Exploring the dynamics of new drug launch in pre-TRIPS India:

A survival analysis approach

Saradindu Bhaduri[♣] and Thomas Brenner[♠]

Abstract:
The small amount of literature on inter country diffusion of new drugs, focusing largely on industrialised countries, has primarily sought to address whether stringency in regulation influences delay of launch. Industrialised countries are, however, quite uniform in terms of a high share of systemic diseases and strong IPR protection. Tropical developing countries, on the other hand, are characterised by a high share of communicable diseases, and weaker forms of IPR protection. The growing literature on the diffusion of new drugs in developing countries indeed conjecture the importance of demand differences and market structure to shape the drug launch dynamics. This paper uses survival analysis technique to investigate the delay of new drug launch in India for drugs launched in the German market during 1990-2004. The paper finds that global commercial success of a new drug, first mover advantage, and the threat of imposition of strong IPR system shortens delay. Innovativeness of a new drug, however, has not impact on delay. This has important policy implications that are discussed.

[♣] Centre for Studies in Science Policy, School of Social Sciences, Jawaharlal Nehru University, New Delhi, India. Email: saradindu@mail.jnu.ac.in

[♠] Department of Geography, Phillips University Marburg, Germany. Email: thomas.brenner@staff.uni-marburg.de

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Introduction:

Inter-country differences in drug launch are studied in the literature for quite some time, at least, since the work by Wardell (1973). He examined whether stringency in the US FDA regulation, post-Thalidomide, resulted in a longer delay of the launch of new drugs. Motivated by this study, many other empirical studies were conducted to understand the dynamics of drug launch across countries (Peltzman 1973, Grabowski 1980, Cullen 1983, Parker 1989). A strong point of many of these studies is their use of comprehensive proprietary databases for the cross country launch of new drugs. However, one can identify two broad limitations of these studies. First, these studies mainly focus on the launch of new drugs in the major pharmaceutical markets of the developed countries, and confine themselves primarily to examining whether stringency in regulation can explain delay. Second, methodologically, most of these studies do not intend to deal with the right censorship problem, which arises from the finite length of their data set. A censorship problem arises because drugs that are first launched in a country during the later years of observation may be diffused in some of the studied countries after the period of observation. As a consequence, it is difficult to judge whether the absence of those drugs in some markets is due to an insufficient period of observation or implies their non launch.

Major pharmaceutical markets in the industrialized countries are largely homogenous in terms of disease profile and institutional arrangement (Cullen 1983: 74). If one roughly categorises diseases into two broad groups, communicable tropical diseases and non-communicable systemic diseases, then developed industrialised countries have a disproportionately high share of non-communicable diseases. Concerning the institutional structure, most of the countries have a very stringent, perhaps uniform, set of norms for new drug approval. They also have a strong product patent system in place. Due to this

strong product patent system, only the innovator or its licensee(s) can launch a new innovation in any of these markets.

In recent years, a number of studies explored the dynamics of drug launch in developing countries (Lanjouw 1999, Lanjouw 2002, Bhaduri and Ray 2006, Ray and Chakravorty 2007). Broadening the sample and incorporating these countries enhances the scope of research in two ways. First, being located in tropical regions, the disease pattern in these countries is quite different (Lanjouw 1999, Lanjouw 2002). The majority of population in these countries suffer from communicable tropical diseases. Demand differences is thus a key verifiable determinant of the diffusion of new drugs in these countries. Secondly, pharmaceutical markets in many of these countries, until very recently, were under weak patent system, which permitted reverse engineering and incremental innovations. New drugs in these countries can, therefore, be launched by any firm present in the market, and not only by the innovating firm (Lanjouw 2002). Issues like competitive pressure to launch, and first mover advantages can also, thus, be incorporated in the analyses of drug launch (Bhaduri and Ray 2006).

Although these studies lead to an interesting set of conjectural hypotheses, there is not much attempt to subject these conjectures to rigorous empirical analyses. This paper makes an attempt to contribute to this growing literature by analysing the drug launch pattern in India. We use Cox proportional hazard model to understand the determinants of drug launch delay in India for the drugs which have been launched in Germany during 1990-2004. The final year of analysis was chosen to be 2004, as this is the last year under weak intellectual property rights regime in India. In the next section we develop the conceptual framework of our study. Section 3 describes the sample. We give a detailed account of our estimation methods in section 4. In section 5, we draw our hypotheses. Results are describes in section 6, and our main arguments are synthesised in section 7.

2. Conceptual Framework:

The importance of analysing drug launch delay is derived from the importance of new medical therapies in promoting economic development. It is widely accepted that access to modern medical therapies have immensely contributed to the developmental catch up process of many less developed countries (Kremer 2002). A delay in the introduction of new medical therapy, therefore, can prove to be detrimental to economic development. Many studies on drug launch have revolved around one central question: to what extent do the various regulations on introducing new drugs contribute to this delay? However, even if regulation might hurt the interest of free markets, a regulatory framework in pharmaceuticals is necessary. The Thalidomide tragedy has made us realise that new medical therapies are ambiguous blessings and the absence of adequate safety standards can, fatally, expose human beings to the threats of false claims and unintended consequences of new technologies. In the ideal Mertonian world of public science, frivolous claims about a new scientific invention would be checked by the prospect of public scrutiny at the hands of scientists with no personal interest (Merton 1973). As a result, need for state regulation might become redundant (or low). But, much of the (applied) research in the field of pharmaceutical sciences is conducted in the private sector with proprietary interests leaving little room for such unbiased evaluations in the public domain. Recent studies have highlighted that contestable claims about the appropriateness of a new technology by a profit seeking agent is more plausible in such a framework (Gold et al 2001), calling for an appropriate regulatory framework. The need for regulation is compounded by the fact that medicine falls into the category of *credence goods*, whose quality cannot be ascertained merely by consuming it (Nelson 1970).

Most of the studies on drug launch have, subsequently, analysed how/whether stringency in regulation leads to delay in launches (Peltzman 1973, Wardell 1973, Grabowski 1980, Cullen 1983, Parker 1989, Danzon et al 2005). The conclusion, however, varies. While studies by Wardell (1973) and Cullen (1983) found that stricter regulation led to drug delay in the USA, Parker (1989) does not find any evidence of delay in drug launch in the USA compared to other countries in his sample. It was also found that average delay declined in the decade of 1980s, compared to 1970s. With more recent data Grabowsky and Wang (2006) find that the US is becoming the country of first launch for a majority of drugs in recent years.

Besides regulatory framework of drug approval, expected market size is also shown to influence the lag in drug launch. Larger expected market size reduces delay (Cullen 1983), and lower expected prices are shown to reduce the number of new launches and enhance delay due to the problems of external referencing and the possibility of parallel exports (Danzon et al 2005). However, as has been mentioned above, most of these studies pertained to developed countries having broadly similar disease profile (hence, demand structure for health care) and similar institutional arrangements. Indeed, differences in medical, legal and commercial environments existing in developing countries were believed to have adversely affected the launch of new drugs in these countries (Cullen 1983).

Differences in demand pattern and institutional arrangements in developing countries can help explore a plethora of other issues related to the diffusion of drugs. Concerning demand pattern, broadly, there are two types of diseases, namely, non-communicable diseases and infective diseases (Troullier and Olliaro 2001). Non-communicable diseases, caused by intrinsic malfunctioning of our systems, are mostly non curable and requires prolonged (life long) treatment. Infective diseases, on the other hand, are caused by

external pathogens (bacteria and virus due to pollution and bad hygiene). These diseases are generally short lived and completely curable through medicine. Being located in non-tropical regions and due to improved hygiene, communicable infective diseases do not pose any serious health problems in developed countries.[1] Their main health burden remains in the area of various non-communicable systemic diseases. People in the developing countries, on the other hand, suffer more from infective diseases (also known as tropical disease). As an illustration of this different disease profile, one may note that the share of communicable diseases in the total Disability Adjusted Life Years (DALY) for Germany is around 4%, while in India around 45% of total DALY is due to communicable diseases. On the other hand, non-communicable diseases count for around 90% of DALY in Germany. The relevant share for India is around 40%.[2]

It may, therefore, be plausible that delay will be shorter for drugs which have higher demand. Under a strong patent regime, Danzon et al (2005) argue that the prevalence of high demand in a country raises the opportunity costs of delay by shrinking the discounted value of total patent-monopoly profits to be earned. Their study, however, takes into consideration only countries which have strong patent systems. Monopoly profit is ensured for the innovating firm during the length of the patent protection in these markets. In the absence of a strong product patent system, however, competition between brands becomes feasible even during the life of a patent, adding uncertainty to patent monopoly. The potential of first mover advantage may crucially determine the lag in such cases. The theory of industrial organisation highlights that the first mover advantage would be high when the scope of repeat purchase is high. Note that non-communicable

[1] This is true, occasional outbreaks of flues notwithstanding. Also, disease like AIDS is a communicable, yet not curable, disease. However, spread of AIDS does not depend on poor hygiene or climatic conditions. In tropical conditions, however, AIDS patients may have higher possibility of getting other kinds of infections. Thus, drugs for AIDS may be needed more in tropical countries.

[2] See http://www.who.int/healthinfo/statistics/bodgbddeathdalyestimates.xls for details. Last accessed on 26 August, 2008.

diseases are non-curable in nature. Medicines have been successful only in controlling their adverse effects on the body. On the other hand, most of the communicable diseases are often fully curable by medicine. Greater need for repeat purchases of drugs for non-communicable diseases, arising out of the need for long term treatment, have important consequence for first mover advantage in markets with weak patent protection, such as India.

Bhaduri and Ray (2006), in this context, argue that psychological costs of brand switchover are higher for drugs for non-communicable diseases compared to the drugs for infective diseases. Non-communicable diseases are also known as life style diseases. In the context of a developing country, demand for these drugs seem to emerge more from the upper socio-economic strata who are comparatively more quality conscious and litigious than people of lower socio-economic strata. The latter group, on the other hand, constitutes the major market for drugs for infective diseases due to their unhygienic living conditions. Due to higher level of quality awareness and the litigious nature of the patients, the physicians of non-communicable diseases would be reluctant to switch brands, solely on grounds of cost efficiency. This adds to the psychological costs of brand switching and strengthens first mover advantage for drugs of non-communicable diseases. As a consequence, delay for drugs for non-communicable diseases can, in fact, be shorter compared to anti-infective drugs (Bhaduri and Ray 2006).

The importance of a new drug therapy also seems to shape the dynamics of drug launch. Quite often, commercial success of a drug has been taken as a proxy for its therapeutic importance. Commercially significant drugs diffuse faster, especially to non-leading countries like Israel, compared to ‘all new drugs’ (Sax 1989). However, all commercially significant drugs may not necessarily bring about major therapeutic advancements.

However, most of the studies seem to overlook this distinction between the commercial significance of a drug and the therapeutic advancement it brings about. Grabowski and Wang (2006), for instance, argue that the drugs that are 'present in all G7 countries are also the drugs of 'high quality', or 'commercially successful' or 'both'. Roy and Chakraborty (2007) make a pioneering attempt to distinguish between these two characteristics of drug, commercial success and therapeutic advancement. Drawing upon the categorisation of therapeutic advancement made by the United States Food and Drug Administration (USFDA), this study shows that the share of 'advanced therapy' was not significantly different from the share of 'non-advanced therapy' for 77 new drugs (out of 297 new drugs launched in the USA), which were launched in India during 1995-2003. This finding, perhaps, implies that innovativeness of a drug has got little to do with its launch in India. However, for a more meaningful conclusionit would be necessary to study the launch pattern of commercially successful drugs and of innovative drugs separately.

A few studies also seek to identify whether the nationality of the innovating firms can explain the pattern of first launch. In this regard, Japanese firms are shown to be exceptionally keen to launch their products in their home markets before it is launched elsewhere (Thomas 2001). US firms, in contrast, seem to choose between their own country and European countries, depending on market size, and the ease of marketing approval (Grabowsky and Wang 2006). Grabowsky (1980) and Grabowsky and Wang (2006) further find that there has been a turn around in the launch behaviour of the US pharmaceutical firms. Until the 1980s they used to prefer launching their new medicines in the European market. In recent years, however, the US market has become a more attractive location for them for the first launch.

In a nutshell, the studies on drug launch have identified stringency in regulation, market size and opportunity costs as major determinants of the delay in drug launch in major pharmaceutical markets of industrialised countries. However, few studies have attempted to understand the diffusion of new drugs in developing countries. These countries have different disease profile and a different institutional structure compared to developed countries. To elaborate, there is more prevalence of tropical communicable diseases as opposed to a high prevalence of non-communicable diseases in the industrialised countries. These two segments have different first mover advantages. Furthermore, these countries often have weak patent protection, giving protection only to processes and not product innovations, so that competition is possible even during the patent protection period. Many of these aspects have remained unexplored in the literature. We investigate some of these aspects by analysing launches of drugs, present in the German market, in India.

3. Sample:

Our analysis concerns the period 1990-2004. Although data was available for later years, we decided to take December 2004 as the end point because this marks the end of the era of weak patent protection in India. Note that India amended its patent legislation in 2005 to comply with the Trade Related Intellectual Property Rights (TRIPS).

We have a sample of 634 drugs that were launched in Germany during this period. Among these, 201 drugs have been launched in the Indian market during the same period. We had to consult two corporate data bases (Rote Liste and Dimdi Pharmasearch) to obtain the comprehensive list of all drugs launched in Germany during that period. It has to be taken into account that one molecule may be sold in different dosage forms. The Dimdi dataset contains the dates of first launch of all these individual entries. Among all

these entries, we took the earliest entry pertaining each molecule, since later entries merely give the range of product differentiation for a particular therapy (drug). However, both datasets share a common shortcoming: they only record information about those drugs that are currently present in the market. This implies that we cannot obtain any information about drugs which have been withdrawn from the market, even if they were launched after 1990.[3] In addition, if a drug is re-introduced after some time, these datasets would only give us the date of re-introduction[4].

The list thus obtained had to be pruned further by omitting homoeopathic drugs and plant medicines, to make it comparable with the list we use for Indian drugs. The source for drugs launched in India is the proprietary corporate database Pharmabiz (www.pharmabiz.com). This list matches with the list of drugs mentioned on the webpage of the Central Drug Standard Control Organisation (CDSCO), Government of India[5]. It may also be noted that, like the German data, Indian data is also available on individual products (dosage forms) for each molecule. Again, we have only considered the first entries for each molecule to make our two datasets comparable.

4. Estimation method:

We use a Cox proportional hazard model to understand the dynamics of drug launch in India. However, 41 drugs have been launched in India before their launch in Germany. The Cox proportional hazard model would ignore all observations for which the launch date in India precedes the launch date in Germany, once we set the 'entry time' for an

[3] Such a situation may arise if a drug cannot qualify the requisite standards of quality and safety in the phase of post-marketing surveillance. Many so called blockbuster drugs have also often fallen prey, leading to their withdrawal or suspension from the market. Nimesulide, Celecoxib, Refocoxib are some of the examples.

[4] Please note that this problem is not present in the proprietary corporate database called AMIS (full name required). However, financial resources at our disposal did not permit us to exploit this data source to the fullest possible extent.

[5] This list is, however, available only from 1999.

observation to be its launch date in Germany. The determinants of launch of these 41 drugs would remain unknown in such a set up. To understand the determinants of drug launch for all drugs, including these 41 drugs, we use a least square regression including all 201 drugs that are present in both markets.

As we know, survival analysis is primarily concerned with analysing 'time' (known as 'analysis time') to the 'occurrence of events' (or 'deaths' or 'failures'). In this paper, time is calculated in month and an event refers to the launch of a new drug in India *after* its launch in Germany. In survival analysis, 'analysis time' signifies the 'onset' of risk for a subject. This risk ends with the 'death' (or failure) of the subject under consideration. In our paper 'death' ('failure') implies the launch of a drug in India. Cox proportional hazard models explain every such 'occurrence of event' with the help of a set of covariates (x).

Analysis time is defined in a manner so that two subjects having similar values of covariates should have similar "onset of risk". At each unit of 'analysis time' one has a binary outcome - either a 'failure' has occurred or it has not yet occurred. In the Cox proportional hazard model these individual observations are first ordered in terms of their onset of risk. The model then calculates the conditional probability of failure for each subject at each point of analysis time, and combines them to calculate the likelihood function. Unlike a parametric hazard model, which relies on a definite functional form of the hazard function [h(t)], the Cox model leaves h(t) unspecified. A typical Cox proportional hazard model is represented as: $h(t) = h_0 (t) \exp (b_0 + x_j b_j)$,

$h_0 (t)$ is the base line hazard function.

However, the conventional emphasis on 'time' in ordering the occurrence of event has been challenged by Cleves et al (2002). It has been emphasised that 'onset of risk' might depend on factors, which are correlated with (and are therefore function of) time, but not

on ‘time’ per se. Note that at any point in ‘analysis time’ a Cox proportional hazard model estimates the (conditional) probability of a ‘failure’ only by taking into account the subjects that have not failed till then. Then, it combines all these probabilities in order to arrive at the composite likelihood function for all subjects. The temporal ordering, therefore, is important for calculating the likelihood of failure of each subject, and not the unit of time (Claves et al 2002: 89-90, 126). Calculating ‘onset of risk’ differently might lead to a different temporal ordering of subjects (in terms of onset of risk, or failure time), changing the (conditional) probability of failure of individual subjects. Clearly, therefore, the way ‘onset of risk’ is measured would have bearing on the probability of failure of each subject. Given a likelihood function L(b/data) = L(analysis 1)L(analysis 2)…, the composite likelihood estimate of ‘b’ is crucially determined by the temporal ordering of observations and, therefore, the measurement of ‘onset of risk’.

Measurement of ‘onset of risk’ (or failure time) can also have implications for the occurrence of tie. Note that the presence of tie reduces efficiency of the maximum likelihood estimate by reducing the number of ‘analysis time’ for which the conditional binary probabilities are calculated (Claves et al 2002: 129, Maribuni and Valsecchi 1995: 182-3). Thus, if an alternative measurement can reduce the number of tied failures it can actually contribute to the efficiency of our estimate.

In the literature on drug launch, it has been pointed out that delay has opportunity cost. To elaborate, when patent length is finite, delay in launch reduces the duration an innovating firm can enjoy monopoly profit in the market. This is, however, true when the market is protected by strong intellectual property rights regime that prohibit reverse engineering. For markets like India, on the other hand, such explanation may not hold much water given that competition is possible even during the working life of a patent. However, given that technologies become outdated and profits that can be made with technologies

decrease with time, the opportunity costs argument associated with delay can still be justified for such markets. Therefore, the ordering of the occurrence of events maybe assumed to be a function of 'opportunity cost of delay', rather than 'time'. The opportunity costs would however, be a function of time. In a nutshell, we argue that two subjects, in this model, will face the same 'onset of risk', when their opportunity cost of delay becomes similar.

Accordingly, we estimate two variants of the Cox model. In the first model, 'analyis time' is the physical time or the absolute delay time. In the second model, 'analysis time' refers to accumulated opportunity costs of delay of launch, measured by total foregone demand due to delay in launch.

We now discuss the hypotheses and construct our variables in the next section.

5. Hypotheses and Variables:

We argue that the delay in launch could be explained by the following set of factors.

Global commercial success of a drug (BB):

Assuming that prescription pattern in major pharmaceutical markets would have demonstration effect in markets of developing countries, a negative relationship between commercial success of a new drug in major markets and its launch in country like India may be hypothesised without much difficulty. Besides such demand side factors, commercial success in other countries might also encourage the domestic firms in the follower country to speed up their R&D and process engineering by raising their profit expectations. As a result, imitation may become faster, increasing the possibility of a faster launch in the domestic market. On the other hand, when a new drug is not commercially successful in leading countries, domestic firms may adopt a cautious strategy for imitation leading to a longer delay, ceteris paribus. Sax (1982), however, does

not find evidence of any shorter delay for drugs that are commercially successful, when compared with the delay associated with commercially unimportant ones in Israel.

Global commercial success can be measured by the annual global sales of a drug. In particular, a drug is considered globally successful, unequivocally, if it gets the status of a blockbuster drug. A drug becomes a blockbuster drug if its global sales turnover reaches US$ 1 bn per annum (Landau et al 1999). However, the FDA does not collect this information. Proprietary databases which claim to maintain such data are also prohibitively expensive. Therefore, we usethe US sales reports of prescription drugs and the pharmacy magazine Drugtopics (www.drugtopics.com), which carried a list of top 200 branded drugs in various years[6]. We also reviewed the company reports of some of the leading innovating firms. Finally we find that 52 such blockbuster drugs are present in our list of drugs in Germany.

The variable BB is a dummy variable that takes the value '1' for blockbuster drugs, and '0' otherwise.

Innovativeness of drugs (INVDRUG)

The knowledge about a major therapeutic advancement can be presumed to diffuse faster among the community of physicians compared to knowledge about a drug that represents only a minor therapeutic advancement. Channels of such knowledge diffusion could be formal medium of transfers like medical journals, or more informal channels like deliberations at conferences and seminars. The individual firms would also allocate more resources on promoting these drugs, reinforcing the positive effect. Both these factors would, conceivably, lead to shorter delay for such drugs.

[6] We thank CDER for this suggestion.

The US Food and Drug Administration (FDA) specifies their opinion on innovativeness of a new drug by marking drugs with high therapeutic advancement as 'Priority drugs (P)' and drugs with insignificant therapeutic advancement as 'Standard (S)'.[7] We used the CDER website to locate these drugs. Data from 1999 was available in http://www.fda.gov/cder/rdmt/. For the pre-1999 period, data were available in the Reports to the Nation and in http://www.fda.gov/cder/archives/default.htm#Archival. We could go up to 1997, and found that 48 of all priority drugs noted by the CDER (USA) to be present in the German market for the period 1997-2004.[8]

We note that out of the 48 drugs that brought about major therapeutic advancements only 6 could attain the status of blockbuster drugs during our sample period. On the other hand, 20 out of 26 blockbuster drugs launched in the German market since 1997 did not bring about any major therapeutic advancement.

Interestingly, most of the studies do not distinguish between commercially important drugs and drugs that bring about significant therapeutic advancement in analysing delay. Grabowski and Wang (2006), for instance, define a NCE of "high quality or commercially important NCE or both" if it has been launched in all G7 countries. The data presented above, however, give us ample reason to believe that there can be little association between commercial success of a new drug and its innovativeness. We, therefore, chose to examine these two effects separately.

The variable INVDRUG is a dummy variable taking value '1' for 'priority drugs' and '0' otherwise.

Therapeutic Category of the new drug (TC):

[7] See also Ray and Chakravorty (2007).
[8] Data prior to that year are not comprehensively available, as reported by the CDER.

Among the two broadly defined therapeutic categories, namely, non-communicable systemic disease (ND) and infective tropical disease (ID), Bhaduri and Ray (2006) argue that the delay in launch would be less for drugs belonging to the former group due to higher first mover advantages. Conventionally, first mover advantage accrues from high psychological cost of brand switching. In health care, ND drugs seem to have high psychological cost of brand switching primarily due to chronic, non-curable nature of these diseases. Physicians, as a result, often become reluctant to experiment with brands, especially when brands vary predominantly on account of their prices. In countries like India, treatments for ND diseases are primarily demanded by the people belonging to upper socio-economic strata, who are more quality conscious and litigious prone. All these characteristics strengthen the first mover advantage. In contrast, ID diseases are curable and short lived. Patients also come largely from lower socio-economic strata, where costs rather than finer distinction of quality become a major determinant of health care. These patients are also, presumably, less litigious prone. Physicians, therefore, enjoy more scope of experimentation with new brands, eroding much of the advantages of moving first.

Following Bhaduri and Ray (2006) we categorise all drugs into two broad therapeutic categories, namely, infectious diseases (ID) and non-communicable diseases (ND). Chronic diseases have been merged with ND on the assumption that they, unlike infectious diseases, are not completely curable through medication. As argued above, infectious diseases are caused by external pathogens, often as a result of contaminated food, drinks or bad sanitation. Non-communicable diseases, on the other hand, are not caused by external pathogens but by malfunctioning of the internal human system.

Our dataset provides the therapeutic category of each drug. We grouped them into two groups with the help of drug information available on the websites and the various issues of Indian Drug Review.

We use a dummy variable TC, which takes the value '1' if a drug is for the treatment of ND, and '0' if it is to treat any ID.

Market share (MS):

It may be quite straightforward to hypothesise that the higher the market share of a product, ceteris paribus, the faster will be its introduction in the market. Implicit behind this explanation is the opportunity costs (foregone profit) of delay. We use market share variable in two ways. (1) as a covariate, attempting to explain the physical time delay in terms of market share of a drug. (2) We use the opportunity costs dimension of market share and reconstruct the 'analysis time' or 'onset of risk' as a function of cumulative opportunity costs (product of time and market share).[9] .

The true market share for a drug which is yet to be launched is non-existent. As a proxy we take the market share of the therapeutic category to which the prospective new drug belongs. ICRA (2005, pp. 5-6) categorises all diseases into 14 therapeutic groups and provides market share for each of them. Each drug in our data set, therefore, gets the value depending on which one of the 14 therapeutic categories it belongs to. We use this information only for India.

Awareness about TRIPS (WTO):

The literature on drug launch emphasises that stricter regulation prolongs delay in drug launch. The literature on technology transfer, on the other hand, emphasises that stricter patent regulation reduces delay in transfer of new technologies (see, for instance, Mansfield 1994). It is, therefore, difficult to assign any one-to-one correspondence

[9] Conceivably, temporal ordering of 'failure time' would be more different when 'onset of risk' is measured in terms of a joint function of time and market share than when 'onset of risk' is measured only in terms of physical time.

between strength of regulation and length of delay, and much would depend on the nature of regulation. Moreover, both these sets of literature only visualise the innovating firms or their licensees as the main agents of transfer or diffusion of (drug) technologies. In the absence of a strong patent regulation, however, a new technology can also be introduced in the market by other firms through process engineering and imitation. However, our present hypothesis is concerned with the impact on delay of an increase in the strength of patent protection from a definite future date. India became a signatory to the World Trade Organisation in 1995 with the commitment to introduce a strong product patent system in line with Trade Related Intellectual Property Rights (TRIPS) in the year 2005. Thus, in the year 1995 it became common knowledge that India will adopt a strong patent regime in the year 2005. It may be reiterated that strong TRIPS compatible patent system prohibits reverse engineering activities. What are the likely implications for drug launch when such a change in regulatory framework is forthcoming?

Suppose there are two groups of firms: multinationals and domestic firms. Further assume that new drug discovery research is carried out only by the former group of firms. The domestic firms do not have the requisite technological capability and, instead, only carry out reverse engineering based minor innovations. When the prospect of a strong patent system appears, multinational firms might postpone its launch decision in the Indian market until such a system is in place to pre-empt competition, with the consequence of prolonging the delay. However, a product may be imitated by the domestic firm when the innovating firm decides to abstain from launching it in the host market. In fact, the domestic firms would attempt to speed up the imitation process and launch new drugs before a strong patent regime comes forth. If new drugs in India are mostly launched by domestic forms, one would expect a shortening of launch delay of new drugs when such an announcement is made.

The TRIPS sought to render reverse engineering as a strategy untenable by providing patents to the entire product. We, introduce a dummy variable (TRIPS) taking the value '1' for drugs which are launched in the global market (represented by launch in Germany) since 1995, and '0' for drugs launched in pre-1995 period.

6. Results:

We measure delay by the number of months elapsed between launch of a drug in Germany and its subsequent launch in India. In few cases, drugs have been launched in India before their launch in Germany. The variable in those cases takes negative values. Note that in the absence of exact dates of launch for many drugs we have used the first day of the month as the representative date.

We divide this section into two subsections. In the first section we report the results of our cross section regression analysis taking only those drugs which have been launched in both countries. In the second section we present the results of a survival analysis in which we have to exclude drugs with a negative delay, meaning that they are launched in India before Germany.[10]

The Regression Analysis:

Due to very high correlation between TC and MS (-0.46) we use these variables separately in our model (model 1a and 1b). Due to heteroscedasticity we take robust estimations. Both models are statistically significant at 1% levels. In model 1a, the dependent variable T_LAG is explained by MS, BB and WTO. All three independent variables appear with desired signs and level of statistical significance. BB is negative and significant at the 5% level, showing that the time lag for blockbuster drugs is significantly shorter than for other drugs. MS is also negative and significant at the 5% level. This implies that drugs with a large market are launched faster. WTO seems to be

[10] We are not sure whether this is indeed the case, or the negative lag is because some drugs were withdrawn from the German market before their current launch. As we have mentioned earlier, our dataset would capture the most recent launch in such cases.

the most important explanatory variable with the level of significance being 1%. The coefficient is negative, so that we find a delay that has decreased after the announcement of stronger patent laws. Similarly, the F-statistics for model 1b is also significant at 1% level. BB and WTO remain significant at the 5% and 1% level, respectively. TC is positive and significant at 10% level. This means that drugs for infective tropical diseases are launched with a smaller delay. This contrasts to our expectation that drugs for non-communicable systemic diseases show a higher first mover advantage and are therefore launched faster. The empirical findings rather suggest that the higher importance of infective tropical diseases in developing countries, such as India, lead to a faster launch of the respective drugs.

Survival analysis:

As discussed, we have two specifications of our proportional Cox model to offer. In the first specification, subjects are ordered in terms of their physical time lag. The observations are then reordered by measuring 'onset of risk' by cumulative opportunity costs of delay. Furthermore, note that our physical time lag is calculated in months, with every launch assumed to take place on the first day of a month. As a result we cannot capture the day to day variation within a month, so that we have many tied failures. For 158 failures we have 84 failure times implying around 2 failures per failure time. In contrast, when we measure analysis time by accumulated opportunity costs, the number of failure times increases to 144 - almost eroding the possibilities of tie. As a result, the efficiency of our model is likely to improve in the second case.

Specification 1(analysis time = physical time lag):

In the first model, our ordering of the subjects is done measuring analysis time or 'onset of risk' by T_LAG (models 2a, 2b, 2c, 2d). Due to high co-linearity between MS and TC

(-0.40) we used them separately. However, they are not statistically significant in explaining the probability of launch in the first two models (models 2a and 2b). In both models, BB and WTO are statistically significant and are associated with hazard ratios of about 5 and 2 respectively. Again we find that blog busters and drugs that appear on the market after stronger patent laws have been announced in India are launched faster on the Indian market.

We also estimated the Cox models with INVDRUG (model 2c and 2d). Since this data was available only for drugs launched since 1997, we discarded all those drugs that were launched in Germany before 1997. A total of 302 observations remained. The models were, again significant at 1% level. But INVDRUFG remained insignificant. BB remained significant with a hazard ratio of above 4.5 (model 2c and 2d). Although MS remained insignificant (model 2c), TC this time appears with a positive and significant coefficient at the 10% level. Note that WTO was dropped since all observations pertained to the post-1995 period.

Specification 2 (analysis time = cumulative opportunity cost):

As discussed earlier, we re-order the observations measuring 'onset of risk' in terms of cumulative opportunity costs due to delayed launch. In other words, individual subjects (drugs) will now be no longer ordered in terms of their physical time lag in launch, but in terms of their cumulative opportunity costs until launch. Between two drugs with the same physical time lag of launch the one with more cumulative opportunity costs would have the higher 'onset of risk'. We measure the cumulative opportunity cost by taking the product of T-LAG and MS.

The likelihood ratio is statistically significant at 1% level implying that our model has satisfactory level of explanatory power. BB remains significant at 1% level with a hazard

ratio of 4.74. WTO also remains significant at 1% level with a hazard ratio of around 2. In this model (Model 3a) TC also appears with a statistically significant (at 1% level) hazard ratio of 1.6. This contrasts with our findings in the above regression analysis. Here we find that drugs for non-communicable systemic diseases are launched faster, while in the regression analysis above we find that drugs for infective tropical diseases are launched faster. Our results remain unaltered when we re-estimate the model with INVDRG (Model 3b).[11] INVDRUG does not appear with a statistically significant hazard ratio.

7. Discussion:

All our analyses reveal that the global commercial success of a drug shortens the delay in launch. According to our survival analyses, blockbuster drugs have a 4 to 5 time higher probability to be launched at each time.

In contrast, our Cox regression models show that the innovativeness of a drug does not influence its delay of launch in India. Indeed, our data reveals that out of 22 blockbuster drugs launched in India since 1997, 18 do not bring about any major therapeutic gains. Moreover, while only 40% of drugs which brought about major therapeutic advancement were launched in India, for the blockbuster drugs, the respective share is 85%. It thus appear that launch in India is often highly influenced by the prospect of commercial success and not by the prospect of major therapeutic gains.

A high market share of the therapeutic category is found to cause smaller delays in the drug launch in the regression analysis. The survival analysis does not confirm this finding. Hence, we have not obtained clear results for this aspect. We might conclude that the market share of the therapeutic category in India can have a impact, but the individual commercial success of the drug worldwide is more important for a fast introduction to the Indian market.

[11] Note that data for INVDRUG is available only from 1997. So, this model is estimated only for the period 1997-2004.

Another very clear result that is obtained in all analyses is thatdrugs introduced in the global market since 1995 have a significantly shorter delay compared to its predecessor drugs. Although we failed to obtain the names of firms associated with every launch of new drugs in India, it may be conjectured, on the basis of the discussion in section 5, that most of the drugs are launched in India by domestic firms, who successfully sped up their effort to discover non-infringing processes for new drugs during the final years of the process-oriented patent regime (1995-2004).

Interesting results are obtained for the variable TC, which distinguishes between two types of drugs. Our regression analysis reveals that drugs belonging to infective communicable diseases seem to have a shorter delay compared to the drugs belonging to non-communicable diseases. The second specification of the survival analysis finds the opposite. The expectation before the empirical analysis is in line with the result from the survival analysis. Hence, let us start with giving an explanation for the results from the regression analysis. We consider the figures for Disability Adjusted Life Years (DALY) given by the World Health Organisation (WHO) for India and Germany quoted in section 2. India has an almost equal share of DALY figures for infective communicable diseases and non-communicable diseases. In Germany, however, 90% of DALY is due to non-communicable diseases leaving only 4% for communicable infectious diseases. Hence, drugs for communicable infectious diseases have a comparably larger market in India, which might motivate firms to launch these drugs faster.

Surprisingly, out of 199 drugs launched in the Indian market during 1990-2004, 125 drugs belong to non-communicable diseases, and 74 drugs are for infectious diseases. The relevant figures for the German market are 369 and 261 respectively. Thus, while a little more than 33% of the drugs for non-communicable diseases present in the German market have been launched in India, the similar share for the drugs for infective

communicable diseases is only around 28%. Furthermore, while the ratio of drugs for communicable diseases to total drugs in the German market is around 44%, in India the comparable share is 37%. This contrasts the share of the DALY for the two kinds of diseases.

Our results change if we use a survival analysis, especially when the 'onset of risk' is measured by opportunity costs of delay. The opportunity costs capture in some way the relevance of the respective diseases. Hence, the above argument is included in this kind of survival analysis.

We have argued in section 2 that drugs belonging to non-communicable diseases have high first mover advantages mainly because of two reasons. First, the nondurable nature of these diseases increases the scope of repeat purchase, and second, high quality consciousness among its consumers prevents late entrants of generic versions to capture much of the market. The opportunity costs of delay should, therefore, be higher for these drugs. We get a confirmation of this conjecture in our survival analysis. The probability of launch of a drug belonging to non-communicable diseases is almost twice (varying between 1.6 and 2.1) the probability of launch of a drug belonging to communicable disease. Hence, if we include the argument based on the different market sizes of the two kinds of diseases, the remaining effect seems to be based on higher first mover advantages. We can conclude that both mechanisms are present with one dominating in the regression analysis and the other dominating in the survival analysis.

Two important policy implications follow. First, effective regulation should be in place to ensure that new drugs for infective communicable diseases are not delayed because of their low first mover advantages. This is important because infective diseases are caused by poor hygiene making people belonging to lower socio-economic strata the biggest

sufferer. Second, effective information dissemination policies should be in place to encourage launch of drugs that bring about major therapeutic advancement, irrespective of their global commercial success, to ensure better access to new medical therapies by Indian people.

Appendix:

Tables:

Model 1: OLS estimation (Dependent variable: T_LAG)

Independent variables	Model 1a	Model 1b
BB	-13.09** (-2.23)	-12.03** (-2.07)
MS	-1.35** (-1.97)	
TC		12.28* (1.77)
WTO	-29.57*** (-4.48)	-31.36*** (-4.43)
Constant	65.66*** (7.13)	46.95*** (6.78)
F Statistics	8.63***	8.01***
No. of Observation	199	199

Model 2: Survival analysis: (Analysis time: T_LAG)

Covariates	Model 2a Hazard Ratios	Model 2b Hazard Ratios	Model 2c Hazard Ratios	Model 2d Hazard Ratios
BB	5.14*** (8.17)	4.9*** (7.95)	4.31*** (5.36)	4.44*** (5.15)
MS	1.01 (0.97)		0.98 (-0.7)	
TC		1.16 (0.89)		1.7* (1.9)
WTO	2.29*** (4.53)	2.23*** (4.35)		
INVDRUG			1.41 (0..99)	1.48 (1.18)
Chi square	72.19***	72.09***	25.73***	29***
No. of Observation	590	589	302	301

Model 3: Survival analysis (Analysis time: DDT_LAG):

Covariates	Model 3a	Model 3b
BB	4.74*** (7.74)	4.09*** (4.88)
TC	1.61*** (2.76)	2.51*** (3.16)
WTO	2.07*** (4.13)	
INVDRUG		1.21 (0.57)
Chi square	75.07***	34.25***
No. of Obs.	589	301

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