Publishable Summary

Access to Pharmaceuticals Project (ATP) 241839 EU FP7 Health 2009

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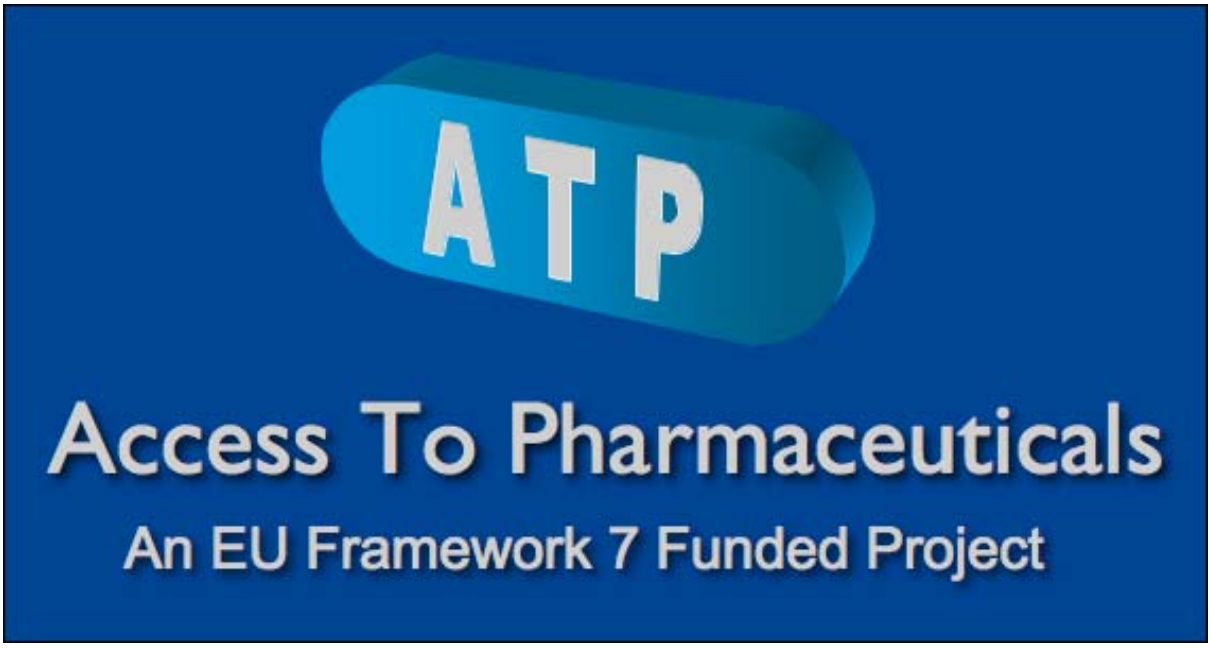

Project context and objectives

Background

Equitable access to pharmaceuticals, particularly for developing countries is an essential human right. Various complex impediments hinder access, which is the subject of ongoing multidisciplinary studies. New health technologies are needed on a continuing basis for the poor in Low and Middle Income Countries (LMIC, as defined by the World Bank). Access barriers include weak health systems, the high cost of many pharmaceutical products, resource and technological capacity constraints, lack of market incentives, market failures and intellectual property (IP) barriers. In addition there are inadequate or no technologies that can potentially address specific disease burdens in LMICs. If promising technologies, such as improved drugs suited for resource constrained settings, exist they often do not progress to full commercialisation due to perceived poor returns on investment. The private sector is often unwilling to commit resources to R&D due to insufficient market demand to develop new products.

Intellectual property regimes incentivise companies and other entities to undertake risk and invest in R&D. Increasingly, public funded research organisations across the globe aim to commercialise their research, often through patent protection. This mostly involves licensing their IP rights (IPR) to a commercial entity in order to bring a technology to the market. Typically both the licensor and licensee wish to make financial returns. In the wake of an infamous case involving the licensing of an antiretroviral drug by a university to a company,

wherein access to this essential drug for HIV patients in the developing world was initially limited, a number of universities woke up to the possibility that their licensing practices may hinder their public mission of making available globally essential health technologies conceived in public-funded research organisations (PSRO). A new concept “Socially Responsible Licensing” (SRL) began to evolve into policy and practices where some PSROs strove to balance financial against social goals to make technologies accessible and affordable to the poor.

In the last decade Product Development Partnerships (PDP) have emerged making important contributions to the development of health technologies. PDPs are a form of public private partnerships that focus on technology development for vaccines, pharmaceuticals and diagnostics. PDPs reflect a new era of partnerships in the history of health technology development in which the public and private sectors have found productive ways to collaborate where public sector incentives to promote global health are balanced with traditional industry-driven incentives to address the gaps in R&D for diseases relatively neglected by industry.

Due to increased harmonisation of IPR rules through multilateral trade agreements such as the Agreement on Trade Related Aspects of IP Rights (TRIPS) that also required new or enhanced protection of pharmaceutical IP, there were concerns raised on the effects on access to medicines in poorer World Trade Organisation (WTO) nations. Hence in the 2001 Doha Declaration on TRIPS and Public Health the WTO sought to strike a balance between IPRs and public health. TRIPS should be implemented in a manner supportive of protecting public health and promoting access to medicines for all by using ‘flexibilities’ provided in TRIPS. Compulsory licenses (CL) granted by Governments to allow the use of the patented innovation without the authorization of the right holder, is one of those ‘flexibilities’ which enables generic manufacture for national use. The provision has been used several times in LMICs to increase access particularly to treatments for HIV/AIDS. In 2003, a further decision was also adopted whereby WTO members may issue CLs, with a view to exporting patented medicines to countries with no or insufficient manufacturing capacity.

Objectives of the project

The main focus of our project was directed to the responsible management of intellectual property rights (IPR) and addressing IP barriers in a manner to promote access to affordable health technologies in LMICs. Specific objectives were:

1. Early Stage Research and Development: To develop practical models and best practices for academic policy in intellectual property (IP) management and licensing, to minimize barriers for the delivery of pharmaceutical innovation to populations in need. To work with a variety of stakeholders including Technology Transfer Officers/Offices (TTO) to develop practical and implementable best practices for identification and commercialization of pharmaceutical innovations that are of importance to health problems of disadvantaged populations.

2. Product Development: To review existing and evolving practices in Public-Private or Product Development Partnerships (PDP) and to analyze their outcomes in terms of pharmaceutical development. To analyse best practices for successful pharmaceutical partnerships in the commercialization of therapies for needs that are inadequately met by traditional industry with a particular focus on IP management by PDPs.

3. Commercial Access to Pharmaceuticals: To identify problems and develop solutions aimed at simplifying processes and removing barriers to trans-national cooperation. This was targeted towards the successful adoption and practical implementation of new legislative instruments via TRIPS to increase access to generic versions of essential patented medicines by countries with or without pharmaceutical manufacturing capacity.

Description of work and results

Our main methodologies used in research consisted of comprehensive analyses of existing literature and health initiatives to improve access to essential health technologies, interviewing or other means of gathering or sharing of information such as through questionnaires stakeholders in the global health community including academics, licensing professionals, medical professionals, pharmaceutical industry representatives, PDPs, negotiators and representatives from governmental and non-governmental organisations. Simultaneously we had an additional mission to raise awareness of global issues in access to essential medicines through several fora including the organisation of stakeholder meetings, presentations at professional associations and international conferences and several peer reviewed publications.

Although SRL has been a topic of discussion and debate elsewhere, there has been very little practical implementation in most of the PSROs in both developed and developing countries to date and SRL remains largely a theoretical issue. The US based Association for University Technology Managers (AUTM) has acted as an effective medium to disseminate and spread awareness of the importance of creative licensing policy and practices for global health. Despite this, SRL is patchily adopted by few universities and even fewer in Europe. Our surveys indicate that a majority of academics and medical professionals support the concept of SRL. One of our major results was crystallisation of a group of stakeholders, primarily technology licensing and IP experts to produce a brief guide to SRL to facilitate understanding, adoption and awareness of SRL practices. It distils a set of principles rather than attempting to be a detailed guide so that TTOs can adopt new ways of facilitating access to health technologies in their licensing practice. In other words, rather than attempt to be a “how to....” guide, it encourages creative thinking and flexibility to structure license agreements that reflect the objectives of the parties involved taking into account not only immediate commercial opportunities, but also future access needs of the poor when technologies enter the global market.

The study on PDPs captured the changes in practices for IP management in the PDP field to guarantee access. To accomplish this, some PDPs were interviewed to gain insight into how they are dealing with IP management issues such as patenting and licensing practices that can enable access. Some strategies are used by PDPs in their agreements, in order to guarantee access such as: 1) negotiating with partners the exact terms of ownership for all IP generated over the course of the project (power of negotiation) 2) when the partner retains IP rights, PDP contract will require “access commitments” for the developing countries and provision of remedies - exclusive license, *march-in rights* 3) When there is a dual market, some PDPs have exclusive or non-exclusive license to IP to commercialize in the developing countries public market and 4) in some cases, license can be a royalty free, sub licensable exclusive one which gives to the PDP rights to distribute and sell for public markets in developing countries. The ultimate goal of “access” is the availability of the product at the lowest price to ensure a sustainable supply and widest access into a given market. But how this objective is defined in practice varies considerably. It depends on some internal and external factors such

as the nature of the contributions brought by the two parties, which means power of negotiation. Generally, specific criteria for a reasonable price are set, and where possible, structures are developed to allow sales in rich markets to subsidize sales in poor markets.

Studies on CLs resulted in the following conclusions: Increasing patent protection of pharmaceuticals worldwide may enhance the importance of the TRIPS flexibility in the future. While diseases, such as HIV/AIDS, malaria or tuberculosis receive high attention and the largest part of donor funding, the prevalence of non-communicable illnesses (NCD), such as diabetes, cardiovascular diseases or cancer will grow and require improved access to cheaper and effective treatment, and CLs for NCDs have been issued by Thailand and India. Our case analyses show that the CL mechanism can impact access to medicines in the short term through increased physical access for a limited period, and in a long-term perspective through the increased competition and subsequent price reductions. However, the various CL uses also illustrate challenges that nations with the intent to apply the instrument for public health purposes may face as discussed in the next section.

Fig 1: Efavirenz: An antiretroviral drug manufactured under a compulsory licence issued by the Government of Brazil.

Conclusions and and societal impacts

Adoption of SRL practices by university technology transfer offices is a critical factor to improve access to healthcare technologies arising from public funded research. Our research reveals that a significant proportion of health technology had its origins in academic research supported by licenses granted to industry. With foresight and diligence with SRL, research

organisations can address unmet needs in underserved markets. And it also has benefits for the organisations and their licensees such as increased reputational goodwill and addressing corporate social responsibility, coupled with increased chances of funding from existing funders or philanthropic sources. Our recommendations include that funders of research projects including the EU Horizon 2020 program consider placing a requirement that grantees of projects of global health significance have access strategies and policies incorporated into proposals and projects including the use of IP to increase access and affordability of technological outputs. And that research organisations consider incorporating in their IP policy a commitment to safeguard humanitarian needs when out-licensing technology. Our handbook and the awareness we have created through diverse advocacy activities will, we hope, move in this direction.

PDPs have in many cases been successful in developing products that have been commercialised or in late stage of development by addressing effectively all components that determine innovation, namely a) the design and execution of research and development programs from preclinical studies to licensure b) analysis and planning for the marketing and distribution of new technologies in individual developing countries c) analysis and planning for the procurement and supply of new health technologies by the global health community d) planning and implementation of manufacturing capabilities e) establishment and implementation of regulatory systems to ensure safe and effective products and f) the establishment and implementation of intellectual property rights (IPR) management systems. According to our analyses and case studies IPRs are but one factor that may affect access to health technologies from PDPs, and very rarely an important factor. Nevertheless, PDPs have put IP management at the forefront of their overall innovation strategies, and access and affordability are a primary concern in IP management, unlike SRL practices by universities where access can be a secondary concern. We advocate wider sharing of access strategies between universities and PDPs to accelerate knowledge and adoption of SRL. Additionally we recommend that greater emphasis is placed on public private partnerships modelled along successful PDPs to address market failures for a wider range of diseases in LMICs, including non-communicable diseases. There is a worrying trend where public and philanthropic funding for PDPs is declining amidst a background of global economic difficulty and much care is needed not to derail such alternate models of product development.

Our case studies on CL reveal several obstacles to the issuing of CLs. Themes that emerged from these experiences include, for example, the varying interpretations and understandings with respect to the TRIPS CL conditions; the lack of operational capacities of IP offices in LMICs including implementing a CL procedure, or the fear and risk of retaliation from other stakeholders when granting a CL. Negotiation for a voluntary price reduction for efavirenz, an antiretroviral, by Brazil turned out to be very protracted and unproductive and forced Brazil to issue a CL. A particular challenge that needs to be addressed is the application of the newer CL system for the export of pharmaceutical products to countries without or insufficient manufacturing capacity. Only one company and country of import have used this provision, and the complexities in the systems both in the exporting and importing country has deterred the company from ever using this flexibility again. In addition Indian generic firms see insufficient incentives to use this new mechanism, particularly due to insufficient volumes potentially ordered. Ultimately national governments should have the capacity and the tools to address access barriers via CL in a legitimate manner during public health emergencies.

Our research is expected to have an impact also at various levels especially policy and practice in the management of IP and addressing IP barriers in a legitimate manner to increase access to essential medicines. These expected impacts will significantly narrow many of the access gaps to pharmaceuticals, but only if there is capacity building at several levels particularly in developing countries, not only in IP issues but also other determinants of access that are more important than case-specific IP barriers. It will also result in significant awareness and implementation of best practices, both for countries and institutions at the policy and practitioner level to address many problems of access to drugs.

Fig 2: The team that contributed to the Socially Responsible Licensing Handbook: Back row (L-R). Anja Meijnecht (Tilburg University, Netherlands), Stanley Kowalski (University of New Hampshire, USA), Rabogajane Busang (Medical Research Council, South Africa), Anatole Krattiger (World Intellectual Property Organisation), Ashley Stevens (Focus IP Group LLC USA). Front Row (L-R) Carol Mimura (University of California Berkley, USA), Rosemary Wolson (Council for Scientific and Industrial Research, South Africa), Harry Thangaraj (St. George's University London), Naseema Sonday (Medical Research Council, South Africa), Lita Nelsen (Massachusetts Institute of Technology, USA)

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