Notes to Global Health Agencies and Civil Society Organizations

Diagnostics, Market Monopoly and Intellectual Property

Over the years, the lack of access to affordable, adapted and simplified diagnostics for infectious diseases such as tuberculosis (TB), HIV/AIDS and hepatitis C (HCV) in health systems in resource limited settings where Médecins Sans Frontières (MSF) works has been an ongoing struggle.

Where diagnostics that are suitable for resource limited settings do exist, the manufacturers have control over the supply chain to the extent that it works like a market monopoly.

From 2017, MSF has conducted a series of analyses aiming to have a better understanding of the causes of market monopoly in the field of diagnostics for infectious diseases especially concerning TB, HIV/AIDS and HCV. Accordingly, a patent landscape on three point-of-care diagnostics for these infectious diseases that are important to MSF field operations – the Xpert MTB/RIF (Cepheid), AlereQ HIV-1/2 Detect (Abbott) and OraQuick HCV Rapid Antibody Test (OraSure) -- and a literature review of patents and diagnostics more broadly have been conducted by MSF with an external consultant and researchers (see attached). This note summarises the key observations by MSF during these analyses and proposes possible follow-up research and analysis that could be taken up by global health agencies and civil society organisations in the context of access to diagnostics.

<u>The key features of diagnostics market monopoly</u>

Like pharmaceuticals, the major markets targeted by major diagnostics developers are the United States and the European market. Markets in upper middle-income countries, such as the BRICS (Brazil, Russia, India, China and South Africa) are also becoming increasingly attractive. In many of the high-income settings, diagnostics testing is normally provided for either by government health programmes or by private insurance companies. In resource limited settings, with the exception of donor-funded tests, the cost of diagnostics is rarely covered by governments or health insurance resulting in high out of pocket expenditure for patients and their care givers. In such a context, the limited capacity of health ministries to negotiate with suppliers translates into high prices or failure to make the diagnostics available, leading to many people being unable to get tested for diseases because they cannot access diagnostic services. Many are also incorrectly diagnosed. As result, they do not receive the treatment they need and, in some cases, may actually receive the wrong treatment.

While donor-supported programmes for HIV, TB and malaria have helped to attract developers and manufacturers (as they enable high volume purchases via pooled procurement mechanisms or by health ministries directly, which have also been aided by some level of price transparency, allowing for more informed and effective negotiations), low and middle income countries (LMICs) continue to struggle to create competition to lower the prices to most essential diagnostics as the way they are developed and marketed in a so-called “closed system” results in monopoly markets.

Indeed, in a closed system, each major diagnostics company develops both the device and the consumable parts – for example the reagent kits or reagent-loaded integrated cartridges -- specifically tailored to that device. To perform the diagnostics testing, the users have no choice but to buy both the device and the assays from the same company. The “lock-in” effect as such

makes it difficult to switch only the cartridges or the device produced by other companies without switching the entire system. Sometimes companies license in hardware, software or reagents from other companies but still retain the closed system. Occasionally a semi-open system exists whereby companies allow assay developers to use their base system of instrumentation and, where applicable, cartridge moulding and interoperability with the instrumentation, but this is typically only for assays that they are not interested in developing internally due to low profit margins (e.g. for outbreak pathogens). To date, outside of reference laboratories staffed with highly trained scientists offering a few "home-brew" lab-based assays for pathogens where commercial assays are lacking, **no truly open systems exist for clinical diagnoses**. In addition, diagnostics companies normally only provide maintenance services to new modes of machines. When new machines come in bundles with newly designed cartridges that are no longer compatible with the old machines, the users may have to replace the entire system too. In addition to the effects of the closed systems, exclusive and restrictive licensing agreements between companies and between suppliers and procuring countries might add further challenges to foment competition or lower prices. In high income countries, where reagent rental contracts are the norm and instruments are never purchased outright, this is never a problem, but **unfortunately instrument purchase has historically been the norm in LMICs** due to a range of reasons.

Consequently, this model makes it **extremely costly to switch diagnostics systems frequently, locks countries in with one provider and limits the possibility of competition**. Even where reagent rental and revolving government tenders do exist, which is extremely rare, there is the additional sunk cost of training staff and setting up supply for the existing system, making it difficult to switch to alternatives. Manufacturers will also not be tempted to apply for tenders or even make supply, distribution and service possible in countries with low volumes as it's not worth their while financially. This is even worse in conflict settings where security problems prevent staff mobility. Even in high income markets, a tender process for diagnostics is normally only every 3-5 years. The cost implication of this reality keeps the demands for multiple diagnostics options in resource limited settings low. For diagnostics for infectious diseases, that mostly affect disadvantaged populations, the less lucrative markets make boosting competition for lower prices even more challenging.

<u>Funding priorities on infectious disease diagnostics sustains monopoly positions</u>

Another factor to consider in the context of monopolies on diagnostics for infectious diseases is what diagnostics the major global **health funders prefer and decide to finance**. Due to the unique features of diagnostics development, as mentioned above, when the major funder is in favour of a particular system to be made available in LMICs, it often means that the company who developed that system will occupy the market for both the device and the assays.

The heavy dependence on major donors to provide adaptive and affordable diagnostics for infectious diseases, the overall lack of alternatives on the market and the slow and ineffective yield of affordable open platforms have contributed to the unintended consequences where funding directions might have reinforced the status quo of monopolies in the diagnostics market for infectious diseases.

For example, the AlereQ (now the Abbott mPIMA) may be a more decentralizable and robust device than Cepheid's GeneXpert, but only offers tests for HIV, whereas the GeneXpert has an impressive menu and has received much implementation support for the Xpert MTB/RIF

test – currently recommended by WHO for everyone needing a TB test – and thus already has an established footprint in LMICs. The Gates Foundation tried to fund a "fast-followers" TB test programme, with the AlereQ TB test coming quite far in the development process, but was not successful on account of the production costs being too high and not competitive enough. As a result, TB diagnostics remain dominated by Cepheid in LMICs.

The role of patents and other intellectual property rights

The role of patents in the context of diagnostics market and monopoly is multifaceted. For some of the commonly used platform technologies, such as polymerase chain reaction (PCR), both the original patent and many patents on the improvements of PCR techniques, such as RT-PCR, have expired. Based on the preliminary findings of the patent landscape on the GeneXpert, AlereQ and OraQuick technologies, **the effects of competition blockage by one or two primary patents are inconclusive**, especially as compared to how blocking patents work in pharmaceutical products. It is however worth noting that the attached patent landscape report contains clear limitations. It did not analyse the perspectives from potential competitors regarding the concerned technologies, nor provide a freedom to operate conclusion in any given jurisdiction. The landscape report also did not analyse the impact of the patent portfolio on follow-on development, and especially did not analyse the extent to which patent thickets might have caused difficulties in developing effective and more affordable open platforms for diagnostics. Therefore, the **potential anti-competitive effects of the high number of secondary patents on diagnostics** on companies and researchers cannot be accounted for, whereas, in other technological fields, such an effect can play an important role on the diversity of existing tools and players on the market. Those gaps, as mentioned above, remain significant subjects for further research by global health agencies and civil society organisations.

Indeed, patents related to diagnostics technologies remain high in number. **Major diagnostics companies hold considerable numbers of patents, often bundled into thickets for various instrumentation, assays, methods and software, related to different aspects of the technologies, methodologies and devices**. Those patents, in most situations, do not seem to be able to block start-up diagnostics developers, often spin-out companies from academia, such as engineering departments, to come up with new testing technologies. However, to attract investment capital and enter into licensing agreements, or to a attract a larger company to buy them out (a common aim and exit strategy), start-up companies also resort to filing patents, which then become a critical indicator for the investors, although there is little proof that the money spent on those patents ever delivers a financial return nor reflects the extent of innovation in diagnostics. The success of a diagnostic has little to do with the list of patents and much more to do with the need, performance, competitiveness and ability to pay (i.e. whether it is reimbursed by the medical insurance).

While the blocking effects may not be as obvious as those on pharmaceuticals, **patent thickets in diagnostics pose a series of questions that are worth tackling**. For instance, it would be worth questioning the total inefficiency of patent thickets to add to diagnostics innovation, how patent portfolios work together with other exclusivities -- such as restrictive licensing, trade-secrets and technical know-how -- in sustaining the monopoly, and the extent to which some of the key public health safeguards, such as excluding the methods and procedures for diagnostic testing from being patentable, have been undermined. The literature review also indicated little in the way of patents on tests for infectious diseases and much more in terms of

genetics and cancer, suggesting that, and following from the low prevalence in HICs, this is not an area of high importance on the business front.

Preliminary proposals for future work by global health agencies and civil society organisations

Looking at the murky picture of patenting together with the monopolistic market dynamic based on a logic of "locking in" the users on one closed system, a critical challenge emerges for the global health community in seeking a simplified solution for accessing more affordable and adaptive diagnostics in resource limited settings. Based on the above preliminary observations, we would propose the below directions to be considered in the future work:

1. Thorough study of the closed systems in diagnostics and their anti-competitive effect on diagnostics development and procurement;

2. Technical assistance to developing countries to increase their capacity to procure essential diagnostics at affordable prices beyond tests for HIV, TB and malaria;

3. Further analysis of other exclusive approaches, such as restrictive licensing, trade secrets and know-how, and others, that have been used jointly with patents in sustaining monopolies in the diagnostics market;

4. Analysis of the potential contribution of the cost of pursuing, maintaining and obtaining patents by the patent holding companies on the cost of goods of the final diagnostics;

5. Further analysis on selected patents on critical diagnostics considering patentability criteria and public health safeguards in patent examination; especially, to analyse whether typical claims might undermine the flexibility contained under Article 27.3(a) of TRIPS for the exclusion of patenting on methods and processes of diagnostics;

6. Publishing of public health-oriented reports and pushing for transparency on all types of IP protections on diagnostics in order to improve the assessment of the effects of patents and other exclusivities and the understanding of practical measures to overcome the barriers;

7. Analysis of whether patent filing or granted patent portfolios by diagnostic developers actually increases the innovative capacity to meet public health needs;

8. Analyse selected patent disputes on diagnostics to understand the impact on alternative diagnostics developers and the limiting of the freedom of choice of products available to end-users (e.g. as with Myriad and their BRCA1+2 lab test in the USA).