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Access to critical medicines: When are compulsory licenses effective in price negotiations?

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ABSTRACT

Governments of developing countries can be in a vulnerable position with respect to patent protected drugs supplied by foreign firms, if the technology cannot be licensed or independently developed by local firms. In such instances, one possible solution is to negotiate for a price-drop with the patent holder in lieu of issuing a compulsory license. The present paper develops a game theoretic model of such bargaining and shows that while compulsory licenses do not occur under complete information, they can be issued under incomplete information. The model is tested against real episodes of compulsory licenses to derive policy insight.

1. Introduction

During the first half of the 2000's, the Brazilian government successfully negotiated discounts on a number of patented drugs, backing up their bargaining with threats to issue compulsory licenses (Ford et al., 2007). On the other hand, in 2006, the Thai Ministry of Public Health actually issued its first compulsory license (or CL in what follows) for an antiretroviral drug after failing to achieve any significant price reduction with the patent holder (Thai White Paper I, 2007). The CL bandwagon seems to be slowly gaining momentum with India issuing one in 2012 for a liver and kidney cancer drug, and China amending its intellectual property laws to allow for them (Francisco, 2012). Still many developing countries remain silent spectators, without even attempting to negotiate prices with the patent holders of branded drugs. This could be because as Kuhn and Beall (2012) point out "patent holders — even though they carry no formal status at the WTO — wield tremendous force by threatening to withdraw their products from the local market or by encouraging their powerful host nations to retaliate against weaker nations" (p. 1168). Naturally, this leads to some loaded questions. Under what conditions will a developing country have the confidence to threaten to use the CL option or actually issue one? Under what conditions will such threats be successful in bringing down the price of the vital drug concerned? These queries, that the present paper seeks to answer, lie at the heart of policy choice among different possible mechanisms to improve access to critical medicines in developing countries.

The price of medicines, especially patented ones, which tend to be high, is one of the factors that can impede access to treatment. The debates on product patents and access to medicines have taken on a heightened allure since the launching of the *Agreement on Trade Related Aspects of Intellectual Property Rights* (TRIPS) in 1995. TRIPS is the most comprehensive multilateral agreement on intellectual property to date and is administered by the World Trade Organization (WTO). As implementation of TRIPS is a necessary condition to become a WTO member, any country seeking to benefit from the market and trade opportunities opened by the WTO must strictly comply with the intellectual property provisions of TRIPS.

One of the cornerstones of TRIPS is mandatory product and process patent protection in all branches of manufacturing, including pharmaceuticals, eliminating the possibility for firms in developing countries to produce and sell drugs at cheaper prices through re-engineering. It also homogenizes the minimum period of protection to 20 years and bans discrimination between imported and domestic products. Thus, to minimize the potential negative impact of patents on access to medicines, TRIPS contains a number of flexibilities. One of them is the right of countries to issue CL, whereby governments can permit third parties to produce the patented product without the consent of the patentee. TRIPS does not restrict the use of CL only to cases whose access is hindered by

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high prices. For instance, Article 31 allows CL in cases of 'national emergencies', 'circumstances of extreme urgency' and 'public non-commercial use'. For all these situations, it is not necessary to negotiate with the patent holder before granting a CL.

Recent literature suggests that the threat to issue a CL can be used to advantage in price negotiations between developing countries and pharmaceutical companies (Beall and Kuhn, 2012; Shankar et al., 2013). A review of this literature points out that three main factors play an important role on the outcomes of CL threats: local manufacturing capacity, import possibilities, and political pressure and retaliation – as shown in Table 1.

The existence of local manufacturing capacity is critical for a developing country's bargaining power vis-à-vis pharmaceutical companies, for only then can it license the technology to local companies. According to the World Health Organization (WHO, 2004), there are at least 84 developing countries with only drug formulations manufacturing capabilities. In addition, there are another 42 countries, mainly in Africa, with limited or no competence in the production of bulk drugs, relying on imports to satisfy their demand. Such developing countries can use a CL to get the cheapest priced generic from the international market. However, if the concerned drug is subject to one or more patents in the exporting country, then the latter has to issue a CL for export (as defined by the Decision of the TRIPS General Council of 30 August 2003). This means that the use of CL – or of the threat of issuing a CL – is not only limited by the existing local manufacturing capacity but also by importing possibilities.

The issuance of CL may provoke "economic punishment" from various players against the developing country exercising the TRIPS flexibility. Scholars note that there is considerable pressure from developed countries that actively dissuades less developed ones from granting CL (see Table 1). Thus, any developing country that threatens to issue a CL must expect to receive counter threats from pharmaceutical firms that can take the form of not launching new drugs in the developing country in the future, and/or not including the country in clinical trials for drug development. In addition, patent holders can also create a strong lobby with their home country's government in order to put pressure on the developing country, especially in terms of trade retaliation. Ultimately, the issuance of CL may provoke pharmaceutical companies and other industries dependent upon intellectual property rights (IPR) to avoid ventures in that nation and seek a more business friendly legal climate elsewhere.

To summarize, the *threat to issue* a CL is used as an instrument by public agencies in developing countries to effectuate drug price reductions in negotiations with patent holders. Local manufacturing capacity and access to imports determine the threat credibility. The cost of reprisals on the local industry is an element that has to be integrated in all calculations by developing countries engaging in price negotiations with patent holders. Nevertheless, to date there is no integrative analytical framework that explains the interrelationships between the possible determinants of CL issuance to obtain more affordable drugs and this is the gap that we aim to contribute to fill in this paper.

Our methodology follows a two-step procedure. In the first step, based on the reading of the literature, we formulate and solve a game theoretic model of price negotiation between a pharmaceutical company and a public agency in a developing country. In the second step, we validate our model by checking to what extent the model fits with reality in order to draw inferences. The game features two players: a *patent holder*, a large pharmaceutical company that sells its patented drug; and a *public agency* in a developing country that buys this drug and tries to negotiate prices with the patent holder using the issuance of a CL as a threat.

Our game theoretic model, like all economics models, seeks to simplify rather than represent a complex reality, in order to trace how certain outcomes can emerge. As an instrument of investigation, for analytical tractability, it limits itself to a set of elements most common to different manifestations of the phenomena under study. Furthermore, in this paper, the model's purpose is to provide a rationale for the surfacing of outcomes to help fine-tune intuition, rather than to serve as a precise tool for decision-making or forecasting.

The remainder of the paper is organized as follows. Section 2 presents the two models of price negotiation between a public agency and a patent holder of a lifesaving drug, where the public agency can use the threat to issue a CL as a bargaining tool. Section 3 validates our findings by checking to which extent the model explains real CL episodes. Section 4 proposes some policy recommendations. Section 5 concludes.

2. The drug price negotiation game

We first consider the context of complete information, when all features of the game are common knowledge to the patent holder and the public agency. Then we examine outcomes under incomplete information, when the patent holder does not know the true value of all the parameters influencing the choices of the public agency.

2.1. Game under complete information

Suppose that in a developing country, a multinational company, an original innovator holding a drug patent, is the sole supplier of a

Table 1
Factors significantly influencing the issuance of compulsory licenses.

Factor	Reasons	Reference(s)
Local manufacturing capacity	Is a necessary condition for credible CL threats	Abbott and Reichman (2007); Beall and Kuhn (2012); Benoliel and Salama (2010); Flanagan and Whiteman (2007); Kerry and Lee (2007); Ng and Kohler (2008); Ravvin (2008); Shadlen (2007); Smith et al. (2009); Yu (2007).
	Increases bargaining strength in price negotiations	Roemer-Mahler (2010).
Import possibilities	Necessary for credible CL whenever domestic manufacturing capabilities are absent	Abbott and Reichman (2007); Beall and Kuhn (2012); Bird (2009); Bird and Cahoy (2008); Dutfield (2008); Hannah (2011); Kerry and Lee (2007); Ng and Kohler (2008); Yu (2007).
Retaliation	Moral pressure from developed countries/patent holders' threat of market withdrawal or market retaliation	Abbott and Reichman (2007; Beall and Kuhn (2012); Benoliel and Salama (2010); Bird (2009); Bird and Cahoy (2008); Kerry and Lee (2007); Liu (2010); Ng and Kohler (2008); Shankar et al. (2013); Schüklenk and Ashcroft (2002); Smith et al. (2009); Yu (2007).
	Lobbying by pharma majors in WTO	Cohen-Kohler et al. (2008); Beall and Kuhn (2012); Ravvin (2008); Stiglitz (2008).
	Pressure to comply with TRIPS and WTO	Weissman (1996); Cohen-Kohler et al. (2008); Shadlen (2007).

drug, which is bought by the local public health agency for a major health burden. Let the public health agency of the developing country be given by *DC* and the foreign patent holder by *PH*.

The public health agency *DC* has a fixed amount of funds *B* to spend on drug provision that we will refer to as its budget. Furthermore, suppose that the patent holder *PH* has negotiated a price p_0 and is currently supplying $q_0 = B/p_0$ to *DC*. But the quantity, q_0, is not sufficient for the public health program to reach the poorer sections of society. For simplicity, we assume that the foreign patent holder can produce any finite amount of the drug at the constant average cost of production *c*.

In this context, the public agency, *DC*, has the choice of either accepting the status-quo or initiating a price negotiation. Note that such negotiation refers solely to public procurement prices for a specific patented medicine at the national level and "spillovers" of this negotiation over the supply chain to final pharmacy retail prices are not considered.

When a negotiation starts, *DC* informs the patent holder *PH* that unless *PH* reduces the price of its branded drug from p_0 to price $p_1 < p_0$, the government of *DC* will issue a CL and procure the technology to be manufactured by local firms or import it from the international market. For instance, p_1 could be the lowest price at which *PH* sells the branded drug in a different market or p_1 could be the low price at which a generic version can be imported. The patent holder *PH* can respond to such a threat in one of three ways.

i. *PH* can accept the large price drop to $p_1 < p_0$, then the game ends.
ii. *PH* can refuse to give the large price drop to $p_1 < p_0$, and instead make a counter-offer of a smaller price drop to p_2, where $p_1 < p_2 \leq p_0$.
iii. *PH* can refuse to give a large price drop and continue to reinforce the status quo.

When *PH* responds as per (ii) or (iii) above, *DC* can either accept *PH*'s proposal or issue a CL. Pharmaceutical companies can also make voluntary licenses available to avoid this threat, but we did not include this option in the model for simplification. For the same reason, we also did not consider the possible impact of parallel imports (when allowed by law) on the negotiation dynamics.

2.2. The payoff structure

The objective of *DC* is to maximize the quantity of the drug that it is able to buy, and thus, its payoff at price p_i is the quantity of the drug that can be bought given its budget. The goal of *PH* is to maximize its profit, and therefore, its payoff is given by the profit associated with the sale of the quantity q_i at price p_i, namely $\pi_i = \pi_i(p_i, q_i)$. Moreover, given the fixed budget *B* of the public agency *DC*, its payoff increases as the price of the drug decreases, i.e.:

$$p_1 < p_2 < p_0 \Leftrightarrow q_1 > q_2 > q_0. \quad (1)$$

By the same logic, since $B = p_i \cdot q_i$ the profit of *PH* decreases as the price decreases, i.e.:

$$p_1 < p_2 < p_0 \Leftrightarrow \pi_1 < \pi_2 < \pi_0. \quad (2)$$

At the start of the game, *PH* charges the negotiated price p_0 with corresponding payoffs $q_0 = B/p_0$ and $\pi_0 = \pi_0(p_0, q_0)$ to *DC* and *PH* respectively. The same payoffs hold if *PH* insists on the status quo and *DC* accepts the same.

Viewing the stakes from the *DC*'s perspective, if *DC* issues a CL, then it has to ensure that the minimum target of the public health program is met by finding alternative sources of drug supply. To do so, *DC* must either buy the drug from local firms or import it from the international market, depending on who can offer the drug at a lower price, which in turn will affect final market prices. It also has to bear the costs of possible reprisal, *R*, from the government of the patent holder's country, which reduces its budget for drug procurement from *B* to $B - R$. We assume that reprisal will have actual direct costs that can only be taken from the budget of the drug. A reprisal can assume very informal and subtle ways that are not always measurable in economic (or other) terms. Therefore, we opted for an oversimplification of the dynamic in order to explore its implications better.

Let α_L and α_F be the indicators of manufacturing capacity of local and foreign generic producers respectively, where $0 \leq \alpha_L \leq 1$ and $0 \leq \alpha_F \leq 1$. This means that if either α_L or α_F is equal to 1, the drug can be offered at the lowest possible price, p_1. Conversely, if α_L and α_F are both equal to 0, there is no alternative source of drugs. Then the drug price under CL is given by:

$$p_{CL} = \min(p_L, p_F) = \frac{p_1}{\max(\alpha_L, \alpha_F)}. \quad (3)$$

Finally, given that the reprisal *R* represents a burden on the developing country's budget, under CL the payoff of *DC* is:

$$q_{CL} = \frac{B - R}{p_{cl}} = \frac{(B - R) \cdot \max(\alpha_L, \alpha_F)}{p_1}. \quad (4)$$

In Equations (3) and (4), local capacity and import possibilities carry the same weight. Therefore, in case of CL granting, DC will opt for local manufacturing only if the local price is lower than the price of an imported generic. Obviously, if there is no generic version available for imports, then *DC*'s bargaining power will be function of only its manufacturing capacity.

This interaction is represented in Fig. 1 assuming that all parameters of the game are common knowledge to the two players.

2.3. Game outcomes under complete information

Applying the standard approach of game theory, the most probable moves along the game tree of the two players *DC* and *PH*, also referred to as the sub-perfect Nash equilibrium of the game, is indicated in Result 1. It presents the moves of players, which are rational given their anticipation of how the other player will respond. The equilibrium or most probable play is one such that no player has incentive to change his strategy given what the other player is doing – implying a convergence around a strategy profile.

Result 1*: DC will consider issuing a CL only if reprisal R is below an upper limit* $\overline{R}$ *and alternative supply capabilities max* (α_L, α_F) *are above a minimum limit* $\underline{\alpha}$. However, a CL will never be issued under complete information because PH will counteroffer a price p_2 *such that it is in the interest of DC to accept it.*

We begin by noting that the public agency, *DC*, will not issue a CL if quantity after a CL (q_{CL}) is less than the current quantity (q_0) available, i.e. if:

$$\frac{B \cdot p_1}{p_0 \cdot (B - R)} \geq \max(\alpha_L, \alpha_F) \quad (5)$$

The right side of equation (5) assumes its minimum value when $\max(\alpha_L, \alpha_F) = 0$. In this case, the above equation will always be true. Therefore, given the continuity of the functions on both sides of the equation, there always exists a small enough value $\underline{\alpha} = (B/(B - R)) \cdot (p_1/p_0)$ such that if the $\max(\alpha_L, \alpha_F) < \underline{\alpha}$, the above equation holds and *DC* prefers the status-quo.

Similarly, the right side of equation (5) assumes its maximum value when $\max(\alpha_L, \alpha_F) = 1$. Here equation (5) holds whenever $R = B(1 - (p_1/p_0))$. Again by continuity of functions, there exists a

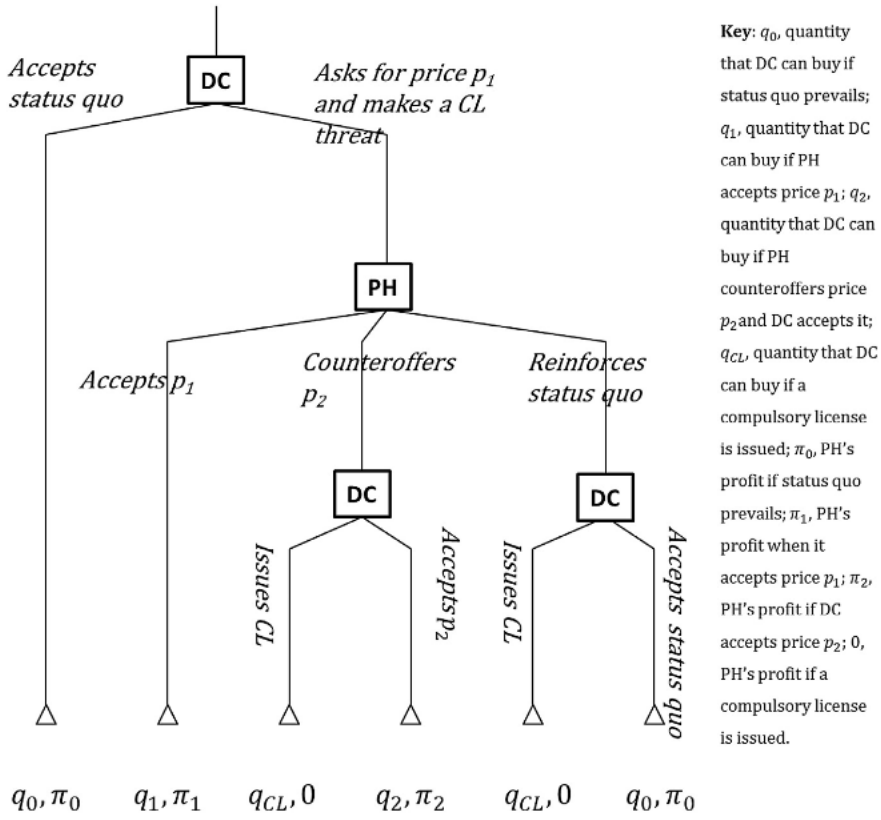

Fig. 1. Extensive form of the game under complete information.

high enough reprisal value $\overline{R} = B \cdot (1 - (p_1/p_0) \cdot (1/(\max(\alpha_L, \alpha_F))))$ such that for $R > \overline{R}$ equation (5) is true.

Thus, *DC* will consider issuing a CL if and only if the expected reprisal is not too high, i.e. if $R < \overline{R}$, and there is sufficient local manufacturing capacity or imports from alternative sources, i.e. $\max(\alpha_L, \alpha_F) > \underline{\alpha}$. However, even under such circumstances, *PH* can propose a price reduction to p_2 just small enough so that *DC* can buy at least the same under p_2 as after issuing a CL and thereby avoid the risk of having a CL being issued. Price p_2 can be easily found because:

$$q_2 \geq q_{CL} \Leftrightarrow \frac{B}{p_2} \geq \frac{B-R}{p_{cl}} \Leftrightarrow p_2 \leq \frac{B}{B-R} \cdot \frac{p_1}{\max(\alpha_L, \alpha_F)} \tag{6}$$

Therefore, the highest possible price that *PH* can offer such that $q_2 = q_{CL}$ is $p_2 = (B/(B-R)) \cdot (p_1/\max(\alpha_L, \alpha_F))$. At p_2, for *PH* the payoffs are higher than at p_1 and for *DC* there is no incentive to issue a CL. Thus, in the complete information context a CL can always be avoided. Moreover, according to equation (6), PH will accept to lower prices to p_1, i.e. $p_2 = p_1$, if and only if $R = 0$ and $max(\alpha_L, \alpha_F) = 1$. Indeed, the lower the expected reprisal and the higher the manufacturing capacity, the larger is the price drop acceptable to the patent holder.

However, in reality there have been instances when CL have been issued. Could this be due to informational constraints? We turn to this question now.

2.4. Game under incomplete information about possible reprisals

A reading of the existing literature indicates that the factor on which there is likely to be asymmetric information is the degree of reprisal from the government of the patent holder whenever a CL is issued. For instance, if we rearrange (4), we obtain $q_{CL} = B/(p_{CL} \cdot (B/(B-R)))$. We can interpret the term $p_{CL} \cdot (B/(B-R))$ as the *DC*'s reservation price, that is, the maximum price that *DC* is willing to pay not to issue a CL. The reservation price depends on reprisal *R*, which, in the game under incomplete information, is *DC*'s private information. Higher the reprisal, higher the maximum price that *DC* is willing to pay. The patent holder does not know how *DC* calculates such cost as this may include not only economic variables (such as share of exports on GDP, share of exports to the US in the total exports, United States Trade Representative listing etc.) but also more 'imprecise' political variables (such as political inclination of the current government, local political context etc.).

Suppose that the reprisal expected by *DC* in case a CL is granted can be high, say R^H, or low, say R^L, with $R^H > R^L$. In this case, *DC* can be one of two types. Either it can be of type DC^H, i.e. from a developing country that is a high reprisal target with a high reservation price of $p_{CL} \cdot (B/(B-R^H))$; Or *DC* can be of type DC^L i.e. belonging to a low reprisal target country with a low reservation price of $p_{CL} \cdot (B/(B-R^L))$.

Now the drug price negotiation game under incomplete information starts with the move by nature (represented by *N*), which chooses *DC*'s type. Nature chooses the developing country to be a high-reprisal type DC^H with probability γ, and a low-reprisal type DC^L with probability $(1-\gamma)$ and this is common knowledge to both players. The public agency, *DC* of either type, makes the second move either accepting status quo or launching a price negotiation. In the latter case, *DC* demands *PH* to lower price from p_0 to p_1 or face the risk of a possible issue of CL. The third move consists of the response of *PH*, to either decline DC's request and reinforce the status quo or make a counter offer of a smaller price drop to p_2, calculated according to type so that *DC* has no incentive to issue a

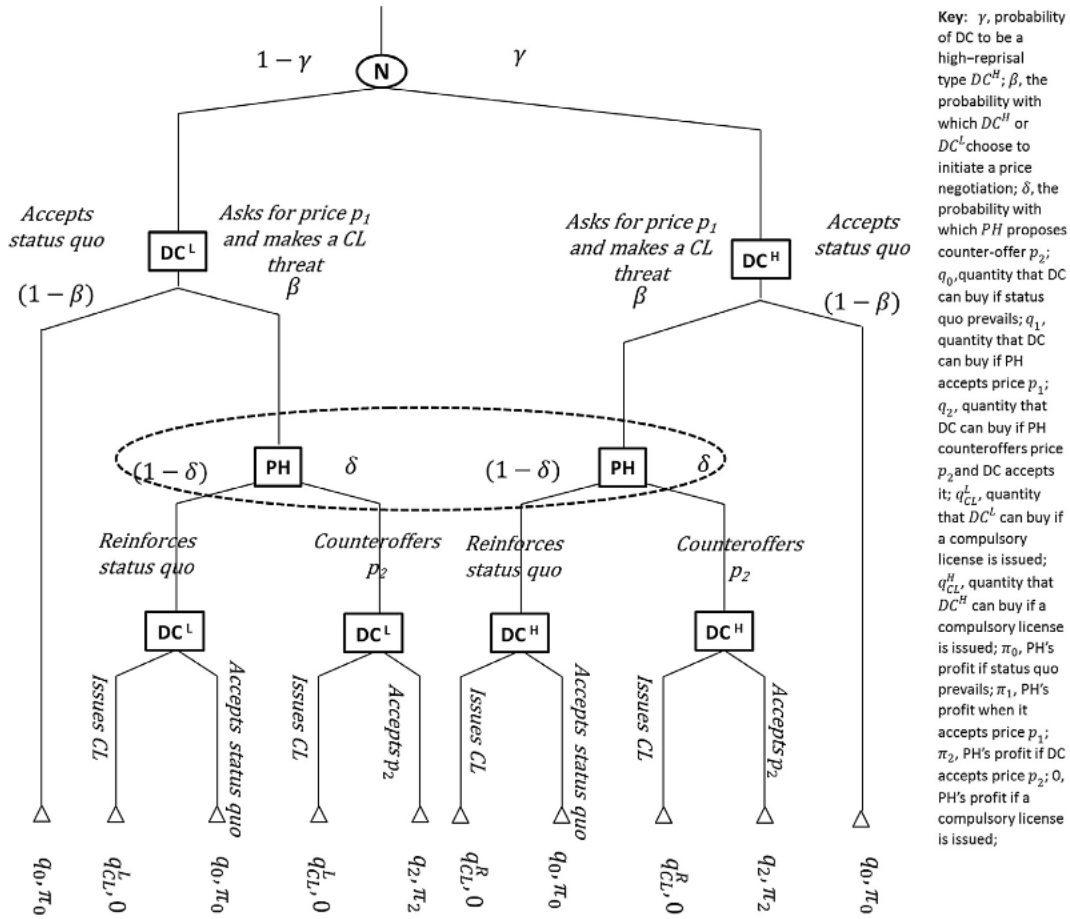

Fig. 2. Extended Game under incomplete information.

CL. In the fourth and last move of the game, *DC* decides whether to accept *PH*'s move or issue a CL. This game is presented in Fig. 2.

We start with an extreme case by supposing that if nature chooses *DC* to be DC^H, it means that $R^H > \overline{R}$. Then we know from the previous section, that DC^H will never issue a CL, preferring status quo to launching a price negotiation as $R^H \geq \overline{R}$ implies that $q_0 > q_{CL}^H$. However, is it in the interest of DC^H to bluff by launching a price negotiation with the threat of CL issue? How will the probable outcomes change? In order to identify the probable outcomes of a sequential game under incomplete information, which are also referred to as Perfect Bayesian Equilibrium, we consider mixed or probabilistic strategies for all players as per the standard approach. Let β be the probability with which the public agency, whether DC^H or DC^L chooses to initiate a price negotiation and $(1-\beta)$ the probability with which it accepts the status-quo. Similarly, let *PH* consider the randomized strategy, whereby with probability δ, it proposes counter-offer p_2, and with probability $(1-\delta)$ it upholds the status-quo. We now prove that CL is possible under incomplete information by a low reprisal developing country target via three results.

Result 2: *Whatever its type, DC^L or DC^H, a developing country will always initiate a price negotiation under the given payoff structure.*

The payoff of *DC* associated with the issuance of a compulsory licence varies according to its type as follows:

$$q_0 < q_{CL}^L = \frac{B - R^L}{p_{cl}} = \frac{B - R^L}{p_1} \cdot \max(\alpha_L, \alpha_F) \tag{7}$$

$$q_0 > q_{CL}^H = \frac{B - R^H}{p_{cl}} = \frac{B - R^H}{p_1} \cdot \max(\alpha_L, \alpha_F) \tag{8}$$

If nature chooses *DC* to be of type DC^L, then given that expected reprisals are low, DC^L will always choose to initiate negotiation for price reduction (i.e. $\beta = 1$). On the other hand, DC^H will choose its strategy, i.e. the probability of initiating price negotiation β, so as to maximize its expected payoff:

$$\max_{\beta}[(1-\beta)\cdot q_0 + \beta.\delta\cdot q_2 + \beta\cdot(1-\delta)\cdot q_0] \tag{9}$$

$$\max_{\beta}[q_0 + \beta\cdot\delta\cdot(q_2 - q_0)] \tag{10}$$

Since $q_2 > q_0$, for all values of δ, the expected payoff of DC^H increases in β. Therefore, to maximize payoff, DC^H will always choose $\beta = 1$, i.e. DC^H will always initiate a price negotiation.

Result 3: *Even if a price negotiation is initiated, the beliefs of PH about DC's type do not change as there is no learning.*

Now, according to the conditional probability (i.e. by Baye's law) determined by the game tree (Fig. 2), whenever a price negotiation is initiated, the probability that it comes from type DC^H is $(\gamma\cdot\beta/((1-\gamma)+\gamma\cdot\beta))$, while the probability it is from type DC^L is $(1-\gamma)/((1-\gamma)+\gamma\cdot\beta)$. However from result 1, we know that $\beta = 1$; and hence the beliefs of *PH* remain unchanged.

Result 4: *A CL will be issued only if the belief-payoff configuration is such that $\pi_2 < \gamma\cdot\pi_0$ and nature chooses DC= DC^L.*

Recall that *PH* believes that *DC* is of type DC^H and DC^L with

probability γ and $(1-\gamma)$ respectively. Thus, *PH* chooses δ, the probability of making the counter-offer p_2, so as to maximize its expected payoff, i.e.:

$$\max_{\delta} [\delta[(1-\gamma)(\pi_2)+(\gamma)(\pi_2)]+(1-\delta)\cdot[(1-\gamma)(0)+(\gamma)(\pi_0)]] \tag{11}$$

$$\max_{\delta}[\gamma\cdot\pi_0+\delta\cdot(\pi_2-\gamma\cdot\pi_0)] \tag{12}$$

Clearly, when $\pi_2 > \gamma\cdot\pi_0$, the expected payoff of *PH* is increasing in δ implying that *PH* will attribute the highest probability $\delta = 1$ to the counteroffer p_2. By construction p_2 offers better payoffs to both DC^H and DC^L as compared to issuing a CL or the status quo. And hence it will be accepted. Similarly, when $\pi_2 < \gamma\cdot\pi_0$, *PH* will affirm the status-quo. Here, it is in the interest of DC^L to issue a CL, while for DC^H it is better to accept the status quo.

Note that π_2 represents the certain payoffs for *PH* from taking the safe route of proposing a lower price p_2, while $\gamma.\ \pi_0$ is the expected payoff from pursuing the risky path of refusing to lower the drug price. Consequently, result 4 indicates that whenever the certain returns from the safe route exceeds the expected payoffs from the risky route (i.e. $\pi_2 > \gamma\cdot\pi_0$), *PH* will follow the safe route of making a counter offer. Thus, result 4 demonstrates that if the patent holder is handicapped by incomplete information, then even if it takes a bold stand on the basis of rational expectations and rejects a demand to lower drug prices, the true state of the world could be such that the bet does not pay off and a CL is issued.

3. Discussion and validation on real episodes

3.1. Data compilation and indicators

To test the predictions of the model with reality, we identified and compiled a sample of 33 episodes of CL announcements and threats that fit the context presented in this article. While 27 of these episodes had been identified previously by Beall and Kuhn (2012) for the period between from 1 January 1995 to 6 June 2011, following their methodology we identified seven additional episodes for the period between June 2011 and June 2013, resulting in a final database with 33 CL threat episodes in 19 nations. As the research did not require data collection from human subjects, an ethics approval was not required.

The next step of the validation procedure was to identify to which context of the model each CL episode fitted. To do this, we constructed indicators for the "existing level of local manufacturing capacity", "import possibilities for the drug(s) that was(were) the object of a CL" as well as for the "patent holder's belief on the reprisal level" that the country would be subjected to (see Table 2).

All these three indicators were obtained from publicly available sources. The Special 301 Report has been used since the mid-1980s by the United States to issue threats to developing countries. Any patent holder is likely to believe that a country that has already been formally threatened under the Special 301 Report is a high reprisal target. The study carried out by the World Health Organization (WHO, 2004) is the most comprehensive evaluation of the manufacturing capacity of pharmaceuticals at the country level. Although ideally the indicator of local manufacturing capacity should be at the drug level, the WHO report provides a picture close to reality. The WHO's pre-qualification programme ensures that a high quality version of a given drug is available. In addition, most of the official documents on CL provide information on whether or not the drug is going to be imported.

3.2. Cases explained by incomplete information game

We find that the model can propose an explanation for a majority comprising 25 of the 33 incidences of CL threats (see Table 3).

Cases 1–11 can be explained by result 4 whereby if the patent holder has a strong belief (i.e. $\gamma > (\pi_2/\pi_0)$) that *DC* is of type DC^H when in fact it is of type DC^L, a CL will be issued. Case 12 is also explained by the incomplete information game, but here *PH* is holds the right belief on *DC*'s type and the status quo prevails. It is interesting to see that episodes 5, 7 and 11 are related to high-burden non-communicable diseases (that is, cardiovascular disease and cancer). According to the WHO, the burden of non-communicable diseases measured by the disability-adjusted life-year (DALY) increased markedly during the last decade in low and middle-income countries (see Table 4). As pointed out by Shankar et al. (2013), this rise coupled with the high emotional impact, high prices, and limited drug substitutes that characterize these diseases, create an ideal scenario for more CL of this kind in the future.

4. Cases explained by complete or incomplete information game

Both complete and incomplete information scenarios can explain cases 13–20. First, according to our framework, when all players are completely informed, the public agency is able to obtain a price reduction such that the quantity it can afford under the new price is greater than the quantity it would be able to get under CL. Furthermore, by reaching a negotiated agreement, the government avoids the sanction costs associated with a CL and signals to existing and potential future investors that it respects the needs and interests of industries sensitive to intellectual property rights. Similarly, the patent holder does not lose the exclusive market

Table 2
Construction of indicators.

PH's belief on retaliation	Indicator	Local manufacturing capacity	Import possibilities
High	If the country was placed on the USTR's priority watch list	Countries classified by WHO (2004) as having either a "sophisticated industry with significant research" or "innovative capability"	If there was a generic version prequalified by the WHO by the time of the threat or the CL announced the drug(s) would be imported.
Medium	If the country was placed on the USTR's watch list	Countries classified by WHO (2004) as having manufacturing capacity for "active ingredients and finished products"	N/A
Low	If the country was not mentioned on USTR's Special 301 Report	Countries classified by WHO (2004) as having either manufacturing capacity for "finished products from imported ingredients" or "no pharmaceutical industry"	If the above criteria was not met

Notes. USTR = United States Trade Representative; N/A = Not applicable; WHO = World Health Organization.

Table 3
Selected incidences of CL threat that are explained by the model.

#	Year	Nation	Drug	Outcome[a]	Retaliation	Local capacity	Import possibility	Proposition support
1	2002	Egypt	sildenafil	CL	High	Med	High	Incomplete information $(\gamma > \frac{\pi_2}{\pi_0})$
2	2003	Malaysia	Didanosine; zidovudine	CL	Med	Low	High	
3	2005	Indonesia	Lamivudine; nevirapine	CL	High	Med	High	
4	2006	Thailand	Efavirenz	CL	Med	Med	High	
5	2007	Thailand	Lopinavir + ritonavir; clopidogrel	CL	High	Med	High	
6	2007	Brazil	Efavirenz	CL	Med	Med	High	
7	2008	Thailand	Letrozole; docetaxel; erlotinib	CL	High	Med	High	
8	2010	Ecuador	Lopinavir + ritonavir	CL	Med	Low	High	
9	2012	Ecuador*	Abacavir + lamivudine	CL	Med	Low	High	
10	2012	Indonesia*	Abacavir; lopinavir + ritonavir; tenofovir + emtricitabine; tenofovir + emtricitabine + evafirenz; nevirapine; lamivudine	CL	High	Med	High	
11	2012	India*	Sarofenib tosylate	CL	High	High	Low	
12	2012	Thailand*	Rituximab	None	High	Med	Low	
13	2001	United States	Ciproflaxin	Discount	Low	High	Low	Complete or Incomplete information $(\gamma < \frac{\pi_2}{\pi_0})$
14	2007	Nepal*	Sunitinib	Discount	Low	Low	High	
15	2001	Canada	Ciproflaxin	Discount	Med	High	Low	
16	2001	Brazil	Efavirenz	Discount	Med	Med	Low	
17	2001	Brazil	Nelfinavir	Discount	Med	Med	Low	
18	2007	Brazil	Atazanavir	Discount	Med	Med	Low	
19	2007	Brazil	Lopinavir + ritonavir	Discount	Med	Med	Low	
20	2008	Brazil	Tenofovir	Discount	Med	Med	Low	
21	2005	Brazil	Lopinavir + ritonavir	Discount	High	Med	Low	Complete information
22	2005	Brazil	Tenofovir	Discount	High	Med	Low	
23	2008	Thailand	Imatinib mesylate	Discount	High	Med	High	
24	2012	China*	Tenofovir	Discount	High	High	High	
25	2013	India*	trastuzumab	Discount	High	Med	Low	

[a] *Note*:* indicates Author's own compilation and otherwise source is Beall and Kuhn (2012).

Table 4
Non-communicable disease burden in low and middle income countries (2000 and 2012).

Year	Low income		Lower middle income		Upper middle income	
	DALYs (000s)	% Total	DALYs (000s)	% Total	DALYs (000s)	% Total
2012	155.429	30.6	530.318	46.6	504.353	71.2
2011	124.714	21.4	441.623	36.8	437.433	62.1

Source: World Health Organization: health statistics and information systems – disease Burden

rights for a drug and avoids the risk of a CL in one country creating incentives for other countries to do the same. Thus, in the game with complete information this equilibrium strategy is indeed the best outcome for both developing country public agency and multinational patent holder, given the existing constraints.

Secondly, there could have been an informational problem, but the patent holder believes the developing country to be a low reprisal target $(\gamma < (\pi_2/\pi_0))$. If that is the case, the patent holder prefers to make a counter-offer rather than provoke a CL and *DC* accepts the price drop regardless of its type.

Finally, cases 21–25 can be explained only by the complete information case when *DC* is subject to a high reprisal, but such that the threat is credible (i.e. $R < \overline{R}$). The incomplete information scenario cannot support these cases, because price discount is not a probable outcome when *PH* believes that *DC* is subject to a high reprisal.

4.1. Unexplained cases

Table 5 brings attention to the instances that do not conform to the predictions of the model. To understand the real circumstances behind each of these negotiation episodes would require a detailed qualitative study with key informants in order to capture factors and details that are not publicly available. Therefore, in this subsection, we were able to offer only conjectural explanations for these contradictory cases.

South Africa (26) could have negotiated a price discount according to our model but only status quo prevailed. Thus, it is likely that factors not captured by the model such as the lack of political will or an inadequate legal framework for granting CL were at play.

In cases 27–31, a CL should not have been issued, because according to our framework, a patent holder would provoke a CL only if it believed the developing country to be a high reprisal target. Nevertheless, in these cases there is no need for the patent holder to hold such irrational beliefs. Indeed, the least developed countries

Table 5
Selected incidences of CL threat that are outside model context.

#	Year	Nation	Drug	Outcome[a]	Retaliation	Local capacity	Import possibility
26	1997	South Africa	Various	Status-quo	Med	Low	High
27	2003	Zimbabwe	Various	CL	Low	Low	High
28	2005	Ghana	Various	CL	Low	Low	High
29	2004	Mozambique	Lamivudine; stavudine; nevirapine	CL	Low	Low	High
30	2004	Zambia	Lamivudine; stavudine; nevirapine	CL	Low	Low	High
31	2007	Rwanda	Zidovudine; lamivudine; nevirapine	CL	Low	Low	High

[a] *Source*: Beall and Kuhn (2012).

(even though Ghana and Zimbabwe have refused to accept the United Nation's recommendation for inclusion in the LDC list) are very unlikely to face any reprisal even if they were to issue a CL. Yet CLs were issued by these countries. Why?

A careful reading of the contexts of these incidences of CL reveals the cause to be linked to the specific nature of the technology and the drug concerned. All these cases refer to HIV/AIDS drugs. In the case of Mozambique, Zambia and Rwanda – patients were given a combination of drugs where each was being supplied by a different patent holder. However, there were Indian manufacturers who were producing generic versions of all the drugs involved and were prepared to sell it as fixed-dose combinations (FDCs). Such FDCs are not only more affordable than the free-drug components of the regimen given separately but they also improve medication compliance, which, in turn, can translate into better clinical outcomes. As the patent holders of each medicine were not able to supply FDCs for those drug cocktail, the CL were an optimal solution to the countries involved from both economic and public health standpoints.

In the case of Zimbabwe and Ghana, CL were issued as an extreme measure to all antiretroviral therapies to deal with the high HIV/AIDS incidence. In short, the total absence of reprisal from developed countries (which is ruled out by assumption in our model) and the availability of generic drugs at the best international prices made these countries indifferent between asking for a price reduction and issuing a CL.

Another limitation of the model is pointed out by the cases on Table 6, namely the possibility of the patent holder granting voluntary license to the developing country. Although the factors affecting the developing country's bargaining position (i.e. alternative suppliers and likelihood of retaliation) may be the same for requesting either voluntary licenses or price discounts, it is not clear when each of these options is optimal not only for the developing country but also for the patent holder. This could be an area for further research in the future.

5. Policy recommendations

In terms of policy recommendations, the central point of this paper is that developing countries must work to build their bargaining strengths rather than focusing on whether or not to increase the use of CL as a means to improve access to medicines through international trade. Clearly, CL cannot and should not be a mechanism for sustainable drug access in the developing world. Moreover, they must be limited to vital drugs (e.g. antiretrovirals), differentiating these from "life-style" drugs (e.g. sildenafil), so that they are not placed in the same basket of needs.

Efforts must be centered on development of bargaining strengths to be leveraged in negotiations over price or licensing fees to cope with shifting disease burdens and innovations. For instance, the disease burden of non-communicable diseases in low and middle income countries is increasing to which the pharmaceutical industry is responding with new drugs. Indeed, 65 out of 78 drugs approved by the Food and Drug Administration in 2012 and 2013 were for the treatment of non-communicable diseases, with more than 25% of drugs in the pipeline is being developed to treat cancers (Fisher et al., 2014). In this regard, to fortify bargaining strengths, at least four routes are possible.

First, both developing and least developing countries need to make the best use of industrial policy to build industrial and technology capabilities in pharmaceuticals for drugs that cannot be imported due to IPR restrictions. Given the obvious economic and technological constraints, it is not reasonable to claim that *every* country must pursue this goal. Middle-income countries such as Argentina, Brazil, China, India, and South Africa may have more autonomy to implement capacity-building policies, but the same may not hold for most of the least developed countries. Moreover, the focus cannot be limited to technological capabilities but has to include scale-up capabilities. Least developed countries can first work towards building technological capabilities in formulation and initiate institutional changes to facilitate the import of cheap generic versions of patented drugs under compulsory-license.

Second, countries could and should use other flexibilities in TRIPS, such as research exemption to develop FDC. However, there are other concerns that make this issue more complex. The development of FDCs demand technological capabilities (innovation capabilities and not only manufacturing capabilities) that are restricted to very few developing countries and involves considerable costs and uncertainty. If we consider that CL is for local market only, the costs could be greater than the savings. In addition, patent holders are also active in FDCs for patented drugs (e.g. elvitegravir + cobicistat + emtricitabine + tenofovir; atanazavir + cobicistat; darunavir + cobiscistat). Therefore, developing countries could be also better off by negotiating prices for these drugs. Based on the above, more research is required on how these options change trade-offs vis-à-vis CL.

Third, South–South R&D cooperation in pharmaceuticals has to be strengthened by pooling and sharing knowledge, technology and products in order to build bargaining strengths. This is particularly crucial because an increasing share of the new approved drugs are based on biotechnology, in which the developing countries have a greater lag than synthetic chemistry. Due to their intrinsic technological features and the specific regulatory requirements associated to the approval of such drugs, even after the patent expiration, there are fewer alternative substitutes and price negotiation on such drugs is going to be even tougher.

Fourth, there is an urgent need to facilitate the issuance of CL to export vital drugs to the least developed countries. In this regard, making the back-to-back CL smoother is likely to yield a high impact even in the short run. Institutional changes in this direction would not only benefit the least developed countries, but all countries that do not have enough manufacturing capacity for a given drug. Just changing the resolutions of the August 30 decision is not enough. While developing and least developed countries are subject to political and economic pressure from both companies and their home government, it is very unlikely that they will take full advantage of the existing TRIPS flexibilities to get more affordable drugs by either issuing CL or by bargaining for price discounts with the patent holder.

Table 6
Selected incidences of CL threat that require refinement of model.

#	Year	Nation	Drug	Outcome	Retaliation	Local capacity	Import possibility
32	2005	Argentina	Tamiflu	Voluntary license	High	High	High
33	2005	Taiwan	Tamiflu	Voluntary license	Med	High	Low

Source: Beall and Kuhn (2012).

6. Conclusions

The availability of drugs for public health programs depends on the quantity of drugs that the State is able to buy given its health budget and existing drug prices. With respect to patent protected drugs supplied by Western pharmaceutical majors, governments of developing countries are particularly in a vulnerable position as often the technology cannot be licensed or independently developed by local firms. Therefore, when there is a major disease that calls for patented medicines, the sustainability of public health programs may be put at great risk. In this context, one possible solution is to negotiate for a price-drop with the patent holder. If this initiative also fails, as a measure of last recourse, developing country governments can consider issuing a compulsory license.

Compulsory licenses should not be considered as a tool to promote long-term sustainable access to critical medicines, but rather a short-term fix for market conditions that exclude patients from receiving the right treatment. Even so, the incidence of compulsory licensing may increase in the future, but our recognition of this trend is not matched by a better understanding of its determinants and impact. Thus, the present paper developed a game theoretic representation of the price negotiation process between a public agency of a developing country and a patent holder to attempt to provide insight. A venue for future research could be a validation exercise of the model through interviewing people with experiential knowledge of these negotiations.

The game theoretic model demonstrated that a compulsory license would not be issued under complete information. However, under informational constraints a compulsory license could be issued if the developing country has sufficient local manufacturing capabilities or access to imports. The informational constraint considered was the degree of reprisal against the developing country in the aftermath of compulsory licensing, assumed to be known only to the public agency but not the patent holder.

Our model and its validation with reality affirm the view that the current institutional framework provided by the TRIPS Agreement and legitimized by both the Doha Declaration and the August 30 Decision gives freedom to developing and least developed countries to issue a compulsory license. Nevertheless, the analysis also clearly indicates that the existing political, diplomatic and economic pressure exerted by pharmaceutical companies and their supportive home governments are still barriers to the widespread use of compulsory licensing to provide more affordable drugs. These pressures can be subtle or even informal, but they are institutionalized as part of the rules of the game and play a strong enforcement role in constraining the available options to countries willing to issue a compulsory license.

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