When access to drugs meets catch-up: insights from the use of compulsory licensing threats to improve access to ARVs in Brazil

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1. Introduction

Catch-up theories of industrial capability build-up, like macro-economic theories of growth, focus on the supply side. Sectoral catch-up studies describe pathways by which local firms accumulate capabilities within their sectoral and national innovation systems, expand their markets, and contribute to economic growth (Abramovitz, 1986; Malerba and Nelson, 2011). Catch-up is important for policy makers, because of the underlying implicit assumption that if production is increased, then its trickle-down benefits would improve access to commodities, in terms of their availability and affordability. For most products, these trickle-down benefits are left to be determined by markets, with the state being held accountable for catch-up in terms of the technological, innovative and industrial capabilities upstream, and the quality and safety of goods reaching final consumers downstream. However, for some essential commodities and services, access is also deemed to be the responsibility of the government, and not to be left to markets alone. For example, access to food, water, sanitation, medicines, education etc. as embodied in the 17 Sustainable Development Goals (SDGs), are considered as human rights, and hence, important policy goals. This leads to a question largely understudied in the catch-up literature. Can the drive to improve access to an essential commodity impact the sectoral catch-up trajectory of the corresponding industry? In order to throw light on this issue, the present paper takes a bottom-up perspective instead of a top-down view and enquires if access goals of the state can impact catch-up.

Drugs for life threatening diseases are essential commodities, whose universal accessibility is important for inclusive growth. For middle and low-income countries, which have to catch-up in pharmaceuticals, this challenge is most daunting. The manufacturing of

drugs involves two main operations in decreasing levels of complexity and knowledge intensity: production of 'active pharmaceutical ingredients' (API)[1] and drug formulation[2]. The wider the scope of technological capabilities over the production process, the higher the catch-up in pharmaceutical manufacturing. The World Health Organization reports that there are at least 126 developing countries without API production capabilities and 42 in this set have limited, or no, competence in drug formulation, relying exclusively on imports to satisfy their demand (WHO, 2011).

When a country is faced with a high disease burden and has to improve access to the corresponding drug, its response is affected by its level of catch-up and whether or not the drug is patented. The problem may become untenable, if the drug manufacturer is unwilling to supply adequate quantities at acceptable prices and/or the corresponding technology cannot be licensed from the supplier and developed independently by other firms. In such cases, Target 3b of Goal 3 of SDG affirms that governments have the right to use, to the full, the provisions in the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) regarding flexibilities to protect public health, and, in particular, provide access to medicines for all in accordance with the Doha Declaration on the TRIPS Agreement and Public Health in 2001. This includes the possibility of issuing a compulsory license.

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[1] These are the core therapeutic components of drugs. Industrial production of APIs involves development and optimization of the process, scale-up from the bench to a pilot plant, and from the pilot plant to the full-scale process.

[2] It is the preparation of final pharmaceutical products (e.g. tablets, capsules, injections, parenteral solutions). It is a relatively simple manufacturing activity wherein inputs go through a physical transformation process (e.g. grinding, mixing, dissolution, compaction), with few or no modifications of their chemical characteristics

Compulsory license or CL is a flexibility contained in TRIPS, whereby a government can permit third parties to produce the patented product without the consent of the patentee. This is a measure that has been purposefully introduced to minimize the potential negative impact of patents on access to medicines. Scholars have confirmed that the CL option empowers developing countries to negotiate prices with pharmaceutical companies more aggressively (Beall et al., 2015; Beall and Kuhn, 2012; Ramani and Urias, 2015; Shadlen, 2007; Smith et al., 2009; Stavropoulou and Valletti, 2015).

Under this context, the central questions of our paper can be redefined as follows. *For an emerging country with limited manufacturing and innovation capabilities, what are the possible inter-temporal impacts of sectoral catch-up in pharmaceuticals on access to life saving drugs and vice versa? Furthermore, what insights can be gained from the interrelationships between price negotiations of essential patented drugs, access and catch-up?*

For our research queries, the Brazilian catch-up experience in the production of antiretroviral (ARV) drugs required by HIV/AIDS patients presents itself as an ideal trajectory to study. In 1996, Brazil initiated a policy of universal and free access to highly-active ARV therapy (HAART) (or simply Universal Access Policy), which put an enormous pressure on the Brazilian Ministry of Health (MoH). In order to ensure an adequate supply of ARVs in the public healthcare system with a limited budget, MoH started negotiating price reductions for high-cost patented drugs, often deploying the threat of using CL. In this context, the paper explores how the drive to access in Brazil was impacted by prior catch-up in the pharmaceutical sector and in turn triggered future sectoral catch-up.

A mixed methodology is applied to answer our central questions. The literature is first examined and its main findings on catch-up and access are identified and summarized as theoretical constructs through figures. Then the Brazilian case study is constructed using

multiple sources of data. Its implications for the interrelationships between catch-up and access are validated through expert interviews. At each stage, results are inferred, and then in the final section, they are combined together to provide a broader analytical insight. The case study method is applied, because it is suitable for studying complex contemporary social phenomena, when boundaries between a phenomenon and its context are not clearly evident (Yin, 1994). Moreover, since the number of observations of CL threats in Brazil is not sufficiently high to justify a statistical analysis, the case study method is more appropriate.

The rest of the paper is organized as follows. Section 2 presents a scoping review of the literature and summarizes its main findings through theoretical constructs (Figure 1 and Figure 2). Section 3 starts by tracing the Brazilian catch-up trajectory and then presents a detailed study of the use of CL in price negotiation episodes for ARVs in Brazil. Section 4 discusses the main results obtained, and the refinement they provide of the earlier frameworks (Figure 3). Finally, section 5 concludes the paper.

2. A brief review of the literature

The term catch-up has been used broadly to study the comparative or individual experiences of communities (countries, regions or firms) in terms of the evolution of their income, productivity, capabilities or other economic variables. The focus is either on patterns of convergence (or lack of) of economic variables in a set of regions or over time or on the tracing of the strategy-outcome paths of economic actors. In the latter, a sub-stream centers on the firm dynamics of knowledge and capability accumulation applying qualitative inductive research methods such as case studies (Malerba and Nelson, 2011; Ramani, 2014). The present paper situates itself in this niche.

Technological catch-up in production of a commodity can be defined as the acquisition of knowledge, savoir faire, equipment, personnel, infrastructure etc. i.e. all the capabilities,

required to manufacture the product in terms of a targeted quantity and quality. Following Abramovitz (1986) such technological catch-up goes through four phases: entry, catching-up, forging ahead, and falling behind. Triggers for thrust into any of the stages may emanate in the innovation system in the form of new problems, actors, knowledge, discovery, technology or innovation, and finally, new policy initiatives (Lee, 2005; Perez and Soete, 1988). Some important triggers for catch-up in the pharmaceutical sector in emerging countries have been changes in the intellectual property rights (IPR) system (Guennif and Ramani, 2012), bandwagon effects of inter-organizational learning (Athreye et al., 2009), reverse brain drain of engineers trained in the USA and Europe (Kale et al., 2008) and import of technology and materials (Ren and Su, 2015).

Catch-up by a firm starts with entry through investment in the build-up of absorptive capabilities necessary to learn about existing and superior technologies. Then it continues through learning and integration of the most efficient technologies in the production process. Thereafter, market shares are expanded and market power is established. Finally, as new entrants armed with better innovations penetrate the market, earlier entrants lose their market leadership. Lee et al. (2016) refer to these four phases as the 'standard' catch-up cycle with three other possible variants: 'aborted catch-up' when only entry occurs (i.e. only first phase); 'sustained leadership' when incumbents are able to retain their leadership over time even with entry and catching up (i.e. only first two phases); 'coexistence of leaderships', when the last phase fails to materialize (i.e. only first three phases). Diverse patterns are possible because absorption and subsequent integration depend on a range of institutional characteristics, technological and social capabilities. Thus, technological catching-up cannot be taken for granted; a variety of necessary and complementary capabilities may be needed for effective absorption of available technological knowledge (Ramani and Szirmai, 2014).

2.1 Meta-Analysis of abstracts via a scoping review

Under the broad setting of catch-up, in order to identify the salient findings of the existing literature on catch-up triggers, the role of policy and its interrelationship with access, a scoping review of the literature was carried out and followed with an analysis of the article abstracts. A scoping review of the literature is suitable whenever the objective is to broadly explore a theme in order to identify the sub-themes covered and the gaps. Here, the search is done on a well defined corpus using search equations with the inclusion/exclusion criteria being developed *iteratively* after initial search results (Armstrong et al., 2011). Following this methodology, for the purposes of our research query, three search equations were applied on SCOPUS the standard abstracts and citation database in the subject area: 'all social sciences', to extract a corpus of abstracts. The first equation was, 'catch up' OR 'catching up' OR 'catch-up' in either title, key words or abstract of the article. The second was 'indus*'[3] AND 'pharm*' AND 'access'; while the third was 'indus*' AND 'pharm*' AND 'Brazil'. Considering each abstract as a data point, a meta-analysis was then carried out manually by reading through abstracts and retaining only those that provided responses to our research queries (Poth and Ross, 2009).

2.2 Role of access of final product for local consumption is invisible in catch-up

With respect to access, first and foremost, according to our corpus, in the catch-up literature, access has been considered uniquely with respect to the firm or public laboratory striving to catch-up. Access to global knowledge and technology pools including the most

[3] * extracts any article with the term preceding * in either the abstract, title or key words.

advanced is helpful to catch-up in knowledge intensive industries (Abraham, 2014; Colli and Corrocher, 2013; Dadush, 2008; Park and Lee, 2006; Schiller, 2011); so is access to global resources and market opportunities (Fan, 2011). Access to latest foreign technology is deemed important (Lee et al., 2005, 2011) and this can also be in the form of imported capital goods (Ahmad and Lee, 2016). Access to internet coverage and ICT platforms (Campisi et al., 2013; Conte, 2001; Gruber, 2001) and access to finance (Pšeničny et al., 2014) can be crucial for catch-up. However, similar access configurations need not lead to similar catch-up trajectories as the latter is determined by a host of other factors such as public policy and focus, infrastructure, managerial capabilities and culture (Raven et al., 2007). For effective exploitation of available access, local firms must have absorptive capabilities (Faucher, 1991; Park, 2011). Access can be enhanced through cross border inventions (Giuliani et al., 2011) as well as social networks (Salavisa and Fontes, 2012). Access to large markets promotes foreign direct investment (Poelhekke and van der Ploeg, 2009) and as the Chinese experience shows, market access can be used to negotiate technology sharing for catch-up successfully, if the sectoral industrial policy is also fine tuned towards this end (He and Mu, 2012). Multinationals can use such opportunities and not obstruct access to know-how for local firms, if the IPR system can guarantee protection of their innovations (Archibugi and Filippetti, 2010; Kiedaisch, 2015).

Our corpus revealed that policy triggers for catch-up can be a combination of two types of actions focusing on the supply side sectoral actors: building an enabling innovation system or intervening through specific initiatives to build capabilities (Giesecke, 2000). Most scholars give more weight to the former for catch-up, as a pluralist approach is required to develop capabilities in new knowledge areas that require closer links with science, while addressing social apprehensions about environmental problems and poverty (Romijn and Caniëls, 2011). Illustrations of each type are provided below.

Table 1
Illustrations of policy triggers for catch-up

Policy initiatives to nurture an enabling innovation system	Interventionist Initiatives
Investment in human capital and infrastructure (Archibugi and Filippetti, 2010; Choi, 2011; Co, 2002; Dadush, 2008; Furman and Hayes, 2004)	Promotion of national champions (Barbieri et al., 2013; Chu, 2009);
A strong patent system (Aghion et al., 2001)	Targeted policies and projects for specific technologies and standards (Choung et al., 2012; Fan, 2010; Khan, 1999)
Industrial policy that promotes a broad economic and social nurturing environment for innovation and technology capabilities accumulation (Filippetti and Peyrache, 2017; Intarakumnerd and Charoenporn, 2010; Mu and Lee, 2005; Oshima, 1984; Thacker-Kumar and Campbell, 1999; van Dijk and Szirmai, 2006; Zhang and Zhou, 2016)	Organizations and institutions for targeted facilitation (Choung et al., 2006; Goldman et al., 1997)
Reform of the public research and university system (Kwon, 2011; Lehrer and Asakawa, 2004) and promotion of knowledge transfers between university and firm (Kwon, 2011)	National R&D programs and Consortiums (Ahn and Mah, 2007; Hutschenreiter and Zhang, 2007; Lucchini, 1998)
Stimulation of firms' participation in frontier innovation activities (Rasiah, 2010, 2013)	Cluster development (Klochikhin, 2013); Regional development (Iosif and Tăchiciu, 2016); Sector development (Wang, 2013)
Building managerial capabilities (McKendrick, 1992)	Improving public sector enterprises (Klochikhin, 2013)
Promotion of FDI (Camilla et al., 2013; Perkins and Neumayer, 2008)	Public financing and procurement (Siaroff and Lee, 1997)
International technology cooperation (Sawada et al., 2012)	Promote short cycle technologies (Lee, 2012)
Appropriate labour market policy (Lange and Marrocco, 2012)	Active control and guidance of the market by the state (Soofi, 2016)

To summarize, the catch-up literature portrays it as a process within the production space of an innovation system. Catch-up is the outcome of the actor-strategies on the supply side of the market, as a function of the nature of demand. But, actors and processes in the consumption space, and the access of commodities to local final users are not perceived to impact catch-up, as illustrated in Figure 1. Indeed, just as macroeconomic theories of growth and catch-up frameworks of income convergence implicitly assume that the quality of life of the poor is likely to improve through trickle down effects, similarly sectoral studies seem to assume that access for local consumption will improve through catch-up.

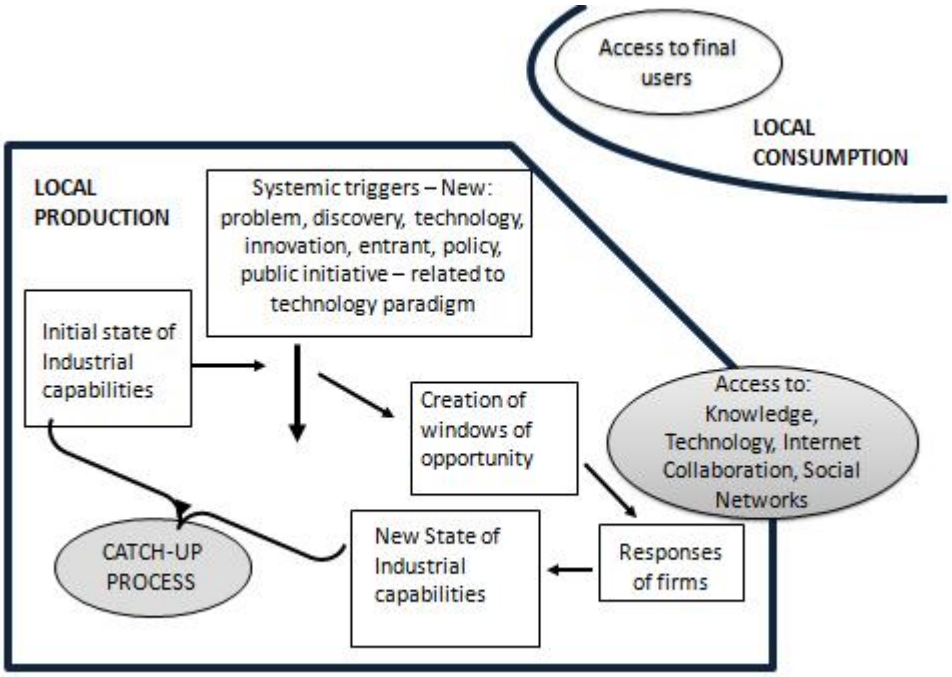

Fig. 1. Catch-up as an outcome of the strategies of supply-side actors

2.3 Role of catch-up blurry in the literature on access to medicines and industrialization

Turning to the other two corpuses on the interrelationships between the industrialization process in pharmaceuticals and access to medicines and then the specificities with respect to Brazil, we however get a different view as depicted in Figure 2.

The different perspective seems to stem from the fact that medicines are an essential commodity to ensure a good quality of life via health. There is a demand from civil society that essential commodities, including medicines, should be provided by the state to all citizens as a fundamental human right. Such a movement has been particularly strong for medicines in Brazil (Loyola, 2009). Civil society pushed the Brazilian government to ensure access to drugs to HIV/AIDS via interventions in the production space (Flynn, 2008; Veras, 2014). In intellectual property-based technologies like pharmaceuticals, the drive for access triggers negotiations with Western multinationals with the bargaining power of the emerging country depending on local market size and innovation capabilities (Benoliel and Salama, 2010). In Thailand and Brazil,

compulsory licensing has been used as a bargaining tool to establish the primacy of health over patent rights (Ford et al., 2007; Rosenberg, 2014). For instance, the drive for access increased local production in Brazil (Shadlen and Fonseca, 2013), while export of low-cost generics from India and China improved access to essential medicines in Africa (Chaudhuri et al., 2010; Haakonsson, 2009).

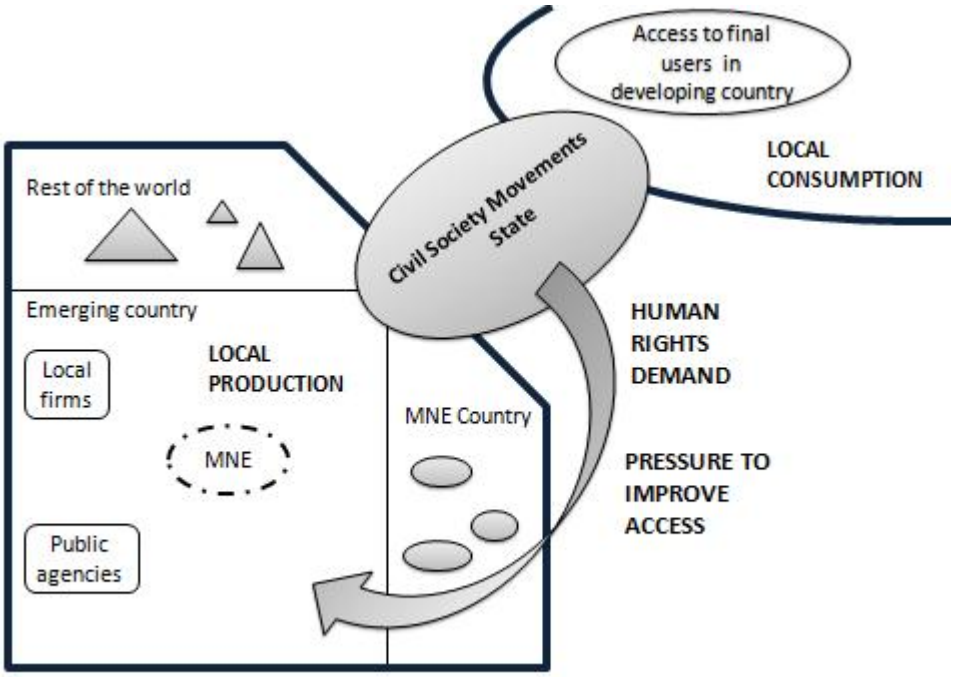

Fig. 2. Bridging consumption and production systems through access as human right

The above discussion yields a noteworthy point: the drive for universal access to essential commodities by actors that bridge production and consumption spaces is putting pressure on actors in the local production system to increase output. However, the literature is not clear about the impact of the access drive on the country's technological catch-up or the impact of prior catch-up on the possible alternatives to improve access to essential commodities. To gain insight on such issues, we turn to the Brazilian case study.

3. Brazilian Drive for access to ARVs and its impact on Catch-up

3.1. Background of the Universal Access Policy

Brazil's first AIDS case was reported in 1982 and, by the end of the decade, there were approximately 76,000 people living with HIV in the country (Levi and Vitória, 2002; Nunn, 2009). Faced with this crisis, while most developing countries focussed on prevention of new cases, Brazil became a trailblazer by taking the stance that all its citizens would be ensured access to medicines as a human right. In 1996, it initiated a well-structured official policy of universal and free access to HAART through its public health system. The availability of ARVs to people living with HIV/AIDS was to be ensured through local production of generic drugs in state-owned laboratories and imports of branded drugs from research-based pharmaceutical multinational enterprises (MNEs). It is worth noting that local production of ARVs in Brazil could be considered only because of prior catch-up in pharmaceuticals nurtured by a set of policies designed between 1969 and 1984 to promote industrialization. Among these, three are particularly important.

Abolition of patent protection in 1969: This move was expected to enhance the competitiveness of indigenous companies and improve access to medicines (Frenkel et al., 1978). Local firms responded by importing generic APIs to reduce their production costs (Rebouças, 1997). Thus, while the loose intellectual property regime fostered price competition and improved access to medicines, it did not stimulate accumulation of technological capabilities for industrial production of APIs.

Creation of institutional technology suppliers: in 1976, a public-private entity called CODETEC was founded to provide support in product and process R&D to private companies of several sectors. From 1983 its mission was reoriented to focus almost exclusively on pharmaceuticals.

In the same year, Farmanguinhos was founded as part of a network of stated-owned laboratories to supply affordable medicines to the public sector (Hamilton and Azevedo, 2001). In 1979, Farmanguinhos set up a research laboratory for chemistry synthesis of APIs (Vieira, 2005). The objective was not to manufacture APIs, but to master the production process to gauge the actual production costs for transfer to local companies (Hamilton and Azevedo, 2001; Vieira, 2005).

Interventions to build local firm capabilities in pharmaceuticals during 1980's: The objective of an industrial policy called *Projeto Fármaco* initiated under the aegis of CODETEC, was to provide technical and scientific support to indigenous pharmaceutical companies in order to reduce imports of APIs. Several policy instruments provided support to Projeto Fármaco, including tariff and non-tariff barriers to trade and fiscal and financial subsidies to local firms. In turn, *Projeto Fármaco* fostered formal and informal collaborative arrangements between local firms and state-owned laboratories, often supported by public funding schemes (Queiroz, 1995; Rebouças, 1997). Universities were critical nodes of such a system, not only through supply of skilled scientists and chemical engineers, but also via collaboration to assist in reengineering of drugs (Cassier and Correa, 2008).

As a result of these initiatives, during the 1980's there was finally a steady accumulation of technological capabilities in API production, demonstrating that lack of IPR alone is not sufficient for catch-up (Guennif and Ramani, 2012; Queiroz, 1993; Rebouças, 1997).

The Brazilian pharmaceutical industry, however, did not move to the forging ahead phase after catch-up for diverse reasons. During the 1990s, most of the companies could not exploit the economic opportunities created, because public support was abandoned due to financial constraints. Further, protection to the local industry was discontinued by the mid-1990s; tariff and non-tariff barriers were removed and CODETEC was shut down. Consequently, local API

production fell drastically and the local pharmaceutical industry remained confined to drug formulation and distribution activities (Queiroz, 1995). Finally, under a macroeconomic context of import substitution, extremely high protection proved to be indiscriminate and exaggerated; and incentives put no emphasis on exports or innovation capabilities, stalling the forging ahead phase (Suzigan and Furtado, 2006). However, such an aborted catch-up cycle enabled accumulation of knowledge and skills in a few niches, such as the production of ARVs. Indeed, the local producers of ARVs active in the new millennium had built their technology capabilities through collaboration with either CODETEC or Farmanguinhos, mainly under Projeto Fármaco.

3.2. Rise of local production of ARVs

Even before the initiation of the Universal Access Policy, from the 1980s itself, there had been public commitment to tackle the HIV/AIDS epidemic. São Paulo and Rio de Janeiro had created state-level programmes of free drug distribution of imported ARVs in 1983 and 1985 respectively. In 1991, MoH included imported ARVs in the public health system with the distribution of zidovudine (AZT) capsules (Teixeira et al., 2004). In 1993, Microbiológica, a university spin-off founded in 1981 and supported by CODETEC since 1983 (Rabi, 2007), started supplying the API of AZT to a state-owned laboratory called LAFEPE (Cassier and Correa, 2003; Orsi et al., 2003). However, with implementation of the Universal Access Policy in 1996, there was an immediate need to increase access multifold

For this purpose, MoH targeted increased local production of ARVs as the main pillar of support for the Universal Access Policy (Orsi et al., 2003). Then, MoH assigned Farmanguinhos the task of being the main supplier of generic ARVs. When CODETEC was shut down by the Federal Government in the early 1990s, one of its leading chemists, Benjamin Gilbert was seized by Farmanguinhos to be its scientific director. In Farmanguinhos, Gilbert created an R&D

department for reverse engineering of pharmaceutical processes (Vieira, 2005). This allowed Farmanguinhos to develop imitative capabilities for reverse engineering the synthesis processes of the several drugs, including second-generation ARVs such as Efavirenz, Nelfinavir and Lopinavir (Cassier and Correa, 2008).

Between 1997 and 2002, the volume of production at Farmanguinhos increased sevenfold, notably due to ARV production (Cassier and Correa, 2003). Nevertheless, Farmanguinhos and other state-owned laboratories responsible for local production of ARVs, remained specialized in drug formulation. Only a few private companies developed their own technological capabilities to produce APIs (Fortunak and Antunes, 2006), and therefore, the public sector was dependent on imports of these critical inputs. More than 90% of the public demand for APIs were satisfied by Indian and Chinese firms (Orsi et al., 2003; Pinheiro, 2012).

3.3. Challenge posed by TRIPS and possible solution pathways

The sustainability of the Universal Access policy was severely constrained by high prices of newer ARVs due to premature compliance with the TRIPS Agreement. In 1997, the patentability of pharmaceutical products and processes was re-introduced in the country as Brazil had waived the ten years adaptation period for developing countries.

Different countries in Latin America retained different features of TRIPS flexibilities in their local IPR regime (Correa, 2015). For instance, Brazil opted to retain CL and the experimental use of patented inventions (also known as 'Bolar exemption'), but opted out of permitting parallel imports and included a provision for 'pipeline patents'[4]. Such choices had a

[4] Brazil automatically granted patents of inventions that were already patented abroad, provided that the product covered by the foreign patent was not made commercially available anywhere (Mitsuuchi Kunisawa, 2009)

strong bearing on the ability of the country to cope with the potential negative impact of patents on access to ARVs.

The challenge became even more daunting with the major depreciation of the local currency in 1999 that led to a 64% rise in the cost of antiretroviral drugs in Brazil as compared to 1998 (Grangeiro et al., 2006). An increasing number of AIDS patients, the introduction of high priced, newly patented ARVs, and the need to ensure the success of the Universal Access Policy, while answering to its own government and other societal stakeholders put an enormous pressure on MoH. Fenced in by these diverse constraints, MoH sought price reductions for the patented drugs, threatening at times to issue a CL (Galvão, 2002; Nunn et al., 2007, 2009). What was their effect on access and catch-up? We turn to this question now.

4. Role of catch-up in Price Negotiations and Impact on Access

4.1. Primary and Secondary Data Collection

The ARV price negotiations were identified by applying designed search criteria to our secondary data. These secondary sources included: scientific articles; official documents, national and international reports; Web portal of the STD/AIDS Department at MoH of Brazil, available at: http://www.aids.gov.br/; Official Gazette of the Federal Government of Brazil, available at: http://portal.in.gov.br/); MoH of Brazil: administrative documents, proposals, progress reports, and other internal records, available at http://portalsaude.saude.gov.br/ and finally, newspaper clippings and other articles appearing in the press and digital media. The search criteria spotted negotiations between MoH and pharmaceutical companies for patented ARVs that involved at least one of the following factors: CL threat, voluntary license request, rejection of patent claim and patent nullification. Thus, we inferred that between 2001, when MoH began price negotiations over ARVs, and 2014, there have been at least 14 episodes of

price negotiations involving 6 different ARVs (see Table 2) that fitted our search criteria. In some instances, MoH carried out simultaneous negotiations. These cases are labelled with numbers and letters (e.g. 1A and 1B, 2A, 2B and 2C, 3A, 3B and 3C, and 8A and 8B).

Table 2:
Price negotiations of ARVs in Brazil

Episode	Drug	Pharmaceutical MNE	Start
1A	Efavirenz	Merck & Co. (USA)	Jan/2001
1B	Nelfinavir	Roche (Switzerland)	Jan/2001
2A	Efavirenz	Merck & Co. (USA)	Jul/2003
2B	Nelfinavir	Roche (Switzerland)	Jul/2003
2C	Lopinavir/Ritonavir	Abbot Laboratories (USA)	Jul/2003
3A	Lopinavir/Ritonavir	Abbot Laboratories (USA)	Mar/2005
3B	Efavirenz	Merck & Co. (USA)	Mar/2005
3C	Tenofovir	Gilead Sciences (USA)	Mar/2005
4	Atazanavir (	Bristol-Myers Squibb (USA)	Nov/2006
5	Efavirenz	Merck & Co. (USA)	Nov/2006
6	Tenofovir	Gilead Sciences (USA)	Apr/2007
7	Tenofovir	Gilead Sciences (USA)	Aug/2008
8A	Raltegravir	Merck & Co. (USA)	Sep/2010
8B	Atazanavir	Bristol-Myers Squibb (USA)	Sep/2010

This data was complemented by primary data collection obtained from 26 semi-structured and exploratory interviews[5] with academics, politicians, lawyers, activists and businesspersons familiar with the Brazilian experience in price negotiation for ARVs. The selection of the first expert subjects to be interviewed was based on bibliographic research in online newspapers, academic journals and on the website of the MoH in Brazil. Furthermore, we also used a 'snowball sampling' technique, asking interviewed people to give referrals to other possible subjects. These interviews were conducted in Portuguese, between January and March 2012. Additional primary sources were also used, such as personal communication (via e-mail) with personnel of both STD/AIDS Department and Department of Science, Technology and

[5] The choice for using both semi-structured and exploratory interviews is justified by several variations in the circumstances in which interviews took place, such as the background of the person interviewed, the time available for the interview and personal knowledge of the subject.

Strategic Resources at MoH and Data requested via the 'Portal for Access to Public Information'[6], available at http://www.acessoainformacao.gov.br/.

After summarizing the interview results, we also submitted an online survey to all the interviewed subjects to reduce the importance of personal opinion and to obtain a greater level of generalization. The rate of response was 21 out of 26 (81%).

4.2. Price negotiations as a process within a complex system

Though price negotiations are bilateral in principle, in practice they are actually a multi-player game whose outcomes emerge through strategic play within a complex system as shown in Box 1.

There are two loose coalitions around the public agency of the developing country and the pharmaceutical MNE respectively. For instance, in the Brazilian case, one coalition comprised MoH supported by state-owned laboratories, notably Farmanguinhos, a few local companies, and Indian generic manufacturers. MoH's bargaining strength was built upon the technological capabilities in fine chemicals accumulated at Farmanguinhos and local firms. Indeed, all the indigenous companies that supported both MoH and Farmanguinhos, that is Cristália (episodes 3A, 5, 6, 7), Nortec (episodes 3B, 6, 7, 8A, 8B), Blanver (episodes 5, 6 and 7), Microbiológica/Genvida (episode 3C), and Globe Química (episode 5) benefited from technological transfers from CODETEC in the past.

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[6] This portal provides general data on financial expenditures and contracts, programmes, actions, projects and other public works at the city, state, and national levels.

The other coalition revolved around pharmaceutical MNEs and their governments. The bargaining strength of the MNEs rested upon the ability of their home governments to inflict costly reprisal if there was a conflict of interest. For example, in 2005 (during episodes 3A, 3b and 3C) the US Government threatened Brazil, using its 'Special 301 Report' to impose trade sanctions against Brazilian exports and to remove preferable trade partner status (Galvão, 2002; Love, 2008; Nunn, 2009). Such pressure may make emerging country actors fear that a CL may provoke MNEs to seek a more business-friendly legal climate elsewhere and lower the flows of foreign direct investment, trade and technology transfer.

Tensions between the two coalitions can be attenuated by other sectoral actors. For example, when international pressure is too strong, then the Ministry of Development, Industry and Trade (MoDIT) may put pressure on the MoH against CL. In Brazil, MoDIT is in charge of the country's innovation policy and it sees CL as an impediment to the creation of an 'innovation-friendly' environment. Moreover, MoDIT is under pressure from other economic sectors that believe that CL may cause loss of exports and/or foreign investments. The outcomes of the price negotiations are presented in Table 3. Out of the 14 episodes of price negotiations, 1 was a failure (i.e. 3B), 10 led to price discounts (i.e. 1A, 1B, 2A, 2B, 2C, 3A, 3C, 4, 6, 7), 2 led to public-private partnerships (PPP) through licensing (i.e. 8A, 8B) and 1 triggered a CL (i.e. 5).

Box 1:
Summary of actors' involvement in price negotiations

Actor / Episode	1A, 1B	2A, 2B, 2C	3A	3B	3C	4	5	6	7	8A, 8B
MoDIT	Not involved	Not involved	Took over the negotiation to avoid CL	Took over the negotiation to avoid CL	Took over the negotiation to avoid CL	Not involved	Did not oppose to CL	Did not oppose over rejection of patent claim	Did not oppose over rejection of patent claim	Co-sponsor of PPPs for local production
International Generic Suppliers	Supply of small quantities for 'experimental use'	Supply of drugs until local production commences in case of CL	Supply of drugs until local production commences in case of CL	Supply of drugs until local production commences in case of CL	There was no generic available for imports	There was no generic available for imports	Supply of drugs until local production commences in case of CL	There was no generic available for imports	There was no generic available for imports	There was no generic available for imports
Local Firms	Not involved	Not involved	Cristália would supply of API under PPP in case of CL (6 months to commercial scale)	Nortec would supply of API under PPP in case of CL (4 months to commercial scale)	Genvida-Microbiológica would supply of API under PPP in case of CL (12 months to commercial scale)	Not involved	Blanver, Globe Química and Cristália would supply of API under PPP in case of CL	Blanver, Cristália and Nortec would supply of API under PPP	Blanver, Cristália and Nortec would supply of API under PPP	Technology for API production to be transferred to Nortec within 5 years
Public Labs	Reverse engineering by Farmanguinhos (process in pilot scale already developed).	Reverse engineering by Farmanguinhos (process in pilot scale already developed).	Reverse engineering by Farmanguinhos (process in pilot scale already developed). Formulation and distribution in case of CL.	Reverse engineering by Farmanguinhos (process in pilot scale already developed). Formulation and distribution in case of CL.	Formulation and distribution in case of rejection of patent claim (reverse engineering of process yet to be developed)	Formulation and distribution in case of CL. (reverse engineering of process yet to be developed)	Reverse engineering by Farmanguinhos (process in pilot scale already developed). Formulation and distribution in case of CL.	Formulation and distribution in case of rejection of patent claim (reverse engineering of process yet to be developed)	Formulation and distribution in case of rejection of patent claim by FUNEDE and LAFEPE (reverse engineering of process yet to be developed)	Technology for drug formulation to be transferred to Farmanguinhos and LAFEPE within 5 years
Foreign Government	Strong opposition from US Government	No opposition due to Doha Declaration	Strong opposition from US Government	Strong opposition from US Government	Strong opposition from US Government	Not involved	Not involved	Not involved	Not involved	Not involved

Table 3
Summary of the negotiation episodes (prices in US$)

Episode	Drug	Initial Price	Final price after negotiation	Lowest price of patent holder (A)	Price of cheapest imported generic version (B)	Price if locally produced	Final price discount achieved	Final price relative to A	Final price relative to B	Other concessions
1A	Efavirenz (200 mg)	2.05	0.84	0.46	0.44	1	-59%	1.84	1.9	
1B	Nelfinavir	1.07	0.64	0.74	0.42	0.6	-41%	0.86	1.52	
2A	Efavirenz (600 mg)	2.1	1.59	0.95	1.27	0.87	-24%	1.67	1.83	
2B	Lopinavir + Ritonavir	1.5	1.3	0.23	0.9	0.68	-13%	5.7	1.91	
2C	Nelfinavir	0.52	0.47	0.26	0.31	0.53	-10%	1.81	1.51	
3A	Lopinavir + Ritonavir	1.17	0.63	0.23	0.72	0.41	-46%	2.76	1.54	
3B	Efavirenz (600 mg)	1.59	1.59	0.95	0.92	0.87	0%	1.67	1.83	
3C	Tenofovir	7.68	3.8	0.57	1.00[1]	*	-51%	6.7	3.8	
4	Atazanavir (200mg)	3.13	3.04	0.48	**	n/a	-3%	6.28	n/a	
5	Efavirenz (600 mg)	1.59	-	0.65	0.46	0.6	-	-	-	CL
6	Tenofovir	3.8	3.25	0.57	0.42[2]	*	-14%	5.73	7.83	
7	Tenofovir	3.25	2.54	0.57	0.42[2]	*	-22%	4.48	6.12	Patent rejection and PPP
8A	Raltegravir	8.04	7.53	0.93	**	*	-6%	8.14	n/a	PPP and Voluntary license
8B	Atazanavir (200mg)	1.98	1.85	0.68	0.48[1]	*	-7%	2.73	3.83	PPP and Voluntary license
	Atazanavir (300mg)	3.58	2.8	1.13	0.69[1]	*	-22%	2.48	4.08	

* There was no cost estimation for local production.

** There was no generic available for imports

[1] Generic manufacturers were unable to export to Brazil due to contractual arrangements with the patent holder

[2] Generic manufacturers were unable to export to Brazil due to lack of regulatory approval by local authorities.

4.3. From catch-up to access via price negotiations

Reorganizing the information in Box 1 and Table 3, we derive Table 4, which shows that even basic catch-up or absorptive capacity can improve access.

Table 4
Final prices relative to cheapest generic alternative and small-scale local capacity

Episodes wherein reverse engineering had not been carried out	Final price relative to the best international price	Episodes wherein reverse engineering had been carried out	Final price relative to the best international price
3C	3,8	1A	1,9
		1B	1,52
4*	6,28	2A	1,83
		2B	1,91
6	7,83	2C	1,51
		3A	1,54
7	6,12	3B	1,83
Average	6,01	Average	1,72

In an extensive survey of the literature on the use of CL in price negotiations, Ramani and Urias (2015) highlight that local manufacturing capacity and import possibilities have an important influence on outcomes of price negotiations evoking CL. In episodes 3C, 4, 6, and 7, local manufacturing capacity posed a challenge by its total absence. Furthermore, Brazil could not import the drug from third parties even if a CL had been granted (See Table 3, notes 1 and 2). However, the MoH was able to negotiate discounts in all these cases. In episodes 3C, 6, and 7, a local public-private consortium announced that it could manufacture Tenofovir within 12 months (see Box 1), even though there had been no previous reverse engineering effort. Therefore, what seems to matter is not only actual technological and manufacturing capabilities, but also the potential for building these, as suggested in an interview with a former Director of STD/AIDS Department, who led three price negotiation episodes:

'*The simple fact that Brazil masters the technology and knowledge necessary for API and drug production has resulted in price reductions. Actually, the patent holder may reduce its*

prices just to make the local production less attractive and, therefore, avoid the creation of local productive capacity.' (Interview with STD/AIDS Department at MoH[2]).

Table 4 also shows that MoH paid, on average, six times the lowest international price for the drugs which no reverse engineering effort had been carried out. Whereas, MoH was able to negotiate better prices – on average, 1.7 times the lowest international price – when technological capabilities for production on a small scale were already developed (i.e. Efavirenz (1A, 2A, 3B); Nelfinavir (1B, 2B); and Lopinavir (2C, 3A)). This was possible because, in 2001, MoH authorized Farmanguinhos to use the 'Bolar exemption' to reverse engineer the production technology of these three APIs to strengthen its position in the negotiation with pharmaceutical MNEs (Cassier and Correa, 2008). The existence of technological capabilities for reverse engineering a given drug means that local production can commence in less time and, therefore, increases the country's bargaining strength in the negotiation as explained by an interviewee.

'*The issue of technological capacity is complex. Brazil does have technological capacity to produce ARVs, including APIs. However, there are many steps involved, such as drug deformulation, development of an alternative synthesis route, regulatory approval to ensure that the generic drug has the same quality and efficiency, as does the original drug. This process is not straightforward. This is not like an electrical power that you just have to plug into the wall socket. The capacity building takes times.*' (Interview with Local Company [1]).

4.4. From CL to catch-up and access

The first – and only – CL was issued in 2007 after failing to achieve any significant price reduction for Efavirenz with the patent holder (episode 5). The drug was initially imported from Indian suppliers, but local production had to be arranged, because the Brazilian IPR law allows imports under compulsory licensing only for 12 months after the issuance. Then, a public-private

consortium was set up, wherein three local private enterprises were responsible for the development and production of the API – Cristália, Nortec and Globe Química, while two state-owned laboratories (LAFEPE and Farmanguinhos) were in charge of the formulation and distribution. This public intervention to foster local production of ARVs was an important policy window for accumulation of technological capabilities necessary for developing a synthesis route for Efavirenz and to scale up production to a commercial scale.

While CL can boost catch-up it may not always improve access. For example, MoH granted a CL for Efavirenz in 2007 and the local production of the drug started in 2009. Since then, the price of the local generic manufactured version has remained constant while the lowest international price has reduced by 77% (see Table 5). The CL allowed MoH to save around US$103.5 million of the resources otherwise needed for the period 2007–2012 (Correa, 2015). If only imports had been considered, then MoH could have saved approximately 25% more. Therefore, even though CL improved access to the drug, such improvement was less than it could have been, due to the lack of competiveness of local producers.

Table 5
Price comparison of Efavirenz after compulsory licensing in Brazil (US$ 2007 constant)

Year	Best generic price[1]	CL price (Imported)[2]	CL price (Farmanguinhos)[2]
2007	0.47	0.46	
2008	0.42	0.30	
2009	0.27		0.69
2010	0.14	0.14	0.69
2011	0.14		0.69
2012	0.12		0.69
2013	0.11		0.69

Sources: [1] MSF; [2] MoH of Brazil, STD/AIDS Department

4.5. Post-CL PPP: another pathway for catch-up and access

From 2005, when MoH was considering CL for three ARVs (See Box 1, episodes 3A, 3B, 3C), the PPP model was viewed as the solution that would be implemented if ever a CL was

issued. However, a PPP came to be formed with three local private enterprises and two state-owned laboratories only in 2007 when a CL was actually issued after episode 5 and it proved to be successful. With this, came policy learning of PPP management induced by CL issuance and the PPP model was extended for a wider range of drugs leading to further catch-up. In Brazil, the latter gave confidence to MoH to initiate PPPs which further boosted catch-up, as confirmed by a MoH staff member directly involved with these PPPs :

"The model of CL for efavirenz was the base, a kind of pilot project, for the existing PPPs for technological transfer supported by the Ministry of Health." (Interview with MoH [1])

In 2009, 11 PPPs for local production of high-cost drugs – including their APIs – were launched, with assured procurement by MoH. These included, two consortia of local companies (Blanver, Nortec and Cristália) and state-owned laboratories (FUNED and LAFEPE) for local production of a generic of Tenofovir, only a few months after the Brazilian Patent Office overruled its patents (episode 7). Finally, episodes 8A and 8B resulted in PPPs as part of a set of institutional changes implemented by both MoH and MoDIT aimed at making voluntary license agreements a more attractive alternative to pharmaceutical MNEs. The 2009 policy window of opportunity for catch-up in form of PPPs also included national R&D programs and consortiums, international technology cooperation, and promotion of national champions (Del Campo, 2016)

Presently there are 83 ongoing PPPs for local production of 38 synthetic drugs, 24 biologicals (including biosimilars and vaccines) and 21 medical devices (Ministry of Health of Brazil, 2016). As of march 2017, 35 consortia were already supplying the respective product to MoH, generating a total savings of US$ 1,5 billion in drug acquisitions for the public health system (Ministry of Health of Brazil, 2017).

Again though PPP are meant to improve access via catch-up, they can also backfire, as illustrated by the case of Tenofovir after episodes 6 and 7. In 2011, the first batch of Tenofovir supplied to MoH by the two public-private consortia mentioned above supplied to the MoH was more than eleven times more expensive than the lowest international price. In addition, after two years, these consortia reduced the price by 5%, while the lowest international price fell 30% during the same period. Thus, like in the case of the local generic of Efavirenz, local production of Tenofovir resulted in a suboptimal access to the drug as compared to importing generics.

5. Discussion of results

We discuss the results at two levels, in terms of the inferences from the Brazilian case study on the interrelationships between policy instruments for access and catch-up, and thereafter, on what such results add to the literature on catch-up.

Catch-up can have an inter-temporal impact on access; i.e. industrial policy initiatives can contribute to the success of health programmes either immediately or with a time lag. Brazilian industrial policy implemented since the 1970s strived to build technological and innovation capabilities. While there is a consensus that this policy failed to build a competitive pharmaceutical industry and reduce trade deficits in pharmaceuticals, this industrial policy is directly responsible for the success of the Brazilian health policy to tackle the HIV/AIDS epidemics. Skills in fine and organic chemistry accumulated locally, notably at Farmanguinhos and in a handful of private companies in the 1980s, created absorptive capability and prior knowledge bases for the local development of other ARV drugs. Furthermore, CL enabled local production of API and formulation of efavirenz, only because of absorptive capabilities developed over prior aborted catch-up.

Price negotiations can create synergies or trade-offs between catch-up and access. Table 6 summarizes the drivers and impact of price negotiations as a pathway for access and catch-up. It shows that under complex systemic settings with actor and actor-group interactions and struggle, the impact of instruments used to ensure access can be nuanced and not clearly favour either access or catch-up. In turn, with respect to the ongoing debate about whether promoting catch-up in the pharmaceutical sector is likely to be harmful for access to medicines, or whether the two can be complementary, the table indicates that neither argument can be generalized. Evaluation has to occur on a case by case basis even within the same country.

Table 6
Drivers and Impact of Price Negotiations on Catch-up and Access

Drivers of pathway	Public agency pathway	Bargaining Outcome (Episodes)	Impact on access	Impact on catch-up
Catch-up – only basic absorptive capabilities, no reverse engineering capabilities	Price negotiations	Price discounts from MNE (3C,4, 6, 7)	Positive (neither CL nor importing generic was possible)	None
Catch-up –reverse engineering capabilities & Institutional Support by state	Price negotiations	Price discounts from MNE (1A, 1B, 2A, 2B, 2C, 3A, 3B	Positive But could be less than by CL	None
		Status-quo (3B)	None	None
		Compulsory licensing (5)	Positive But could be less than by importing generic	Positive
Policy learning from compulsory licensing	PPP with MNEs	MNEs agree to voluntary licensing to avoid CL risk (8A, 8B)	Positive (neither CL nor importing generic was possible)	Positive
Policy learning from compulsory licensing	PPP with local firms and labs	Local production increases and diversifies with catch-up	Positive But could be less than by importing generic	Positive

Compulsory licensing can contribute to technological catch-up via two pathways: (i) through build-up technological capabilities; (ii) through policy learning that comes from the efforts to issue and implement the CL through PPP, as highlighted by the Brazilian case study. The role of PPP and government procurement in catch-up is likely to increase as more new drugs emerge as biopharmaceuticals as they are much more complex than ARVs or other

conventional chemical entities, more difficult to replicate, and at the same time, with a rising share in the public healthcare expenditure (Tanaka and Amorim, 2014).

The impact of access drivers on catch-up may be obstructed by power struggles between actors, or simply politics. In the Brazilian case, there was tension between the coalition led by the MoH and the other supported by the US Government. The pressure of possible retaliation was strongly indicated in episodes 3A, 3B and 3C. Thus, the first best solution for MoH was to accept price reductions instead of issuing CLs. In these episodes, both the MoDIT and the US Government were actively mobilized by pharmaceutical MNEs to put pressure on MoH against compulsory licensing.

It does seem that ultimately only forging ahead can lead to sustainable and large scale access. An aborted catch-up experience may improve access in certain specific contexts, such as in price negotiations of patented drugs. However, by definition, such an experience means that companies have failed to reach the technological frontier of the industry. At the same time, the impact of investment in catch-up on access to medicines will take time to materialise, as in the initial learning stages, local actors will operate below the international technological frontier. Therefore, it is imperative that policy and market mechanisms are in place to reduce the risk of an eventual negative impact on access to medicines due to prolonged inefficiency of local actors. The two main sources of future catch-up are individual capability accumulation of firms and those generated within PPP. However, to realise this potential from local firms and PPP, it is necessary to implement an environment that builds international competitiveness for forging ahead.

Given the above findings, the contribution of the present paper to the literature on sectoral catch-up can now be summarized as in Figure 3, which shows how the results of the case study refine the preceding theoretical constructs (Figures 1 and 2).

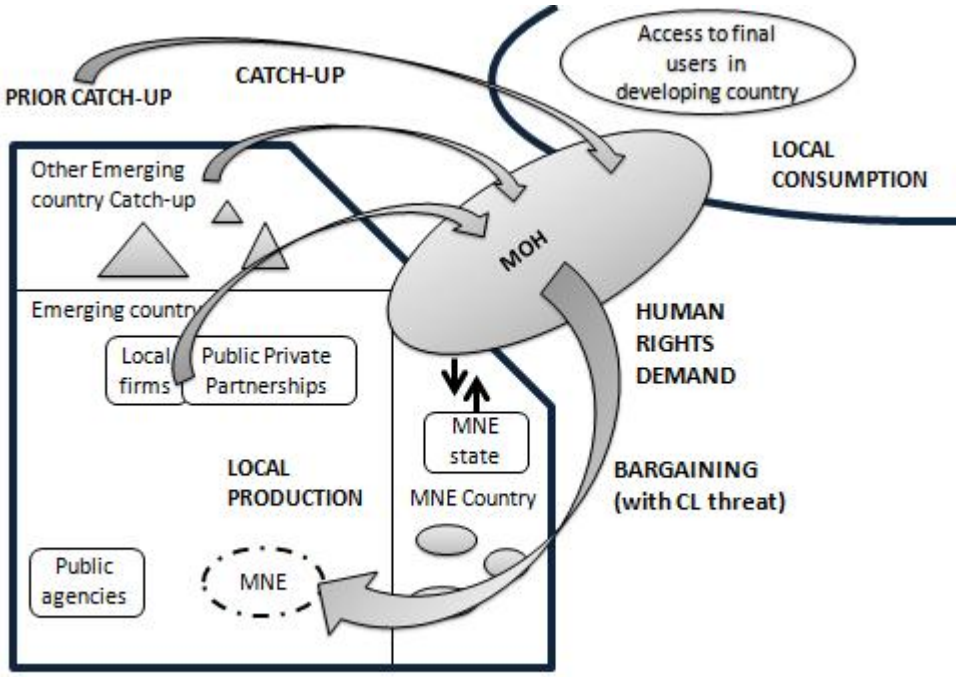

Fig. 3. Interrelationships between catch-up in pharmaceuticals and access to drugs

First, catch-up in the manufacturing of an essential commodity need not automatically lead to better access. In the economic growth literature, it has been repeatedly pointed out that growth benefits may not trickle down to improve poverty alleviation unless the system, especially the state and public agencies, nurture structural changes and capability building for pro-poor growth (Kakwani et al., 2000; Nussbaum and Sen, 1993). Similarly, for catch-up to improve local access to essential commodities, going beyond markets, there is a need for public actor bridging of the production and consumption sub-systems.

Second, with respect to an essential commodity like medicines, sectoral catch-up can have a strong inter-temporal relationship with access. Past catch-up, even if aborted, can nurture better access in the future. Catch-up of other emerging countries can boost access. Similarly, present access drives can trigger future catch-up.

Third, the literature indicates that catch-up triggers can appear in the form of novelty in the innovation system, either as a new technology, an entrant, a new macroeconomic or

industrial policy or some form of external shock that directly impacts local firms. In contrast, in the essential commodity sectors, it is possible for catch-up triggers to emanate from public agencies focussing on access rather than on knowledge or firm capabilities enhancement.

5. Conclusion

The objective of the present paper is to explore the possible inter-temporal impacts of catch-up in pharmaceuticals on access to medicines and vice versa, an issue that has not received much attention in the existing catch-up literature. The Brazilian success story in making with ARVs available free of charge to all HIV/AIDS patients through prices negotiations with patent holders lent itself as an ideal case study to draw insight on the research query, because it was intimately linked to prior catch-up by local firms and those from other emerging countries. A scoping review of the literature on catch-up was complemented by a detailed study of the Brazilian catch-up in ARVs production and price negotiations with patent holders between 2001 and 2010.

Our findings indicate that catch-up is neither necessary nor sufficient for improving access, but it is favourable. The existence of production capacity for a specific drug is not a necessary condition to obtain price reductions for it. But, the existence of absorptive capacity for reverse engineering can be enough to bring prices down. Moreover, when local actors master the savoir-faire to produce generic versions of the drug, then price discounts are likely to be greater. Thus, it is not only the current level of manufacturing capacity that influences the country's ability to reduce prices of patented drugs, but also the potential to 'create' manufacturing capacity in the future. This leads to three recommendations for emerging countries.

First, emerging countries with basic technology and innovation capabilities ought to invest in closing the knowledge gap in essential drugs production. The Brazilian case study

indicates that given the paramount role of local manufacturing capacity in bargaining with patent holders, public policy should support technological capacity building. This is even more critical for biopharmaceuticals, as these products face lower competition even after patent expiration due to technological complexity and regulatory challenges. Countries with no previous capabilities should also invest in creation of absorptive capacity and reverse engineering skills, as these two can already be sufficient to obtain more affordable prices, when negotiating prices of patented drugs with research-based pharmaceutical MNEs.

Second, for emerging countries, there can be real trade-offs between catch-up and access. As the Brazilian case study amply illustrates, price discounts by MNEs for their patented drugs improve access, but they slow down catch-up, because then it becomes even more challenging for local firms to become equally competitive. Similarly, following a CL or initiation of a PPP, while there will be catch-up, access might be improved more by importing cheap generics than by procuring costlier locally produced drugs.

Third, especially for emerging and developing countries, a strong public sector would be a good source of bargaining power. It is not necessary for the public sector to undertake manufacturing of drugs, this can be left to the private sector. However, the public sector must have state of the art technological and innovation capabilities so that it can transfer technology to local firms whenever necessary. For instance, Brazil has not mastered the technological routes to produce newer anti-HIV drugs such as Atazanavir, Raltegravir, Maravoric, Darunavir, Etravirine and Enfuvirtide, for which there is an increasing demand. While in the past, CODETEC and Farmanguinhos played the role of centres of excellence for drug re-engineering, the first no longer exists and the second does not consider drug re-engineering to be a part of its mission. Thus, emerging countries must invest in the development of well performing public sector entities to close the knowledge gap in drugs production for their important disease burdens.

Arrow (1962) first established the classic result that firms tend to under-invest in R&D, when knowledge spillovers are high, or when competitors can capture any new knowledge that is created, easily and cheaply. To this, we can add that firms of emerging countries will under-invest in R&D, when the catch-up gap is too large or costly. Thus, a public sector with strong technological and innovation capabilities is favourable to catch-up, especially in essential commodity sectors like medicines, where there is a drive for universal access as a human right.

The present paper points to at least three research avenues for a broader and deeper understanding of the role of policy instruments to promote access and their possible synergy with catch-up. For instance, a number of other countries like Ecuador, Thailand, and Malaysia have issued CL in the name of access, and others like India have evoked the threat of using it and their comparative experience can be analyzed. Further, the role of instruments to improve access to patented innovations evoked in this paper such as price negotiations, voluntary licenses and PPP can also be examined in other essential commodity sectors such as seeds, with respect to their impact on catch-up and access. Finally, the contextual politics and the management of these instruments greatly influence their outcomes and call for a deeper examination.

To conclude, catch-up, access improvement and price negotiations are processes that involve multiple and parallel discourses within a complex system, which taken together impact both catch-up and access to medicines. There can be positive as well as negative externalities due to unforeseen outcomes arising from interaction of different policies. This can give rise to a systemic risk such that improved access is not embedded effectively in the catch-up trajectory. To minimize this risk, emerging countries must continue to invest in technology catch-up and also pay attention to governance and the coordination between different national policies such as health and industry.

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