

Pharmaceuticals and Global Health Policy:

Medicines, Markets, Manufacturers, and Medical Countermeasures

One-day workshop, 9 June 2016, University of Sussex

Workshop Summary

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The importance of safe, effective and affordable medicines for global health has long been recognised. However, in a rapidly globalising world of emerging public health threats, interconnected markets and increasingly complex trade and property rights rules, a number of questions are becoming prominent around the role of pharmaceuticals in global health security. Global health security can be thought of as the capacities required for countries to respond to emerging (or re-emerging) public health threats and reduce the risk of these threats crossing borders. The risk is believed to be particularly high for low- and middle-income countries with underfunded and less-developed systems.

How can the research and development of drugs for new health threats located in distant – and often neglected – parts of the world be guaranteed? How can we ensure that the world stockpiles enough of the right drugs and should the pharmaceutical industry be responsible for this? Would global and local markets be able to live up to these new needs? What could be the equity and sustainability implications of such new aspects for pharmaceuticals, and what role is there for governments to make sure that standards are upheld and the right incentives are in place?

On 9 June 2016 a workshop addressed these concerns, ‘Medicines and Markets: the Role of Pharmaceuticals in Global Health Policy’, co-hosted by the Institute of Hygiene and Tropical Medicine of Lisbon and the Centre for Global Health Policy of the University of Sussex. Across four panels and 12 presentations, UK-based and international experts from diverse academic disciplines presented and discussed ongoing research work on pharmaceuticals and health security, the global supply of medicines, the political economy of manufacturing pharmaceuticals in lower-middle-income countries (LMICs), and on Anti-Microbial Resistance (AMR) in resource-poor settings.

A number of key issues were explored in discussing the relevance of pharmaceuticals in this health security domain. First of all, the emergent **pluralistic international order** – with the rise of India and China in particular – has important ramifications for the way that health security threats can be managed in the future. Global security efforts must be reconciled with the needs of many other countries around the world – needs that may be at odds with the particular interests of the Western and U.S. pharmaceutical industry. In particular, the relevance of medical countermeasure development for the world must be balanced with improving access to existing medicines.

Analysing the evolution of the political economy of **patents for medicines**, the role of patent implementation for the availability of pharmaceutical products, and the effect of a national patent

systems' discontinuity, evidence was shown that governments' early choices in setting up national patent system carry an influence for the current availability of drugs, length of patents and introduction of generics. As the world is entering a post-transition period for TRIPS implementation, this creates the need to better understand the changes happening right now in the implementation of patents, the launch of generics, and the development of trade patterns in emerging economies like India, that happen to play a key role in the global supply of medicines.

The influence of countries home to large pharmaceutical sectors was also highlighted, balancing the international need to discover new molecules with the **host country's needs** to innovate and develop local capacity. The role of African countries in particular were flagged as increasingly influential in defining a global health and medicines agenda, as 'global' health security can only be achieved through 'local' health security and local economic development. To guarantee all this, the right economic incentives must be harnessed in local pharmaceutical markets, so that the most needful medicines get produced. Interestingly, a need was also identified to find a common way of dealing with pharmaceuticals and medical devices when discussing global health security, as the latter are an often neglected case of dependency and insecurity could be made for less industrialised countries.

Finally, considering the impact of the widespread attention on **anti-microbial resistance (AMR)** for low-income countries, it was highlighted how this raises significant concerns around ensuring the access and the right to antibiotics for the poor. In order not to jeopardize the substantial health gains made in the past, thanks to the availability of antibiotics in low-income countries, an international agreement must be reached as to how newly developed antibiotics will be used. It was suggested that the debate should therefore shift from restricting the use of antibiotics in low-income settings to how to achieve a just and sustainable use by focusing on its governance. Some of the key problems that must be addressed in managing this balance between continued access and the efficacy of newly developed medicines include: understanding community perceptions of antibiotics and their use, the role of informal providers in dispensing antibiotics, and understanding more clearly the role that antibiotic use in animals plays in generating resistant bacteria in humans.

Panel 1 - Pharmaceuticals and Global Health Security

This panel explored the relationship between pharmaceuticals and global health security. Against the background of government concern with health-based threats such as pandemics and bioterrorism, pharmaceuticals have become incorporated into national security strategies. However, special challenges begin to emerge when pharmaceutical and security logics intermesh. Many of these challenges were exposed through investigations into the case of the antiviral medication *Tamiflu*, which was stockpiled by governments in response to the threat of pandemic flu. Economic challenges focused predominantly on the lack of a natural commercial market around which a business case can be made. This has made it less attractive for pharmaceutical companies to invest in this area, exacerbating the late stage development challenge already present in drug development. Regulatory issues, challenges in demand management, distribution, liability and data also arose.

The second presentation reviewed the most sophisticated attempts to overcome these challenges that have arisen in the United States. The Biomedical Research and Development Authority (BARDA) supports the development of medical countermeasures which are stockpiled and released in response to a bioterrorist attack. Key policy interventions that have arisen in conjunction with this development have included the setting aside of public funds – \$5.6 billion in the form of Project BioShield dedicated to the development of medical countermeasures. This pull incentive was complimented by the creation of BARDA and its core services that act as developmental support mechanisms for the small to medium sized biotech companies that are interested in this area of medical countermeasure production. A number of other policy interventions have been introduced to overcome the challenges of drug development including liability protection for drug producers, the animal efficacy rule for the regulatory approval of drugs that cannot be tested for efficacy in humans and the use of unapproved drugs during an emergency, broadening the portfolio of drugs that can be used.

The third presentation examined BARDA's response to the recent Ebola crisis and the way collaborations could be structured to respond to future outbreaks. A vision for a more sustainable response to emerging infectious disease was outlined. It is one that seeks to move past the boom and bust cycle of Research and Development funding and development for outbreak responses by focusing on long term investments in technologies, platforms and institutions required to respond quickly and effectively to the next outbreak. Such efforts must ensure equitable access to developing countries and the pooling of funds to support a long term approach. A mechanism of prioritisation for the allocation of resources has emerged into a two pronged strategy: 'just in case' and 'just in time'. 'Just in case' prioritises pathogens and develops them to the latest stage possible, enabling the rapid scale up to clinical trials should the pathogen emerge. 'Just in time' is a long term project focused on the development of technology platforms such as vaccine delivery to be mobilised in response to an outbreak. There is a third aspect of this approach, which seeks to develop an organisation like BARDA to coordinate efforts in the field and develop drugs on a global scale. Such efforts must also be able to interface with organisations both upstream and downstream. Initial efforts have taken the form of a coalition offering funding to support this business plan.

Panel 2 - The Global Supply of Medicines: TRIPs, Generics, Pharmaceutical Companies Old and New

This second panel explored the global supply of medicines, specifically looking at the post-transition period equilibria in Trade-Related-Intellectual-Property-Rights (TRIPs) in emerging economies, and on new partnerships for the research and development of medicines. Firstly, it analysed the evolution of the political economy of medicine patents, the role of patent implementation and its effect on pharmaceutical products, and the effect of continuity and discontinuity in national patent systems. In the 1970s and 80s the countries of Western Europe and the Organization for Economic Cooperation and Development (OECD) started to allow pharmaceutical patents. This began with the establishment of patent law in the United States, United Kingdom, France and Western Germany in 1970. In understanding the policy choices regarding how and when pharmaceutical patents should be introduced, research has shown that early choices matter, particularly with patent implementation and in understanding the effects of policy choices. A lot of decisions made by countries in the 1990s about how and when they should introduce pharmaceutical patents triggered all sorts of consequent reactions within the state, industry and society. When new issues emerged in the 2000s in relation to what will be done about this system, in light of the adoption of these pharmaceutical patents and on issues of price and access, these decisions were made in the shadows of earlier choices. Countries that tried to change course in the 2000s from regulations adopted in the 1990s have found that those originally adopted have not only triggered certain changes but also enabled and complicated consequent options.

With regards to the discursive and institutional development of global health governance and global health security, some evidence was shown that national governments' early choices in setting up a country's patent system had an influential effect on the current availability of drugs, length of patents and introduction of generics. As the world is entering a post-transition period for TRIPs implementation, evidence was shown of a radical change in the way medicine patents were implemented and generics were launched in emerging economies, particularly in India. In this area product development partnerships are very important and often formed of public-private partnerships. The second presentation analysed the product development partnerships that have emerged in the last fifteen years in quite a range of areas including HIV/AIDS, neglected tropical diseases and antimicrobial resistance. These partnerships are seen as the answer to the failure of the conventional model of pharmaceutical development. The last twenty years in the field of neglected tropical diseases we have seen the emergence of between a dozen and thirty product development partnerships launching roughly fifty drugs, vaccines and diagnostics. Market failure has often been cited as the reason for the emergence of these partnerships. The political demand of governments and private organisations for medicines has generated a crucial change and market failure on the demand side of production. In talking about market failure we are talking about a change in political demand made on the basis of social and health justice and on the basis of security. Product development partnerships have emerged then as the institutional

response set out to match the political demand with the financial incentives. These partnerships have launched a lot of products and impacted lives positively, though they have considerable limitations. Foremost, they still rely on the idea that we need to incentivise companies to invest in a field that is essentially not commercially interesting.

The third presentation investigated how the rise of countries such as India and China will impact health security and the global supply of medicines. India has come to dominate the global supply of generic medicine, it is the third largest supplier of medicines in the world and is often referred to as the pharmacy of the developing world. The impact new patent regimes may have on this supply of medicines has generated concerns. Questions have also been raised as to the quality of the medicines produced and the degree to which countries benefit from India's production in the creation of innovative South-South trade of medicines as India splits its pharmaceutical exports roughly equally between the global north and global south. Looking at the South-South dynamics of the Indian industry two competing perspectives have emerged. There is the win-win South-South trade promoted by the Indian industry and the Indian government and major international health organisations such as Medicines Sans Frontier. Perspectives that have questioned this have focused on the variable quality of supply and the emerging dynamics within sub-Saharan Africa where policy makers are increasingly keen on local pharmaceutical production. The dominance of the Indian industry in these areas, shaped by early choices, can actually crowd out efforts to promote local manufacturing production capacity and can lead to a position of health insecurity.

Panel 3 - The Political Economy of Developing Local Health Technology Capacity: What Role for African Countries in Shaping Global Health Security

This panel looked at global health security in an African health care context and explored the links between security and the production of medical devices and biologicals, going beyond the narrow notion of health technologies as solely pharmaceuticals. Through the three presentations it was argued that in spite of some of the recent global health events originating from low-income locations, African countries have so far had little influence on the global discourse on health security. By strengthening their local health technology and manufacturing capabilities African countries may better contribute to global health security by rapidly responding to emerging health issues.

The first presentation examined the role of medical devices, bringing the view that it is necessary to go beyond pharmaceuticals when addressing global health security issues. It also outlined the need to develop a common way of dealing with pharmaceuticals and medical devices. Medical devices play a key role not only in diagnosis but also in administration. Access to affordable and appropriate devices has proved to be a challenge for middle and low income countries. Most of the producers of medical devices are based in developed countries, with few having any sort of presence in low income nations. Developed countries dominate the production of high technology products with low income countries dominating in low technology products. The supply of devices to low income countries often comes through import and donation. Almost 80% of medical devices used in sub-Saharan Africa have been donated. Imports in low income countries are often ten times higher than their exports. Products imported from developed countries have predominantly been designed for their own markets and may have little suitability for local conditions. The majority of this equipment is out of use and has created a mismatch in terms of what is supplied and what is needed. Going forward, the key challenges of low and middle income countries include addressing the issue of a lack of regulation and enforcement capabilities from regulatory authorities. The lack of entrepreneurship and the absence of a national health technology policy must also be addressed in addition to supporting and developing a research ecosystem.

The role of African countries in developing local biologicals/vaccines production and innovation capabilities was subsequently discussed, as well as its link to health security. By asking what will happen when it will no longer makes sense for countries such as India to make medicines for Africa, the second presentation analysed Africa's dependence on India for its pharmaceutical security. It also

asserted that vaccine production is a key element of biosecurity as many of the threats we face come from viruses, and that this is an area of neglect for developing countries but one that Africa could contribute to. The manufacture of pharmaceuticals in Africa was argued to be connected to issues of economic and industrial development, health system strengthening, technology transfer and up scaling, while in Sub-Saharan Africa most countries manufacturing capabilities are focused on formulation and its activities. Some governments in this area have introduced policies ensuring that locally produced drugs are prioritised to protect innovation in that sector. In this way local policy was introduced to protect local industry. The value of local industry in strengthening local health systems and health security is often overlooked by global health and international health concepts, as well as the importance of proximity of production to increase a country's R&D system to respond to changing local needs. These concepts, in contrast to public health which is concerned with issues of international justice, emphasise transnational health issues and the colonial management of disease. This is despite the fact that many transnational issues must be addressed at a local level. Global value chains and production networks are perceived as having the capability and agility to spring into action in response to a global pandemic. History tells us differently, and also shows us how African countries are often overlooked when it comes to the allocation of medicines in an emergency. Such realisations bring into focus the need for these countries to project their own capacity in relation to organisational, dynamic, technical, finance and innovation capabilities that need to be developed if Africa is to support itself in vaccine production.

The third presentation on the political economy of local health security contrasted the idea of 'global' vs 'local' health security with the importance of keeping the right economic incentives in the local pharmaceutical markets to make sure the most needed drugs get researched, developed and manufactured. The case of Tanzania was given as the 'perfect storm of unintended consequences', where health sector and pharmaceutical firms have been caught up in a storm of globalisation pressures that have shifted market structures. The health sector there has shifted towards much more donor support and a large rise in import dependence. Firms have been experiencing increasing price pressure including falling import prices from second-tier Indian generics producers. This has been particularly dramatic in antibiotics and has wiped out almost all the local production of basic antibiotics in the country. There have also been rising barriers to market access in all market segments for the locally based firms. Local firms, having lost their basic market for drugs, also lose income for investment purposes making it more and more difficult to survive. These events occurring over the last six years, have led to a disaggregation of domestic economic linkages which were already fragile in a very low-income economy. Firms whose core market was the domestic market, would previously invest in distributions systems and fill in supply gaps commercially with imports. As these economic linkages were broken, those economic incentives that help drive economic development were undermined. This disaggregation in Tanzania happened in both the health and industrial sectors and has impeded the development of the country.

The key idea developed in this session was that the way to improve global security is through local security, and that can be best pursued through local economic development. The sovereign ability to drive its own economic development was lost as a consequence in Tanzania. A rethinking of the connections between health system functioning and industrial development can help drive economic development and security.

Panel 4 - Health Markets: Delivering Pharmaceutical Innovation for Low-income Settings

This panel considered the challenge of antimicrobial resistance (AMR) with a specific focus on low income settings, and the importance of guaranteeing access to antibiotics for the poor when discussing pharmaceuticals resistance. AMR is seen as a growing public health challenge; however, it cannot be forgotten that the most important successes in maternal mortality, the burden of disease reduction and general life expectancy in low-income settings were achieved through the increase in access to antibiotics. The new movement towards limiting AMR spear-headed in the UK by the O'Neill report should not compromise the gains made in the past thanks to the 'liberal' use of antibiotics by the poor.

The same report also seems to suggest that pharmaceutical companies should be forced to invest in discovering new antibiotics, and then foregoing the potential financial reward from launching them in the markets, in order to keep these new molecules as second or third-line treatment. The report seems to ignore that new antibiotics could be easily reverse engineered and produced by Chinese and Indian pharmaceutical firms. This means that the development of these drugs, if they are to remain efficacious, has to take place within a global agreement on restricted use. Access to antibiotics currently in use must also be just and fair, as well as sustainable, to ensure global and national action. The public expectation of access to antibiotics should be acknowledged in relation to the incentives along the value chain that support the selling of drugs. Access to antibiotics is seen then as a global right and the efficacy of these antibiotics is a global public good which needs to be preserved. A clear tension has emerged in dealing with this issue between individual benefit, saving lives and the global public good, between security and access. Any global agreement must carry out and develop surveillance, antibiotic production and diagnostic technologies with users and local communities in mind. Communities must also be empowered to rethink their right not just to antibiotics but to effective antibiotics. Coalitions must be built that are much broader than those usually developed in global health and must include key attitude makers if it is to be a legitimate movement. By focussing on the issue of governance in this field, this session tried to move the debate on the just and sustainable use of antibiotics forward.

The supply side of antibiotics in India was analysed in the second presentation by assessing the role of informal providers in the private health sector. In rural areas there are few qualified doctors with many more informal doctors. Within the informal sector there are huge differences in personal qualification from doctor to doctor. One of the major sources of new knowledge about drugs and treatment for informal providers was qualified doctors. The main areas of knowledge and treatment for informal providers included fevers, diarrhoea and respiratory problems. Research has shown that in response to these problems antibiotics are administered for most patients and given for two to three days on average. Often antibiotics are not always given appropriately or in the right dosages. It was also found that there is an equal amount of inappropriate administration of antibiotics by formally qualified doctors as informal. Efforts are being made by state providers to recognise informal providers, certify them and give them training. Such interventions are often hampered by medical and legal barriers. As informal providers are excluded from the medico legal framework it is difficult to work with them in a systematic way. Moving forward, effective programmes must address social, behavioural and economic issues including the personal belief systems of informal providers and the community's perceptions of antibiotics. In the local market environment, doctor's prescribing culture and the influence of regulatory frameworks must also be understood in order to address this issue.

The veterinary use of antibiotics in the analysis of zoonoses was assessed in the third presentation. Zoonoses are pathogens that can cross species barriers and there is concern that antibiotic resistant bacteria found in animals may transfer over to humans. This concern has emerged following increased use of antibiotics in animal production and welfare. Antibiotics are used in Asia and many other continents to treat sick animals and as growth promoters. The growth and intensification of pig farming in Asia has increased the risk of disease amongst animals, particularly if the necessary infrastructure and bio security measures are not implemented. Antibiotics are often added to pig feed to prevent sickness from developing and spreading. The lack of regulation and labelling on the antibiotics used in feed has contributed to different antibiotics being added to feed at different times. This has raised concern that a zoonotic organism could develop resistance in this context and that it could be passed to humans, generating resistance to commonly used antibiotics. Other issues of concern have focused on the large volume of antibiotics used in animal production and on the lack of separation between antibiotics used in human medicine and in treating animals. This issue will be investigated by analysing the supply chain of drugs and the household economics of farmers and the common theme of their community understanding and perception of antibiotics. Further, by linking the social economic data of antibiotic use to the molecular microbiology of resistant genes the connection between antibiotic use in animals and the emergence of resistant genes in humans can be better understood.

All in all, this panel showed that there is increasing global agreement on the need for action to address the challenge of antimicrobial resistance. However, it also pointed to the degree to which drug

markets are unregulated in many countries. Any global agreement on investment in new drugs must be tied to action that ensures access to antibiotics and to withhold them from general use. Finally, serious global agreements are needed in order to address the global public good that efficacious antibiotics represent.

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