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Improving Access to Medicines in Low-Income Countries: A Review of Mechanisms

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Individuals in low-income countries ("LICs") often lack access to appropriate medicines. The multi-disciplinary nature of this problem requires a holistic approach. Whereas, other writings on the topic tend to focus on one or a small number of issues, often from the perspective of a single discipline, this paper seeks to consider the major issues from a multi-disciplinary perspective. It first considers mechanisms for improving the availability of medicines in LICs, through grants, prizes, treaties, advance market commitments, priority review and product development partnerships to incentivize and fund R&D for neglected diseases. The paper then assesses mechanisms for improving affordability of medicines in LICs, such as differential pricing mechanisms, monopsonies, patent law flexibilities and human rights obligations. Next, the paper reviews mechanisms for improving the efficacy of medicines in LICs, including authentication, criminalization, international and national enforcement and communication and education. Finally, the paper examines mechanisms for improving the obtainability of medicines in LICs, through low-cost intervention, task-shifting, efficient regulation, grass-roots service provision and education. The paper concludes by identifying areas warranting further research.

Keywords TRIPS; WHO; Africa; Caribbean

On the 24th and 25th of July 2013, the University of Melbourne and Vanderbilt University held the Melbourne–Vanderbilt Roundtable on Access to Medicines (the "Roundtable") at the University of Hawaii. In attendance were ten participants[1] with expertize in a variety of disciplines, including intellectual property law, health policy, medical ethics, medicine, genetics, public health, economics, pharmaceutical markets and development. The Roundtable was moderated by Andrew Christie and Daniel Gervais, being representatives of the University of Melbourne and Vanderbilt University, respectively. The participants were brought together to contribute to a group discussion on one of the most important global public health issues: improving access to medicine in low-income countries (LICs)[2] (Commission on Intellectual Property Rights 2002; Commission on Intellectual Property Rights, Innovation and Public Health, 2006; Lanjouw, 2005; Watal, 2000; World Bank, 2013, 2014; World Health Organization (WHO) Commission on Macroeconomics and Health, 2001).

The multi-disciplinary nature of the problem of access to medicines in LICs requires a holistic approach, especially one that identifies and examines the areas where cross-disciplinary collaboration is valuable. The need for such a discussion was the primary reason for convening the Roundtable. The Roundtable proceedings included presentations on all participants' areas of expertize, reflections across

disciplines on the various access issues, a consolidation of the major factors that contribute to access and suggestions for further research.

This paper provides an overview of the various issues considered at the Roundtable, and contains further research and analysis undertaken following the Roundtable. Whereas, other writings on the topic tend to focus on one or a small number of issues, often from the perspective of a single discipline, this paper seeks to consider the major issues from a multi-disciplinary perspective. Its significance, therefore, lies in its breadth.

Individuals in LICs often live in situations of inadequate food, shelter and sanitation. In addition to these obstacles, they lack appropriate healthcare and access to medicines. As a result, it is not surprising that these individuals suffer from high rates of illness and premature death from diseases that would otherwise be preventable and/or treatable (Orach, 2009). Access to medicines in LICs is influenced by a combination of interlocking factors. For diseases and illnesses that are prevalent in LICs but which have no presence in high-income countries, there are often no effective medicines in existence. Such medicines have not been developed due to a lack of sufficient incentive for private sector investment in the necessary R&D. For those medicines that do exist, their accessibility in LICs is reduced when they are priced to make a profit, thereby often putting them out of reach of the majority of the population. Access to available and affordable medicines is also reduced by purveyors of substandard medicines, who expose millions of patients in LICs to harmful and even deadly concoctions. For those medicines that are available, affordable and efficacious, access in LICs is dependent upon the medicine being obtainable. Obtainability is reduced due to a number of impediments to distribution: inadequate health systems, a lack of physical (incl. transport) infrastructure and social barriers.

Part II of this paper considers mechanisms for improving the availability of medicines in LICs. It provides an overview of pharmaceutical R&D, its impact on the treatment of neglected tropical diseases (NTDs), current methods to incentivize and fund R&D, and options for further incentives. Part III considers mechanisms for improving affordability of medicines in LICs. It discusses patients' ability to pay for medicines in LICs, methods to reduce the cost of R&D and the price of medicines, and other approaches to reducing prices. Part IV considers mechanisms for improving the efficacy of medicines in LICs. It examines the proliferation of substandard medicines internationally, their disproportionate effect upon poor nations, current structures to reduce their existence, and additional preventative means. Part V considers mechanisms for improving the obtainability of medicines in LICs. It reviews impediments to distribution of medicines in poor nations, existing methods to increase supply to patients, and further possibilities for enhancing distribution. The Annex identifies areas warranting further research.

Improving Availability

Medicine availability is satisfied when medicines specific to the largest disease burden of LICs, namely NTDs,[3] are in existence (News Medical, 2011; WHO, 2013). While there are thousands of medicines on the market, the overwhelming majority are designed for the needs of high-income countries. This results from a lack of incentive for R&D of medicines for NTDs.

Pharmaceutical companies function within a system incentivized by attaining profits through the intellectual property rights (IPR) regime. The IPR system incentivizes innovation through the extension of market exclusivity via patents. A benefit of this system is its sustainability: the patent system runs within a market whereby consumers (instead of governments) "choose" by providing the incentive for production[4] (Vacca, 2013). However, in LICs the population is largely unable to provide an incentive for production as their ability to pay is minimal if not non-existent.

Furthermore, the government purchase of medicines for the public sector is restricted due to limited funds. The cost of medicines is substantial, accounting for 60% of health spending in some developing and

transitional countries, a stark contrast to only 18% in Organization for Economic Co-Operation and Development (OECD) countries (Cameron *et al*., 2009; Organization for Economic Co-Operation and Development, 2005; WHO, 2004). Example health expenditures per capita[5] include $37 in Benin, $17 in Ethiopia and $30 in Guinea (World Bank, 2013). This is in comparison to $8,608 in the United States, $4,952 in France and $5,939 in Australia (World Bank, 2013). The majority of people do not have health insurance and must pay out of pocket for medicines; this can send large groups of the population deeper into poverty[6] (Niens *et al*., 2010). For example, in 2010, 77% of the population in Nigeria and Tanzania were living below US$2 a day—before medicine expenditures.

Given the lack of market-based incentives for producing medicines specific to NTDs, pharmaceutical companies have targeted their efforts at high-income markets where they are capable of generating a profit. The development of medicines which are applicable only to NTDs have little (if any) incentive under the patent system as there is an inability to profit or even recoup costs[7] (Pugatch *et al*., 2012; WHO, 2013). Only in situations where a disease affects both LICs and high-income countries, or has an analogous disease pathway, will R&D investments likely be made and then typically not directed at the LIC (Lipkus, 2006, p. 390). The consequence of this inequality is that key pathways of drug discovery do not exist for NTDs,[8] as the large majority of R&D (and thus new medicines) is directed at diseases common to high-income countries (Pugatch *et al*., 2012; p. 20; WHO, 2013).

Initiatives

There have been a number of mechanisms created to provide incentives and funding to the R&D sector outside of or in addition to "traditional" patent-based incentives. It is hoped that by increasing incentives for R&D into NTDs, it will increase the availability of these medicines in LICs.

R&D Grants

One of the most commonly utilized methods to incentivize R&D is the research grant system, which awards funding to those pursuing predetermined research outcomes (Pugatch *et al*., 2012, p. 28). The grant model spurs development by financing some of the up-front costs of R&D. Grants are frequently distributed by the Bill and Melinda Gates Foundation, which facilitates access to medicines through its global access model. The Bill and Melinda Gates Foundation ensures global access by refraining from taking IP rights in their supported projects, and by requiring grantees to ensure that their innovation will be available worldwide.

However, there are limitations to this mechanism, as grants are subject to the changing will of the particular donor: governments, philanthropic organizations and individuals. Additionally, grant money may run out before the necessary R&D is completed, or it may be sporadic, not guaranteed from year-to-year. In the end, these considerations reflect the fact that the purse strings are held by organizations or individuals who themselves are not conducting the R&D and so may act in ways detrimental to researchers.

R&D Prizes

R&D prizes incentivize R&D by providing applicants with a financial reward when they achieve a stipulated outcome (as set by the grantor). The prize may be shared with other "winners" and it may be conditional upon the achievement not being patented (Muller-Langer, 2011).

InnoCentive has successfully used this model to develop a process for simplifying the manufacturing process of a tuberculosis (TB) drug (InnoCentive, 2008). The Health Impact Fund (HIF) also utilizes a prize system, by offering an incentive to drug sponsors based on the medicine's health impact, conditional upon its sale at cost. HIF measures health impact by "DALYs" (disability-adjusted life years) which enables the burden of disease to be quantified and compared. The DALY gives an estimated number of lost years of life due to premature death and reduced productivity (WHO, 2010, p. 13)

While prize funds delink access from ability of the patient to pay, some of the Roundtable participants noted that prize funds suffer from the inability to be predictable funding for innovators. Furthermore, even if the developer does meet the objectives that qualify for the prize, the developer may not realize all of their sunk costs if the value of the prize is not sufficient to match their expenses. Lastly, prize funds assume that donor organizations are acutely aware of patient needs on the ground, and their monetary value. While delinking of this nature can correct the lack of incentive for R&D, there is undoubtedly a risk that the objectives sought may be of limited utility or seemingly impossible to achieve.

R&D Treaty

R&D grants and prizes require a source of funding. The implementation of a global R&D treaty was recommended by the WHO Consultative Expert Working Group (CEWG) on Research and Development: Financing and Coordination. This treaty would promote R&D through delinking and sustainable funding (WHO CEWG, 2012, p. 113). The CEWG recommended that all countries commit at least 0.01% of their GDP on government funded R&D devoted to meeting the health needs of developing countries, with a similar commitment to developing countries with a potential research capacity (WHO CEWG, 2012, pp. 110–11). The treaty is supported by over 80 health research institutions, product development partnerships, and public interest NGOs, including Médecins Sans Frontières, Oxfam and Health Action International (Balasubramaniam, 2012). However, negotiations on the treaty have been opposed by the US and the EU until 2016 mainly due to the financial pressures (Kiddell-Monroe *et al*., 2013).

The Roundtable noted that a treaty of this nature is subject to political influence and would need to be carefully drafted to ensure that it does not disadvantage LICs. A case in point discussed by the Roundtable was the negotiation of TRIPS, which was not implemented with a view to spurring innovation in developing countries, nor in consideration of global developmental objectives and strategies—it was accepted by several developing countries due to ignorance, coercion and hard bargaining (Gervais, 2013, p. 2). Furthermore, the development of a R&D treaty could be counterproductive and hamper availability if it reduced the willingness and ability of governments to fund other successful incentive mechanisms.

Advance Market Commitments

Advance market commitments create an agreement, in advance of the development of a product, to purchase guaranteed amounts which meet criteria set by the donor (Commission on Intellectual Property Rights, Innovation and Public Health, 2006). The agreement increases the price received by the developer, as the guarantee "tops up" the price paid by the consumer, which must be low in order to ensure affordability. In practice, the Roundtable identified only one purchase agreement introduced, the PneumoAMC, which was advanced by a partnership between the Bill and Melinda Gates Foundation, the Global Alliance for Vaccination and Immunisation and other donor governments. PneumoAMC has resulted in guarantees for at least two pneumococcal vaccines, which would not normally reach LICs until 10–15 years after their introduction in industrialized countries (GAVI Alliance, 2013).

Critics have said that the PneumoAMC has neither accelerated the innovation cycle in pneumococcal vaccines nor increased availability (Plahte, 2012); others have noted that it is too early to measure outcomes (Cernuschi *et al*., 2011). Representatives from manufacturers in developing nations have noted concern over depletion of the fund before their products were finished (Plahte, 2012, p. 2465). Light has noted that the cost of PneumoAMC is expensive (and serves the interests of the pharmaceutical companies) compared to other more holistic approaches, such as extending inexpensive vaccines for diseases such as polio, measles and yellow fever (Light, 2009; Scudellari, 2011). The cost per child saved under the GAVI-sponsored AMC has been assessed at approximately US$4,722, which critics have estimated as much more costly than the implementation of multidrug package interventions for NTDs which would only cost approximately 40 cents per person per year (Molyneux *et al*., 2005; Scudellari, 2011).

Priority Review Vouchers and Tax Credits

Priority review vouchers (PRVs) provide incentives for R&D by shortening the review process on future medicines. In the US priority review system, sponsors of newly approved medicines which target a NTD, malaria or tuberculosis are given a voucher. The vouchers can be traded or sold, to be used on a future drug application which would not have qualified for priority review. A single voucher is estimated to save between 4–12 months and 50–500 million dollars[9] (Robertson *et al*., 2012; Stefanakis *et al.*, 2012). In the United States, PRVs can be used in combination with the Orphan Drug Tax Credit, which provides a 50% tax credit on R&D costs (Ridley *et al*., 2006). The United Kingdom has implemented a similar mechanism, the Vaccine Research Relief Programme, which gives a tax credit for vaccine research aimed at the developing world.

While these methods incentivize NTD-specific R&D, their value is questionable, as neither has been extensively utilized. The Vaccine Research Relief Programme has been relatively unused, with only an average of 10 claims per year between 2003 and 2010 (Pugatch *et al*., 2012, p. 32). A similar situation has occurred with the PRV system, in which only two PRVs have been awarded, one for the antimalarial drug Coartem and a second for the Tuberculosis medicine Bedaquiline[10] (Sakhia, 2013). At this point in time, it is unclear whether companies are actively pursuing PRV-eligible products and, if they are, the impact that the scheme has had on their motivations (Stefanakis *et al.*, 2012). However, interviews with representatives of a convenience sample of 12 pharmaceutical companies conducted by Robertson and co-workers showed that respondents[11] thought that PRVs could be improved as an incentive if some of the following changes were implemented: a PRV sale on the market to build credibility and determine the sticker price; reduction in the voucher user fee (currently set at $5.2 million); relaxing the 1 year notice period before using a PRV; relaxing the limit on voucher transferability (only one transfer of ownership allowed); and providing greater clarity on the revision process of the list of PRV-eligible diseases (Robertson *et al.*, 2012, pp. 3–4).

Product Development Partnerships

Product Development Partnerships (PDPs) are public–private partnerships, which bring together public, private and funding organizations to incentivize R&D specific to diseases in low and middle income countries (Pugatch *et al.*, 2012, pp. 37–38). In this way, PDP's utilize multi-sector engagement to bring together a multiplicity of stakeholders to jointly pursue a discreet public health goal. PDPs strike a balance to create a mutually beneficial relationship between private and public interests (Lipkus, 2006, p. 414). The largest PDP sponsor is the Bill and Melinda Gates Foundation, which funds 55% of the total PDP funding.

The Medicines for Malaria Venture (MMV) is a PDP which functions as "public venture capital fund" to incentivize development of medicines where the market has failed to do so (Burci, 2009, p. 365). MMV incentivizes private involvement by giving marketing rights and IP rights to private partners for use outside of the target area. The TB Alliance also functions as a PDP, to develop new TB drug regimes that are simpler and faster acting. The TB Alliance uses the PDP structure to leverage the knowledge of their staff and partners to accelerate TB drug development. A benefit of this model is the unique opportunity to have a number of the world's leading pharmaceutical companies test their experimental compounds in combination with one another (Global Alliance for TB Drug Development, 2014).

The overall impact of PDPs has been mixed. While the TB Alliance has assembled the largest portfolio of potential new TB drugs in history, they have only produced one new TB drug: Bedaquiline. MMV has had more success, although the advances have been in altering existing medicines for markets rather than creating new treatments. For example, MMV launched a malarial therapy for children by reformulating an existing drug (Coartem) into a chewable tablet. MMV was also involved in Eurartesim, which was made more patient friendly in that it can be administered once a day for 3 days instead of twice a day. Lastly, MMV collaborated with Guilin Pharmaceutical to attain WHO prequalification over an Artesunate injection, thus qualifying it for purchase by international organizations for disbursement to

patients. While the activity behind PDPs has been immense, critics have noted that public–private partnerships can suffer from high transaction costs, varying accountability and a lack of alignment with country priorities and systems (Burci, 2009, p. 381).

Patent Pools and Open Databases

Patent pools involve the cross-licensing of IP by participants to increase access to essential technologies for particular products (Pugatch *et al.*, 2012, p. 35). A patent pool is "an agreement between two or more patent owners to license their patents to one another or to third parties" (Serafino, 2007). In a nutshell, they are supposed to be a "one-stop shop" for licensing several patents from multiple owners. In this way, they make the process of drug discovery and development more efficient and effective as the acquisition of essential technologies is streamlined (Pugatch *et al*., 2012, p. 35).

Major pools are the Medicines Patent Pool and the World Intellectual Property Organization's (WIPO) Re:Search pool. The Medicines Patent Pool aims to promote access to antiretroviral medicines and promote development of adapted formulations. Re:Search is a collaboration of public and private sector stakeholders designed to encourage the R&D of medicines to treat NTD's, malaria and TB. Researchers can search for compounds, unpublished scientific results, patents and regulatory dossiers. Licenses are royalty-free to Least Developed Countries, and negotiated with other countries on a case-by-case basis[12] (WIPO, *Guiding Principles of WIPO Re:Search*). Re:Search provides open access to a number of compounds in different areas of development to spur collaboration and development activities in R&D.

However, it should be noted that use of patent pools for pharmaceutical R&D is relatively new, and they have not been widely used. Patent pools may not be a viable option for promoting R&D, as they have achieved very little output (Pugatch, 2011).

Unresolved Issues

The review of the previous mechanisms points to the reality that there is no silver bullet to increase the availability of medicines for NTDs. There are a number of options for incentivizing R&D; however, their utility in producing new medicines for LICs has been minimal. Compared to the production of medicines for high-income countries through the free market system, the above options have resulted in limited success, although some commentators query whether the previous successes are likely to continue in the future (Almog, 2005; PRWeb, 2013; Scannell *et al.*, 2012). With this in mind, the Roundtable noted the importance of measuring the effectiveness of various mechanisms to motivate R&D and exploring ways to further incentivize these systems. By drilling down into what specifically incentivizes R&D in these areas, mechanisms may be adjusted to facilitate this process.

The Roundtable also noted the importance of ensuring long term and consistent funding. For example, mechanisms such as prize funds do not provide participants with a guaranteed payment, and R&D grants may be insufficient to enable a project to be completed. A system of "tradable patent terms" has been proposed, where pharmaceutical advances which serve a humanitarian purpose would receive an extended patent term which can be used with a different pharmaceutical product (Ilg, 2010). In this way, the creation of the humanitarian medicine, would allow the developer to extend the patent term on another, more commercially valuable, medicine—the primary market for which would be in developed countries. It is argued that this establishes a more reliable economic incentive as it can be measured by the profits garnered from the proposed term recipient, making it more consistent than prize funds.

However, given the lucrative pharmaceutical markets in high-income countries, it could be that the willingness of pharmaceutical companies to dedicate significant time and money towards medicines for LICs will be limited regardless of the mechanism used, as the profits will never be as large. Therefore, a refocusing of direction of the major R&D players may be needed—one which concentrates on goodwill and corporate social responsibility. While a number of pharmaceutical companies have designed donation

programmes (Bayer, 2014; Max Foundation; Merck, 2013; Merck, 2014), these voluntary systems are not self-sustaining and are dependent upon the chosen direction of management. It may be necessary to create obligations upon these companies to expend a certain amount of time and money on the concerns of LICs instead of relying upon facilitated market incentives (Oke, 2013, p. 8). An additional option discussed by the Roundtable was investigating the viability of state-run R&D programs, which would remove some of the burden placed on private R&D companies.

Lastly, the Roundtable considered the influence of intellectual property (IP) rights mechanisms, especially patents, on innovation (WIPO, 2013). While participants recognized that patents are one tool of many to stimulate innovation, their overall impact on R&D was queried. Patent pools, open databases and differential pricing have had limited use since their inception. Greater research into the factors that would motivate pharmaceutical companies to use these mechanisms is warranted. The Roundtable discussed whether patents were indeed necessary and, if they were, whether they were sufficient. For example, if patents are seen as necessary, it would be useful to identify why and in which contexts. If patents are seen as insufficient and possibly counterproductive, particular methods to rectify this should be explored. The Roundtable also questioned whether patents were actually a spur to innovation (Czarnitzki and Toole, 2011),[13] or whether they stymied innovation (Boldrin and Levine, 2013; Gold *et al*., 2010). The participants were not united on the effect of patents on innovation, and supported further investigation into this topic. Any mechanisms utilized to spur R&D should carefully consider the implications of the inclusion (or exclusion) of IP rights.

Improving Affordability

Medicines are affordable if patients in LICs have enough money to purchase them without unduly compromising their ability to meet other essentials, such as housing, education and food. The cost of medicines is primarily determined by the cost of pharmaceutical R&D. Currently, it costs an average of US $1.38 billion and takes 10–15 years to develop a single drug (International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), 2012b, p. 8). This reportedly adds up to an annual expenditure of US $135 billion by the pharmaceutical industry on R&D (International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), 2012b, p.8). In 2011, the annual spending by the pharmaceutical sector was 5× more than the aerospace and defense sectors, 4.5× more than the chemicals industry and 2.5× more than software and computer services industry (Joint Research Centre, Directorate-General for Research and Innovation, 2011).

Some associate the high cost of R&D with the time consuming and risky nature of pharmaceutical R&D, as the innovator does not know in advance whether the medicine will be safe or effective (IFPMA, 2011). In 2011, there were only 35 new pharmaceutical products launched (International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), 2012b, p. 7). The numbers are more problematic when account is taken of the number of investigated compounds that make it to market, as there is approximately only one marketed medicine for every 5,000–10,000 compounds investigated (International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), 2011, 2012b, pp. 7–8) However, the stated cost of pharmaceutical R&D is not without its critics (Light and Warburton, 2011; Light and Warburton, 2012). The Roundtable queried whether the stated costs were inflated to justify the price paid by consumers, insurers and governments. Also at issue was whether R&D costs should include lost opportunity cost, a factor experienced in many sectors but not typically included in the R&D calculation. Furthermore, some Roundtable participants noted that the claimed increases in R&D expenditures have not resulted in an increase in new medicines.

To compound the problem, pharmaceutical R&D in LICs has lagged far behind their counterparts in high income countries[14] (Lanjouw and MacLeod, 2005). This is largely due to a lack of capacity, technology and funding (White-Guay, 2011). Additionally, LICs function within a system which impedes innovation as there are not efficient systems for clinical trial design, top-level medical schools and experienced clinicians (IFPMA, 2012b, p. 7).

Initiatives

There have been a number of mechanisms implemented to increase affordability by reducing the cost of R&D and the price of medicines, such as differential pricing, monopsonies and patent law flexibilities.

Differential Pricing

Differential pricing involves "the adaptation of prices charged by the seller to the purchasing power of governments and households in different countries" (WHO, 2001). In this way, differential pricing aims to make medicines contextually affordable, depending upon the patient's location. The importance of differential pricing is immense, especially given that in countries with very high income inequality, market forces produce incentives for patent holders to maximize profits by pricing their medicines to serve only the wealthiest sliver of society (Flynn *et al*., 2009).

Differential pricing is not widely used by pharmaceutical companies because of the risks of arbitrage and the erosion of high income markets (Yadav, 2010, p. 6). To combat this, Yadav recommends that pharmaceutical companies work with companies who have a reputational risk resulting from arbitrage and create contractual obligations that medicines are only distributed in low income areas (Yadav, 2010, pp. 6–7). Some Roundtable participants also noted that the use of trademarks may be able to assist in stopping arbitrage across borders.

Monopsonies

In many high-income countries, governments and insurers have become the negotiators of price. They are the largest purchasers (directly in the case of governments, and indirectly in the case of insurers) of medicines. Government procurement, when done for the entire jurisdiction, functions as a monopsony allowing for the negotiation of lower prices. While insurers are not monopsonists per se, they still have a great deal of control over pricing given their large client base. Medicinal monopsonists can benefit patients by driving down prices, in turn saving costs and allowing for more treatments. Furthermore, the monopsonist establishes a mutually beneficial relationship, in which the government can serve as the counterweight to the monopolist tendencies of pharmaceutical companies.

New Zealand employs a monopsonist system in which there is national procurement of medicines for the public sector via PHARMAC, a crown entity. PHARMAC utilizes priority assessment criteria to determine which medicines (and services) have sufficient clinical benefit to justify public funding [Health and Disability Services Act 1993, s5 (NZ)]. PHARMAC engages directly with manufacturers to negotiate price for the public system, attaining prices lower than within other nations. Due to finite resources, PHARMAC must monitor its "opportunity cost", which is the health gains that are lost if health funds are spent on less worthwhile services (Moodie *et al*., 2003).

A reality of monopsonies such as PHARMAC is that they have finite resources. As a result, some patients may not receive the drug of their choice (Manning, 2011), or any treatment at all, because the cost outweighs other health gains that could be achieved with other treatments[15] (Feek *et al*., 1999).

A further consideration is that, in the current market, medicinal monopsonists function without full knowledge of the pricing agreements made by other governments, as the agreements are all confidential. This lack of knowledge and transparency means that public health systems could be paying highly variable prices, which are not tied to the cost of the drug but to other factors, such as the size of the potential market, favorable trading terms or other incentives.

Patent Law Flexibilities

A trilateral report produced by the World Trade Organization (WTO), WIPO and WHO recognized that more equitable public health outcomes are dependent upon having a national public health policy that includes effective health systems, adequate financing and sound regulation (WHO *et al*., 2012, p. 30). Lack of government policy that properly regulates patent applications can result in decreased access to

medicines and high prices. For example, in South Africa, patent applications were not reviewed by the government, which resulted in the creation of multiple patents for the same drug, blocking generic competition and inflating prices (Treatment Action Campaign, 2013). South Africa's Department of Trade and Industry (DTI) has drafted a National Policy on Intellectual Property that calls for reforms to its patent act to introduce patent examination and an opposition system (Department of Trade and Industry, 2013). The draft policy was open for comment in late 2013 and at the time of publication DTI was reviewing public submissions (Daniels, 2013). It is hoped that any proposed changes will increase competition and the introduction of generic medicines, ultimately reducing the cost of medicines (Anley, 2013).

South Africa has also been called upon by the UNDP to utilize its TRIPS flexibilities, such as compulsory licensing, to increase access to medicines (Park *et al.,* 2013). Additionally, Brazil has been undergoing patent reform to take advantage of TRIPS flexibilities (Baker *et al*., 2013; Infojustice, 2013; Kardas-Nelson, 2013). Potential changes include reducing patent terms, streamlining the compulsory licence process, strengthening patent criteria and allowing patent oppositions[16] (Gervais, 2014). Movement on these issues was heavily promoted by civil society groups (Kardas-Nelson, 2013).

Policy approaches utilizing TRIPS flexibilities and domestic law can greatly aid in increasing access to medicines. However, the use of flexibilities such as compulsory licensing is not welcomed by pharmaceutical companies as it jeopardizes the value of the market, decreasing potential profits To this end, Abbott responded to the compulsory licence of an antiretroviral drug in Thailand by announcing that it would no longer register new drugs for sale within that country (Flynn, 2008). Therefore, even though flexibilities are a part of TRIPS, their use should be chosen carefully and strategically so that LICs do not become subject to responses of pharmaceutical companies that can affect access to medicines. The discussion of these flexibilities among nations shows the political realm of access to medicines: actions are not without a political cost, and must be chosen carefully.

However, policy approaches within LICs depend upon a functioning governance system (Thomas and Gostin, 2013),[17] which requires the necessary administrative resources and authority to implement health policies and regulations. LICs often lack these basic capacities, making it difficult for them to meet basic public health needs (Mok, 2010, pp. 508–09). Furthermore, while the existence of an activist medicines policy is important, it is often secondary to other needs such as clean water, food and shelter.

Human Rights Obligations

Affordable medicines for LICs can also be pursued through a human rights framework (Brennan *et al*., 2013; Gold, 2013),[18] although to date this method has been used in limited ways only (Vacca, 2013). A right to health has been enshrined in art 12 of the *International Covenant on Economic, Social and Cultural Rights* ("ICESCR"), as a "right of everyone to the enjoyment of the highest attainable standard of physical and mental health" (International Covenant on Economic, Social and Cultural Rights, 1966). The Universal Declaration of Human Rights affirms that "everyone has the right to standard of living adequate for the health of himself and of his family, including food, clothing, housing and medical care and necessary social services" (Convention on the Elimination of All Forms of Discrimination against, 1980, p. 13, arts 11.1(f), 12; Convention on the Rights of the Child, 1989, p. 3, at art. 24; General Assembly resolution 217A(III), A/810, 1948, art 25.1; International Convention on the Elimination of All Forms of Racial Discrimination, 1966, p. 195, art 5(e)(iv)). The content of this right has been elaborated in General Comment No 14, which specifically mentions the importance of access to essential medicines, affordable and accessible healthcare and the right to prevention, treatment and control of diseases (Committee on Economic, Social and Cultural Rights, 2000, ¶¶ 8], 11], 12a], 16]).

As the obligations of upholding the right to health are held by the state, the right can be used in domestic litigation within states that have ratified the ICESCR (Brennan *et al.*, 2013). There is also a growing body of literature which argues for the use of human rights norms to ensure greater corporate

responsibility (Oke, 2013). These mechanisms can aid in increasing affordability of medicines, but are dependent upon a well-resourced and knowledgeable litigant, the existence of a functioning judiciary as well as enforcement mechanisms for judicial orders. While there are also international mechanisms to monitor the action of states with regard to their human rights obligations (International Network for Economic, Social & Cultural Right, 2012),[19] these are light on enforcement procedures and mainly concern a reporting of the state of affairs in each country.

Unresolved Issues

Like mechanisms to increase availability, affordability mechanisms such as differential pricing suffer from a lack of use by pharmaceutical companies. A further difficulty is a general lack of transparency in price negotiations between, on the one hand, pharmaceutical companies and, on the other hand, governments and insurance companies. While confidential contracting has been common, it must not be used to the detriment of the health of LICs. Methods to increase transparency in these transactions are needed; legislative intervention may be required.

Additionally, political will, capacity and funding in LICs is needed to create and utilize patent law flexibilities. LICs must have the political will to increase affordability, and the capacity and financing to develop policy and effective systems. These are large-scale issues which require a holistic approach and careful attention.

For medicines which are used in both high-income countries and LICs, their affordability is affected by the proliferation of "backdoor deals" and "evergreening". "Backdoor deals" refer to the activity of generic companies being paid to stay off the market, allowing the monopolist to remain on the market with what is likely to be an illegitimate patent (Kesselheim, 2011; Sutton, 2013). These deals allow both originator and generic companies to profit, when supply to LICs is either non-existent or limited to the wealthy. "Evergreening" refers to a proliferation of secondary patenting around the most successful medicines (Amin and Kesslheim, 2012; Christie *et al.*, 2013), which may further reduce the ability of generics to enter the market. Any reduction in the possibility of generics entering the market has a dramatic effect on LICs, as they would produce medicines at lower prices, increasing their affordability. These issues are global and cross-border; they affect both LICs and high-income countries. Methods to reduce their effect upon LICs should be explored.

Lastly, while a number of pharmaceutical companies have designed donation programmes to make medicines affordable in LICs (Bayer, 2014; Max Foundation; Merck, 2013; Merck, 2014), these voluntary systems are not self-sustaining and are dependent upon the chosen direction of management. It may be necessary to impose, by statute, obligations pharmaceutical companies to ensure that life-saving medicines are provided in LICs at affordable prices (Oke, 2013, pp. 5–8).

Improving Efficacy

Substandard medicines disproportionally affect consumers in developing countries, where for some diseases reports indicate that half of the drugs may have little or no active ingredient (Attaran *et al*., 2012; Newton *et al*., 2006). In 2003, state officials estimated that 70% of drugs in Nigeria were either counterfeit or adulterated (IRIN, 2013). In mainland Southeast Asia,[20] there has been a worsening epidemic of substandard "artesunate" malaria treatments, such that in some areas the majority of the malaria medicines were found to be fake (Newton *et al*., 2006a). In Thailand, 40% of sampled anti-infectives were found to contain active ingredients outside pharmacopoeial limits (Shakoor *et al*., 1997).

These "medicines" may simply have no active ingredient or may have harmful toxic substances which independently jeopardize the health and life of the recipient. The effects of substandard medicines are far reaching as they can cause treatment failure extending illness, adverse reactions, disability and death (IFPMA, The Treat of False Friends: Joining Efforts to Protect Patients Against Online Sales of Fake

Medicines, 2012). Substandard medicines often look so similar to the quality product that they deceive health professionals as well as consumers (WHO, 2012).

The lucrative nature of substandard medicines fosters trans-boundary criminal enterprises, making detection and prosecution difficult[21] (United Nations Office on Drugs and Crime, 2009; WHO, 2012). Purveyors of substandard medicines target countries in which regulatory protections are the lowest and profits are the highest (Attaran *et al*., 2012). As pharmaceuticals are usually expensive, cheaper options entice consumers, health care organisations and governments alike (Newton *et al.,* 2006b, p. 603; WHO, 2012). Often the lack of legislation, ineffective enforcement, public corruption and light penalties means there is limited deterrence of criminals (Newton *et al*., 2006a). Detection is also difficult as the supply chain utilizes complex international trade routes, within a system where police, customs and drug regulators are not unified (Newton *et al*., 2006b; WHO, 2009).

While mechanisms to combat substandard medicines occur on both an international and domestic level, drug regulation itself is managed domestically. The issue of substandard drugs is particularly acute in LICs, as mechanisms for regulation are sparse and most incidents[22] (Arie, 2012) get lost in the matrix of high mortality and strained health systems (Gostin *et al*., 2013). Only 20% of WHO member states have well-developed drug regulation systems, and 30% have either no system or mechanisms that barely function (Carpenter, 2004).

Proper detection and prosecution is further complicated by the conflation of IP rights infringement with medically substandard medicines. There is no internationally recognized terminology for substandard medicines, which are often referred to as "counterfeit" by states and civil society groups. The over policing of suspected counterfeit medicines has threatened the generic medicine chain in multiple situations where generics have been legally produced in a country, and then confiscated (en route) on grounds of IP infringement even though the destination country could legally distribute the medicines[23] (Saez, 2013; The Partnership for Safe Medicine, 2011).

Initiatives

Methods to combat substandard medicines have been widespread and varied, falling under five major areas: product authentication, criminalization procedures, international collaboration on enforcement, national enforcement and communication and education.

Product Authentication

Regulatory mechanisms are important to ensure high quality, safe and efficacious medicines. Every drug that makes it to the market must undergo rigorous scrutiny and clinical trials, as determined by the domestic regulatory body of the state[24] (Sutar *et al*., 2013). Regulatory bodies also ensure that medicines are properly registered and labeled to ensure that they are correctly prescribed to consumers (Sutar *et al*., 2013).

Some states have developed domestic regulatory bodies and policies that focus on eradicating substandard and counterfeit medicines. One method utilized is pharmaceutical product authentication, which uses color shifting inks, holograms and chemical markers embedded in drugs to identify legitimate medicines[25] (Kahn *et al*., 2012). China has implemented an "e-coding" system whereby each party within the supply chain is required to send a "signal" to confirm receipt or dispatch to a regulatory database. Health care workers and consumers are then able to enter their medicine's e-code into the database to confirm their origin (China Food and Drug Administration Database; Buckley and Gostin, 2013). Some pharmaceutical manufacturers have dedicated mechanisms to secure their products through sourcing agreements and product authentication. Abbott utilizes track and trace technologies, and both covert and overt security features to secure their supply chain (Abbott, 2013, pp. 47–48). Abbott also works with law enforcement organizations, regulatory bodies, industry, government and non-profits to identify and dismantle criminal organizations and pursue stricter sanctions (Abbott, 2013, pp. 47–48).

While these methods may work quite well within middle and high-income nations, their success in LICs depends upon educating patients and healthcare workers about proper identification. There is also a technological hurdle, which requires access to an electronic database, which may be limited in rural areas. Lastly, some Roundtable participants noted that it might be more effective if an international marking system was created so that medicines would not need to be re-marked when entering a new country, creating a redundant regulatory burden.

Criminalization

The Council of Europe has created the Medicrime Convention, which focuses on "counterfeit" medicines which are "false representation s] as regard ing] identity and/or source". The convention puts an obligation on states to criminalize manufacturing, trafficking and supplying counterfeit medicines, and offers a framework for international coordination. This convention has yet become law, as only two of a required five states have ratified it.

The effect of the Medicrime Convention is limited as its membership is restricted to EU members, although non-members can adhere to it. In this way, it is a euro-centric harmonization mechanism which does not include LIC-specific provisions.

International Collaboration on Enforcement

On an international level, Interpol has partnered with pharmaceutical companies to create a Pharmaceutical Crime Program. The program focuses on protecting the public by dismantling organized crime networks and raising public awareness (Interpol, *Pharmaceutical Crime*). INTERPOL is also conducting law enforcement operations bringing together customs, health regulators, national police and the private sector from countries around the world (Interpol, *Pharmaceutical Crime*). In June 2013, INTERPOL conducted operation Pangea VI, in which they seized 9.8 million potentially dangerous medicines worth approximately USD 41 million (Interpol,2013). This operation was conducted internationally over the course of a week, through the targeting of the online sale of counterfeit and illicit medicines. However, the Pharmaceutical Crime Program is not specifically targeted at the sale of substandard medicines in LICs.

These mechanisms are dependent on domestic involvement and action within LICs. As purveyors of substandard medicines target countries with the lowest enforcement rates, an increase in regulatory measures and bodies within LICs can greatly aid the efforts of international bodies such as INTERPOL and provide an avenue for domestic consumers to report crimes.

National Enforcement

On a domestic level, enforcement measures are carried out by local law enforcement agencies. Consumers can also report substandard medicines to the national drug regulator, such as the Medicines and Healthcare Products Regulatory Agency (UK) or the Food and Drug Administration (US). The World Health Organization has developed guidelines for the development of measures to combat counterfeit medicines. The guidelines outline steps for developing national strategy to halt counterfeit drugs and increase inspection of medicines (Department of Essential Drugs and Other Medicines, 1999).

Despite the useful framework provided by the guidelines, the substandard drug trade has not subsided since their publication. Guidelines of this type must be used in collaboration with strengthening political will, promulgating legislation and establishing a national drug authority.

Communication and Education

A number of organizations have been involved in increasing communication about substandard medicines and educating the public, health professionals and regulators. The World Health Organization has been active in establishing the International Medical Products Anti-Counterfeiting Taskforce ("IMPACT") in

2006 (IMPACT, *About Us*), and the Member State Mechanism on Substandard/Spurious/Falsely-Labelled/Falsified/Counterfeit Medical Products in 2012 (WHO, 2012). IMPACT is a task force which produces a variety of documents relating to legislation, regulatory infrastructure, enforcement, communication and technology to combat substandard medicines. The Member State Mechanism has added to the knowledge pool by identifying the actions, activities and behaviors which result in illegitimate medicines (WHO, *Report A/MSM/2/2*, 2013).

Both government agencies (Food and Drug Administration, 2013; MHRA, 2013) and industry bodies (Pharmaceutical Security Institute, 2014; The Partnership for Safe Medicines, 2014) have been involved in increasing awareness and providing information about counterfeiting, although these efforts appear directed to developed countries. Roundtable participants noted the importance of the sharing of knowledge and communication between the public, healthcare workers and regulators in LICs—a vital aspect to developing knowledge and spurring action on substandard medicines.

Unresolved Issues

Some overarching issues stemming from the mechanisms previously discussed include the need to facilitate political will and intergovernmental partnerships in LICs (Kahn *et al*., 2012). The majority of mechanisms described above involve high and middle-income countries rather than their LIC counterparts. Action within LICs and their inclusion in international frameworks is necessary to combat cross-border crime. Furthermore, for those states with domestic measures, increased collaboration between domestic and international mechanisms is advised. These measures all require political will, capacity and funding to implement—difficult tasks for any LIC.

Furthermore, more research regarding substandard medicines is needed as the prevalence of substandard medicines is still the result of informed guesses (Attaran *et al*., 2012, p. 2). To aid this, the Roundtable considered the benefits of giving the public access to the Pharmaceutical Security Institute's database of medicine crimes in order to increase transparency of their occurrence (Attaran *et al*., 2012; Pharamceutical Security Institute, *About Us*). In this vein, increased regulation and supervision by the government would also allow for a better understanding of the extent of the substandard medicines trade as well as mechanisms to restrict it.

There is also a cause for developing an international harmonisation of practice and law to combat substandard medicines. Buckley and Gostin have advocated for a "soft law" approach involving the creation of an international code of practice to be implemented by the WHO (Gostin *et al*., 2013). This would aid in coordinating regulatory, customs and law enforcement agencies. The code would also harmonize terminology and provide guidance for surveillance, collection of data and supporting low and middle income countries. This system could be implemented on a domestic level by regulatory bodies (as in the case in China) and then expanded through international collaboration.

Attaran and co-workers have argued that a binding international treaty to combat illegitimate medicines should be implemented as it would complement existing trade treaties and raise the status of public health (Attaran *et al*., 2012). The proposed treaty would set an international definition for the different types of illegitimate medicines, create public health crimes to aid prosecution, mandate international cooperation between states and provide administrative assistance to encourage the regulation of medicines in developing countries (Attaran *et al.*, 2012). The Roundtable noted that an international mechanism of this nature would also aid in avoiding the territorial jurisdictional issues that currently make prosecution difficult, as states may be unwilling to cooperate with enforcement proceedings.

Improving Obtainability

The ability to obtain existing medicines within LICs is limited by an inadequate healthcare system, a lack of infrastructure and regulation, domestic mark-ups and social barriers (Smith and Yadav, 2011,

pp. 10–11). At the outset, a patient will not access medicines if they are not aware of their illness or possible treatments. This requires basic healthcare infrastructure, such as medical practitioners, a treatment area and a distribution point for medicines.

LICs spend drastically less on financing healthcare systems than high-income countries, and have much fewer doctors per capita. LICs spend on average 5.4% of their GDP on financing healthcare systems, where high-income countries spend more than 11% (IFPMA, 2012b). The numbers of physicians are similarly dismal as LICs have on average 2.8 physicians per 10,000 inhabitants, in comparison to 28.6 in high-income countries (IFPMA, 2012b). This deficit is within an environment where there are widespread infectious diseases and emerging chronic illness (WHO, 2008, p. 6). The lack of doctors and healthcare workers in LICs reduces the possibility of preventative medicines and diagnosis.

However, the doctors, hospitals and pharmacies that do exist are often located in and around urban areas, and moreover may be few and far between in rural regions. Thus, as nearly 70% of the population in LICs lives in rural areas, the nearest medical practitioners, hospital or distribution point may be too costly and time consuming to travel to for medicines (Mehrotra and Jarrett, 2002, p. 1686). A study done in Lusaka, Zambia found that 50% of patients attended hospitals if they were within 5 km of their homes, but only 2% attended if they were between 30 km and 44 km away (Brenneman and Kerf, 2002). Even if medicines make it to a particular community, they may often be distributed via open air markets, or by unregulated pharmacies. In LICs, the pharmaceutical wholesale market is "excessively fragmented, making for] poor coverage and] traceability" (Smith and Yadav, 2011, p. 11). In this way, the lack of physical infrastructure physically restricts access to medicines (IFPMA, 2012b, p. 23).

Furthermore, when the patient arrives at the distribution point, the mark-up on the medicine may be prohibitively large so that its purchase is either not possible, or will plunge them (further) below the poverty line. Mark-up costs include: import tariffs, port charges, clearance and freight fees, pre-shipment inspection fees, pharmacy board fees, importers' margins, VAT, central government tax, state government tax, wholesaler mark-ups and retail mark-ups (IFPMA, 2012b, pp. 23, 29). These costs are on top of the drug manufacturer's price and any insurance premiums. While some additional costs are necessary to ensure that an efficient and reliable supply chain is maintained, LICs often suffer from exorbitant mark-ups on medicines (Cameron *et al*., 2009, p. 246; IFPMA, 2012b, pp. 28–29; MDG Gap Task Force, 2008). For example, in 2007 patients in Uganda experienced internal mark-ups from 30% to 66% in the public sector, and 100% to 358% in the private sector (Cameron *et al*., 2009, p. 246; IFPMA, 2012b, pp. 23, 29). While the reduction of the manufacturer's price tends to have the biggest impact on reducing the final cost to the patient, that impact is lessened in situations where mark-ups are a large proportion of the cost of the drug.

Lastly, even if medicines are obtainable, patients may not choose to use them due to the unfamiliarity or because of former adverse reactions. Social and cultural contexts influence access to medicines, as patients may be wary of a one-pill solution when previously they have used natural medicine or religious healers. Some individuals do not use modern medicine at all, with cultural and social influences playing the primary role in the choice of provider (Mehrotra and Jarrett, 2002, p. 1686). Others may avoid medical attention as they face social stigma and wish to avoid harassment. This behavior hastens the advancement of their illness, puts others at risk of contracting the illness, and reduces their income-generating capacity (IFPMA, *The Changing Landscape on Access to Medicines*, 2012, p. 38). Additionally, victims of colonial history may also be suspicious of medicines gifted or emanating from those who previously were in a position of dominance. Finally, the existence of substandard medicines further erodes public confidence in western medicines and the health system, erecting a further barrier for treatment (WHO, 2012).

Initiatives

The initiatives designed to correct these distributional difficulties are varied. They include low-cost interventions, task-shifting, efficient regulation, grass-roots health services and education. These

mechanisms aim to work within areas that are resource- and regulation-deficient, utilizing more efficient processes.

Low-Cost Interventions

Roundtable participants discussed the success of low-cost interventions to treat HIV in Mozambique and Nigeria via the President's Emergency Plan for AIDS Relief ("PEPFAR"). (PEPFAR, *About PEPFAR*) HIV treatment requires up to three or more different drugs and intensive monitoring—things previously thought to be very difficult to deliver in areas where patients are undiagnosed and fail to have their basic needs of housing, food and clean water met. However, with appropriate protocols, infrastructure and training, medicinal treatment of HIV was delivered (PEPFAR, *Latest Results*). The Roundtable noted that the protocols, infrastructure and training used in HIV treatment, could be developed into formal guidelines for use with other diseases (Carothers *et al*., 2013).

Potential pitfalls with low-cost interventions are ensuring that each intervention is specifically designed with the particular delivery community in mind, as protocols will change not only between diseases, but also with location. It is important to have personnel who are not only experienced in delivering low-cost interventions, but also versatile and able to react positively to changes and challenges. Furthermore, some Roundtable participants noted that low-cost interventions must be designed in a sustainable way, not purely dependent upon volunteers and donations.

Task-Shifting

Due to the short supply of doctors in LICs, "task-shifting" has occurred whereby there is a redistribution of tasks from doctors to trained healthcare workers. Task-shifting has been recommended by the WHO to rapidly increase the health workforce relating to HIV and other health services (WHO, 2008). This process involves the movement of specific tasks from highly qualified workers to those with shorter training and fewer qualifications, in order to make more efficient use of the available human resources for health (WHO, 2008, p. 2). For example, in Mozambique, 90% of rural Caesarean sections are performed by non-physician surgeons (Pereira *et al*., 2007). The WHO has prepared guidelines for task-shifting HIV treatment, which outlines the tasks that are involved in the prevention, care and treatment of HIV and AIDS, and notes those which can be performed by medical doctors, non-physician clinician, nurse and community health workers (with appropriate training and supervision) (WHO, 2008, pp. 51–63). The results are encouraging, and show that the large burden of medical tasks does not need to be performed by medical doctors.

A prerequisite to task-shifting is its adoption by the state as a public health initiative, as it will need to be set-up utilizing a legal framework. The quality of care will also need to be ensured through proper training, oversight and inspection. Furthermore, health workers will need to be monetarily rewarded, in order to maintain the sustainability of the project (WHO, 2008, p. 4). In this way, there needs to be political will, capacity and financing to implement this initiative.

Efficient Regulation

Traditional methods of government regulation of medicine distribution include inspections and licensing systems. Inspections may be problematic, as they can be an expensive form of regulation in that they require significant time and experienced staff (Mok, 2010, p. 511). While licensing sifts out unqualified distribution businesses by setting standards for compliance, it can also be administratively expensive, cumbersome and used to extort (Mok, 2010, p. 511).

With the limited budgets of LICs, use of more flexible and less time- and money-consuming methods will extend the impact of regulatory mechanisms. Mok and co-workers recommend the following low-cost mechanisms, as supported by their successful use in OECD countries: formal warnings, public disclosure, use of sanctions, alternative dispute resolution, use of ombudsmen,

self-regulation and public–private cooperation (Mok, 2010, pp. 511–18). While no method is a fix-all solution, these more efficient methods used in a holistic format can be a better use of limited capacity and resources.

However, a risk of utilizing these methods is that they may fail to deter improper behavior, or that criminals will evade public scrutiny through corrupt government officials. To mitigate these risks, there needs to be dedicated political will, capacity, financing and oversight. International cooperation could also be utilized to develop proper infrastructure and protocols.

Grass-Roots Health Service Provision

Mehrotra and Jarrett recommend utilizing Grass Roots Organisations (GROs) as a channel for promoting economic and social development to address societal health problems (Mehrotra and Jarrett, 2002, p. 1688). A GRO is distinct from an NGO, in that it is made up of interested parties coming together for self-help (as opposed to interested parties coming together to help others) (Mehrotra and Jarrett, 2002, p. 1688). Mehrotra and Jarrett note that GROs are more effective than NGOs as they allow for the community (Hurlburt, 2012, p. 36) to actively participate in the public services of the state, putting greater pressure on the state to effectively treat patients (Hurlburt, 2012).

An example organization is the Bamako Initiative, which has been implemented in some areas of sub-Saharan Africa since the late 1980s. The Bamako Initiative has been successful in decentralizing decision-making from the government to the district level, and instituting community financing and management of basic health services. The aim is to improve health services through generating enough income to maintain consistent supply, health workers and incentives. As the income does not travel back to the national government, but instead remains within the community (controlled by a locally elected health committee) patients can become more than mere recipients and manage their own health care (Hurlburt, 2012). The Bamako Initiative has been successful in raising sustained immunization levels and enabling nearly half of the rural population in Benin and Guinea to regularly use healthcare (Mehrotra and Jarrett, 2002, p. 1689). The potential for similar programs has also arisen in India where local self-government institutions (panchayati raj institutions—PRIs) provide the opportunity for the community to exert its influence on the government providers.

However, the sustainability and effectiveness of GROs depends upon proper implementation and social inclusiveness. Review of GROs has shown that there is a tendency for local elites to direct the action of the committee, leaving other, marginalized, groups out (1689–91). As a result, widespread community empowerment has not occurred as marginalized groups are not participating. Like the other initiatives, proper implementation and structure depends upon political will, capacity and financing.

Education

To combat cultural wariness of Western medicines and the social stigma attached to certain illnesses, educational programs such the Positive Action Programme have been implemented (Viiv Healthcare, *Community Partnerships*). These programs work to address disease-related stigma and promote the use of healthcare treatments, especially for those within marginalized groups (ViiV Healthcare, 2011). Additionally, measures to combat and reduce the existence of substandard medicines, as discussed in Pt IV, should be implemented. The existence of these "medicines" only harms the reputation of western medicine and the health system generally.

Education programs should be objective and holistic, in that they address not only the benefits of medicine use, but also preventative measures to reduce the need for medical attention. Raising a person's health literacy can have a large impact on one's health as it "will help them better interact with medical staff, understand prescriptions and make lifestyle choices that lead to better health and well being" (IFPMA, *The Changing Landscape on Access to Medicines*, 2012).

Unresolved Issues

An underlying requirement of the above initiatives is political will, capacity and funding. Political commitment is the lifeblood of public health, and its focus will benefit the already strained budgets of LICs as "after improvement to basic sanitation, access to clean water and immunization, access to pharmaceuticals is one of the most cost-effective health-related measures" (IFPMA, *The Changing Landscape on Access to Medicines*, 2012; Simoens, 2012). Furthermore, a healthy workforce is better able to contribute to the national economy, increasing GDP. The benefits of increasing access to medicines outweigh initial outlays in financing in the long term.

The previously discussed initiatives also highlight the importance of tailored mechanisms for change. Tailored mechanisms are more effective as they complement the actions of the existing healthcare systems, government organizations, NGOs and GROs (Hurlburt, 2012, p. 35). As there is no system which will work across all LICs, adaptability and information sharing is crucial.

Lastly, the socio-economic determinants of health must be recognized. Adequate nutrition (Koethe *et al*., 2009), sanitation and clean water are important to ensuring good health as their deficiency puts individuals at higher risks of acquiring diseases. Under-nutrition contributes to at least 1/3 of all childhood deaths, usually in combination with an infectious disease (Centers for Disease Control and Prevention, 2011; IFPMA, *The Changing Landscape on Access to Medicines*, 2012, p. 49). Unclean water and unsanitary conditions cause a variety of diseases including cholera, typhoid, parasitic worms and intestinal diseases (IFPMA, *The Changing Landscape on Access to Medicines*, 2012, p. 41). Thus, a holistic approach to health treatment, which includes medicinal access while ensuring adequate nutrition, clean water and sanitation, is necessary for the efficient use of limited medicine repositories.

Conclusion

As this paper has shown, the Roundtable discussed and reflected on a wide array of issues pertaining to access to medicines. These issues ranged from the effectiveness of the patent system to drug delivery in rural areas. The broad variety of topics considered highlights the complexity of the problem, and confirms the need for a multi-disciplinary approach to improving access to medicines in LICs.

Despite the vast range of issues that affect the availability, affordability, efficacy and obtainability of medicines, some overall themes do arise. First, political will, capacity and funding within LICs must be directed at improving access to medicines. Without domestic efforts, the actions of local, foreign and multi-national organizations will falter. Secondly, many of the alternative approaches to incentivizing R&D into medicines specifically for LICs are addressed to the private sector. This confirms that the role of private sector R&D companies in improving access to medicines in LICs is vital, and must be supported. Thirdly, greater understanding of the pharmaceutical marketplace is warranted. Evidence of rent-seeking behavior by patentees, collusive arrangements between research and generic companies, and intentional lack of transparency in price negotiations, indicate that great care is needed in regulating this marketplace if accessibility is to be maximized.

It was the intention of the Roundtable participants that their deliberations would provide a contribution to knowledge in the field, and a resource for future considerations of the issue. The Annex sets out some specific topics warranting further research that were identified at the Roundtable and subsequently.

Annex: Potential Areas for Further Research

Improving Availability

The Roundtable discussed the difficulty of incentivizing the commercial R&D market where the end-user is unlikely to be able to afford the medicine. Research on the relative success of the

various non-patent incentives for investing in the development of medicines specific to LICs is warranted. Such research might involve case studies to determine which incentives did and didn't work, and why.

"Open access" research is commonly thought to be more efficient, thereby reducing R&D costs—and, presumably, making it more likely to occur. However, there is little, if any, empirical evidence establishing whether this is in fact the case. Research on this issue is warranted. It might include an exploration of the utilization of patent pools in developing new medicines.

The existence of a human right to health may impose obligations on certain stakeholders to actively engage in R&D for LIC-focused medicines. Research on the link between human rights and corporate social responsibility would be desirable.

Improving Affordability

The Roundtable discussed whether drug patents had the net effect of hindering or spurring innovation. Further research into the existence and effect of patents on important medicines is desirable. This research should explore the effect of patents on drug prices and on follow-on R&D.

A potential problem with differential pricing of medicines is arbitrage—that is, the diversion of the medicines from LICs back to high-income countries. Research is warranted on whether trademark rights provide an effective mechanism for preventing such arbitrage.

The Roundtable noted that it would be useful to compare the availability and price of a single important medicine in multiple countries, and to identify the different regulatory processes and purchasing practices adopted in each country. Doing so may provide insight into the processes and practices that improve access to medicines.

The Roundtable noted the lack of transparency about what regulatory approvals, and what IP rights, have been granted in relation to particular medicines. Research is desirable on the means for increasing transparency. One possible topic for exploration is the practicality of creating a database on important medicines, detailing the existent of regulatory approvals, patents, supplementary protections and related matters.

Improving Efficacy

The Roundtable noted that more information is needed regarding the prevalence of substandard medicines on the market, as the majority of knowledge is reliant upon "informed guesses". Empirical pharmacology research to determine the prevalence is warranted. One approach would be to sample drugs from multiple countries and test their quality.

There is an international trade in substandard medicines. One area of potential research is to investigate the methods that will foster political will for establishing intergovernmental partnerships to combat this illegal trade. The research might evaluate the current international collaborative initiatives, to identify the incentives and barriers to international collaboration.

Improving Obtainability

The Roundtable noted that the protocols, infrastructure and training used in HIV–AIDS treatment may be suitable for use with respect to other diseases. Research is warranted into developing guidelines that transfer the experience of successful delivery of HIV–AIDS treatment to the delivery of other diseases prevalent in LICs.

Throughout the paper, the need for political will, capacity and financing was highlighted. It would be desirable to know what methods drive political will, development of capacity and disbursement of funds in LICs in relation to health. Research on this issue could be conducted utilizing a cross-country comparison of practices in LICs.

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Notes

1. The contributing participants were: Amir Attaran, University of Ottawa; Marie Bismark, University of Melbourne; Andrew Christie, University of Melbourne; Ellen Wright Clayton, Vanderbilt University; Daniel Gervais, Vanderbilt University; Douglas Heimburger, Vanderbilt University; Aidan Hollis, University of Calgary; Aaron Kesselheim, Harvard Medical School/Brigham and Women's Hospital; James Love, Knowledge Ecology International; Megha Patel, Bill and Melinda Gates Foundation. All participants attended in a personal capacity. The authors gratefully acknowledge the assistance of Debora Halbert, University of Hawaii, in organising the Roundtable.
2. For clarity, we have used the World Bank's terminology for low income economies. Low-income countries are those which have a gross national income per capita of US $1,035 or less.
3. Neglected tropical diseases (NTDs) are a group of tropical infections which are especially widespread in low-income countries. These diseases cause between 500,000 and 1 million deaths annually, and have a larger disease burden than HIV/AIDS. WHO has identified 17 NTDs: buruli ulcer, chagas disease, dengue/severe dengue, dracunculiasis (guinea-worm disease), echinococcosis, foodborne trematodiases, human African trypanosomiasis (sleeping sickness), leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis (river blindness), rabies, schistosomiasis, soil transmitted helminthiases, taeniasis/cysticercosis, trachomas and yaws (endemic treponematoses).
4. Defining the term "consumer" in this context (hospitals, doctors and patients) would warrant a more extensive discussion but it is neither necessary nor possible to do so in the context of this paper.
5. Health expenditure per capita is the sum of public and private health expenditures as a ratio of total population. It includes the provision of health services, family planning activities, nutrition activities and emergency aid designated for health but does not include provision of water and sanitation.
6. Impoverishing has been defined by the authors as pushing the patient below an income level of US$2 per day when purchasing the medicine.
7. As discussed in Part II.
8. The key elements of discovery are disease mapping, isolation of target points on diseases, identification of "hit' molecules and transforming them into "lead series". While we recognize that Non Communicable Diseases have a rapidly increasing influence on LICs, we have chosen to focus the discussion on NTDs which uniquely impact LICs.

9. Although these numbers are only estimates, as no voucher has been sold on the market.
10. Recently, the FDA has approved priority review status to Impavido(R) for the treatment of leishmaniasis. If the drug is approved by the FDA, a PRV will be awarded to Paladin.
11. Executives of seven for-profit companies pursuing active R&D of a drug or vaccine that would likely receive a PRV upon approval.
12. Least developed countries are those defined by the United Nations Office of the High Representative for the Least Developed Countries, Landlocked Developing Countries and the Small Island Developing States, as of November 2010.
13. See reference for a discussion of how R&D investment falls in response to high levels of market uncertainty, but that patent protection partially mitigates the influence of uncertainty.
14. It is also interesting to note that for lower-income countries such as India which have a booming R&D market, their investments became less targeted towards the health needs of low income nations over time.
15. For example, two NZ patients made national attention when they were refused renal dialysis, in what the media described as a "death sentence".
16. The reference provides examples of how the three usual patentability criteria (novelty, inventive step and industrial applicability) can be used differently.
17. The reference provides a focus on non-communicable diseases.
18. We define human rights as a set of formal law-based systems and obligations, such as formal UN treaties and declarations, expert reports, domestic court decisions, regional court decisions and civil society proclamations, as well as normative claims about human flourishing and development.
19. An example of such an international mechanism is the Committee on Economic, Social and Cultural Rights, which examines the extent to which countries are achieving their obligations under the *International Covenant on Economic, Social and Cultural Rights*. *There are similar committees to monitor the implementation of the Convention on the Elimination of All Forms of Discrimination against Women and the Convention on the Rights of the Child.*
20. Namely, Burma, Cambodia, China, Lao People's Democratic Republic, Thailand and Vietnam.
21. The value of the illegal antimalarial drug market in West Africa is estimated to exceed 400 million.
22. One incident in Pakistan did not go unnoticed however, where 120 people died after taking a poorly made isosorbide mononitrate.
23. This issue arises as patents are issued on a domestic basis, thus a patent for a drug may exist in the US, but if it is not patented within Thailand, a generic form can be legally distributed.
24. The major regulatory bodies include the Federal Drug Administration (US), the European Directorate for the Quality of Medicines and HealthCare (EU), the Medicines and Healthcare Products Regulatory Agency (UK), the Therapeutic Goods Administration (Australia), Drugs Control Administration (India) and the Therapeutic Products Directorate (Canada).
25. Review the reference for an overview of methods employed by the United States, United Kingdom, Europe, China, Russia, Brazil and India.

References

Abbott. (2013) *Global Citizenship Report*. Available at http://prod2.dam.abbott.com/global/documents/pdfs/abbott-citizenship/globalreports/Abbott_longform_report.pdf [Accessed on November 10, 2014].

Almog D.M (2005) 'Drug Industry in "Depression"'. *Medical Science Monitor*, 11(1), SR 1–4.

Amin T. and Kesslheim A. (2012) 'Secondary Patenting of Branded Pharmaceuticals: A Case Study of How Patents on Two HIV Drugs Could be Extended for Decades', *Health Affairs*, 31(10), 2286–94.

Anley, P. (2013) quoted in L. Daniels, *New Draft South African IP Policy Receives Initial Positive Reactions* [online]. Intellectual Property Watch. Available at http://www.ip-watch.org/2013/09/09/new-south-african-ip-policy-receives-initial-positive-reactions/?utm_source=post&utm_medium=email&utm_campaign=alerts [Accessed on November 10, 2014].

Arie, S. (2012) 'Contaminated Drugs are Held Responsible for 120 Deaths in Pakistan', *British Medical Journal* [online], 344:e951. Available at http://dx.doi.org/10.1136/bmj.e951 [Accessed on November 10, 2014].

Attaran, A., Barry, D., Shamnad, B., Bate, R., Benton, D., Chauvin, J., Garrett, L., Kickbusch, I., Kohler, J., Midha, K., Newton, P., Nishtar, S., Orhii, P. and McKee, M. (2012) 'How to Achieve International Action on Falsified and Substandard Medicines', *British Medical Journal* [online], 345:e7381. Available at http://www.bmj.com/content/345/bmj.e7381.pdf%2Bhtml [Accessed on November 10, 2014].

Baker, B., et al. (2013) Open Letter from Global Academics in Support of Proposal to Amend Brazil's Patent Law to Take Advantage of TRIPS-Compliant Flexibilities [online]. Infojustice. Available at http://infojustice.org/support-brazil [Accessed on November 10, 2014].

Balasubramaniam, T. (2012) *Wellcome Trust Tells WHO it Opposes R&D Treaty and the De-Linkage of R&D Costs from Drug Prices* [online]. Knowledge Ecology International. Available at http://keionline.org/node/1608 [Accessed October 28, 2014].

Bayer. (2014) *Bayer is committed to fight the Chagas disease* [online]. Bayer. Available at http://www.bayer.com/en/chagas-disease.aspx [Accessed on November 4, 2014].

Boldrin M. and Levine D. K. (2013) 'The Case Against Patents', *Journal of Economic Perspectives*, 27(1), 3–22.

Brennan H., Distler R., Hinman M. and Rogers A. (2013) 'A Human Rights Approach to Intellectual Property and Access to Medicines'. Yale Law School and Yale School of Public Health, Global Health Justice Partnership, Policy Paper No. 1. Available at http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2323144 [Accessed on November 10, 2014].

Brenneman A. and Kerf M. (2002) Infrastructure and Poverty Linkages: A Literature Review. Available at http://www.ilo.org/wcmsp5/groups/public/–-ed_emp/–-emp_policy/–-invest/documents/publication/wcms_asist_8281.pdf [Accessed on November 10, 2014].

Buckley G.J. and Gostin L.O. (eds.) (2013) *Countering the Problem of Falsified and Substandard Drugs*. The National Academies Press, Washington, DC.

Burci G. L. (2009) 'Public/Private Partnerships in the Public Health Sector', *International Organizations Law Review*, 6, 359–82.

Cameron A., Ewen M., Ross-Degnan D., Ball D. and Laing R. (2009) 'Medicine Prices Availability and Affordability in 36 Developing Middle-Income Countries: A Secondary Analysis', *The Lancet*, 373, 240–49.

Carothers C., Heimburger D., Schlachter S., Gardner P., Primack A., Warner T. and Vermund S. (2013) 'Training Programs Within Global Networks: Lessons Learned in the Fogarty International Clinical Research Scholars and Fellows Program', *The American Journal of Tropical Medicine and Hygiene*, 90(1), 173–79.

Carpenter J. (2004) A Review of Drug Quality in Asia with Focus on Anti-Infectives [online]. US Pharmacopeia. Available at http://pdf.usaid.gov/pdf_docs/PNADH154.pdf [Accessed on November 10, 2014].

Centers for Disease Control and Prevention. (2011) Ten Great Public Health Achievements – Worldwide (2001–10) [online]. Centers for Disease Control and Prevention. Available at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6024a4.htm [Accessed on November 10, 2014].

Cernuschi T., Furrer E., Schwalbe N., Jones A., Berndt E. and McAdams S. (2011) Advance Market Commitment for Pneumococcal Vaccines. *Bulletin World Health Organization* 89, 913. Available at http://www.who.int/bulletin/volumes/89/12/11-087700/en/ [Accessed November 4, 2014].

China Food and Drug Administration. Database of Approved Active Pharmaceutical Ingredients and API Manufacturers in China (CFDA). Available at http://app1.sfda.gov.cn/datasearcheng/face3/base.jsp?tableId=85&tableName=TABLE85&title=Database%20of%20approved%20Active%20Pharmaceutical%20Ingredients%20(APIs)%20and%20API%20manufacturers%20in%20China&bcId=136489131226659132460942000667 [Accessed on November 10, 2014].

Christie A., Dent C., McIntyre P., Wilson L. and Studdert D. (2013) 'Patents Associated with High-Cost Drugs in Australia', *PLoS One* [online], 8(4), 1–7. Available at http://dx.doi.org/10.1371/journal.pone.0060812 [Accessed on November 10, 2014].

Commission on Intellectual Property Rights. (2002) Integrating Intellectual Property Rights and Development Policy. Commission on Intellectual Property Rights. Available at http://www.iprcommission.org/papers/pdfs/final_report/ciprfullfinal.pdf [Accessed on October 27, 2014].

Commission on Intellectual Property Rights, Innovation and Public Health. (2006) Public Health, Innovation and Intellectual Property Rights. World Health Organization, Geneva. Available at http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf?ua=1 [Accessed on October 27, 2014].

Committee on Economic, Social and Cultural Rights. (2000) General Comment No 14, The Right to the Highest Attainable Standard of Health (Article 12 of the Covenant) [online]. Available at http://tbinternet.ohchr.org/_layouts/treatybodyexternal/Download.aspx?symbolno=E%2fC.12%2f2000%2f4&Lang=en [Accessed on November 10, 2014].

Convention on the Elimination of All Forms of Discrimination against, 1 March 1980, United Nations Treaty Series, vol 1249.

Convention on the Rights of the Child, 20 November 1989, United Nations Treaty Series, vol. 1577.

Czarnitzki D. and Toole A. (2011) 'Patent Protection Market Uncertainty, and R&D Investment', *The Review of Economics and Statistics*, 93(1), 147–59.

Daniels L. (2013) Comments Received to South Africa's Process for New IP Policy [online]. Intellectual Property Watch. Available at http://www.ip-watch.org/2013/11/18/comments-received-to-south-africas-process-for-new-ip-policy/ [Accessed on November 10, 2014].

Department of Essential Drugs and Other Medicines (1999) *Counterfeit Drugs: Guidelines for the Development of Measures to Combat Counterfeit Drugs*. Geneva: World Health Organization.

Department of Trade and Industry. (2013) *Draft National Policy on Intellectual Property (IP) of South Africa: A Policy Framework*. Available at http://www.ip-watch.org/weblog/wp-content/uploads/2013/09/SA-IP-Policy-Sept-2013-36816_gen918.pdf [Accessed on November 10, 2014].

Farlow A. W. K. (2005) 'Accelerating the Innovation of Vaccines: Can the Global HIV Vaccine Enterprise, Malaria Vaccine Initiatives, and Purchase Commitments Deliver?', *Innovation Strategy Today*, 1(2), 154–65.

Farlow A. W. K., Light D.W., Mahoney R. and Widdus R. (2005) 'Concerns Regarding the Centre for Global Development Report "Making Markets for Vaccines"', *Submission to Commission on Intellectual Property Rights, Innovation and Public Health*. Available at http://www.andrewfarlow.com/cipih1may2005.pdf [Accessed on November 4, 2014].

Feek C., McKean W., Henneveld L., Barrow G., Edgar W. and Paterson R. (1999) 'Experience with Rationing Health Care in New Zealand', *British Medical Journal*, 318(7194), 1346–48.

Flynn S. (2008) Appeal of Thailand Commission Order on Abbott's Refusal to Sell AIDS Medications in Thailand [online]. Available at http://www.wcl.american.edu/pijip/thai_comp_licenses.cfm [Accessed on November 10, 2014].

Flynn S., Hollis A. and Palmedo M. (2009) 'An Economic Justification for Open Access to Essential Medicine Patents in Developing Countries', *Journal of Law, Medicine & Ethics: Pharmaceutical Regulations*, 37(2), 2–25.

Food and Drug Administration. (2013) Counterfeit Medicine online]. Food and Drug Administration. Available at http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/CounterfeitMedicine/default.htm [Accessed on November 10, 2014].

GAVI Alliance. (2013) Pneumococcal AMC [online]. GAVI Alliance. Available at http://www.gavi.org/funding/pneumococcal-amc/ Accessed on October 28, 2014].

General Assembly resolution 217A(III), A/810 (10 December 1948), Health and Disability Services Act 1993, s5 (NZ).

Gervais D. (2013) 'TRIPS & Development', *SAGE Handbook on Intellectual Property*. In: David M, and Halbert D (eds). SAGE, London, UK.

Gervais D. (2014) 'Patentability Criteria as TRIPS Flexibilities: The Examples of China and India', In: Bagley M and Okediji R (eds), *Patent Law in a Global Perspective*. Oxford University Press, Oxford, UK, pp. 541–569.

Global Alliance for TB Drug Development. (2014) Operating Model [online]. TB Alliance. Available at http://tballiance.org/about/operating-model.php [Accessed on November 10, 2014].

Gold E. R. (2013) 'Patents and Human Rights: A Heterodox Analysis', *The Journal of Law, Medicine and Ethic*, 41(1), 185–98.

Gold E. R., Kaplan W., Orbinski J., Harland-Logan S. and N-Marandi S. (2010) 'Are Patents Impeding Medical Care and Innovation?', *PLoS Medicine*, 7(1), e1000208. Available at http://dx.doi.org/10.1371/journal.pmed.1000208 Accessed on November 4, 2014].

Gostin L., Buckley G. and Kelley P. (2013) 'Stemming the Global Trade in Falsified and Substandard Medicines', *Journal of the American Medical Association*, 309, 1693–94.

Hurlburt S., Mann C., Byam P., Linnander E., Bradley E. and Berman P. (2012) Developing Primary Health Care Delivery in Lower and Middle Income Countries: Challenges Faced and Lessons Learned. Report on the Expert Policy Consultation, July 30–31.

Ilg M. (2010) 'Market Competition in Aid of Humanitarian Concern: Reconsidering Pharmaceutical Drug Patents', *Chicago-Kent Journal of Intellectual Property*, 9, 149–78.

International Covenant on Economic, Social and Cultural Rights, 19 December 1966, United Nations Treaty Series, vol. 993.

International Convention on the Elimination of All Forms of Racial Discrimination, 7 March 1966, United Nations Treaty Series, vol. 660.

International Covenant on Economic, Social and Cultural Rights, 19 December 1966, United Nations Treaty Series, vol. 993.

IMPACT. About Us [online]. World Health Organisation. Available at http://www.who.int/impact/about/en/ [Accessed on November 10, 2014].

Infojustice. (2013) *Brief Technical Overview of Brazil's CNY Proposed Patent Law Reforms*. [online]. Infojustice. Available at http://infojustice.org/wp-content/uploads/2013/10/Brief-Technical-Review-of-Brazilian-Leglislation.pdf [Accessed on November 10, 2014].

InnoCentive. (2008) Challenge Solution: TB Alliance Works to Eradicate One of the World's Deadliest Diseases [online]. InnoCentive. Available at https://www.innocentive.com/challenge-solution-tb-alliance-works-eradicate-one-world%E2%80%99s-deadliest-diseases [Accessed October 28, 2014].

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). (2011) Data Exclusivity: Encouraging Development of New Medicines [online]. IFPMA. Available at http://www.ifpma.org/fileadmin/content/Publication/IFPMA_2011_Data_Exclusivity__En_Web.pdf [Accessed on November 4, 2014].

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). (2012a) The Changing Landscape on Access to Medicines. Available at http://www.ifpma.org/fileadmin/content/Publication/2012/ChangingLandscapes-Web.pdf [Accessed on November 10, 2014].

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). (2012b) The Pharmaceutical Industry and Global Health: Facts and Figures 2012 [online]. IFPMA. Available at http://www.ifpma.org/fileadmin/content/Publication/2013/IFPMA_-_Facts_And_Figures_2012_LowResSinglePage.pdf [Accessed on November 4, 2014].

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). (2012c) 'The Threat of False Friends: Joining Efforts to Protect Patients Against Online Sales of Fake Medicines'. Available at http://www.ifpma.org/fileadmin/content/Publication/2012/FIP-IFPMA_brochure._The_threat_of_false_friends._Joining_efforts_to_protect_patients_against_online_sales_of_fake_medicines.pdf [Accessed on November 10, 2014].

International Network for Economic, Social & Cultural Rights. (2012) Human Rights Enforcement Mechanisms of the United Nations [online]. Available at http://www.escr-net.org/docs/i/405650 [Accessed on November 10, 2014].

Interpol. Pharmaceutical Crime [online]. Interpol. Available at http://www.interpol.int/Crime-areas/Pharmaceutical-crime/Pharmaceutical-crime [Accessed on November 10, 2014].

Interpol. (2013) International Operation Targets Online Sale of Illicit Medicines [online]. Interpol. Available at http://www.interpol.int/News-and-media/News-media-releases/2013/PR077 [Accessed on November 10, 2014].

IRIN. (2013) The Controversy Over 'Counterfeit' Drugs [online]. IRIN News. Available at http://www.irinnews.org/report/98866/the-controversy-over-counterfeit-drugs [Accessed on November 10, 2014].

Joint Research Centre, Directorate-General for Research and Innovation. (2011) Monitoring Industrial Research: The 2011 EU Industrial R&D investment Scoreboard (2011) [online]. European Commission. Available at file:///C:/Users/Caitlin/Downloads/The%202011%20EU%20Industrial%20R&D%20Investment%20Scoreboard.pdf [Accessed on November 4, 2014].

Kahn U., Kreutzer S., Gill J. and Taylor D. (2012) 'Falsified Medicines and the Global Public's Health', *Report of Matrix Insight and UCL School of Pharmacy*. Available at http://www.ifpma.org/fileadmin/content/Publication/2012/UCL-Matrix_Insight-Falsified_Medicines_and_the_Global_Publics_Health.pdf [Accessed on November 10, 2014].

Kardas-Nelson M. (2013) Brazil's Sick CNY of Patent Exploitation [online]. Mail & Guardian. Available at http://mg.co.za/article/2013-10-11-00-brazils-sick-of-patent-exploitation [Accessed on November 6, 2014].

Kesselheim A. S. et al. (2011) '"Pay for Delay" Settlements of Disputes over Pharmaceutical Patents', *The New England Journal of Medicine*, 365(15), 1533.

Kiddell-Monroe R., Iversen J. H. and Gopinathan U. (2013) Medical R&D Convention Derailed: Implications for the Global Health System [online]. Journal of Health Diplomacy. Available at http://www.ghd-net.org/sites/default/files/Medical%20R%20and%20D%20Convention%20Derailed%20-%20Implications%20For%20The%20Global%20Health%20System.pdf [Accessed on October 28, 2014].

Koethe J., Chi B., Megazzini K., Heimburger D. and Stringer J. (2009) 'Macronutrient Supplementation for Malnourished HIV-Infected Adults: A Review of the Evidence in Resource-Adequate and Resource-Constrained Settings', *Clinical Infectious Diseases*, 49(5), 787–98.

Lanjouw J. (2005) Patents, Price Controls and Access to New Drugs: How Policy Affects Global Market Entre. Working Paper No 11321, Centre for Global Development. Available at http://nber.org/papers/w11321 [Accessed on October 27, 2014].

Lanjouw J. and MacLeod M. (2005) 'Pharmaceutical R&D for Low-Income Countries: Global Trends and Participation by Indian Firms', *Economic and Political Weekly*, 40(39), 9–17.

Light D. W. (2005) 'Making Practical Markets for Vaccines', *Public Library of Science Medicine*, 2(10), Available at http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0020271#pmed-0020271-g001 [Accessed November 4, 2014].

Light D. W. (2009) *Advanced Market Commitments: Current Realities and Alternate Approaches*. Amsterdam: Health Action International Europe.

Light D. W. and Warburton R. (2011) *Demythologizing the High Costs of Pharmaceutical Research*. [online]. Biosocieties. Available at http://www.pharmamyths.net/files/Biosocieties_2011_Myths_of_High_Drug_Research_Costs.pdf [Accessed on November 4, 2014].

Light D. W. and Warburton R. (2012) *Pharmaceutical R&D's Costly Myths*. [online]. PLOS Blogs. Available at http://blogs.plos.org/speakingofmedicine/2012/03/07/pharmaceutical-rds-costly-myths/ [Accessed November 4, 2014].

Lipkus N. (2006) 'How to Understand Product Development: Public-Private Partnerships as Vehicles for Innovation in Combating Neglected Disease', *Michigan State University Journal of Medicine & Law*, 10, 385–427.

Manning J. M. (2011) 'The Herceptin Interception: New Zealand's Pharmac and the Herceptin Funding Issue', *New Zealand Law Review*, 4, 663–714.

Max Foundation. Gilvec International Patient Assistance Program [online]. Max Foundation. Available at http://themaxfoundation.org/gipap/default.aspx [Accessed on November 4, 2014].

MDG Gap Task Force (2008) 'Access to Affordable Essential Medicines', in *Delivering on the Global Partnership for Achieving the Millennium Development Goals*.' New York: United Nations Report.

Mehrotra S. and Jarrett S. (2002) 'Improving Basic Health Service Delivery in Low-Income Countries: "Voice" to the Poor', *Social Science & Medicine*, 54(11), 1685–90.

Merck. (2013) 25 Years: Merck Mectizan® Donation Program [online]. Merck. Available at http://www.merck.com/about/featured-stories/mectizan1.html [Accessed on November 4, 2014].

Merck. (2014) Merck Medical Outreach Program [online]. Merck. Available at http://www.merckresponsibility.com/access-to-health/merck-medical-outreach-program/ [Accessed on November 4, 2014].

MHRA. (2013) Winning the War Against Counterfeits [online]. MHRA. Available at http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Adviceandinformationforconsumers/counterfeitmedicinesanddevices/Casestudies/index.htm [Accessed on November 10, 2014].

Mok E. et al. (2010) 'Implementing Public Health Regulations in Developing Countries: Lessons from the OECD Countries', *Journal of Law, Medicine and Ethics*, 38(3), 508–19.

Moodie P., Metcalf S. and McNee W. (2003) 'Response from PHARMAC: Difficult Choices', *The New Zealand Medical Journal*, 116(1170), 1–6.

Molyneux D., Hotez P.J. and Fenwick A. (2005) '"Rapid-Impact Interventions": How a Policy of Integrated Control for Africa's Neglected Tropical Diseases Could Benefit the Poor', *PLoS Medicine*, 2(11), 1064–70.

Muller-Langer F. (2011) *Neglected Infectious Diseases: Are Push and Pull Mechanisms Suitable for Promoting Research?* Max Planck Institute for Intellectual Property and Competition Law, Working Paper.

News Medical. (2011) *What are Neglected Diseases?* [online]. News Medical. Available at http://www.news-medical.net/health/what-are-neglected-diseases.aspx [Accessed October 27, 2014].

Newton P., McGready R., Fernandez F., Green M., Sunjio M., Bruneton C., Phanouvong S., Millet P., Whitty C., Talisuna A., Proux S., Christophel E., Malenga G., Singhasivanon S., Bojang K., Kaur H., Palmer K., Day N., Greenwood B., Nosten F. and White N. (2006a) 'Manslaughter by Fake Artesunate in Asia: Will Africa Be Next?', *PLoS Medicine* [online], 3(6), e197. Available at http://dx.doi.org/10.1371/journal.pmed.0030197 [Accessed on November 10, 2014].

Newton P., Green M., Fernández F., Day N. and White N. (2006b) 'Counterfeit Anti-Infective Drugs', *The Lancet Infectious Diseases*, 6(9), 602–13.

Niens Lauren M, Cameron A., Van de Poel E., Brouwer Werner B. F. and Laing R. (2010) 'Quantifying the Impoverishing Effects of Purchasing Medicines: A Cross-Country Comparison of the Affordability of Medicines in the Developing World', *PLoS Medicine*, 7(8), e1000333. doi: 10.1371/journal.pmed.1000333

Oke E. K. (2013) 'Using the Right to Health to Enforce the Corporate Responsibilities of Pharmaceutical Companies with Regard to Access to Medicines', *Journal of Health Diplomacy*, 1(1), 1–15.

Orach C. (2009) 'Health Equality: Challenges in Low Income Countries', *African Health Sciences*, 9(Suppl 2), S49–S51.

Organization for Economic Co-operation and Development (OECD). (2005) Drug Spending in OECD Countries Up by Nearly a Third Since 1998, According to New OECD Data [online]. Organization for Economic Co-operation and Development. Available at http://www.oecd.org/general/drugspendinginoecdcountriesupbynearlyathird-since1998accordingtonewoecddata.htm [Accessed October 27, 2014].

Park C., Prabhala A. and Berger J. (2013) 'Using Law to Increase Treatment Access in South Africa: An Analysis of Patent, Competition and Medicines Law', *United Nations Development Programme*. Available at http://www.undp.org/content/dam/undp/library/hivaids/English/using_law_to_accelerate_treatment_access_in_south_africa_undp_2013.pdf [Accessed on November 6, 2014].

Pereira C., Cumbi A., Malalane R., Vaz F., McCord C., Bacci A. and Bergstrom S. (2007) 'Meeting the Need for Emergency Obstetric Care in Mozambique: Work Performance and Histories of Medical Doctors and Assistant Medical Officers Trained for Surgery', *British Journal of Obstetrics and Gynaecology*, 114(12), 1530–33.

Pharmaceutical Security Institute. (2014a) Safe Medicines [online]. Pharmaceutical Security Institute. Available at http://www.psi-inc.org/safeMedicines.cfm [Accessed on November 10, 2014].

Pharmaceutical Security Institute. (2014b) About Us [online]. Pharmaceutical Security Institute. Available at http://www.psi-inc.org/index.cfm [Accessed on November 10, 2014].

Plahte J. (2012) 'Is the Pneumococcal Vaccine Advance Market Commitment Motivating Innovation and Increasing Manufacturing Capacity? Some Preliminary Answers', *Vaccine* 30(14), 2462–66.

PRWeb. (2013) *Layoffs in Pharmaceutical Industry due to Productivity Crisis in R&D; CBCD Offers a New Technology*. [online]. PRWeb. Available at http://www.prweb.com/releases/2013/10/prweb11222203.htm [Accessed on November 4, 2014].

Pugatch M. (2011) 'Patent Pools and Collaborative Initiatives: Assessing the Efficacy of Alternatives to IP in the Development of New Pharmaceutical Drugs, Especially for Neglected Diseases - An Empirical Analysis', *European Journal of Risk Regulation*, 4, 566–71.

Pugatch M., Chu R. and Torstensson D. (2012) *Assembling the Pharmaceutical R&D Puzzle for Needs in the Developing World*. Commissioned by International Federation of Pharmaceutical Manufacturers and Associations. Available at http://www.ifpma.org/fileadmin/content/Publication/2012/Assembling_the_RD_puzzle_FINAL.pdf [Accessed October 27, 2014].

Ridley D., Grabowski H. and Moe J. (2006) 'Developing Drugs for Developing Countries', *Health Affairs*, 25(2), 313–24.

Robertson A., Stefanakis R., Joseph D. and Moree M. (2012) 'The Impact of the US Priority Review Voucher on Private-Sector Investment in Global Health Research and Development', *PLoS Neglected Tropical Diseases*, 6(8), e1750. Available at doi: 10.1371/journal.pntd.0001750 Accessed on November 4, 2014].

Saez C. (2013) *New EU Customs Regulation Might Allow Wrongful Seizures of Generic Drugs in Transit, NGOs Say*. [online]. Intellectual Property Watch. Available at http://www.ip-watch.org/2013/10/17/new-eu-custom-regulation-might-allow-wrongful-seizures-of-generic-drugs-in-transit-ngos-say/?utm_source=post&utm_medium=email&utm_campaign=alerts [Accessed on November 10, 2014].

Sakhia S. (2013) *Paladin Receives Priority Review Status from FDA for Impavido® NDA Submission*. [online]. Paladin Labs, Inc. Available at http://online.wsj.com/article/PR-CO-20130619–909846.html [Accessed on November 4, 2014].

Scannell J. W., Blanckley A., Boldon H. and Warrington B. (2012) 'Diagnosing the Decline in Pharmaceutical R&D Efficiency', *Nature Reviews Drug Discovery*, 11(3), 191–200.

Serafino D. (2007) *Survey CNY of Patent Pools Demonstrates Variety of Purposes and Management Structures*. [online]. Knowledge Ecology International Research Note 6. Available at http://keionline.org/content/view/69/1 [Accessed on November 4, 2014].

Scudellari M. (2011) 'Are Advance Market Commitments for Drugs a Real Advance?', *Nature Medicine*, 17(2), 139.

Shakoor O., Taylor R. B. and Behrens R. H. (1997) 'Assessment of the Incidence of Substandard Drugs in Developing Countries', *Tropical Medicine & International Health*, 2(9), 839–45.

Simoens S. (2012) 'What Is the Value for Money of Medicines? A Registry Study', *Journal of Clinical Pharmacy and Therapeutics*, 37(2), 182–86.

Smith L. and Yadav P. (2011) 'Improving Access to Medicines for Non-Communicable Diseases through Better Supply Chains', In: Galambos L and Sturchio J (eds), *Addressing the Gaps in Global Policy and Research for Non-Communicable Diseases, P 9-L 12*. Available at IR http://www.ifpma.org/fileadmin/content/Publication/2013/Johns_Hopkins_Addressing_the_Gaps_in_Global_Policy_and_Research_for_NCDs.pdf [Accessed on November 10, 2014].

Stefanakis R., Robertson A.S., Ponder E.L. and Moree M. (2012) 'Analysis of Neglected Tropical Disease Drug and Vaccine Development Pipelines to Predict Issuance of FDA Priority Review Vouchers over the Next Decade', *PLoS Neglected Tropical Diseases*, 6(10), e1803. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3493373/pdf/pntd.0001803.pdf [Accessed November 4, 2014].

Sutar M., Gawhane D. and Tenpe C.R. (2013) 'Study of Drug Regulatory Approval Process an Comparative Requirement of Common Technical Documents (CTD) in Europe, USA and India in Coordination with Drug Developmental Process', *International Journal of Pharmaceutical Sciences Review and Research*, 20(2), 68–79.

Sutton M. (2013) *Pay for Delay: The US Supreme Court Rules on CNY Reverse Patent Settlements*. [online]. Mondaq. Available at http://www.mondaq.com/australia/x/248706/Patent/Pay+for+delay+The+US+Supreme+Court+rules+on+reverse+patent+settlements [Accessed on November 6, 2014].

The Partnership for Safe Medicine (2011) *Counterfeit Drug Incident Encyclopedia*. [online]. The Partnership for Safe Medicines. Available at http://www.safemedicines.org/nigeriabound-hivaids-drugs-seized-in-netherlands.html [Accessed on November 10, 2014].

The Partnership for Safe Medicines (2014) *Working Together to Protect the Safety of Your Prescription Drugs*. [online]. Available at http://www.safemedicines.org/ Accessed on November 10, 2014].

The US President's Emergency Plan for AIDS Relief (PEPFAR). About PEPFAR [online]. Office of US Global AIDS Coordinator and the Bureau of Public Affairs, US State Department. Available at http://www.pepfar.gov/about/index.htm [Accessed on November 10, 2014].

The US President's Emergency Plan for AIDS Relief (PEPFAR). Latest Results [online]. Office of US Global AIDS Coordinator and the Bureau of Public Affairs, US State Department. Available at http://www.pepfar.gov/funding/results/index.htm [Accessed on November 10, 2014].

Thomas B. and Gostin L. (2013) 'Tackling the Global NCD Crisis: Innovations in Law and Governance', *The Journal of Law, Medicine and Ethics*, 41, 16–27.

Treatment Action Campaign (2013) *DTI's Draft IP Policy Lays Foundation to Prevent Abusive Patenting*. [online]. Fix CNY the Patent Laws. Available at http://www.fixthepatentlaws.org/?p=657.

United Nations Office on Drugs and Crime (2009) *Transnational Trafficking and the Rule of Law in West Africa: A Threat Assessment*. Available at http://www.unodc.org/documents/data-and-analysis/Studies/West_Africa_Report_2009.pdf [Accessed on November 10, 2014].

Vacca R. (2013) *Intellectual Property and Public Health - A White Paper*. Akron Research Paper No. 13-11, School of Law, University of Akron.

ViiV Healthcare. Community Partnerships [online]. ViiV Healthcare. Available at http://www.viivhealthcare.com/community-partnerships.aspx [Accessed on November 10, 2014].

ViiV Healthcare. (2011) ViiV Healthcare's Positive Action and the International HIV/AIDS Alliance Tackle HIV Stigma in Six Central American Countries [online]. ViiV Healtcare. Available at http://www.viivhealthcare.com/media/press-releases/2011/february/viiv-healthcare%E2%80%99s-positive-action-and-the-international-hivaids-alliance-tackle-hiv-stigma-in-six-central-american-countries.aspx [Accessed on November 10, 2014].

Yadav P. (2010) 'Differential Pricing for Pharmaceuticals: Review of Current Knowledge, New Findings and Ideas for Action', *Study Conducted for the UK Department for International Development (DFID)*. Available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/67672/diff-pcing-pharma.pdf [Accessed on November 4, 2014].

Watal J. (2000) 'Pharmaceutical Patents, Prices and Welfare Losses: Policy Options for India under the WTO TRIPS Agreement', *World Economics*, 23(5), 733–52.

White-Guay B. (2011) 'Regulation of Medicines in Low and Middle-Income Countries: Current Challenges and Future Prospects', In: Galambos L and Sturchio J (eds), *Addressing the Gaps in Global Policy and Research for Non-Communicable Diseases*. Report of the IFPMA Non-Communicable Diseases Working Group pp. 4–8.

World Bank (2013) *Health Expenditure Per Capita*. [online]. World Bank. Available at http://data.worldbank.org/indicator/SH.XPD.PCAP [Accessed October 27, 2014].

World Bank *How Does the World Bank Classify Countries*. [online]. World Bank. Available at http://datahelpdesk.worldbank.org/knowledgebase/articles/378834-how-does-the-world-bank-classify-countries [Accessed on October 27, 2014].

World Health Organization (WHO) (2001) Report of the Workshop on Differential Pricing & Financing of Essential Drugs. Available at http://apps.who.int/medicinedocs/en/d/Jh2951e/1.html [Accessed November 4, 2014].

World Health Organization (WHO) (2003) *The 17 Neglected Tropical Diseases*. [online]. World Health Organization. Available at http://www.who.int/neglected_diseases/diseases/en [Accessed October 27, 2014].

World Health Organization (WHO) (2004) *The World Medicines Situation*. Available at http://apps.who.int/medicinedocs/pdf/s6160e/s6160e.pdf [Accessed October 27, 2014].

World Health Organization (WHO) (2008) *Task Shifting: Rational Redistribution of Tasks Among Health Workforce Teams*. Geneva: World Health Organization.

World Health Organization (WHO) (2009) *Counterfeits FAQ*. [online]. World Health Organization. Available at http://www.who.int/medicines/services/counterfeit/faqs/QACounterfeit-October2009.pdf [Accessed on November 10, 2014].

World Health Organization (WHO) (2010) *Working to Overcome the Global Income of Neglected Tropical Diseases*. Available at http://whqlibdoc.who.int/publications/2010/9789241564090_eng.pdf [Accessed on October 28, 2014].

World Health Organization (WHO) (2012) *Spurious/falsely-labelled/falsified/counterfeit (SFFC) medicines (fact sheet)*. [online]. World Health Organization. Available at http://www.who.int/mediacentre/factsheets/fs275/en/ [Accessed on November 10, 2014].

World Health Organization (WHO) (2013) *Neglected Tropical Diseases*. [online]. World Health Organization. Available at http://www.who.int/neglected_diseases/en/ [Accessed on October 27, 2014].

World Health Organization (WHO). (2013) 'Report of the Steering Committee of the Member State Mechanisms on Substandard/Spurious/Falsely-Labelled/Falsified/Counterfeit Medical Products, including the Draft Workplan as Proposed by the Steering Committee'. Report A/MSM/2/2. Available at http://apps.who.int/gb/ssffc/pdf_files/A_MSM2_2-en.pdf [Accessed on November 10, 2014].

World Health Organization (WHO) Commission on Macroeconomics and Health (2001) *Macroeconomics and Health: Investing in Health for Economic Development*. World Health Organization. Available at http://whqlibdoc.who.int/publications/2001/924154550x.pdf [Accessed on October 27, 2014].

World Health Organization (WHO) Consultative Expert Working Group on Research and Development: Financing and Coordination (2012) *Research and Development to Meet Health Needs in Developing Countries: Strengthening Global Financing and Coordination*. World Health Organization. Available at http://www.who.int/phi/CEWG_Report_5_April_2012.pdf?ua=1 [Accessed on October 28, 2014].

World Health Organization (WHO), World Intellectual Property Organization (WIPO) and World Trade Organization (WTO) (2012) *Promoting Access to Medical Technologies and Innovation: Intersections between public health, intellectual property and trade*. Available at http://www.wto.org/english/res_e/booksp_e/pamtiwhowipowtoweb13_e.pdf [Accessed on November 11, 2014].

World Intellectual Property Organization (WIPO) *Guiding Principles of WIPO Re:search*. [online]. World Intellectual Property Organization. Available at http://www.wipo.int/research/en/about/guiding_principles.html [Accessed on November 4, 2014].

World Intellectual Property Organization (WIPO) (2013) *R&D, Innovation and Patents*. [online]. Available at http://www.wipo.int/patent-law/en/developments/research.html [Accessed on November 4, 2014].