Key element for implementation of such databases include:

- political will and strong support to address safety and access to medicines
- a public health interest in accessing and using such data
- financing for the initial set up and long term running of the system
- technical expertise for development, management and analysis of the data

Ideally, such systems would be developed across multiple countries to allow for international comparisons. Systems would also link into a number of other existing national databases, in order to avoid duplications and the risk of data incoherence.

As recommended in the CGD report mentioned above, the data should be made available to those involved in different stages of drug development, policy making and medicines supply, while recognizing potential commercial sensitivities for manufacturers and importers.

Such systems would require sustainable funding sources, but would provide a service to a large number of different parties. A sustained service of this kind would also reduce the need for expensive one-off surveys, and would also serve as an independent information and evidence source in times of R&D funding changes, or new trade dynamics. By levelling the playing field between different parties, such a service would also reduce information asymmetries between larger or established players in the medicines field and smaller or newer players.

Conclusion

We believe that addressing this asymmetry of information could help to minimize investment risks and optimize prioritization in policy making and service delivery which is critical to ensuring access to life saving treatments. By creating information sources available to different parties, this solution not only removes a barrier but also provides sources of new evidence to help uphold the various rights indicated in the terms of reference of this High Level Panel.

Bibliography

1. UN Secretary General's High-Level Panel on Access to Medicines, (2015) *Call for Contributions*, http://www.unsgaccessmeds.org/call-for-contributions/

2. UN Secretary General's High-Level Panel on Access to Medicines, (2015), *Terms of Reference of the High-Level Panel on Access to Medicines*, 2015 https://static1.squarespace.com/static/562094dee4b0d00c1a3ef761/t/568d535a1c12106651299f6e/1452102490740/TOR+on+new+template+5Jan16+FINAL.pdf

3. Legros, D. et al., (2002), *Clinical efficacy of chloroquine or sulfadoxine-pyrimethamine in children under five from south-western Uganda with uncomplicated falciparum malaria,* Trans R Soc Trop Med Hyg. 2002 Mar-Apr; 96(2):199-201

4. National Malaria Control Center of Zambia, (2012) *Malaria Indicator Survey 2012* http://www.nmcc.org.zm/files/FullReportZambiaMIS2012_July2013_withsigs2.pdf

5. Uganda Ministry of Health (2015), *National Malaria Indicator Survey 2014-2015*, http://dhsprogram.com/pubs/pdf/MIS21/MIS21.pdf

6. Wells WA, Ge CF, Patel N, Oh T, Gardiner E, et al.; (2011), *Size and Usage Patterns of Private TB Drug Markets in the High Burden Countries*. PLoS ONE 6(5), 2011

7. WHO (2015), *Global Tuberculosis Report 2015*, World Health Organization, Switzerland

8. Coghan, R., Gardiner E., et al, (2015) *Understanding Market Size and Reporting Gaps for Paediatric TB in Indonesia, Nigeria and Pakistan: Supporting Improved Treatment of Childhood TB in the Advent of New Medicines*, PLoS ONE, 10(10): e0138323

9. G-finder Fact Sheet, (2014), *Government funding for neglected diseases, why it doesn't add up* http://policycures.org/downloads/Government_Funding_for_NDs.pdf

10. European Commission (2000), Regulation 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan medicinal products, Official Journal of the European Union, L18/1, 22 Jan 2001 http://ec.europa.eu/health/files/eudralex/vol-1/reg_2000_141/reg_2000_141_en.pdf

11. AUC, Pharmaceutical Manufacturing Plan for Africa, (2012) http://apps.who.int/medicinedocs/documents/s20186en/s20186en.pdf

12. Ministry of Health and Ministry of Industry, Ethiopia, (2015), National Strategy and Plan of Action for Pharmaceutical Manufacturing Development in Ethiopia (2015–2025). Developing the Pharmaceutical Industry and Improving Access, http://apps.who.int/medicinedocs/documents/s21999en/s21999en.pdf

13. WHO, 2011, Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, World Health Organization, Switzerland

14. I. J. Onakpoya, C. J. Heneghan, J. K. Aronson, *Post-marketing withdrawal of 462 medicinal products because of adverse drug reactions: a systematic review of the world literature* BMC Medicine 201614:10

15. WHO, Department of Essential Medicines and Health Products, www.who.int/medicines/regulation/ssffc/en/

16. Center for Global Development, (2007), *A Risky Business*, Washington DC