International Centre for Trade
and Sustainable Development

Guide to the IPRIA (Intellectual Property Rights Impact Aggregate) Model

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WORKING DRAFT

NOT FOR QUOTATION

Content

1. INTRODUCTION

1.1. Objectives and scope

The primary objective of the project is to develop a **simulation model** to assess the impact of changes in intellectual property regime on access to medicines. Its aim is to assist analysts and decision-makers to customise the model to their specific needs, mainly to apply it in order to make quick assessments of the impact of alternative IP options.

The IPRIA model was expected to provide a user friendly tool that decision makers with limited expertise in economics and modelling could use to make quick assessments of the impact of alternative IP options. This lead to developing an aggregate (sectoral) simulation model of the pharmaceutical market with many simplifying assumptions, implemented in an Excel spreadsheet.

The model was initially applied to Colombia, Guatemala and Costa Rica. The team from Colombia, which had previous experience in IPR impact simulation models, made a key contribution to the development of the IPRIA model. The national experts from Guatemala and Costa Rica attended a two days training workshop to understand the model and to begin preliminary analysis. The three country applications are available (in Spanish) as a companion report to this document (Appendix 7: Pilot Country Studies: Colombia, Costa Rica and Guatemala). These country applications helped in the identification of the strengths and weaknesses of the model. The experience from the pilot studies was used to fine-tune the model and make it applicable to different settings. The model has also been used in training workshops and by independent academic researchers in order to provide preliminary results in other countries such as, Bolivia, Malaysia, Vietnam, Thailand, South Korea, Uruguay and India and Jordan. The most recent applications of the model with extensive data collection have been carried out in the Dominican Republic and Costa Rica.

The introductory chapter starts with a literature review that tried to identify and take advantage of previous work on the topic. It also addressess the general issues of when the impact should be evaluated, which options should be evaluated, how this could best be done and finally, which are the potentially relevant impact variables.

The second section describes the structure and characteristics of the IPRIA model and how it operates and provides some advice and discussion for users on how to translate potential IP changes into model parameters and on how to apply the model, in general.

The third section discusses the strengths and limitations of the model. It is based on a formal review process and on the overall experience gained thorugh the multiple country applications and seminars on the IPRIA model.

The appendices include:

- Appendix 1: An Abbreviated User's Guide,
- Appendix 2: Information and data required for the application of the IPRIA model to a given country
- Appendix 3: Reporting format for country analyses
- Appendix 4: Model specification
- Appendix 5: Reviewers' reports
- Appendix 6: Range of values of the main parameters
- Appendix 7: Pilot Country Studies: Colombia, Costa Rica and Guatemala
- Appendix 8: Summary review and description of IPR impact studies in LA countries (in Spanish)

1.2. Literature review.

This section provides an overview of the studies that have tried to assess the impact of changes in IPR regimes on access to medicines. It also comments on the relevance of these studies for the development of the proposed model.

Schondelmeyer (1995) considered the effect of the increase in the term of the patent in the U.S.A. as a consequence of becoming signatory to the WTO. The term of all patents in force on June 8 1995 was extended retrospectively to 20 years. 109 products benefited from this extension of the patent term. The time frame for the study was the period 1996 to 2012, but it did not cover the products for which patents were granted after 1995. It estimated the additional costs to the consumers and to the federal and state governments, as well as the unexpected benefits obtained by the companies. The report available with the authors does not provide a detailed specification of the model used by the study.

Scherer and Weisburst (1995) used an aggregated time series approach to assess the effect of the introduction of pharmaceutical patents in Italy in 1982. Using econometric techniques, the authors compared the observable trends in the period prior to the introduction of the patents and extrapolated it to the later years. The results were then compared with the actual data for this period. They concluded that the introduction of patents neither lead the domestic companies to invest more in R&D nor to a rise in innovation.

La Croix and Kawaura (1996) analyzed the effects of the change in IPR regime in 1996 in Korea using an econometric model. Prior to 1996 Korea granted only process patent for medicines. With the new legislation product patents for pharmaceuticals were introduced. The study analysed if this change benefited the Korean companies in form of an increase in profits. The study covers a one year period.

Spain introduced the product patent for pharmaceuticals on October 7, 1992. A study by the Ministry of Industry and Energy (Ministerio de Industria y Energía, 1999) analyzed the evolution of patenting pre and post this introduction. However, the study does not focus on the impact on prices and other variables of interest to our proposed model.

Suh et al. (2000) analyzed the impact of stronger intellectual property regime by comparing the price of a product under exclusivity with its price under competition from generics. The study focused on the U.S.A. Therefore, the results cannot be directly extrapolated to other countries. Nonetheless, the study provides a useful methodology to model differences in prices under conditions of exclusivity and competition. This makes this paper particularly relevant to the proposed model as it proposes to study the impact of TRIPS Plus provisions on prices.

A study by Nicol and Nielsen (undated) evaluated the impact of the introduction of patents for the Australian biotechnology industry. The analysis was based on the responses of research institutions and pharmaceutical and biotechnology companies, public and private, to a questionnaire. The responses suggest that the introduction of product patents was perceived as beneficial to the biotechnological industry in Australia.

Several studies have focused on India as a case study. Lanjouw (1998) analysed the implications of the TRIPS agreement by way of introducing product patents for medicines. The author based her analysis on literature review, interviews with different stakeholders and questionnaires. Fink (2000) uses a partial equilibrium framework to capture the specific features of the Indian pharmaceutical industry. The author simulates the effects of introduction of patent protection for pharmaceutical products on market structure and consumer welfare.

Chaudhuri, Goldberg and Jia (2003), provided an empirical examination of the arguments by the proponents and opponents of the TRIPS. They estimated the price and expenditure–elasticity and supply side parameters for fluoroquinolones. They used the estimates to simulate a counterfactual scenario to determine the prices, the profits (of the domestic companies and the multinationals) and the consumer welfare that would prevail if fluoroquinolones were under patent in India, as they were in the United States at this time. Their estimates suggest a total annual welfare losses to the Indian economy to the tune of US$713 million. Of this amount, forgone profits of the domestic industry was approximately $50 million. The rest constituted a loss of consumer welfare. Foreign companies would earn additional profits of $57 million.

In wake of the FTA negotiations several studies have been carried out, often commissioned by national Governments, to investigate the impact of patents on the pharmaceutical market of Latin American countries. These generally predict substantial increases in drug expenditure, negative impact in terms of access to medicines and harm to the domestic industry.

These studies are:

Chile: LENZ Consultores (2009)

Colombia: Zuleta and Lylian (1999); IFARMA (2004); Centro de Investigaciones para el Desarrollo y Universidad Nacional de Colombia (2005); Fedesarrollo y Fundación Santa Fe (2005); Corporación Sisma Mujer / Fundación IFARMA / Proyecto Girasol (2008);

Peru: Ministerio de Salud de Perú (2005); APOYO Consultoría (2005), INDECOPI (2005a,b);

Ecuador: CORDES. Corporación de estudios para el desarrollo (2005);

It is also worth mentioning two recent studies on the impact of higher IPR standards on access to medicines in Jordan (Oxfam International, 2007) and Guatemala(Shaffer and Brenner, 2009). These studies do not use formal models to assess the impact; they just make an estimate of the price increases of a sample of products, which are attributable to stronger IP standards and apply the price differential to the units sold on a given year.

In the case of Jordan the authors conclude that that "additional expenditures for medicines with no generic competitor, as a result of enforcement of data exclusivity by multinational drug companies, were between $6.3m and $22.04m".

The study in Guatemala focussed on the impact of test data protection on drug prices. They used the Ministry of Health's Open Contract prices from 2005 and 2007 as the best available indicators of relative prices. To further establish the price implications of introducing data-protected drugs to the market and conferring data-protected status to drugs already offered in Guatemala, the authors identified several data-protected drugs used for conditions that are common causes of morbidity and mortality, and also for HIV/AIDS—the latter because the virus often develops resistance to first-line drugs, requiring the use of newer medicines. They compared these drug prices with those of therapeutically equivalent brand-name and generic medicines that are not dataprotected and that were already offered on the Open Contract lists in 2005 and 2007 (Shaffer and Brenner, 2009). The authors found estimated price increases from 50% to 500% of the equivalent generic price.

The literature review was a usefull source of general ideas and of suggestions of methodological approaches, which have been often used in the present model. However, it was not feasible to directly use or adapt any of the reviewed models due to one or more of the following reasons.

1.The model was not aimed at making projections or building scenarios

2. The model was not clearly specified in detail, so as to allow its use its application with new data to other settings.

3. The model used a microeconomic, desaggregated approach.

4. The model did assess past actual changes in IPR, but it was not suited to estimate the future impact of hypothetical changes in single or combined IP provisions.

1.3. When to evaluate the impact

The IPRIA model can be applied to study the impact of changes in intellectual property regime both ex-ante (before of the change in the IPR regime) and ex-post (after the change in the IPR regime). Both approaches have their merits.

The ex-ante evaluation will involve making projections of the likely impact of future changes in IPR regime. For the policy makers a crucial time for evaluating the prospective impact of a change in the IPR is when this change is being considered, for example, at the time of negotiating IP related issues in the framework of a FTA negotiation. Simulation models can be employed by constructing different scenarios under different strategies for negotiation. The ex-ante estimation of the impact can be useful to identify options that can be of interest to a country. These can guide designing of national policies and international negotiations. This option implies that the analyst has to construct two or more future scenarios, one representing the likely trends in the absence of changes and the others, representing one or several potential agreements.

But it is also feasible and relevant to evaluate ex-post the impact of changes in intellectual property regimes, i.e. when the effects have already set in, and to compare the effects of actual past decisions with other options available at the time. Ex-post analysis allows to garner the necessary evidence for projecting the impact of similar policy options. Ex-post impact evaluation nevertheless also requires some form of modelling. This is because the estimation of the impact requires construction of a baseline scenario based on the observable real data and construction of a counterfactual i.e. a scenario that represents what would have happened if there was no policy change. One advantage of ex-post analysis is that one of the scenarios constitutes an actual, observable situation as opposed to ex-ante analyses, where all scenarios are hypothetical.

1.4. Options to evaluate

The policy makers may want to assess the impact of any variation in the intellectual property regime. This will include a range of policy options like the introduction of the product patent, test data protection, extension of the term of the patent, the introduction of the Bolar exception, etc (see Box 1). The scenarios can be constructed by using different combinations of IPR provisions. For example, the baseline scenario will be compared with alternative scenarios. Some examples of different alternative scenarios are:

Scenario A: An increase in the term of the patent;

Scenario B: Restriction on use of compulsory licenses;

Scenario C: simultaneous implementation of both the policy options.

The model could also be applied to assess changes in policies such as drug price control or drug registration, which are not directly related to IPR but have an impact on the same variables as IPR and might be part of a global policy or a FTA negotiation.

BOX 1. LIST OF TRIPS PLUS PROVISIONS

TEST DATA PROTECTION

INCREASE IN THE TERM OF THE PATENT BEYOND 20 YEARS

EXTENSION OF THE TERM OF THE PATENT DUE TO DELAYS IN APPROVAL ATTRIBUTABLE TO THE PATENT OFFICE

ELIMINATING OR RESTRICTING EARLY WORKING (BOLAR) EXCEPTION

ELIMINATING OR RESTRICTING COMPULSORY LICENSES

PATENTS FOR SECOND USE (INDICATION)

ESTABLISHMENT OF A MINIMUM TIME FROM PATENT APPROVAL BEFORE COMPULSORY LICENSES CAN BE ISSUED

EXTENSION OF THE OBJECT OF THE PATENT (ELIMINATION OF RESTRICTIONS TO PATENTABILITY)

ELIMINATING OR RESTRICTING THE POSSIBILITY OF PRE-GRANT OPPOSITION

ELIMINATING OR RESTRICTING CAUSES FOR REVOCATION OF PATENTS

LINKAGE BETWEEN REGISTRATION AND PATENT OFFICE

ELIMINATING OR RESTRICTING THE USE OF THE INN

ELIMINATING OR RESTRICTING PRICE CONTROL

ELIMINATING OR RESTRICTING PARALLEL TRADE

ELIMINATING OR RESTRICTING INTERVENTIONS AGAINST ABUSE OF MONOPOLY POWER GRANTED BY PATENTS

OTHER MARKET EXCLUSIVITY CONDITIONS

1.5. How to evaluate the impact

The policy makers often must take decisions under conditions of information asymmetry and uncertainty about the likely impact of their decisions. Simulation models are a comprehensive and transparent tool for evaluating different policy options. However, simulation models are not substitutes for alternative approaches for e.g. econometric models, qualitative analysis, or expert opinion. Simulation models allow drawing of an inference from multiple sources of information. This makes them superior to the plain value judgements. Simulation models also have some advantages over statistical and econometric models, which rely on historical tendencies of the data to make projections by extrapolation. Simulation models allow for a greater flexibility in use of multiple sources of evidence. They allow for a specification of a relationship between variables based on observation even when no historical data for the stated variables are available. Simulation models also allow to extrapolate from past experiences relevant for the decision maker from the same or other settings.

However, a simulation model should not be viewed as a crystal ball that predicts the future course of events. It is only an instrument that allows to present the information in a logical manner, making it easier to draw inferences.

1.6. Impact variables

The changes in IPR affect the welfare of the society in a number of ways. The selection of the impact variables will be determined by the needs and purposes of the end user of the model. Some variables are relevant for majority of the stakeholders.

1. First, the changes in the IPR affect the degree of competition in the pharmaceutical markets. This in turn has an effect on prices. Stronger intellectual property protection will lead to an increase in prices.

2. Rise in prices will lead to an increase in pharmaceutical expenditure and will thereby have an affect on access to medicines. If the price-elasticity of the demand is high there will be an overall decrease in pharmaceutical expenditure. When the price elasticity of demand is low the access issue will be predominant. The access issue will be more pronounced for low income groups, which usually have a more elastic demand. Access issue emerges even when drugs purchases are financed by a third party like the state health system. Higher prices might not immediately lead to lower utilization, but will have budgetary implications and may translate in cut-backs on procurement of other drugs and other important goods and services.

3. The changes in IPR also have a bearing on competitiveness through entailed changes in the market share of innovator and generic firms. This effect will be more pronounced for countries where the domestic sector is largely engaged in production of formulations and has a limited research and development capacity. In such countries stronger IPR will lead to reduction in production by the domestic sector. Consequent upon which there will be fall in the level of employment and worsening of the

pharmaceutical trade balance. Multinational companies may also relocate their production to plants in other countries to realise economies of scale.

4. It is also claimed that stronger IPRs might lead to an overall increase in research and development, particularly in development of drugs for diseases specific to low income groups or countries and that they might promote foreign investment and technology transfer, as well as the growth of innovation activities in the country concerned.

2. DESCRIPTION OF THE IPRIA (INTELLECTUAL PROPERTY RIGHTS IMPACT AGGREGATE) MODEL

2.1. Structure and general characteristics of the IPRIA model.

The IPRIA model is a computer assisted simulation model that allows the user to calculate the impact of changes in IPR on pharmaceutical expenditure, consumption and market share of the domestic industry over a defined time horizon. The model consist of a set of quantitative relationships. The user has to populate the model with a set of parameters and input data for each specific application. The source of data and parameters is empirical evidende in the form of primary data and results from empirical studies. When empirical evidence is missing the analyst might use estimates from other countries or expert opinion or assumed values, but the validity of the results is obviously conditioned on the validity of the input data. When making prospective impact assessemnts of hypothetical IPR changes the analyst will have to input the hypothetical data and parameters that best reflect the options assessed.

The IPRIA can be defined as an agreggated model, as it is not based on the analysis of individual products, but on the total pharmaceutical market.

The model is deterministic. Uncertainty on the data and parameters can be assessed by means of sensitivity analysis.

The key elements of the model are:

1. The level of competition-exclusivity in the market. Average market exclusivity depends on the number of products that enter the market with either patent protection or test data protection and on the duration of the related market exclusivity.

2. The variation in average prices. It is assumed that a product under exclusivity will have a higher price than under (generic) competition. Given an average price differential between exclusivity and competition, the average market price will be higher the larger the proportion of the market under exclusivity. The model can also consider the effect on prices of changes in the market share of branded and unbranded generics, a relevant issue when the branded versions of a generic drug have a higher price than the unbranded versions.

3. Impact on access, i.e. consumption and expenditure. The precise impact of variations in price level on access depends on the shape of the demand curve. A zero price-elasticity means that higher prices will not affect consumption, but will only affect (increase) expenditure. If the absolute value of price-elasticity is larger than zero, a price increase will affect both consumption and expenditure. The larger price-elasticity, the larger the effect on consumption. The IPRIA model assumes a costant

price-elasticity demand curve, but the analyst must select the specific value for each particular application.

4. Industrial impact. The model also allows for an assessment of the impact of changes in intellectual property regime on domestic production, but it does not intend to assess the impact of stronger IPR on the domestic and global rates of innovation via an increase in R&D, on foreign direct investment and technology transfer, because no compelling evidence was found in the literature on these effects.

The IPRIA model defines the impact of a change in the IPR by comparing a baseline scenario with an alternative scenario. The baseline scenario will usually reflect the estimated evolution of the pharmaceutical market under the present IPR situation and market trends. An alternative scenario provides a simulation of the pharmaceutical market under the conditions that will prevail once the changes in the intellectual property rights that the analyst wants to assess are introduced.

The market can be defined according to the purpose of the analysis. It might refer to all drugs or to a specific therapeutic segment (for eg, antiretrovirals, ACE inhibitors, statins, etc).

The model should in principle be applid to a country as a whole, because IP related policies, FTAs and other pharmaceutical sector related policies usually have a national scope. However, nothing prevents the model from being applied to a sub-national level, for e.g. to a state, municipality or a district.[1]

The market can be defined as well according to segments defined by the source of finance. Many countries are characterised by the co-existence of different sources of finance. For instance, the drug finance may come through state sponsored social insurance schemes, private insurance and private out of pocket expenditure. A policy maker might be interested in the market as a whole or only in a particular market segment. Many parameters of the model such as prices, demand functions and the range of medicines may differ across the segments. For example, the public system will usually have a smaller number of drugs and face lower prices than the private sector. Also, the price-elasticity of demand is likely to be lower where there are third party payments in comparison with that where the expenditure is out-of-pocket. However, publicly financed health systems are more likely to face strict budget constraints and stock-outs.

[1] However, the industrial impact of IPR changes might not be relevant at the sub national level, because the distribution of the pharmaceutical production across the country is usually not directly related to the geographic distribution of drug consumption and expenditure.

2.2. Operation of the model

The practical application of the model is described in the Abbreviated User's Manual in Appendix 1. The following paragraphs describe some important aspects of the model.

Defining the time horizon

The analyst must specify the time horizon of the simulation exercise. The initial year may be the one when IPR related changes have been introduced, but this is not necessarily so. For instance, the model allows to simulate the impact between 2009 and 2029 of a new IP norm that came into force in 2001 or in 2020. As there will always be a substantial time lag between a policy change and its effects to set in, the final year should be distant enough to capture the full effects of the change. Keeping this in view, a 40 year time frame might be appropriate to capture most of the impact of changes in IPRs. For example, if product patent is introduced in year 2000, patented products may begin entering the market between the years 2008-2012, but it will take some more years for the market share of proprietary and generic drugs to stabilize and attain the full effects.

Calculating the proportion of drugs under exclusivity

The number of drugs in the market enjoying data exclusivity in year 'i'. This figure is calculated by adding the number of drugs entering the market with data exclusivity in the year 'i' to the total number of drugs in the market with data exclusivity in the year 'i-1' and subtracting the number of drugs that lose data exclusivity in the year 'i'.

The number of drugs under patent protection in the market in year 'i' is computed by adding the number of newly patented drugss entering the market in year 'i' to the total number of patented drugss in the market in year 'i-1' and subtracting the number of drugss losing patent protection in year 'i'.

The model assumes that if product patents are introduced in year 'i', then the first drug with patent protection will enter the market in year 'i+DT', DT is the average time taken from patent filing to market registration. Since patents for a product get filed at early stages of development, additional time 'DT' may be required in its further development and getting marketing approval.

The period of exclusivity is calculated by adding the following to the period of effective patent protection:

1. The average extension of the patent term as a compensation for delays in the patenting process.

2. The time lag between patent expiry and generic entry.

3. The extension of the patent duration as a compensation for delays in marketing approval.

The model calculates the periods of exclusivity for different drugs that enter the market each year and the number of drugs that will be under patent protection each year.

A similar procedure is followed to calculate the number of drugs that will be covered by test data protection by year. The procedure is simple because it only involves inputing the year in which the provision is introduced and the duration of test data protection.

The total number of drugs in the market under exclusivity is the sum of the number under patent protection, the number under test data protection and the number under both types of exclusivity. It is assumed that the monopoly power of a drug covered by both forms of protection is not higher than the one covered by only one form. As the duration of patent protection for a given drug is normally longer than the duration of test data protection, in order to avoid double counting the model computes the total number of drugs under exclusivity by adding those which are patent-protected with those that are not patent protected, but enjoy data protection exclusivity.

Calculating the impact on consumption, expenditure, and domestic production

The size of the pharmaceutical market in real terms and the real pharmaceutical expenditure or real value of the market (i.e. at constant prices) is calculated by applying a constant rate of growth to the expenditure in the initial year in the baseline scenario.

For the alternative scenarios the procedure of calculation of the expenditure and the impact on consumption is the following one:

The model calculates a price index of the alternative scenario for each year, that relates the average price in the alternative scenario to that in the baseline scenario. The value of the index is by definition one for the baseline scenario for each year. The index for an alternative scenario in a given year reflects the weighted price differentials between drugs with and without exclusivity and between the drugs sold as branded generics and unbranded generics (sold under INN).

A non-linear constant price-elasticity demand function is assumed to calculate the impact that of an increase in price on the quantities demanded and on expenditure.

The demand curve is of the form:

$q = k\, p^{e}$, or $\ln q = \ln k + e \ln p$,

where k is a constant, e is the constant price elasticity and $k>0$ and $e=<0$

Table 1

Constant price-elasticity of demand: e						$q = kp^e$ e<=0					
e = -2			e = -1			e = -0,5			e = 0		
P^x	q	$MV^x=P^xq$	P^x	q	$MV^x=P^xq$	P^x	q	$MV^x=P^xq$	P^x	Q	$MV^x=P^xq$
1	1	1	1	1	1	1	1	1	1	1	1
1,1	0,826	0,909	1,100	0,909	1,000	1,100	0,953	1,049	1,1	1	1,1
1,2	0,694	0,833	1,200	0,833	1,000	1,200	0,913	1,095	1,2	1	1,2
1,3	0,592	0,769	1,300	0,769	1,000	1,300	0,877	1,140	1,3	1	1,3
1,4	0,510	0,714	1,400	0,714	1,000	1,400	0,845	1,183	1,4	1	1,4
1,5	0,444	0,667	1,500	0,667	1,000	1,500	0,816	1,225	1,5	1	1,5

Table 1 illustrates the relationship between price elasticity, quantities consumed and total expenditure.. Total expenditure (MV^x) by definition is price times quantity (or P^x * q). When the demand is price inelastic (e=0), a price increase (e.g. from 1 to 1,1) will lead to an increase in expenditure by the same proportion (from 1 to 1,1), and consumption will remain unchanged (at 1). When the demand is elastic (e =-2), an increase in price (from 1 to 1,1) will result in more than proportionate decrease in both consumption (from 1 to 0,826) and expenditure (from 1 to 0,909). When the demand is less elastic (e=-0,5), an increase in price (from 1 to 1,1) will lead to a less than proportionate decrease in consumption (from 1 to 0,953) and expenditure (from 1 to1,049). When the demand is unit elastic (e=-1), an increase in price (from 1 to 1,1) will lead to a fall in consumtion by the same proportion (from 1 to 0,909) and the total expenditure will remain the same (at 1).

Four cases are worth considering regarding the effect of the value of e on q and on mvi:

1. If e = 0, q does not change and expenditure (p*q) increases proportionally to price increases when price p goes up.

2. If e = -1, q comes down and expenditure does not change (p*q = k) when price p goes up.

3. If e < -1(e.g. e = -2), q comes down and expenditure (p*q) decreases when price p goes up. This is called an elastic demand

4. If e > -1 (e.g. e = -0,5), q comes down and expenditure (p*q) increases when price p goes up. This is called a rigid or inelastic demand

Finally, the model calculates the value of the sales of the domestic industry in the market. It assumes that the domestic industry has a fixed market share in the segments under exclusivity and under competition. For countries with an industry that has a low innovative capacity, the market share in the market under exclusivity will usually be smaller than in the market under competition or may even be zero. These market shares are assumed to be constant across all years.

2.3. Translating IPR changes into model parameters

The change in IPR provisions can take a variety of forms, as listed in Box 1. A key feature of the model is the need to express the changes in the IPR provisions and other pharmaceutical policies in quantitative terms, i.e. in the form of a parameter:

1. The term of the patent and variations to it. This is easy to quantify. It simply means representation in actual number of years.

2. The duration of test data protection and variations to it. This also can be simply quantified by representing it in terms of the number of years.

3. The extension in the term of the patent on account of delays in the patent approval process and in market registration. The model accounts for these aspects in form of an increase in the period of exclusivity for a certain proportion of drugs. This information might be obtained from countries that already have these provisions in place.

4. Similarly the presence or removal of the Bolar exception can be introduced in the model by adjusting the period of exclusivity. If the Bolar exception is applicable then there will be no increase in the period of market exclusivity. If the clause of Bolar exception is removed then there will be an increase in the period of market exclusivity. These values can be inferred from the delays in generic entry in countries where Bolar exception is not applicable, but it should be customised to the country analyses, because the time lag will be shorter for countries where a strong generics industry exists (like the US and the UK) in comparison with those where the generics industry is still not developed.

5. Changes in the definition of patentable subject matter. Expanding the definition of patentable subject matter is likely to increase the proportion of new drugs with patent protection. The value of this parameter might be estimated on the basis of the experience of countries with a similar definition of patentable subject matter.

6. Variations in generic drug policies, such as restrictions in the use of INN, generic prescribing, etc that affect the relative importance of unbranded generics vs. the branded generics. These measures can be modelled through projections of the expected impact on the market share of unbranded generics vs. branded generics.

7. Introduction of patents on second use. This can be modelled in terms of an increase in the period of patent related exclusivity. However, this option will require adjustments for anticipated changes in prices. The patents on second uses might not have the same impact on prices as the patent of a new product.

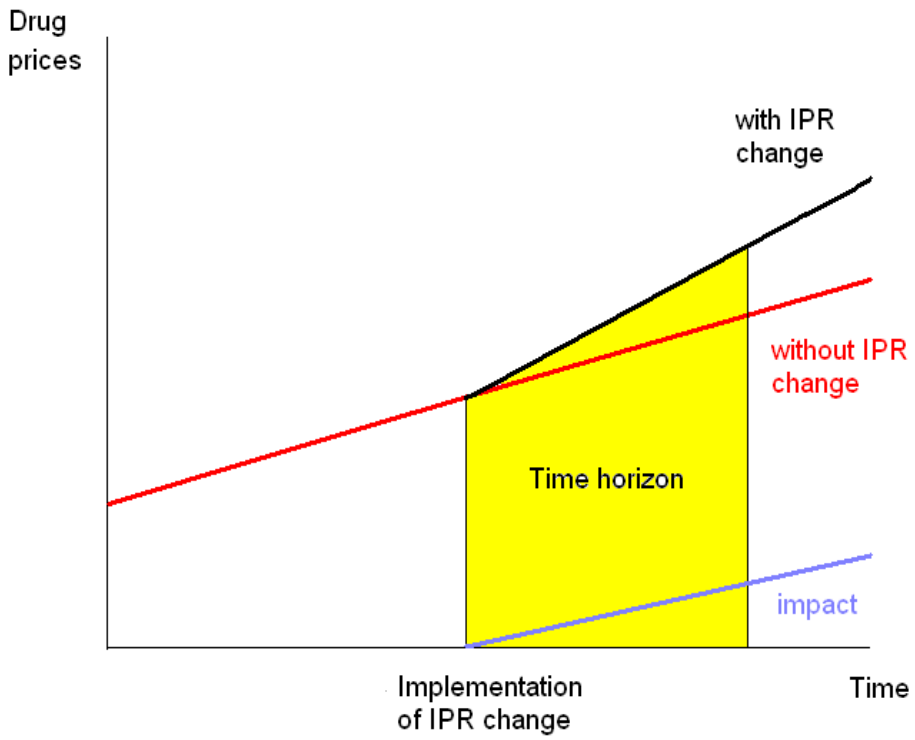
The previous paragraphs illustrate how to incorporate some types of changes in IPR in the present version of the model. The structure of the model has been revised a number of times to accommodate new requirements at the occasion of country applications. Incorporation of other policy changes and agreements such as those on parallel trade or compulsory licensing might require major modifications to the structure of the model.

2.4. Definition and calculation of impact

Any policy measure has multiple effects. The definition of impact variables is a matter of choice by the policy-maker and, hence for the analyst. The effects on variables wich are relevant for society and, as a consequence, for the decision-makers is to some entent a matter of judgement. The variables which are assumed to directly affect societies welfare can be defined as final and those that are the direct effect of the changes and affect the final variables, but are not relevant in themselves, can be called, intermediate variables.

The impact is calculated as the difference between the baseline scenario and that of an alternative scenario for any given outcome variable (see Figure 1.

Figure 1. Graphical illustration of IPR impact on drug prices



In the IPRIA model the final impact of a change in intellectual property regime is defined as:

- The change in the total pharmaceutical expenditure, i.e. in the value of the pharmaceutical market(in monetary terms).
- The change in pharmaceutical consumption (in units).
- The difference in the sales of the domestic industry (in monetary terms.

Key intermediate outcomes include

- the average difference in prices and
- the share of the market under exclusivity.

2.5. Key assumptions of the model

Arriving at country level assumptions and the values of the parameters will involve comprehensive data collection and analysis. For example, analysis of the market for pharmaceuticals will involve looking at the market share of three categories of drugs: drugs under intellectual property protection, branded generics and unbranded generics. It can be assumed that off-patent drugs are

covered under the catgory of branded or unbranded generics and that the pricing policy is uniform across all drugs .

The model assumes that the difference in prices of drugs under exclusivity and under competition remains constant. It also assumes that once the drug loses exclusivity, the its price immediately falls to the average competitive price. This is a strong assumption that is not supported by empirical evidence since prices tend to adjust over a certain period of time. However, it is assumed that relaxing this assumption will not dramatically alter the results of the model.

By modelling the market in an aggregate way the analysis does not take into account the differences in the market shares of drugs. These can be significant. It is implicitly assumed that all drugs have equal market share, which remains the same along the product life cycle.

The demand curve is assumed to have a constant price-elasticity. This is again a simplification. This implies that the elasticity along the demand curve remains unchanged. This in turn means that at all points along the demand curve the change in price will lead to the same variation in the quantity demanded.

Finally, in order to calculate the impact on the production of the national industry, the model assumes that the market shares of the domestic and foreign firms remain constant over time in the submarket segments under conditions of competition and exclusivity. Therefore, the variation in the share of the total market held by the domestic industry is directly and exclusively related to the variations in the relative size of these two markets.

3. LIMITATIONS AND STRENGTHS OF THE IPRIA

The formal process of review of the IPRIA model (see the reviewers' reports in Appendix 5), as well as the experience gathered through its application to particular countries, has raised a number of criticism and suggestions on the structure and assumptions of the model.

The following pages tries to address these concerns and to better define the purposes and assumptions on which the model is build, in order to highlight its strengths and limitations and to suggest to potential users how to make the best use of it.

3.1. Econometric vs. simulation models

Economic, econometric and simulation models share some common features, but they differ in some important aspects.

Econometric models are usually applied to test a theory or to a estimate some hypothised relationships. They can also be used to forecast the evolution of economically relevant variables, such as GDP or prices. One of the first steps in developing an econometric model is to specify the assumed relationships in the form of a single equation or a set of equations. Econometric models may start with a formal economic modelling. For instance, market equilibrium models often start defining some utility and profit functions and assuming a maximising behaviour from the demand and supply agents, from which generic demand and supply equations are specified. Often, however, the equations are derived in a more intuitive, informal way. In any case, the analyst might define a demand function by specifying a certain relationship, such as $q = ax1 + bx2 + cx3$, where q is the number of units demanded, x1 is the price of the product, x2 is the consumers' income, x3 the price of a substitutive product, etc.

Econometric analysis aims at estimating the parameters a, b and c using a certain set of empirical data. These parameters describe the direction and strength of the assumed relationships. As any specification is likely to ignore some relevant causal factors and there are likely to be errors in the data, etc, econometric models include an error term, u, (sometimes, more than one) turning the former equation into $q = ax1 + bx2 + cx3 + u$. The methods used to estimate the parameters are based on certain criteria, such as minimising the errors between the observed, empirical data and those predicted by the estimated equation.

Once the parameters have been estimated, the equation becoming, e.g.

$q = -2x1 + 8x2 + cx3$, it is possible to predict by extrapolation the value of q for combinations of values of the explanatory variables x1, x2 and x3, that might have not been observed. This kind of prediction is more reliable if the values assumed for the explanatory variables fall within the range of the observed values on which the estimation of the variables has been made .

As economic theory does usually not allow to univocally specify a single functional form, econometricians often specify alternative functional forms for the equation to be estimated, for instance, in the previous example, it could be

q = ln ax1 + ln bx2 + ln cx3.

If time has been factored into the demand equation, e.g.

q = ax1 + bx2 + cx3 + dt, the model allows in principle to predict the value of q at any point of time, say, in 20 years. This requires, however, several strong assumptions, mainly that the structural relationships between explanatory variables and, hence, the functional form and the values of the parameters will not change along time. Such an assumption is more acceptable if the model is used for short term predictions (or forecasting), e.g. one or two years, than if it pretends to assess the results in 30 years.

Simulation modelling has a different purpose and takes a different approach to econometric modelling. Although both might use similar equations, simulation models are not aimed at estimating the parameters of the equations from empirical data, but to make projections. The parameters and the functional form of the equations are usually not based on a statistical estimation derived from a single set of data, but it allows relationships (equations) in the model to be derived from different sources, including expert opinion and assumptions. This is of course both the major strength and the major weakness of simulation modelling. On one hand it gives a lot of flexibility to the modeller, but this is at the cost of a weaker, or at less, of a less conventionally accepted empirical foundation. Of course, the predictive capacity of simulation models that make projections of values over time can be tested in the same way than one would test econometric models, either prospectively or retrospectively. Retrospective validation implies testing the predictions of the model against already some available data which have not been used to select the functional forms of the equations or the values of the parameters. A practical limitation of prospective simulation is that the model cannot be tested before it is used for a decision, but only some time later and only for decisions that have actually been implemented.

3.2. Main characteristics of the IPRIA Model

Economic analysis distinguishes microeconomic from macroeconomic models. Microeconomic models focus on single markets of homogeneous goods; demand and supply functions determine the price and quantity at some equilibrium point; often a set of similar goods that are substitutes (e.g. cars, apples) are aggregated into a single product. In microeconomic demand (supply) functions quantity is usually assumed to be negatively (positively) related to price.

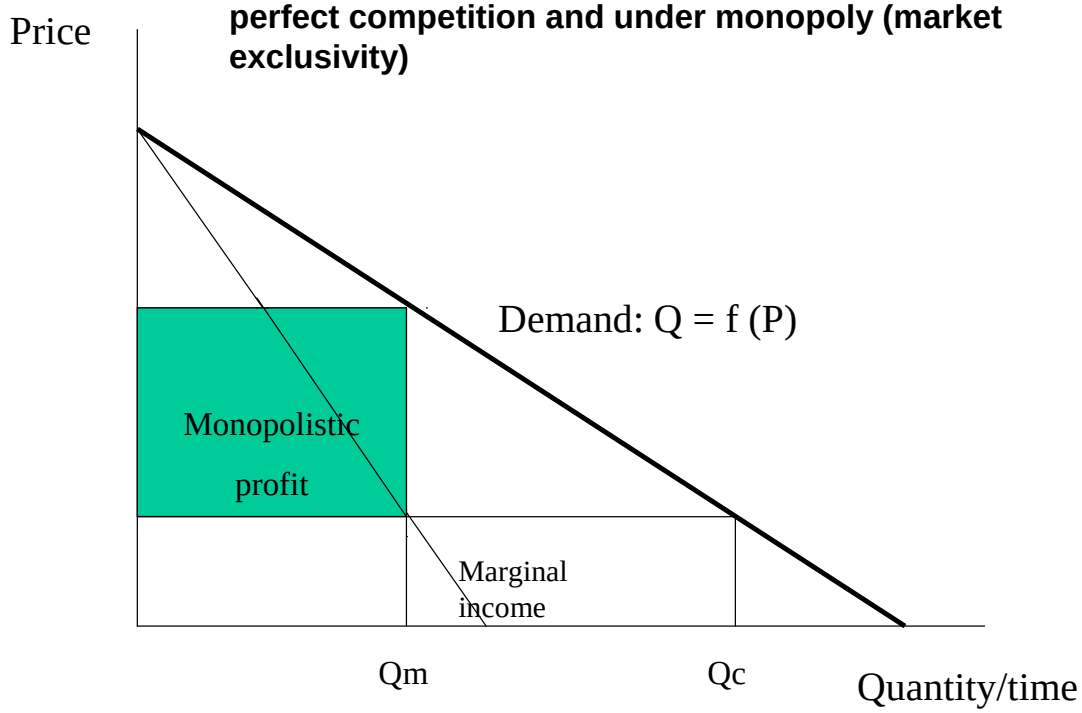
Macroeconomic models deal with highly aggregated variables, such as the GDP or total consumption.

The IPRIA is neither a pure macro nor a micro model. All drugs are aggregated into a single variable, although it is obvious that most drugs are not substitutes

at all (e.g. a statin and an antiinfective). The IPRIA can be defined from an economic-analytical perspective as an aggregate static simulation model. It is probably closer to a macro than to a micro model, because although individual products are considered in order to assess the degree of exclusivity on the pharmaceutical market, prices and expenditure refer to aggregate sets of medicines: all drugs, drugs under exclusivity, branded generics and unbranded (INN) generics.

The core mechanism of the IPRIA is based on the entry of new drugs into the market, and on a certain (market) life cycle profile. When the intellectual property system of a country recognises (product) patents and test data protection, most drugs spend the initial period of its life cycle under exclusivity, which is followed by a second period of non-exclusivity when generic competition steps in. IP regulation and changes in IP regulation determine the proportion of drugs that will enter the market under exclusivity and the length of the period of exclusivity and, consequently, what proportion of the whole market will be under exclusivity or under competition at a give point in time. The IPRIA model further assumes a certain price differential between a drug under exclusivity and under competition (which is the same for all drugs and fixed over the years).

Figure 2 : Single drug market equilibrium under perfect competition and under monopoly (market exclusivity)



The microeconomic economic logic of the model is illustrated in Figure 2, which represents the market of a single drug. The market of an originator under exclusivity can usually be thought of as a monopoly. It is assumed that under exclusivity the originator will maximise profits by charging whatever the market

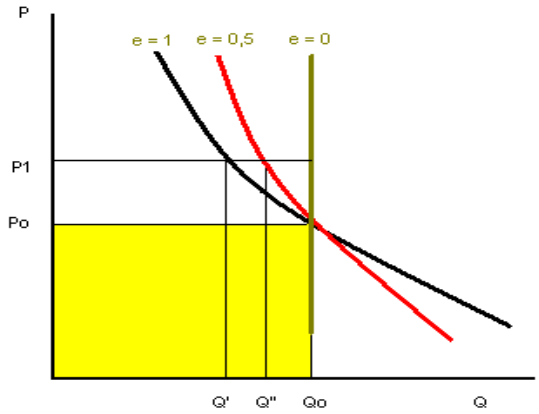
can bear. The market equilibrium is attained at price Pm and quantity Qm, where the monopolist maximises profits. Under generic competition – a situation that might be close to the theoretical concept of perfect competition - the price would be Pc, the level of production costs (plus a normal competitive profit rate) and the quantity of units sold, Qc. These two prices represent static equilibrium prices. They can conceptually represent the prices of a new drug under a scenario that provides exclusivity to originator drugs and a scenario which does not provide it. Alternatively, it might represent the equilibrium points for a drug under a exclusivity scenario at the time the drug enters the market and when it looses exclusivity. Of course, in reality the competition price would not be reached instantaneously, but it would probably take three to five years to do so. For the sake of simplicity, the model assumes however an immediate adjustment to the competitive price after exclusivity expires.

We assume that under competition the supply curve of a product can be represented by an horizontal line (infinite price-elasticity), which is an aggregate function of the originator and the generics manufacturers supply curves. The model does not try to assess the share of each individual manufacturer in total supply .

There is an apparent inconsistency between the use of a demand function to determine the effect of prices on consumption and the use of fixed price differentials. The answer is that the IPRIA does not intend to predict the prices Pm to Pc or the relative price differential (Pm – Pc) / Pc, a key parameter of the IPRIA model, which is exogenously determined, i.e. is taken from other studies or expert opinion. The price differential represents a long term equilibrium, which is determined only by supply. This should not be a major problem for a simulation model, as long as the exogenous determination is a valid one.

The aggregate drug market for all pharmaceutical products is illustrated in figure 3 and is characterised by an aggregate CED (constant elasticity of demand) function. The total number of units sold is determined by the average price of drugs, which is defined by means of a (inter-scenario) price index that captures the changes in the share of the market under exclusivity (and between branded and an unbranded generics) between the baseline scenario and any alternative scenario for the same year. If the price index goes up from Po to P1, the variation in quantity of units will come down from Qo to Q1. The variation will be smaller the closer the elasticity is to zero. For a zero elasticity, the quantity will remain unchanged.

Fig 3: Aggregate drug market



There is not a direct link between the implicit single drug demand curves and the aggregate demand curve, which might lead to some theoretical inconsistencies in the model. The IPRIA does not make any assumptions on the precise form of the single drug demand curve, other than having a negative slope, which results in price going down when exclusivity expires. The price reduction has to be estimated from empirical data reflecting the relative difference in equilibrium prices under exclusivity and under generic competition.

The changes in the prices of individual drugs due to the shift from exclusivity to competition determine the inter scenario price index, which in its turn determines the variations in the aggregate consumption of drugs. As already mentioned, there certainly are some conceptual microeconomic inconsistencies in this model. Trying to address these inconsistencies would require a full microeconomic model, where the prices and quantities of each drug were set individually. In fact, there is such a model been developed as a follow-up of the IPRIA.

Although the IPRIA formally generates annual figures for the endogenous variables over the predefined time horizon, it cannot be properly considered a dynamic model in economic terms. The supply part of the model that determines the proportions of the market under exclusivity and under competition has a dynamic character, as the values at any year depend on the values of exogenous variables in previous years. However, the evolution of the value of the market over time in the baseline scenario is obtained by taking or estimating the value for the initial year and simply assuming a constant growth rate at constant prices. And the value of the market, as well as the changes in

prices and units demanded at any year in the alternative scenarios does not depend on the values of previous years, but on the equilibrium values of supply and demand at that year. Supply is assumed to be totally elastic, meaning that supply will provide any quantity demanded at the prevailing prices, which are exogenously determined.

Many of the criticisms and suggestions made by the reviewers (see Appendix 5) in relation to the model structure and assumptions are relevant, but they can only be appropriately addressed with a full microeconomic approach. Moreover, the fact that the price-differentials depends on IP protection standards and changes and should therefore be considered in the model, does not imply, that prices must be necessarily modelled as an endogenous variable. On the other hand, it must be acknowledge that simulation models cannot always follow the logic of the theoretical models of economic analysis, in the same way that econometric models sometimes cannot replicate textbook models because of specification problems.

3.3. The realism of the model

Models are always a simplification of the reality. The degree of simplification must be judged in terms of the purposes of the model and on the availability of reliable data and evidence on the relevant relationships.

The IPRIA model can be criticised for being too simplistic and not a realistic representation of how the drug market actually works according to accepted microeconomic analysis and evidence. Few variables are endogenised, i.e. determined by the equations of the model, when compared to microeconomic market models, general equilibrium models or dynamic growth models.

The purpose of the IPRIA model was to develop a user friendly model that could be used and applied by local teams to any country. Of course, a one-size-fit-all-simulation model is necessarily less realistic when applied to a particular country than a country-specific model. As a response of complains about the limitations of the IPRIA model, several modifications have been introduce in the successive prototypes developed before the present version was reached. Modifications have been made when they had a clear purpose for the user and were likely to be useful in different contexts and countries. An requirement additional condition for a modification to be made was that the relevant additional information or data required were be available. This conditions are justified by the purpose of the IPRIA of becoming a decision-making tool, rather than an academic or theoretical piece of work.

In principle, trying to derive a simulation model from a previously estimated econometric model might be the ideal option. However, data and resource constraints might preclude or advise against such an optimal approach to be taken. This was, and still is the case of the IPRIA, at least if one aims at applying it to developing countries. The type of policy variables which effects the model is expected to predict (various forms of higher IP standard) have never been tried before in these countries. Therefore, there is no way to estimate these effects from local empirical data. Moreover, the data required for such an exercise (time series of prices and quantities, among others) are not

available either. When empirical studies are available and assuming the results are transferable, they will allow to make reliable estimates of the type of relationships implied in the IPRIA model,.

Although it is desirable for a simulation model such as IPRIA to derive from a well defined and accepted set of economic principles, it is less obvious whether and how far it should closely replicate a theoretical economic or an econometric model. Simplicity or parsimony is also a relevant criterion to be considered when developing a model, especially when such a model is aimed at being used by non-experts in the technical aspects. A more complex model might please experts in economic modelling, but might reduce comprehension and acceptability by decision makers with limited expertise in economic analysis. In any case, some of the theoretical economic concerns raised by the reviewers IPRIA are being addressed in the second generation of microeconomic IPR impact models which are in process of development.

3.4. The role of prices and price indexes in the IPRIA model.

Three types of price indexes might be distinguished in relation to the IPRIA model

1. The general price index (e.g. the Consumer Price Index)

2. The pharmaceutical price index

3. The inter-scenarios pharmaceutical price index

The first two indexes might be used to deflate time series of pharmaceutical expenditure. If we use the general price index, the resulting values represent the evolution of pharmaceutical expenditure at the purchasing power of the initial year. By deflating pharmaceutical monetary values with an appropriate pharmaceutical price index, we obtain an estimate of the evolution of pharmaceutical consumption in units. Pharmaceutical prices do not necessarily follow the variations of the general price index. By dividing the pharmaceutical price index by the general price index we obtain the relative inflation of pharmaceuticals.

Most economic models define monetary variables in real terms, i.e. at constant prices of a given year. This is because using current monetary values of different years amount to comparing (adding, subtracting) heterogeneous magnitudes, i.e. monetary units of different value. As already stated, the IPRIA model is primarily aimed at assessing the impact of changes of IP provisions on access and expenditure. In order to do that, it first has to estimate the impact of IP changes on average drug prices in alternative scenarios at the same point in time; but the IPRIA is not aimed at forecasting the evolution of either general inflation or the evolution drug prices over time. The model is assumed to work at constant prices of the initial year. It does not make any assumption on the evolution of the relative prices of pharmaceuticals over time and , hence, on variation of the units sold.

The only mechanism in the model that drives prices variations between scenarios is the substitution of generic products by the same products under exclusivity and viceversa. Therefore, the pharmaceutical price index used in the model reflects price variations between the pharmaceutical prices in the baseline scenario and in alternative scenarios for the same year. It is therefore more appropriate to call it an inter-scenarios pharmaceutical price index; its purpose is to capture the variation in prices of what is assumed to be the a set of homogeneous, but differentiated products.

The baseline scenario assumes that the value of the market grows at a real constant rate α. As $\Sigma p_i q_i = \alpha \Sigma p_{i-1} q_{i-1}$. This means that the increase in the real market value can be explained by an increase in p_i , in q_i , or in both. Multiple combinations of the growth rate of units and of prices can result in the same growth rate of expenditure. That is, the way the evolution in drug expenditure is modelled in the baseline scenario, assuming a constant real growth rate in real terms of drug expenditure does not imply any particular combination of growth of the units and the prices of pharmaceuticals sold, but just an increase in the demand and expenditure.

This approach was selected, on one hand, because there are usually no valid price indexes of drugs available, especially in developing countries; and producing a valid price index would probably be out of the scope of a country application of the model. Moreover, it was estimated that the effect of including inflation into the model would have only a moderate influence on the impact that changes in IP provisions was expected to have on access.

Besides deflating the time series to account for inflation, when monetary amounts of different years have to be added, as it is done in the IPRIA model to calculate the total amount on the time horizon, it is customary to discount the values using a certain discount rate. Discounting has nothing to do with inflation but with time preference; i.e. even in the absence of inflation it is usually assumed that individuals value more a certain asset, the closer it is in time. There is more debate on how to set an appropriate value for the discount rate. The IPRIA model allows the user to enter the value that is appropriate or acceptable in the local context.

Trying to assess the evolution of current prices (inflation) is a legitimate and valuable exercise. Models aimed at predicting the short term evolution of the economy, usually include inflation among the variables predicted. But trying to predict the changes in the average prices of drugs (or the price of a single drug) is much more difficult than predicting general inflation, as it requires far more detailed and comprehensive information on the demand and supply of drugs and other factors, such as regulation, which are almost impossible to assess it in an objective, scientific way. In the case of pharmaceuticals it is difficult even to theoretically predict what is likely to happen to prices when the demand goes up or down, because there is nothing close to a theoretical competitive market determining the equilibrium price. A larger demand can increase prices as in the usual short term market equilibrium, but it also may

a) reduce prices by allowing economies of scale to local producers,

b) reduce prices by attracting foreign competitors and new entrants into the market,

c) give social insurers and price regulators a larger negotiating power that allows them to attain lower acquisition prices, etc.

In conclusion, even from a theoretical point of view, it is difficult to predict whether an increase in public funding or in private demand would lead to any variation in drug prices.

Statistically oriented analysts might try to assess future trends in prices by extrapolating past trends. This is a very questionable approach – why should past trends hold over time? – but it might be the best one can do.

Such an approach would however require valid price indexes for the last, say, 5 or 10 years. Moreover, general consumer price indexes are usually accepted to be reliable because they are based on a large, representative sample of goods and services. But the disaggregated components of the general index, e.g. the pharmaceutical component, are usually based on a relatively small number of products which are less likely to be representative. Pharmaceutical price indexes tend to over-represent relatively old products, which prices usually grow less that those of new products. In fact, pharmaceutical prices grow to a great extend because old products are constantly been substituted by new ones at higher prices, which often do not add any therapeutic value to the old ones which are substituted. These type of phenomena are difficult to capture with traditional price indexes (such as Laspeyres) which use a fixed basket of products for many years. In order to have meaningful price indexes one probably needs to produce them for a given purpose or study, by transforming the units sold of every drug into DDD or mg, etc. This requires having access to a large database of prices and quantities sold of every drug over a number of years.

If an analyst still wants to generate monetary variables at current prices, a conventional price index can be added to the results predicted by the IPRIA model. The analyst can export the results table (only the data, not the formula) to another file and perform the additional calculations required. New columns for the estimated pharmaceutical time price index and for each monetary variable, such as, MV/Pt, should be added to the matrix.

The pharmaceutical price index might have an empirical basis or just reflect an assumption about factors other than IP changes, that make drug prices change. One can assume that the composite impact of IP related and IP unrelated growth in drug prices is multiplicative. The value of the time index for the initial year must be set to 1. Dividing expenditure at constant prices by the pharmaceutical price index provides an estimate of the evolution of consumption in the drug units used for the price index (packages, DDD, etc). Setting this consumption indicator to 1 in the initial year it can be used to estimate the evolution of the number of units consumed, by simply multiplying the indicator by the number of units consumed on the initial year.

3.5. Static and dynamic effects of exclusivity

A second type of impact considered in the IPRIA – besides the effects of IPR changes on prices, access and expenditure - refers to the effects on domestic industry. This option was introduced in the model mainly because of its strategic policy implications – namely, because it might raise awareness of the potential negative impact of higher IP standards not only on the health status of the population, but also on the domestic industry. There is in fact strong evidence that the introduction of higher IP standards in countries not having an R&D industry has resulted in a reduction of the market share of the domestic generics industry, and even to its practical elimination. This inclusion does not imply that, establishing, maintaining or increasing domestic production of drugs is a desirable policy goal from a social welfare perspective. High IP standards and trade agreements, in general, are likely to have both negative and positive effects for different groups within a country and policy makers concerned by societal welfare need to consider all the effects in order to take an appropriate decision. In fact, the IPRIA is not designed to make any explicit measurement of social welfare impacts.

The modelling of the impact in the IPRIA on the domestic industry is, in fact, rather simplistic: it assumes that the domestic industry will maintain a fixed share of the generics market over time. As the core model provides a calculation of the share of the generic market, the computation of the domestic industry market share is straightforward. Of course, the assumptions taken are very strong and are not based, so far, on any rigorous empirical analysis. Even the meaning of domestic/national industry is far from clear. Should only imports be counted as foreign supply or should the subsidiaries of MNC be also included. What about companies with a shared (foreign-national) ownership? Should the simple majority-of-capital rule apply irrespective of other forms of control? Domestic industry often imports a large part of the production factors, especially active ingredients and technology. Should the market share be measured in terms of sales or of added value? All these question marks must be addressed by the model user, as the model leaves these aspects undefined.

Moreover, the use of that part of the model was meant and should preferably be used for countries that have a well developed industry with a strong position on the domestic market – meaning that imports of generics can be ignored - but no significant innovative capacity during the time horizon of the analysis.

Advocates of high IP standards claim that they will produce important benefits to the countries that implement them. The main effects mentioned in relation to the pharmaceutical sector are: increased incentives and hence, likelihood, of technology transfer, foreign direct investment, increase in domestic R&D, and global investment in R&D on diseases that predominantly affects developing countries. These claims are neither theoretically obvious nor is the empirical evidence available to justify its introduction into the model structure. Moreover, even if these positive effects would happen, they would have an industrial-economic impact, but there is no reason to think that the prices would fall or the access to drugs would somehow improve. Innovators located in the country would probably set their prices according to global considerations, which means

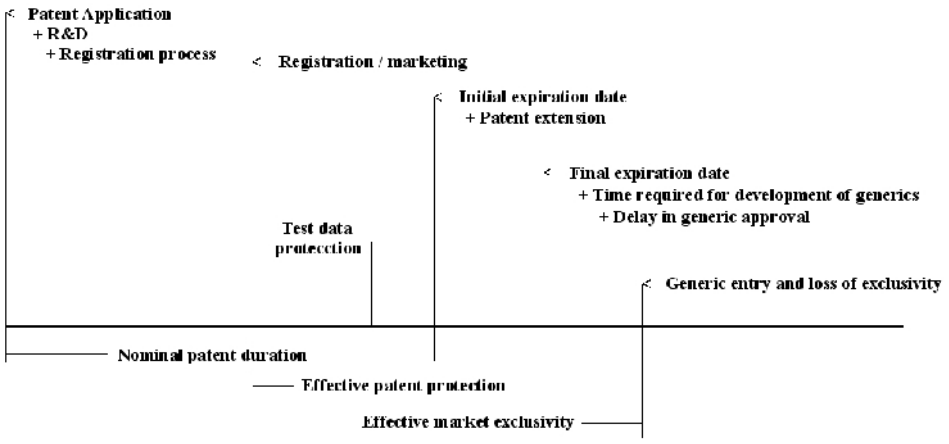
that the industrial advantages might not provide any access advantages in the country concerned.

3.6. Exclusivity due to patent and to test data protection.

The core variable of the model is the legal status of exclusivity granted to pharmaceutical products. Patents protection (PP) and test data protection (TDP) are likely to be in the future the two main sources of market exclusivity for drugs in developing countries. It is therefore important for the user of the model to understand how these two factors are treated in the model and how the user can model the situations that s/he wants to simulate.

Exclusivity due to test data patent protection and to patent protection might overlap in the life cycle of a product (as depicted in figure 4). In that case, it might be assumed that the two forms of protection are redundant and that TDP does not add any market power to the patent holder, nor does it increase the share of the total market under exclusivity. This situation can be easily modelled by first stating the number of new products that get patent protection. Then, if we assume that that all products, or at least all those that have no PP, get TDP, the figure that has to be entered in the model is the difference between the total number of new products and those with PP. If we assume that only 50% of products without PP will be granted TDP, that one should halve the previous figure, and so on.

Fig 4: Patents, test data protection and market exclusivity



However, although the previous situation is likely to apply in most cases, for a certain proportion of products that loose for any reason PP, TDF might well provide an additional time of effective exclusivity. This fact (or assumption) can be modelled in the IPRIA as an extension of the duration of exclusivity by x

years times the probability of a product benefiting from such an extension, as the model does with linkage and patent extension due to delays in patenting. In fact these two options offered by IPRIA can be used to model any factor causing an extension of the period of exclusivity that can be expressed in terms of an extended duration and a certain probability of attaining that extension. Determining the appropriate values requires empirical analyses, which should be made in countries with a long enough period of experience with that mix of causes of exclusivity.

It might also happen that in some countries new products are not patented at all, but receive only TDP-related exclusivity: this assumption can be easily modelled with the IPRIA and does not pose any particular difficulty.

3.7. Parameter values and sensitivity analysis.

The parameters of the model reflect a) relationships between variables within a give equation, b) policy parameters and c) study design decisions. For most of them is not easy to provide general advice on an appropriate or acceptable range of values. Estimates should be obtained whenever possible from empirical studies designed to fit the needs of the IPRIA model or from studies carried out for other purposes. Unfortunately these studies are scarce or not available at all, and parameter values would be often based on subjective opinion and hence subject to a large uncertainty

The analyst may want to consult the values used in previous country applications of the model, although this source of inspiration does not provide any scientific validity to the values concerned: even if they are fine for the original application, they might make no sense when applied to a different country and period of time.

Appendix 6 shows the range of values used at previous applications of the model for the key variables, which might be used as an orientation for future country applications, if no local data are available. It also provides information on literature reviews on the price elasticity of the demand of medicines.

One of the most traditional forms of addressing uncertainty is applying some form of sensitivity analysis. Sensitivity analysis allows the analyst and the audience to be aware of how far the uncertainty in the parameters affect the results. The implementation of the IPRIA model on an Excel spreadsheet makes it very easy to carry out in practice the calculations of a conventional sensitivity analysis.

One-way sensitivity analysis means changing one at a time the values of the uncertain parameters. Multi-way sensitivity analysis implies simultaneously changing the values of two or more parameters at a time. One extreme form of multi-way sensitivity analysis is taking the combinations of values of the parameters that provide the lowest and the highest results of the impact variables.

One of the key decisions of sensitivity analysis is determining the values of each parameter – usually a central, an upper and a lower value. If a set of

potential values is available, the mean and the mean plus and minus one or two standard deviations is a possible criterion. Taking the maximum and minimum values of the range of values as an alternative criterion will provide a larger variability of the impact variables.

The situation is more complicated when only subjective point estimates are available. In any case, a practical criterion is that the values of the sensitivity analysis should acceptable to the ultimate decision maker.

4. REFERENCES

APOYO Consultoría (2005). Impacto de las negociaciones del TLC con EEUU en materia de propiedad intelectual en los mercados de medicamentos y plaguicidas. Lima.

Centro de Investigaciones para el Desarrollo, Universidad Nacional de Colombia (2005). Impactos del tratado de libre comercio Colombia-Estados Unidos en el sector salud del distrito capital, Bogotá, (no publicado)

Chaudhuri, S., P. Goldberg, et al. (2003). The Effects of Extending Intellectual Property Rights Protection to Developing Countries: A Case Study of the Indian Pharmaceutical Market. NBER Working Papers 10159, NBER.

CORDES. Corporación de estudios para el desarrollo (2005). Informe sobre el impacto económico sobre el sector farmacéutico y agroquímico ecuatoriano de la adopción de un capítulo sobre protección de derechos de propiedad intelectual en el marco del tratado de libre comercio. Ecuador.

Corporación Sisma Mujer / Fundación IFARMA / Proyecto Girasol (2008), Impacto del tratado de libre comercio firmado entre Colombia y Estados Unidos sobre el acceso a medicamentos requeridos por mujeres viviendo con VIH o SIDA y su implicacion sobre la calidad de vida sentida. Colombia.

Fedesarrollo y Fundación Santa Fe (2005). Estudio sobre la propiedad intelectual en el sector farmacéutico Colombiano. Bogotá, Junio de2005.

Fink, C. (2000). How Stronger Patent Protection in India Might Affect the Behavior of Transnational Pharmaceuticals Industries.

INDECOPI (2005a). “Incidencia de los derechos de propiedad intelectual en el gasto de las familias en el marco del TLC” Serie Estudios de Investigación, Lima.

INDECOPI (2005b). “Análisis del impacto económico de un régimen de protección de datos de prueba en el mercado farmacéutico peruano” Serie Estudios de Investigación, Lima. *Segunda versión corregida: julio 2005*

La Croix, S.J. and Kawaura, A (1996). "Product patent reform and its impact on Korea´s Pharmaceutical Industry." International Economic Journal 10(1).

Lanjouw, J. The Introduction of Pharmaceutical Product Patents in India: "Heartless Exploitation of the Poor and Suffering" . NBER Working Paper No. 6366.

LENZ Consultores (2009). Efecto de las patentes de medicamentos en el costo del plan AUGE, Chile

Ministerio de Industria y Energía, D. G. d. E. y. N. T. (1999). La investigación y

desarrollo en el Sector Farmacéutico. Análisis del Impacto de la Patente de Producto y del Mercado único. Madrid, Ministerio de Industria y Energía.

Ministerio de Salud de Perú (2005). ""Evaluación de los potenciales efectos sobre acceso a medicamentos del tratado de libre comercio que se negocia con Estados Unidos de América", Lima, Perú, Abril 2005.

Nicol, D. and Nielsen, J. (undated). Patents and Medical Biotechnology: An Empirical Analysis Of Issues Facing The Australian Industry. Occasional Paper No. 6, Centre for Law and Genetics.

Organización Panamericana de la Salud/Organización Mundial de la Salud y Fundación IFARMA (2004). Modelo prospectivo del impacto de la protección a la propiedad intelectual sobre el acceso a medicamentos en Colombia, OPS/OMS, Sin publicar

Oxfam International (2007). All costs, no benefits: How TRIPS-plus intellectual property rules in the US-Jordan FTA affect access to medicines, Oxfam Briefing Paper, March 2007

Scherer, F. and S. Weinsburst (1995). "Economic Effects of Strengthening Pharmaceutical Patent protection in Italy." International Review of Industrial Property and Copyright Law 26(6).

Schondelmeyer, S. (1995). Economic Impact of GATT Patent Extension on Currently Marketed Drugs.

Shaffer ER and Brenner JE (2009).A Trade Agreement's Impact On Access To Generic Drugs. Health Affairs, 28, no. 5: w957-w968Suh, D., W. Manning, et al. (2000). "Effect of Multiple-Source Entry of Price Competition After Patent Expiration in the Pharmaceutical Industry." HSR: Health Services Research 35(2): 529-537.

Zuleta, L. and M. Lylián (1999). Incidencia del régimen de patentes de la industria farmacéutica sobre la economía colombiana, FEDESARROLLO.

Additional literature

Anónimo. "Evolución de los nuevos medicamentos comercializados en España (1980-2004)." Panorama actual del Medicamento – Digital (Revisión).

Anónimo. IMS Market Prognosis Latin America 2003-2007. COLOMBIA.

Anónimo. (2004). Combating generics: Pharmaceutical Brand Defense. Durham, Cutting Edge Information**:** 1-9.

Bala, K. and Sagoo, K.(sin fecha). Patents and Prices, Consumers International - Health Action International**:** 1-8.

Creese A and Quick J (sin fecha). "Working paper on differential prices

arrangements and feasibility context setting paper". WHO, 2001. Citado por

Bermúdez, Oliveira y Chaves (2004) en "Intellectual property rights in the context of the WTO-TRIPS agreement: What is at stake?. Fiocruz-ENSP-PAHO/WHO. ENSP, Rio de Janeiro.

Danzon, P. and M. Furukawa (2003). "Prices and Availability of Pharmaceuticals: Evidence from Nine Countries." Health Affairs. The Policy Journal of Health Sphere.

Grabowski, H.G. and Vernon J.M. (1992), "Brand Loyalty, Entry, and Price Competition in Pharmaceuticals after the 1984 Drug Act", *Journal of Law and Economics,* October 1992

Kantor, M. U.S. Free Trade Agreements and the Public Health, Mayer Brown Rowe & Maw**:** 1-12.

Lexchin, J. (2004). "The effect of generic compatition on the price of brand-name drugs." Health policy 68: 47-54.

Lexchin, J. and P. Grootendorst (2004). "Effects of prescription drug user fees on drug and health services use and on health status in vulnerable populations: a systematic review of the evidence." International Journal of Health Services 34(1): 101-122.

Magazzini, L., F. Pammolli, et al. (2004). "Dinamic competition in pharmaceuticals Patent expiry, generic penetration, and industry structure." HEPAC: 1-16.

Mullins, C., F. Palumbo, et al. (2000). Projections of Drug Approvals, Patent Expirations, and Generic Entry from 2000 to 2004. Washington, Leavey Conference Center, Georgetown University**:** 1-5.

Relman, A. and M. Angell (2002). "America's Other Drug Problem." The New Republic: 27-41.

Wiggins, S. and R. Maness (2004). "Price competition in pharmaceuticals: the case of anti-infectives." Economic Inquiry 42(2): 247-263.

Appendix 1. An Abbreviated User's Guide

Introduction

The IPR impact model simulates the impact of the changes in the intellectual property regime on the price, cost, consumption, and national production of medicines. The model captures the impact of a change in the IPR or in pharmaceutical sector specific policies by comparing a baseline scenario with an alternative scenario. The baseline scenario reflects the market conditions prevalent during the specified baseline year. An alternative scenario provides a glimpse of the market conditions that will prevail once the specified changes in the intellectual property rights are introduced.

A Guide to the Model

The model is developed in an EXCEL spreadsheet. There is a set of six sheets titled: BASE, ALT 1, ALT2, ALT3, ALT4, ALT5. The sheet titled BASE pertains to the baseline scenario. Sheets ALT 1, ALT2, ALT3, ALT4, ALT5 are for the alternative scenarios.

Imputing the Data

The sheet titled BASE comprises of three tables. Table 1 has two sections: Fixed Parameters and Scenario Dependent Parameters. Table 2 lists information on both endogenous and exogenous variables for the simulation period. These will be explained in detail in the following sections. Table 3 provides information on the percentage distribution of drugs according to the effective period of exclusivity.

The data needs to be manually entered in Table 1 and for the exogenous variables in Table 2. The information on the exogenous parameters in table 2 has to be entered manually for each year of the time horizon. It should be noted that the data entered for **Fixed Parameters** in Table 1 of the sheet titled BASE will get automatically copied to all the sheets for alternative scenarios alias ALT 1, ALT2, ALT3, ALT4, ALT5. Any modification to the information in this section will be automatically reflected in the alternative scenarios.

The Excel program is case sensitive. The decimal place has to be represented by a 'comma' or a 'dot' on a consistent basis. Commas and dots cannot be used interchangeably. The growth rates and the proportions have to be expressed in decimal numbers. For example, a 7% annual rate of growth has to entered as 0.07 or 0,07.

All the durations must be expressed in annual terms and entered as positive integers.

The procedure for saving the entered data or any modifications is: after entering the data, click on any cell, other than the one in which the data has been entered or modified. Follow it by clicking on the key titled "PRESS HERE TO UPDATE the ENDOGENOUS VARIABLES" (this is done by pointing the arrow on that box and pressing the left key of the mouse). This procedure applies to all the six sheets.

After the data has been entered in the sheet for the baseline scenario, enter the data for each alternative scenario for scenario specific variables. The data that needs to be entered includes the Dependent Parameters section of Table 1 and endogenous variables in Table 2.

As in BASE each time the data for scenario specific variables is modified, the key tilted PRESS HERE TO UPDATE the ENDOGENOUS VARIABLES" needs to be clicked. The other key titled: “TO EXPORT the RESULTS From the SCENARIO To the RESULTS SHEETS” needs to be clicked to save the results of the calculations and to export the same to the results sheets. The results sheets: RESULTS, RESULTS (2) etc display the values of the impact variables for the scenarios and the sheet titled ‘GRAPHICS’ displays the graphical representation.

DESCRIPTION OF THE VARIABLES

A) EXOGENOUS VARIABLES

The exogenous variables are those variables whose values are independent from the state of other variables in the model.

The exogenous variables can be classified into three categories: Fixed, Scenario Specific and Annual Input Data.

1) The Fixed parameters

As the name suggests, fixed parameters remain the same across all scenarios. These present the ex-ante situation such as characteristics of the pharmaceutical market prior to the changes in the IPR regime or introduction of other pharmaceutical industry related policy measures. As mentioned earlier, once the data for the fixed parameters is entered in the BASELINE SCENARIO, it automatically gets displayed in the corresponding columns of the **parameters’ input table** of all the alternative scenarios and cannot be changed throughout a simulation exercise unless the changes are made in the baseline scenario.

The fixed parameters include:

YI

The first/ initial year of the simulation exercise. It will vary according to the policy option being evaluated. It can be the year of the introduction of IPR related changes. If the impact of adopting FTA provisions is being evaluated, then the year when the FTA provisions start operating will be the first year of the

simulation exercise. In the case of a retrospective assessment of a policy decision made in the past, such as the impact of having introduced the product patent in year 2002, the initial year would be the year when the measure came into effect, that is, 2002.

YL

The final year of the simulation exercise. The choice of the final year should take into account the fact that the effect of a policy measure such as extension of the patent duration might take a number of years to set in.

The current version of the model allows for a maximum of 50 years.

TAPto

The number of drugs existing at the beginning of the year **YI**. The model uses the term 'active pharmaceutical ingredients' for the number of end products in the market. Each product includes all forms, presentations and brands containing the corresponding drug. For simplicity, drug's with a small market share can be excluded.

MVto

The value of the pharmaceutical market/ the market for the specific drug category in the initial year YI. The value of the market can be inferred from the total sales or by focusing only on private out-of-pocket expenditure, state expenditure or institutional procurement.

α

The Annual Growth Rate of the Relevant Market Segment/ pharmaceutical market: The annual growth rate should be presented in real terms, that is in constant prices of a given year. This implies making adjustments for the rate of inflation, i.e. deducting the inflation rate from the nominal growth rate.

d

The discount rate. The rate at which a monetary unit of value is discounted in order to obtain its present value (the value at t_0). Discounting is justified in economic analysis either by consumers' time preference or by the positive productivity of capital.

k_{de}

The market share of domestic industry in markets under exclusivity.

k_{dc}

The market share of domestic industry in markets under competition.

2) The Scenario Specific Parameters

These parameters may across the alternative scenarios in order to capture the effect of changes in the IPR or other pharmaceutical sector related policies.

YP

The year of introduction of product patents.

YDP

The year of introduction of test data protection.

PD

The term of a patent, i.e. the number of years from filing to expiry. For example, TRIPS Agreement, makes it mandatory for every member of the WTO to make a minimum 20-year term of protection available for all patents from the date of filing.

DT

The average time taken from patent filing to market registration.

PDE

The extension of the patent duration as a compensation for delays in marketing approval.

pPDE

The proportion of drugs obtaining an extension of patent duration due to as delay in marketing approval.

TTC

Time lag between expiry of a patent of an originator product and entry of generics .

DGE

Average delay in market entry of generics due to patent extension –(patent-market registration linkage).

pDGE

The proportion of drugs for which generic entry is delayed due to patent-registration linkage.

DE

The period of market exclusivity due to test data protection.

Rpec

The price differential between the average price of a drug under market exclusivity and that under competition.

Rpbd

The price differential between the average price of a branded generic of an off-patent drug and an unbranded (INN) generic version of the same drug.

e

The price-elasticity of demand for drugs

The price elasticity of demand is defined as a percentage change in the quantity demanded in response to a percentage change in price. In general, a fall in price of a good leads to a rise in its demand. The graphic representation is a downward sloping demand curve. The price elasticity of demand generally has a negative value. It can range from 0 (perfectly inelastic demand) to infinity (perfectly elastic). The value of price elasticity should be entered with a negative sign in the model.

3) The Annual input data

Unlike the previous parameters, that have a fixed value throughout the time horizon of the model, the input data of this section might take a different value every year. The corresponding values must be entered for each of the alternative scenarios.

AIi

The number of new drugs entering the market in a particular year.

AOi

The number of drugs exiting the market in a given year.

The variables **AIi** and **AOi** will be defined in accordance with the definition of **TAPYI.** If **TAPYI** refers to all the registered or marketed drugs, then **AIi** and **AOi** must accordingly reflect the entry and exit of all drugs ingredients. If **TAPYI** refers to certain percentage of registered or marketed drug then for consistency **AIi** and **AOi** should also focus on the corresponding proportion.

AIPPi

The number of newly patented drugs entering the market in a given year.

There might be a situation when product patent regime has been introduced before the period specified by the model. For example, suppose the product patents were introduced in the year 2002. The term of the patent is 20 years.

The average time taken between filing of a patent and market approval is 10 years. However, the first or the initial year for the simulation exercise is 2005. There is a possibility that patented products could have entered the market between 2002 and 2005. Assume that 5, 6 and 5 patented products entered the market in the years 2002, 2003, and 2004 respectively. Since the column for **AIPPi** starts in 2005, it is not possible to enter data for previous years. The data on patented products for the previous year should however get reflected in the column for **AOPPi** i.e. the column reflecting the number of drugs that lose patent protection in a given year. In this example the number of drugs losing patent protection will be 5, 6 and 5 in the years 2012, 2013 and 2014 respectively. In the model these numbers will automatically get added and will get reflected as total number of accumulated patented drugs (TAIPi) in the corresponding column of the initial or first year of the simulation exercise.

AIDPi

The number of new drugs with market exclusivity due to test data protection.

The drugs that entered the market before patent protection was introduced will not have patent protection but may be conferred with market exclusivity on account of test data protection. Those drugs that enter the market after patent protection has been ushered in might enjoy both data protection and market exclusivity. There is a possibility that for a number of drugs there might be an overlap between the periods of protection conferred by patents and market exclusivity. In this situation the model will overestimate the number of drugs enjoying exclusivity.

In the model the total number of drugs under exclusivity (**TAIDPi**) is a sum of the number of drugs with patent protection and those with exclusivity due to test data protection. If all the drugs entering the market either have patent protection or market exclusivity on account of test data protection, in such a situation the total number of drugs with exclusivity would be greater than the total number of drugs (**TAPi**) in the market. The analyst must ensure that such a paradox does not occur. The data must be manually corrected by adjusting the numbers in AIDPI, the column for new drugs with data protection, in a manner that the value of **TAIDPi** does not exceed that of **TAPi** in a given year.

There is possibility that exclusivity due to test data protection (data exclusivity) is being conferred before the period specified by the model. Suppose test data protection started in 2003 and the period of exclusivity is five years. The simulation exercise is for the year 2005 onwards. Therefore,

the products that entered the market in 2003 and 2004 with exclusivity due to test data protection will not get reflected in the column titled AIDPI. These products must be however accounted for in the column for products coming out of the period of data exclusivity, **AODPi,** for the years when these will lose data exclusivity. For example, if 2 products entered in 2003 with test data protection and 3 products in 2004, these figures must be introduced in 2008 and 2009, respectively, in the column titled **AODPi**.

pdi

The proportion of unbranded generics to all generics without exclusivity.

The unbranded generics refers to drugs with no exclusivity sold under their International Non-Proprietary Name (INN) or the generic name. Branded generics also do not have exclusivity. However, follow product differentiation through the use of brand names.

B. THE ENDOGENOUS VARIABLES

Endogenous variables are those variables whose values are determined by the state of other variables in the model. The cells for endogenous variables in the worksheet are protected to avoid mistakes from unintended modifications.

EEP

The effective period of patent protection. Total duration of a drug not getting exposed to generic competition.

Assuming generic completion soon after patent expiry, the average effective period of patent protection is the total term of the patent less the average time taken for drug development and approval. If there is a time lag between patent expiry and entry of generics then this time lag should be added to the above equation to obtain the effective period of patent protection.

TAPi

The total number of drugs in year i. The total number of drugs in year ‘i’ is calculated by adding the new drugs that enter the market in year ‘i’ to the total number of drugs in the market in year ‘i-1’ and subtracting the number of drugs that exit the market in year ‘i’.

AOPPi

The number of drugs losing patent-protection in year ‘i’.

TAIPi

The number of patented drugs (proprietary drugs) in the market in year ‘I’. This number is computed by adding the number of newly patented drugs entering the market in year ‘i’ to the total number of patented drugs in the market in year ‘i-1’ and subtracting the number of drugs losing patent protection in year ‘i’.

AODPi

The number of drugs that lose data exclusivity year ‘i’.

TAIDPi

The number of drugs in the market enjoying data exclusivity in year ‘i’. This figure is calculated by adding the number of drugs entering the market with data

exclusivity in the year ‘i’ to the total number of drugs in the market with data exclusivity in the year ‘i-1’ and subtracting the number of drugs that lose data exclusivity in the year ‘i’.

TAIEi

The total number of drugs with exclusivity either due to patent or test data protection in year ‘i’.

TAEIi

Calculated by adding the number of drugs in the market with patent protection and those with test data protection, subtracting the number of drugs covered by both forms of protection. This adjustment must be manually made in the column for the corresponding scenario

pei

The proportion of the pharmaceutical market under exclusivity in year ‘i’. The **pei** is the ratio of the number of drugs under exclusivity to the total number of drugs in the market the year ‘i’.

MVi

The total value of the pharmaceutical market (expenditure) in year i.

ΣMVi

The total cumulated value of the pharmaceutical market or total pharmaceutical expenditure.

It is the sum of the value of the market for all years in the scenario.

ΣdMVi

The cumulative discounted value of the pharmaceutical market expenditure.

The discounted value is calculated by dividing the present market or pharmaceutical expenditure value by the selected rate of discount.

MVDi

The sales/share of the domestic industry in the domestic market in the baseline scenario, year i

The notations for the alternative scenario X (X = 1,2,3,4,5) are indicated by a superscript ‘X’. For example, the variable ΣMVi for the *alternative scenario 2,* will be $\Sigma MV^{2}i$.

$P^{x}i$

The drug price index for the alternative scenario X in relation with the baseline scenario.

$MV^{X}i$

The value of the pharmaceutical market or the total pharmaceutical expenditure in year i for the scenario X.

$k^{X}i$

The share of the domestic industry in the domestic market in year i and for scenario X.

C. THE IMPACT VARIABLES

The impact of an alternative scenario on a given variable is computed both in absolute terms and relative to the baseline scenario.

1. Consumption

$rC^{x}i$ The relative reduction in the consumption of pharmaceuticals (in units) in year i in comparison with the baseline scenario

A value of the 0.2 will mean a reduction in consumption by 20% in comparison with the baseline scenario

2. Expenditure/value of the market

$IMV^{x}i$

The impact of scenario X on the value of the pharmaceutical market (pharmaceutical expenditure) in year i.

$I\Sigma MV^{x}i$

The impact of scenario X on the cumulative value of the pharmaceutical market.

$\%I\Sigma MV^{x}i$

The impact of scenario X on the cumulative value of the pharmaceutical market relative to the baseline scenario.

$I\Sigma dMV^{x}i$

The impact of scenario X on the cumulative discounted value of the pharmaceutical market/ expenditure.

$\%I\Sigma dMV^{x}i$

The impact of scenario X on the cumulative discounted value of the pharmaceutical market/ expenditure relative to the baseline scenario.

3. The sales of the national industry:

$RMVD^x_i$

The reduction in the sales of the domestic industry in the domestic market in year i.

Appendix 2. Information and data required for the application of the IPRIA model to a given country

Note: The following list includes but goes beyond the strictly necessary set of input parameters required for running the model. For instance, the model requires the user to specify the rate of growth of the relevant market segment. In order to choose a value the analyst might want to use the recent values of the rate and compute an average value or else identify and extrapolate a time trend for the rate. But if there are good reasons to expect the rate to rise in the future, e.g. because the percentage of population insured is expected to grow, the analyst might prefer to base the estimated rate of growth on expert opinion or use other approaches to select the appropriate value. In any case, knowing the rate of growth in the previous years will always help the analyst make a reasonable choice of the appropriate parameter value.

1. The first/ initial year of the simulation exercise.

2. The final year of the simulation exercise.

3. The value of the pharmaceutical market in nominal terms, i.e. total pharmaceutical expenditure in nominal prices. Ideally this data should be for the last five to ten years to enable calculation of the rate of growth of the market. If the drug procurement is at different levels such as institutional, private and through insurance then expenditures will be calculated on the basis of prices applicable to the corresponding level. It is recommended that separate estimates should be made for each level, for e.g. separate estimates should be made for each sector like Ministry of Health, Social Insurance, and private market. These values can be presented in US$ or in local currency terms.

4. The exchange rate over the time frame of the simulation exercise to covert the value in US$ terms.

5. The estimates of the rate of growth of the relevant market segment. The terms in which the values which form the basis of the growth rate are expressed should be clearly stated, for e.g. whether these are in US$ values, or in nominal and real prices.

6. The total number of drugs in each market segment. It will be useful to indicate the number of drugs that account for 50%, 80% and 90 % of the market. Ideally, these data should be for the past five to ten years.

7. The number of drugs that were given market registration in each year for the past 5 – 10 years. If available it will be useful to have estimates for the number of drugs that are expected to gain market registration in the following 5-10 years.

8. The number and market share of drugs that are less than 5, between 5-10 and more than 10 years old.

9. The year of introduction of product patents.

10. The year of introduction of test data protection and other forms of market exclusivity.

11. The number and market share of drugs with patent protection by year. This information should ideally be for the past 5-10 years.

12. The number and market share of drugs with test data protection or other forms of intellectual property by year. This information should ideally be for the past 5-10 years.

13. The nominal life of a patent.

14. The nominal duration of test data protection and of other forms intellectual property that provide market exclusivity.

15. The average time taken between patent filing and market registration for products that entered the market in the past 5-10 years.

16. The average time lag between patent expiry and generic entry. (if applicable)

17. The total population and the population covered under different health insurance schemes (if applicable) and projections for future coverage.

18. A brief description of the country's health system. For e.g. description of the main features of the insurance schemes: eligibility, financing mechanism, benefit package, co-payments.

19. The per capita expenditure in health services and pharmaceuticals under each insurance scheme.

20. The distribution of the population both covered by insurance schemes and uninsured by income levels (e.g. in deciles).

21. Description of payment and co-payment mechanisms for pharmaceuticals under different insurance schemes.

22. The estimates of price-elasticity of the demand for pharmaceuticals.

23. The value of domestic pharmaceutical production. Market share of domestic and foreign manufacturers in each market. Market share of domestic firms in the submarket under exclusivity.

24. The share of domestic products in the domestic market. (This includes products manufactured by subsidiaries of foreign firms)

25. The export and import figures for pharmaceuticals (It is important to distinguish between trade in finished products and active pharmaceutical ingredients (APIs).

26. The cost structure of domestic and foreign firms. The share of imported drugs and other inputs is of particular relevance. .

27. The employment by domestic and foreign firms.

Appendix 3. Reporting format for country analyses

The following suggested format is aimed at allowing the analyst to communicate in a summary way the relevant information of an application of the IPRIA model

The name of the Country:

The country in which the model is applied and the sub sector, if relevant. For instance: Costa Rica, Social Insurance Institute.

The User Team

Names of the team members, profile, affiliation and role in the analysis.

The Purpose/ Objective of the Analysis:

For example: To analyse implications of the application of the FTA provisions on access to medicines.

The Description of Data and Data sources:

Data sources could include official sources such as, Statistical Yearbooks,

Ministry of Health,

The methodology

This will involve defining the variables. Conducting analysis, such as sensitivity analysis, to ascertain robustness of the specification.

The specification of the baseline and alternative scenarios

This involves defining the baseline and alternative scenarios. (For example: **Baseline Scenario:** No change in the IPR regime. **Alternative Scenario:** Introduction of 5 years test data exclusivity.)

Quantitative analysis of the results.

The policy implications

Discussion of the policy implications. For example the implication of extending duration of the patent on account of delays due to market registration.

General comments

Suggestions on further empirical analysis and additional data collection.

Limitations and suggestions for the improvement of the model.

Appendix 4. Model specification

Exogenous Variables

Fixed parameters

YI: The first/ initial year of the simulation exercise.

YL: The final year of the simulation exercise.

TAPYI: The number of drugs existing at the beginning of the year **YI**.

MVYI: The value of the pharmaceutical market/ the market for the specific drug category in the initial year YI.

α: The annual growth rate of the relevant market segment/ pharmaceutical market.

d: The discount rate.

$\mathbf{k_{de}}$: The market share of domestic industry in markets under exclusivity.

$\mathbf{k_{dc}}$: The market share of domestic industry in markets under competition.

The Scenario-specific parameters

YP: The year of introduction of product patents.

YDP: The year when test data protection was introduced.

PD: The term of a patent.

DT: The average time taken from patent filing to market registration.

PDE: The extension of the patent duration as a compensation for delays in marketing approval.

pPDE: The proportion of drugs obtaining an extension of patent duration due to a delay in marketing approval.

TTC: Time lag between expiry of a patent of an originator product and entry of generics in absence of Bolar exemption.

DGE: Average delay in market entry of generics due to patent extension.

pDGE: The proportion of drugs for which generic entry is delayed due to patent-registration linkage.

DE: The period of market exclusivity due to test data protection.

RPec: The price differential between the average price of an drug under market exclusivity and that under competition.

RPbd: The price differential between the average price of a branded generic of an off-patent drugs and an unbranded (INN) generic of the same drug.

e:The price-elasticity of demand.

The Annual input data

AIi: The number of new drugs entering the market in a particular year.

AOI: The number of drugs exiting the market in a given year.

AIPPI: The number of newly patented drugs entering the market in a given year.

AIDPI: The number of new drugs with market exclusivity due to test data protection.

pdi: The proportion of unbranded generics to all generics without exclusivity.

The Endogenous Variables

EEP is the effective period of patent protection.

EEP = PD – DT + PDE + TTC + DGE

where:

PD= The term of a patent.

DT=The average time taken from patent filing to market registration.

PDE= The extension of the patent duration as a compensation for delays in marketing approval.

TTC: Time lag between expiry of a patent of an originator product and entry of generics in absence of Bolar exemption.

DGE: Average delay in market entry of generics due to patent extension.

TAPi is the total number of drugs in year i.

$TAPi = TAP_{i-1} + AIi – Aoi$

Where:

TAP_{i-1} = The total number of drugs in the market in year 'i-1'.

AIi = The number of new drugs entering the market in a particular year.

AOI = The number of drugs exiting the market in a given year.

AOPPI is the number of drugs losing protection linked with patents in year 'i'. This will include drugs covered by patent term extension due to delay in patent approval and market registration. Number of drugs losing exclusivity linked to patent protection in year.

$$AOPPi = pPDE*pDGE*AIPP_{i-(PD-DT+PDE+TTC+DGE)}$$

$$+ (1-pPDE)*pDGE*AIPP_{i-(PD-DT+TTC+DGE)}$$

$$+ pPDE*(1-pDGE)*AIPP_{i-(PD-DT+PDE+TTC)}$$

$$+ (1-pPDE)*(1-pDGE)*AIPP_{i-(PD-DT+TTC)}$$

where:

pPDE: The proportion of drugs with patent term protection due to delays in patent approval

pDGE: The proportion of drugs with patent term extension due to delays in marketing approval

AIPPi: Number of drugs with exclusivity linked to patent protection in year i

Example
Suppose 10 drugs enter the market with patent protection in the year 1993. The total term of patent protection is 20 years. Time taken from patent filing to market registration is 7 years. Let 20% of the patented drugs be covered by patent term extension due to delays in patent approval and 50% of the patented drugs be covered by patent term extension due to delays in marketing approval. The patent term extension due to delays in patent approval is 2 years and for delays in marketing approval is 4 years. This scenario is summarised in the following matrix:

	DGE	**No DGE**

PDE	0.2, 0.5	0.2, (1- 0.5)
No PDE	(1-0.2), (0.5)	(1-0.2), (1-0.5)

The drugs losing patent linked protection will follow the following sequence:

Drugs with No PDE and No DGE, i.e. without exclusivity due to delays in patent or marketing approval: (1-0.2)*(1-0.5)*10 = 4. This implies that 4 drugs will lose patent protection in the year 2013.

Drugs with PDE and DGE: (0.2)*(0.5)*10 = 1. This means that 1 drug will lose patent protection in the year 2017.

Drugs with PDE and No DGE: (0.2)*(1-0.5)*10 = 1. This implies that 1 drug will lose patent protection in the year 2015.

Drugs with No PDE and DGE: (1-0.2)*(0.5)*10 = 4. This implies that 4 drugs will lose patent protection in the year 2017.

In sum, 4 drugs will lose patent protection in 2013, 1 in 2015 and 5 in 2017.

$TAIPi = TAIP_{i-1} + AIPi - AOPi$

AODPi: Number of drugs losing exclusivity due to test data protection in year i

$AODPi = \underline{AIDP_{i-DE}}$

TAIDPi: Number of drugs with exclusivity due to test data protection in year i

$TAIDPi = TAIDP_{i-1} + \underline{AIDPi} - AODPi$

TAIEi: Number of drugs with market exclusivity in year i

TAIEi = TAIPi + TAIDPi

pei: share of the relevant market under exclusivity in year i

pei = TAIEi/ TAPi

MVi: Total sales/expenditure of the relevant market in year i.

$MVi = MVi_{-1}*(1+\alpha)$

ΣMVi: Cumulative sales/expenditure of the relevant market over time horizon.

ΣdMVi: Discounted cumulative sales/expenditure of the relevant market over time horizon.

Variables for alternative scenarios x are indicated by the superindex (^{x})

Pi : price index of baseline scenario in year i;

By definition, Pi=1, for i = 1,2,3,...n

$P^x i$: price index of scenario X in relation to baseline scenario in year i

$P^x i = AP^x i / APi$, where

$AP^x i$: average price per AI in year i, in scenario X

APi : average price per AI in year i, in baseline scenario

$AP^x i = pe^x i * APe + (1 - pe^x i)*(1 - pd^x i)*APb + (1 - pe^x i)*pd^x i * APu$

APi = pei*APe + (1 - pei)*(1 - pdi)*APb + (1 - pei)*pdi*APu

APe: Average price of originators under exclusivity

APb: Average price of branded generics

APu: Average price of unbranded generics

These average prices are assumed constant over time

$pe^x i$ = the share of products subject to exclusivity in year i under alternative scenario

pei = the share of products subject to exclusivity in year i in the baseline scenario,

pdi = the share of products without exclusivity that are available as unbranded generics in year i, in the baseline scenario,

$pd^x i$ = the share of products without exclusivity that are available as unbranded generics in year I, in the alternative scenario, and

RPec : The average price of a product under exclusivity relative to its price when subject to generic (unbranded) competition ,

RPec = APe / APu, hence, APe = APu*RPec

RPbd : The average price of a product sold as a branded generic relative to the average price if sold as an unbranded generic.

RPbd = APd/APu, hence, APd = APu*RPbd

$AP^{x}i = pe^{x}i*APu*RPec + (1 - pe^{x}i)*(1 - pd^{x}i)*$ APu*RPbd + $(1 - pe^{x}i)*pd^{x}i*$ APu

APi = pei*APu*RPec + (1 - pei)*(1 - pdi)*APu*RPbd + (1 - pei)*pdi*APu

$AP^{x}i = APu\ [pe^{x}i*RPec + (1 - pe^{x}i)*(1 - pd^{x}i)*RPbd + (1 - pe^{x}i)*pd^{x}i]$

APi = APu [pei*RPec + (1 - pei)*(1 - pdi)*RPbd + (1 - pei)*pdi]

Finally,

$P^{x}i = [pe^{x}i*RPec + (1 - pe^{x}i)*(1 - pd^{x}i)*RPbd + (1 - pe^{x}i)*pd^{x}i] / [pei*RPec$

+ (1 – pei)*(1 - pdi)*RPbd + (1 - pei)*pdi]

Note that the price index defined in this model does not show the evolution of prices over time, but the relative level of prices in alternative scenarios in relation to the baseline scenario for which the price index is set to zero all years.

Monetary time series are expressed at constant prices of the initial year

Numerical example

RPec = 4; RPbd = 2; pei = 0.5; pdi = 0.5; $pe^{x}i = 0.65$; $pd^{x}i = 0.25$

$P^{x}i = [0.65*4+(1-0.65)*(1-0.25)*2+(1-0.65)*0.25] / [0.5*4+(1- 0.5)*(1- 0.5)*2$

+(1-0.5)*0.5] =

= [2.6+(0.35)*(0.75)*2+(0.35)*0.25] / [2+(0.5)*(0.5)*2 + (0.5)*0.5] =

= [2.6+0.525+0.0875] / [2+0.5+0.25] = 3.2125 / 2.75 = 1.1681818

This result has been tested on the program IPRIA Model v2008.2_Proves. This is exactly the value obtained for the price index, $P^{x}i$, for Alternative Scenario 2 in year 2025.

This means that under the alternative scenario prices would be on average 16.8% higher than in the baseline scenario for the same year.

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The demand curve has the form:

$q = k\ p^{e}$, or $\ln q = \ln k + e \ln p$,

where k and e are constant and k>0 and e=<0

This demand curve has a constant price-elasticity e.

The firs derivative ($dq/dp = k \alpha p^{e-1}$) is negative when e<0 and k>0:

$MV^x i$: Total sales/expenditure of the relevant market in year i under alternative scenario x

$MV^x i = MVi^* P^x i^{e+1}$

Demonstration:
$MVi^x/MVi = k(Pi^x)^{e+1}/ k(Pi)^{e+1} = (Pi^x)^{e+1}$ as Pi is by definition Pi = 1, then $MV^x i = MVi^* P^x i^{e+1}$

Impact of scenario x on consumption

$RC^x I$: Relative reduction in consumption (units) in year i (from baseline scenario)

$RC^x I = P^x I^E - 1$

Demonstration:
$rC^x i = (q^x i - qi) / qi = q^x i/qi - 1 = (k P^x i^e / kPi^e) - 1$ as Pi is by definition Pi = 1 , then $rC^x i = P^x i^e - 1$

$\Sigma MV^x i$: Cumulative sales/expenditure of the relevant market over time horizon under alternative scenario x.

$\Sigma dMV^x i$: Discounted cumulative sales/expenditure of the relevant market over time horizon under alternative scenario x.

Impact of scenario x on sales/expenditure

$IMV^x i$: Impact of scenario x on total sales/expenditure of the relevant market in year i.

$IMV^x i = MV^x i - MVi$

$I\Sigma M^x Vi$: Impact of scenario x on cumulative sales/expenditure

$I\Sigma M^x Vi = \Sigma MV^x i - \Sigma MVi$

$I\Sigma dMV^x i$: Impact of scenario x on discounted cumulative sales/expenditure

$I\Sigma dMV^x i = \Sigma dMV^x i - \Sigma dMVi$

Impact of scenario x on domestic industry sales

MVDi: Market sales of domestic industry in year i under baseline scenario

MVDi: k_{de}* pei* MVi + k_{dc}*(1-pei)* MVi

$MVD^x i$: Market sales of domestic industry under scenario x

$MVD^x i = k_{de}$*pei* $MV^x i + k_{dc}$*(1-$pe^x i$)* $MV^x i$

$RMVD^x i$: Reduction in market sales of domestic industry under scenario x

$RMVD^x i = MVDi - MVD^x i$

$RMVD^x i = k_{de}$* pei* MVi + k_{dc}*(1-pei)* MVi

- (k_{de}*pei* $MV^x i + k_{dc}$*(1-$pe^x i$)* $MV^x i$)

$k^x i$: market share of domestic industry under scenario x

$k^x i = k_{de}$*pei* + k_{dc}*(1-$pe^x i$)

Appendix 5. Reviewers' reports

Reviewers' reports

The IPRIA model underwent a formal review process. The reviewers were Carsten Fink, World Bank Institute; Carlos Casacuberta, (Universidad de la República) and Néstor Gandelman (Universidad ORT) Uruguay; Dean Baker; Joan Costa Font, LSE; and Marcelo Olarreaga, University of Geneva. The review was based on a draft version of the Guide, ("Development of a Model to Assess the Impact of Changes in IPR" by Joan Rovira, version 22-02-2008[2]) and an associated Excel spreadsheet. The reviewers were given the following guidelines for the review:

INSTRUCTIONS FOR THE REVIEWERS

In evaluating the model, the reviewers should separately consider

a) the model as described in the Guide, especially the mathematical specification

b) the implementation of the model in the Excel program

c) the applications to particular countries

The reviewers are encouraged to suggest alternative options to the flaws and shortcomings identified in the model.

The reviewers should address on the following questions, taking into account the corresponding TOR, but also additional developments that can enhance the usefulness of the tool:

1. Are the model's key assumptions justified in light of the prior economic literature and the special characteristics of pharmaceutical markets?

2. What are the main advantages and limitations of the model?

3. In what ways can the model be improved and does the sensitivity analysis recommended by the model address these potential shortcomings?

4. Is the model conducive to producing the necessary findings for measuring the impact of new patent standards on the price of medicines?

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[2] Available from the author: joanrovira@ub.edu

5. Are the model's data requirements realistic for implementation in a developing country context?

6. What types of empirical/additional studies should be undertaken to strengthen the applications of the model.

7. Is a partial equilibrium model the best instrument for measuring the impact of TRIPS and TRIPS-Plus provisions? What other types of instruments are available and should be considered?

8. Is the program implementation

a) correct?

b) transparent?

c) flexible enough to accomodate the expected decision-makers needs?

d) user-friendly for a user with basic experience with spreadsheets?

9. What changes and additional features would be desirable to make for a future version of the program.

The reviewers sent written reports (see below) than were commented by Joan Rovira (comments in capital letters in the text). The reviews were also discussed at a ICTSD meeting, Geneva, May 4, 2008. The suggestions of the reviewers were included in the new version of the Guide in the form of modifications of the original text or as discussion topics.

Review 1.

Carsten Fink, The World Bank Institute.

(COMMENTS BY JOAN ROVIRA IN CAPITAL LETTERS)

The paper offers relevant background information on the motivation for empirically assessing the effects of IPRs changes on pharmaceutical markets, a literature review, and a description of the model proposed. Several annexes offer definitions of all model variables, an overview of data requirements for applying the model, a suggested reporting format, and an abbreviated user's manual. The Excel spreadsheet provides an application of the simulation model that can be adapted to user needs.

At its core, the model evaluates the effects of changes in the share of on-patent versus off-patent pharmaceutical compounds on total pharmaceutical consumption, pharmaceutical expenditure, and sales by the domestic industry. Key model assumptions are: i) price changes due to the presents of IPRs-induced market exclusivity are exogenous; ii) all pharmaceutical compounds have the same market share; and iii) overall market demand is characterized by a constant-elasticity of demand (CED) function.

General comments

1. Any modeling analysis of the impact of IPRs changes on outcomes in pharmaceutical markets will invariably need to make some restricting assumptions. The choice of assumptions is first determined by data availability: key structural parameters such as demand elasticities, cost functions, and several 'future' variables (the rate of new product introductions, the length of market exclusivity) are unknown and only few outside estimates are available. In addition, assumptions reflect the focus of the model: what are the key variables of interest and how do they interact with each other.

Against this background, the proposed model focuses on the 'compositional' effects due to IPRs changes in a dynamic setting. This focus appears especially suited to assess the impact of policy changes in the long term (say, within 10-20 years) and at the macro level (national pharmaceutical markets as a whole, rather than individual

pharmaceutical compounds or groups of compounds belonging to a single therapeutic group). The cost of this modeling approach is that the price impact—arguably the most direct consequence of new market exclusivity—is not explained by the model, but rather taken to be exogenous. This assumption is difficult to justify in analyses of more disaggregate pharmaceutical market segments, where one would like to see the impact of exclusivity rights on market structure and eventually prices as the core focus of the model.

From this view, while it is true that the proposed model can, in principle, be applied to any level of market aggregation (as the author asserts on page 10), the design of the model is better suited for macro applications. Indeed, it is this reviewer's understanding that the joint ICTSD-WBI-WHO project aims at developing a special impact assessment model for micro applications. Such a 'micro-model' would not only offer an important complement to the macro model, it could also serve as a direct input into the latter by offering more rigorous estimates of price differentials. (THE APPROACH IS EXACTLY AS THE REVIEWER SAYS.)

2. Even though the paper offers a literature review, **it does not explain to what extent the model is rooted in the prior literature. It would be good to have a discussion of why the approaches taken in previous studies have or have not been used in the current context.** (THIS MIGHT BE A USEFUL EXERCISE, THAT WE HAVE STARTED APPLYING IN THE REPORT ON THE MICRO MODELLING) The current literature review merely discusses the motivation of different studies, but doesn't really go into the methodological aspects of these studies.(IN FACT, WE FOUND THAT THE STUDIES REVIEWED WERE NOT MUCH APPLICABLE TO THE DEVELOPMENT OF THE MACRO MODEL THAT WE ENVISAGED)

3. Related to the previous comment, the model's microeconomic foundations are not well developed (INDEED, A PROBLEM OF MOST MACROECONOMIC MODELS) . **In particular, the use of a CED demand function** (IT WAS THOUGHT AS A COMPROMISE BETWEEN SIMPLICITY AND FLEXIBILITY. MOST DEMAND STUDIES REPORT ONLY PRICE ELASTICITIES. WE FOUND THAT ASSUMING LINEAR DEMAND CURVES, AS SOME PREVIOUS STUDIES DID, INTRODUCE ADDITIONAL UNJUSTIFIED RESTRICTION INTO THE MODEL) on the one hand, and the assumption of exogenous price differentials, on the other, raises a serious

consistency issue. In imperfectly competitive markets (and market exclusivity will make competition highly imperfect), firms will orient their prices according to perceived elasticity of demand: the less elastic demand, the higher will be the price in equilibrium. In other words, a given value of the demand elasticity may, in a simple model, already imply a certain price differential.

(WE WOULD BE PLEASED TO RECEIVE ANY SUGGESTIONS ON ALTERNATIVE SPECIFICATIONS TO MAKE PRICES ENDOGENOUS, AND HOW THIS COULD BE TAYLORED TO AN AGGREGATE MARKET MODEL, WHICH INCLUDES ALL PHARMACEUTICAL PRODUCTS, EACH ONE LIKELY TO DIFFER IN ITS PARTICULAR SUPPLY AND DEMAND CURVES AND IN THE MARKET STRUCTURE).

The two issues can probably be reconciled. In addition to the market-wide demand elasticity, firm demand will also depend on cross-price elasticities (YES, BUT THIS REQUIRES A MICROECONOMIC APPROACH) between different products within a certain therapeutic group and between branded generics and unbranded generics. The study by Fink (2000, quoted in the paper) develops a three level demand function, whereby prices for individual pharmaceutical compounds depend not only on overall market demand, but also on elasticities of substitution (between different drugs in a therapeutic class and between different brands of the same drug). With this demand structure in mind, one could justify a self-standing assumption on price differentials, by arguing that these differentials are, in part, determined by local substitution elasticties, not <u>just</u> overall market demand. (In fact, this is consistent with the prior literature: studies suggest that pharmaceutical prices depend to a large degree on the availability of on and off-patent therapeutic substitute drugs).

Another consistency problem appears to exist in the calculation of the change in domestic industry sales. The model assumes constant and equal market shares of pharmaceutical compounds. Based on that assumption, one calculates the change in the overall price level, with which one computes the associated change in consumption and aggregate pharmaceutical expenditure. The 'new' pharmaceutical expenditure figure is then taken to compute the share of the domestic industry, based <u>again</u> on equal market shares of pharmaceutical compounds. However, prices have changed in the meantime, and one would expect

these price changes to have altered market shares (unless, the demand function at the level of individual products is unit-elastic). (I THINK THE REVIEWER IS RIGHT IN STATING A INCONSISTENCY IN THE MICROECONOMIC FOUNDATIONS OF THE MODEL. PENDING MORE FORMAL CHECK I THINK THAT IN THE COMPETITION PHASE THE MARKET SHARES MUST BE ALLOWED TO CHANGE DEPENDING ON THE PRICE ELASTICITY. HOWEVER SHARES CAN BE ASSUMED TO BE EQUAL FOR PRODUCTS UNDER EXCLUSIVITY, ON ONE HAND, AND UNDER COMPETITION, ON THE OTHER). (I HOWEVER THINK THAT THIS POINT DOES NOT NEED TO DETERMINE OR IMPOSE ANY CONSTRAINT ON THE SHARES OF THE DOMESTIC INDUTRY WHICH ARE DEETRMINED BY A DIFFERENT AND QUITE ARBITRARY RULE)

These points seem academic, but that's precisely the point. In order to defend its credibility, it is important to convincingly demonstrate that the proposed model fits within industrial organization theory. (I AGREE THAT THE MODEL SHOULD HAVE A AS SOUND AS POSSIBLE THEORETICAL FOUNDATION, BUT I AM NOT SURE IF IT MUST NECESSARILY FIT WITHIN INDUSTRIAL COMPETITION THEORY, WHICH IS BASICALLY A MICROECONOMIC THEORY)

4. The model evaluates the impact of IPR changes on domestic industry sales, because policymakers may be worried about industrial "competitiveness" (see page 8). However, the notion of higher domestic sales as an indicator of superior domestic performance is not at all clear. At one level, one might argue that it reflects the success of an industrial policy. However, arguments for an active industrial policy are often made with respect to technology-intensive sectors and it isn't clear whether the manufacture of generic medicines is particularly technology-intensive. Even then, economists tend to be skeptical about governments' success in picking 'winning' industries. Policymakers may be worried about self-sufficiency, though this argument is likely confined to a few products for which supply shortages may arise (e.g., influenza vaccines).

From an economic efficiency as well as medicines' access standpoint, it isn't clear why domestic industry sales should be a relevant variable. Inevitably, some

countries have a comparative advantage in the manufacture of generic medicines, others don't. If countries protect their local pharmaceutical industry, local prices may be above world prices. Admittedly, this debate goes beyond the scope of the model and there is nothing wrong with analyzing the effects on domestic industry sales (not least because policymakers may demand it). However, it would be good to include a few caveats in the paper along the lines suggested here. (Also, how is the "domestic" industry defined: all locally established firms, or only domestically owned or controlled firms?).

THE INDUSTRIAL "COMPONENT" OF THE MODEL WAS INTRODUCED TO HIGHLIGHT THE POINT THAT CHANGES IN IPR MIGHT AFFECT NOT ONLY ACCESS TO MEDICINES, BUT ONLY DOMESTIC PRODUCTION. IT IS BASED ON HIGHLY SIMPLE, MECHANISTIC BUT PLAUSIBLE ASSUMPTIONS AND REFLECTS WHAT IS USUALLY OBSERVED: MOST COUNTRIES HAVE SEEN THE SHARE OF THE DOMESTIC INDUSTRY DECLINE AFTER THE INTRODUCTION OF PRODUCT PATENTS – IRRESPECTIVE OF HOW YOU DEFINE DOMESTIC INDUSTRY.

5. The model documentation and the associated Excel spreadsheet appear user-friendly. Even researchers that do not have an extensive modeling background should be able to implement the model. In addition, the list of data requirements appears reasonable and, in any case, the model set-up is flexible to accommodate cases where some data may not be available.

What still appears to be **missing is some guidance on what are 'reasonable' values for the different model parameters—including, how to 'predict' changes in the period of market exclusivity, price differentials, the discount rate, elasticity of demand, etc.** Some evidence can be obtained from the academic literature on pharmaceutical markets and prior studies that have employed the present model. **Such guidance should also suggest sensitivity analyses that test how the model's endogenous variables change as a result of changes in key model parameters.** Invariably, model predictions will be wrong, but it is important for policymakers to know how large the mistake could be.

I THINK THAT THIS CAN BEST BE DONE NOW THAT SEVERAL COUNTRY STUDIES WILL HAVE BEEN COMPLETED AND REVIEWED.

Specific comments

1. Page 2, third paragraph, first sentence. **The distinction between "emerging economies" on the one hand and "developing countries" on the other is unusual and confusing. How are the two groups defined (are they mutually exclusive)?**

2. Page 2, last paragraph. The author suggests that "FTAs are increasingly being used as a tool to strengthen intellectual property regimes in developing countries." While this statement would have reflected ongoing policy developments 2 or 3 years ago, it's not clear whether it still holds today. Notwithstanding selected test data provisions in a number of EFTA agreements, the most far-reaching FTA-IPRs chapters have so far been concluded by the United States. However, in May 2007, the Democratic Leadership in the US Congress negotiated a 'revised' IPRs template with the US administration that substantially waters down key patent and test data provisions in US FTAs. More importantly, the executive branch of the US Government has lost its Trade Promotion Authority (TPA) under which it can negotiate trade deals and then present them to the US Congress for an up-or-down vote. It is not clear whether a new TPA will be awarded to the next US President. In other words, the US FTA agenda—generally, and with respect to pharmaceutical-related IPRs in particular—may be stalled for the next few years.

This policy development shouldn't be seen as invalidating the purpose of empirical assessments. **The proposed model is designed to evaluate the impact of IPRs changes more generally, not just those emanating from FTAs.** For example, in many countries, significant changes loom as a result of implementing TRIPS-style pharmaceutical patent protection, which only became a requirement for developing countries as of January 2005. **It would therefore be good to emphasize the multiple uses of the model in the introductory section of the paper.** OK

3. Page 3, second paragraph. It seems too optimistic to think that empirical assessments will have a dramatic influence on the outcome of trade negotiations. However, even if they don't, they are still useful, especially as a means of quantifying adverse implications of stronger IPRs standards and to design mitigating policies.

4. Page 5, fourth paragraph. The findings of Chaudhuri, Goldberg, and Jia seem surprising. They suggest a loss of consumer welfare to the tune of $663 million, compared to additional profits of foreign companies of $57 million. In terms of traditional Harberger triangle analysis, the consumer welfare loss seems very large in relation to additional company profits. It would be good to know what is driving this result (e.g., welfare losses due to reduced product variety?).

5. Page 7, Box 1. Two comments. **First, do FTAs really extend the patent term beyond 20 years (independent of patent term extensions due to delays in the processing of the patent/delays in obtaining marketing approval)? Second, reflecting the comment above, it may be good to not only focus on TRIPS-plus provisions, but also on TRIPS provisions (notably, the introduction of patent protection for pharmaceutical products).** OK

6. **Page 8, point 2 under impact variables. The first sentence contradicts the second sentence. It may be best to start off by saying that the effect of a rise in prices on expenditure is theoretically ambiguous and depends on the value of the demand elasticity.** OK

7. Page 9, point 4. **The paper points to empirical evidence, but does not cite any study.** OK In addition, the assertion that stronger IPRs do not lead to an overall increase in R&D seems questionable. Studies have shown that the pharmaceutical and chemical industries are most sensitive to patent protection, due to the long and expensive R&D cycle on the one hand, and the ease with which new pharmaceutical compounds can be copied once introduced to the market, on the other.[3] (Of course, even if stronger IPRs promote R&D, it does not mean that they are the most effective vehicle for promoting R&D or that a policy of stronger IPRs is net welfare increasing).

8. Page 11/12, last/first paragraphs. Paragraphs are repeated. OK

9. Page 12, sixth paragraph. The paper assumes correctly that the monopoly power of an API covered by both forms of protection is not higher than the one covered by only one form. This raises the question of whether the period of test data exclusivity ever

[3] See, for example, Scherer, F.M. and Watal, J. (2001) Post-TRIPS Options for Access to Patented Medicines in Developing countries, WHO Commission on Macroeconomics and Health, Working Paper No. 1.

exceeds the patent term. While this does not pose a modeling problem, it may pose a practical problem as it seems difficult to predict when there will be a test data "overhang". If there is no such overhang, test data protection will still be relevant in possibly rendering compulsory licenses on patents ineffective. Again, this is not a modeling problem, but it would be good to give the reader some guidance on how to specific the relevant policy variables. OK

Review 2

Carlos Casacuberta (Universidad de la República) and Néstor Gandelman (Universidad ORT Uruguay)

(COMMENTS BY JOAN ROVIRA AT THE END OF THE REVIEW)

Introduction

In this report we undertake the evaluation of the performance of a model recently proposed to evaluate the effects of changes in Intellectual Property Rights (IPR) legislation on the pharmaceutical market, particularly using data on several institutional agents and markets in Uruguay. The Effects Simulation Model (ESM) emerged from the recommendations of the PAHO Working Group on the effects of the Trade Related Intellectual Property Rights (TRIPS) and is described in a series of working papers.[4]

We first provide a presentation of the model with a critical appraisal of some of its features, particularly regarding the sensitivity of simulation results to several parameters that must be supplied by the researcher. Our research evolved in parallel with the development of the methodological guide by the core ICTSD-WHO-WBI project team. In the first phase we took stock of available data in the pharmaceutical sector including data on prices and quantities, the date of introduction of new pharmaceutical products and the patent status of pharmaceutical products sold in Uruguay. The second phase of this work involved the implementation of the models, as proposed by the ICTSD-WHO-WBI draft methodological guide. During the project development process the model suffered some modifications and updates that are incorporated in this version.

Secondly, we provide a detailed report on how Uruguayan data might be adapted in order to generate suitable counterparts for the model parameters.

[4] See Rovira (2006), Clift (2007).

The estimation procedures and their results are presented. Then we perform a series of simulation exercises with the model, intending to generate adequate alternatives scenarios that may represent reasonable changes faced by the Uruguayan market in the recent past and foreseeable future. Finally, we conclude.

1. The model

The algebraic presentation of the model is useful to analyze the impacts of the various assumptions and parameters in the output variables. Here we sketch the main definitions and relationships between variables. The modelling strategy seeks to compare alternatives to a baseline scenario. The baseline scenario is not a steady state in which variables or their rates of growth remain constant, but rather a status quo against which the effects of changes in IPR are measured. For instance, the baseline scenario might include the recent introduction of patent laws whose effects might take years to be felt completely.

1.1. Active pharmaceutical ingredients

The active pharmaceutical ingredient is the main “product” concept in the model. Pharmaceutical producers supply the same API in different presentations and quantities each one with its observed prices. In this model all of them are aggregated into APIs. There are three kind of APIs to be considered: patented products protected by exclusivity, branded generics, and unbranded generics.

It is important to consider that the model is very sensitive to classification issues. In general database are defined of terms of products, commercial names and packaging. Data needs to be translated into AI. The aggregation level at which AI are described is crucial to the results since IPR dynamics come into the model as the fraction of total AI whose protection level is changed due new legislation.

1.2. Market value definition

The market is defined in terms of total revenue MV_t.[5] Though not stated explicitly, market value is defined by $MV_t = q_t P_t$. In the baseline scenario prices are constant [6], and market value grows at rate α (one of the user defined parameters). A definition is given that $MV_t = MV_{t-1}(1+\alpha)$ (Rovira (2006), p. 20.). We will use instead the notation $\overline{MV}t = q_t P_0$ to denote market value in the baseline scenario, to keep in mind that prices must be those of the initial year. Hence the growth condition should be interpreted as $\overline{MV}_t = \overline{MV}_{t-1}(1+\alpha)$. Quantities are growing a the constant rate α. Establishing $MV_t = MV_{t-1}(1+\alpha)$ has very different consequences for the behaviour of prices than $\overline{MV}_t = \overline{MV}_{t-1}(1+\alpha)$.

A constant elasticity demand curve is assumed in order to obtain the changes in quantities that will take place when prices change. When prices change, quantities sold are adjusted via a demand curve defined by $q_t = k(P_t)^e$, where *k* is a parameter and *e* is the constant demand elasticity, hence $MV_t = q_t P_t = k(P_t)^e P_t = k(P_t)^{e+1}$. Though in the model documentation it is not explicitly stated, this identity holds for MV_t at current prices.

1.3. What is going on at the fundamentals of the demand curve?

The model assumes that market value growth at a constant rate. This can be interpreted in two ways: changes in prices or changes in the demand function.

1.3.1. Changes in prices

The model does not mention and does not provide (in its Visual Basic-Excel sheet version) the baseline scenario price time series. However this should be an important piece of the model's output, since the result is a ratio between alternative/baseline prices. Without knowing what is going on in absolute terms in the baseline it is not

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[5] Instead of using index *i* to denote time as in Rovira (2006), we use *t* for time and keep *i* for products when is required.

[6] "The expenditure or value of the market (in real terms, i.e. at constant prices) in the baseline scenario is obtained by applying a constant rate of growth to the expenditure of the initial year" (Rovira (2006), p.12).

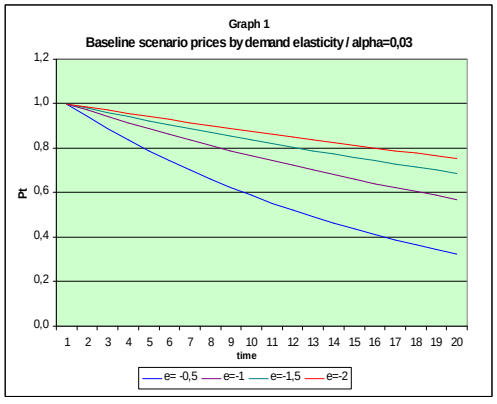
possible to know if prices in the alternative scenarios are going up or down and how large is its impact.

If real expenditures increase at a constant rate α, and the demand function is constant ($q_t = k(P_t)^e$) aggregate prices must go down. If quantities growth at rate α and market value is expressed at period 0 prices, then $\overline{MV}_{t+1} = \overline{MV}_t(1+\alpha) = q_t P_0(1+\alpha) = q_{t+1}P_0$. This expression determines the path of prices completely since

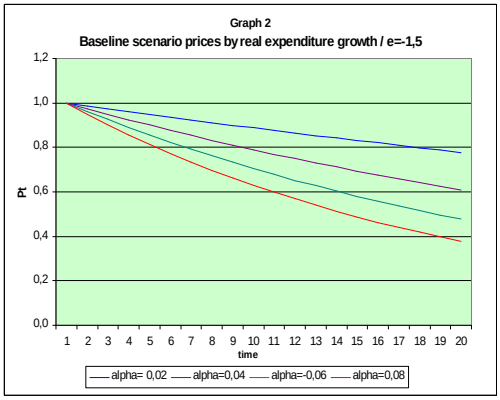
$$\overline{MV}_{t+1} = q_{t+1}P_0 = k(P_{t+1})^e P_0$$

Then prices in the baseline scenario grow according to $\frac{P_{t+1}}{P_t} = (1+\alpha)^{1/e}$. For positive α and negative e the growth rate is always negative, since quantities increase while prices adjust on the demand curve.

As to the assessment of simulation results, prices in the baseline do not only display a falling path, but the speed is very sensitive to parameters e (demand elasticity) and α (rate of growth). Graph 1 shows the path of prices in the baseline for several plausible values of e. Larger (in absolute value) elasticities give smaller rates of decrease in prices since for fixed $\Delta q/q = \alpha$ the constant elasticity assumption gives $\Delta p/p = \alpha/e$ which is smaller for larger $|e|$.



On the other hand prices also show large responses to changes in the real expenditure growth rate α. This is shown in graph 2 for $e=-1{,}5$.



1.3.2. Change in the demand function

An alternative interpretation of the constant growth rate (more in line with the assumption needed to construct the average price) is that the parameters of the demand curve are not constant. Instead of postulating $q_t = k(P_t)^e$, we should postulate $q_t = k_t(P_t)^e$ and assume as well that $k_{t+1} = k_t(1+\alpha)$. If this is so it follows that prices are constant over time and there is no distinction between market value at constant or current prices.

If this is the preferred interpretation of the model, and we abstract from income effects, for the calibration of the model the market value growth rate should equal the expected long turn population growth.

1.4. The alternative scenario description strategy

For calculating market value in alternative scenarios, a new and different in concept price index is calculated. It was originally defined as the "price index of scenario X in relation to baseline scenario in year t". Regardless of the precise definition of the weights and baskets, such price index would have to represent in one way or another the ratio P_t^x / P_t, being P_t^x and P_t prices for the same period under the alternative and the

baseline scenario respectively. Hence we prefer the notation PI_t^x to make clear that it is a price index, rather than P_t^x, which is used in Rovira (2006).

There is a single elasticity and a single aggregate market. The comparison between the alternative and the baseline scenario is generated through a change in prices between the two. The change in prices then translates in changes in aggregate quantities.

Market value under an alternative scenario X at current prices MV_t^x is also defined as $MV_t^x = q_t^x P_t^x = k\left(P_t^x\right)^e P_t^x = k\left(P_t^x\right)^{e+1}$. It is related to market value in the baseline once PI_t^x is defined, since $MV_t^x / MV_t = k\left(P_t^x\right)^{e+1} / k\left(P_t\right)^{e+1} = \left(PI_t^x\right)^{e+1}$. Then MV_t^x equals the baseline market value MV_t times adjustment due to aggregate price change.

However, the model seems to apply such transformation not to MV_t but to $\overline{MV_t}$, which seems incorrect. In fact, it would be reasonable to be interested not in MV_t^x, but in $\overline{MV}_t^x$, the series of market values under the alternative scenario at constant prices. The obvious candidate for base period for prices would be period 0, and it would be reasonable to assume that in year 0 prices under the alternative and the baseline scenarios coincide, hence $P_0^x = P_0$ and $\overline{MV}_t^x = q_t^x P_0$. Then the previously defined $\overline{MV_t}$ is related to $\overline{MV}_t^x$ by the expression: $\overline{MV}_t^x / \overline{MV_t} = q_t^x P_0 / q_t P_0 = k\left(P_t^x\right)^e / k\left(P_t\right)^e = \left(PI_t^x\right)^e$, and we understand that if the constant prices series $\overline{MV_t}$ is to be used, the alternative scenario constant prices series should be obtained by $\overline{MV}_t^x = \overline{MV_t}\left(PI_t^x\right)^e$.

1.5. The alternative/baseline price index

The definition of PI_t^x has changed throughout the project development. In what follows we outline the latest version not yet documented, obtained from personal communications from the author. It is a very important piece of the simulation strategy, since all we have without it is growth at a constant rate of real market value. In what follows we analyze the role of the crucial assumptions made in defining such price index.

1.5.1. Constant prices assumption

A very important recent modification is the assumption that throughout the simulation period the (average) prices of the three types of medicines considered, i.e. patented drugs with exclusivity protection, branded generics and unbranded generics do not change, in both the baseline and the alternative scenarios. The assumption before was that the price ratios between types of medicine did not change. Thus the current price specification is consistent with the constant demand shift suggested in section 2.3.2. The previous version could be interpreted as in 2.3.2, 2.3.1 or a mix of both versions.

The constant price is a very heavy assumption to make particularly when price changes are the driving force of the simulated changes in the model. In particular, this assumption has the consequence that the price indexes to be used should change when none of the prices of any of the goods change. The consequence is that the latest definition of PI_t^x states that it is not a conventional price index, but rather is defined as an average price ratio. PI_t^x is defined as the ratio of the average price in the alternative scenario to the average price in the baseline scenario. In each of the cases the average price is defined as a weighted average of the prices of the three types of goods.

To compute such average prices it is crucial to define the appropriate weights, and such weights are the current market shares of each product type. Therefore the price ratio changes not due to price changes, but to quantity changes. This calls into question the modelling strategy to decompose the change of a market value as $MV_t^x / MV_t = QI_t^x PI_t^x$, i.e. the product of a quantity index times a price index. The QI_t^x term in the right hand side is completely defined once we know PI_t^x by $q_t^x / q_t = k\left(P_t^x\right)^e / k\left(P_t\right)^e = \left(PI_t^x\right)^e$. In this sequence, first "micro" quantity changes alter PI_t^x, what they should not do if PI_t^x was a price index, and then this in turn changes the aggregate quantity in a way that might not be related to the original "micro" quantity changes.

Though as it is defined PI_t^x is not a price index, its role in the model is that of a price index. The argument that the comparisons should be valid between scenarios for the same period but not for different periods under the same scenario does not stand, since any decomposition of the quantity $MV_t^x / MV_t = QI_t^x PI_t^x$ should hold also for different periods. If it works to compare scenarios, it must work also to compare periods within a scenario. If it does not, it will not work in neither of them.

Market shares are crucial, and an additional assumption on market shares is also introduced.

1.5.2. Equal market share assumption

It is further assumed that all the APIs have equal market share. Let us denote Ne_t, Nb_t, Nu_t the number of products under exclusivity, branded and unbranded generics respectively and $N_t = Ne_t + Nb + Nu_t$ the total number of products, while APe, APb, APu are each classes' prices, the same for all within each class. For the market share to be the same for all APIs, it must hold that the quantities sold for each API within each class must be the same. Let's denote Qe_t, Qb_t, Qu_t the quantities sold of each individual of each product type. Then total market value is given by the expression $MV_t = APeNe_tQe_t + APbNb_tQb_t + APuNu_tQu_t$, individual market shares equal $1/N_t$ and the shares of each type of medicine are completely described by $pe_t = Ne_t/Ne_t$, i.e the share of products subject to exclusivity in year t in the baseline scenario, and $pd_t = Nu_t/(Nb_t + Nu_t)$, i.e the share of products without exclusivity that are available as unbranded generics in year t, in the baseline scenario. Their counterparts in any alternative scenario are given by pe_t^x and pd_t^x.

Once the prices are taken to be constant in all periods of time the ratios between them are also constant (this was the only explicit assumption in the earlier version of the model). Then we can define $RPec = APe/APu$, the average price of a product under exclusivity relative to its price when subject to generic (unbranded) competition and $RPbd = APb/APu$, the average price of a product sold as a branded generic relative to the average price if sold as an unbranded generic. Average prices weighed by current market shares are defined as $AP_t = pe_tAPe + (1-pe_t)(1-pd_t)APb + (1-pe_t)pd_tAPu$, and for the alternative scenario as $AP_t^x = pe_t^xAPe + (1-pe_t^x)(1-pd_t^x)APb + (1-pe_t^x)pd_t^xAPu$, where the only difference is given by the weights pe_t^x and pd_t^x.

There is a clear consequence of the equal market share assumption when prices are kept constant, and that is that quantities must adjust so that the market value of each medicine sold is equal to every other's. This adds another source of inconsistencies with aggregate adjustment built into the model.

1.5.3. Index definition

Based on the average price definitions, the index PI_t^x is defined as $PI_t^x = AP_t^x / AP_t$, and it can be shown that

$$PI_t^x = \frac{pe_t^x RPec + (1 - pe_t^x)(1 - pd_t^x) RPbd + (1 - pe_t^x) pd_t^x}{pe_t RPec + (1 - pe_t)(1 - pd_t) RPbd + (1 - pe_t) pd_t}$$

This expression responds clearly to an average price ratio, and it is true only if both the constancy of all prices at all times and the equality of market shares for all APIs hold [7].

The numerator and denominator of this expression are not necessarily increasing functions of pe_t^x and pe_t respectively. This requires that $RPec > (1 - pd_t^x) RPbd - pd_t^x$ and $RPec > (1 - pd_t) RPbd - pd_t$ respectively. It will usually be the case that $RPec > RPbc$ and that will suffice in both cases. Hence PI_t^x will be larger than one if the share of medicines under exclusivity increases all the rest of the things equal.

Hence all the changes in market value at constant or current prices is channelled through the changes in PI_t^x that arise from differences between scenarios due to pe_t^x being different from pe_t and pd_t^x from pd_t. The changes in the IPR regimes alter the proportion of APIs with or without exclusivity and between branded and unbranded APIs sold as generics. The change in such shares alters the price index (some parameters define respectively each price differential, which is assumed to remain constant). Then factor $(PI_t)^{e+1}$ is applied (correctly or not) to $\overline{MV_t}$.

1.6. Number of APIs dynamics and IPR changes

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[7] In earlier versions of the model, the alternative/baseline price index was written as $PI_t^x = 1 + (pe_t^x - pe_t)(RPec - 1) + (1 - pe_t^x)(pd_t - pd_t^x)(RPbd - 1)$ for all t. This expression does not seem to follow from a ratio of prices.

The initial number of APIs is set as a parameter. In each year $N_t = N_{t-1} + AI_t - AQ_t$, i.e adding and subtracting entering and exiting APIs. Of all this, some of them remain each year under market exclusivity, denoted by Ne_t. Our key parameter pe_t is defined $pe_t = Ne_t / N_t$ .The construction of Ne_t reflects the multiple nuances of patent legislation (patent duration, filing procedure delay, duration compensation due to delay, data protection, etc.). For instance, if in the alternative scenario patent protection is lengthened k years, then entry of *p* new patented products in t must be matched by a fall in Ne_t in *p* units k periods later. The model takes care of this arithmetic updating. On the other hand pd_t, the proportion of unbranded generics to all generics without exclusivity remains a fixed parameter throughout all the baseline period (in alternative scenarios it might be a different constant).

1.7. Change in consumption

The model seeks to calculate the reduction in quantities sold compared to the baseline scenario, which is given by $q_t^x - q_t = k\left(P_t^x\right)^e - k\left(P_t\right)^e$, which is calculated as a rate of growth by the expression $q_t^x / q_t - 1 = \left(P_t^x\right)^e - 1$, since $P_t = 1$. Under the baseline scenario q_t grows from period to period at the exogenously given rate. The same constant/current prices problem of the updating of $\overline{MV_t}$ to $\overline{MV_t^x}$ applies here.

1.8. Domestic and foreign sales

Domestic sales are obtained under the baseline scenario using two parameters k_{de} and k_{dc}, which give the domestic share in markets under exclusivity and under competition. These parameters are fixed for the entire simulation. When the relative size of the exclusivity and competition segments change due to IPR dynamics, the domestic share also changes in response. Given the share of exclusivity market pe_t , the overall share of domestic industry is given by $MVD_t = k_{de}\, pe_t MV_t + k_{dc}\left(1 - pe_t\right)MV_t$. Under the alternative scenarios there are changes in both MV_t and in pe_t due to IPR changes. Then under the alternative scenario the share of the domestic industry would be $MVD_t^x = k_{de}\, pe_t^x MV_t^x + k_{dc}\left(1 - pe_t^x\right)MV_t^x$.

1.9. Bottom line

In what follows we sketch a general evaluation of the model. Firstly, we will comment on how the model works in its present state, i.e. how sensitive results are to assumptions, parameter choices, etc., independently of any future scope for improvement or change of criteria. Finally some comments will address how the model captures the economics of the intellectual property law and its effects on the pharmaceutical market.

Despite the relatively elaborate device to accurately portray the many nuances of the changes in the IPR legislation, all the action in the simulations boils down to a relatively small number of parameters. There is an "adjustment factor" by which expenditure en the baseline should be multiplied to obtain expenditure in any alternative scenario. We claim that if the baseline expenditure series is at constant period 0 prices then the adjustment factor should equal $\left(PI_t^x\right)^e$, while in the working papers and the Visual Basic-Excel Sheet version it is multiplied by $\left(PI_t^x\right)^{e+1}$. In either case PI_t^x is a function of the parameters pe_t and pd_t (and their alternative scenario counterparts pe_t^x and pd_t^x), that together with the price differential ratios $RPec$ and $RPdl$ command most of the action. While $RPec$ and $RPdl$ remain constant throughout any scenario, pe_t and pd_t respond to the fraction of the APIs in each class with respect to the total number of APIs. Critical decisions must be made as to how to represent the market value and the shares of each medicine type in terms of APIs.

Firstly, it would be desirable to have an international uniform classification of APIs in order to produce comparable results, and as it is unavailable there is inevitably some degree of arbitrariness in the choices so as to represent the market in terms of APIs. The same holds with respect to the attribution of APIs to newly patented products. Secondly, despite the equal market share assumption there is concentration in the market and large disparities in market share. However, the equal market share assumption implies that individual entry and exit will affect pe_t and pd_t less if the total number of APIs is large. As a result, probably the safest choice would be to manipulate the initial number of APIs and the number of exclusivity patented products, branded and unbranded generics so as to mimic the market share of such products. However, a delicate sensitivity

analysis must test how does pe_t respond to changes in IPR regulation, that in the mode all translate into entry and exit into the market and in and out of each product categories.

With respect to the general working of the model, it is noteworthy that in the baseline the complete set of changes in entry, exit, number of products in the different categories is allowed, but this has absolutely no part in affecting quantities nor prices. The only effects of changes in the number of products and their composition translates in the weights for the average price ratio that will in turn generate the estimation of market value under the alternative. The model has two different price formation rules, one for the baseline in which all quantities grow at a constant rate α and (not explicitly stated) prices adjust via the demand curve, and another for the alternative scenario, based in the average prices and share changes. The question is if it would not be better to base the simulation in a economy that has the same working, demand schedules and price formation rules under the baseline and the alternative scenario. That would allow for testing the effect of parameter changes separately from changes of regime. In that sense, the proposed comparisons between baseline and alternative scenario lump both effects together and it is impossible to disentangle them.

Then a qualification must be given to the statement that the baseline scenario can accommodate the setting of a patent law and its effects in the number of products in each category. One cannot consider as baseline case the one in which there is already a patent law in force, because the API dynamics and price formation is assumed away when the constant rate of growth mechanism is established.

A motive of concern is the substitution of proper price indexes by “average price ratios” that in the context of the extreme assumption of constant prices for all goods in all scenarios and periods, only reflect quantity effects that translate in changes in the weights of prices in such averages.

We understand that the role in which such ratios are used, in generating quantity adjustments via the demand curve, calls for proper price indexes, in which price changes are not confused with quantity adjustments. That is so because the construction of the alternative scenario is based on a decomposition of the variation of market value between two situations, $MV_t^x / MV_t = QI_t^x PI_t^x$, precisely decomposing it in quantity and

price effects. It our claim that such decomposition should work not only for alternative scenarios in the same period, but also between periods within the same scenario.

Price changes are central in the working of the model through the constant elasticity demand function, but they are assumed to be constant by assumption. Though it is beyond the scope of this report, we may mention that proper price indexes might be constructed without major deviations of the main assumptions of the model. However, the product basket should be changing year to year due to entry of new patented products and generics, exit of products, and loss of patent protection. Standard price index techniques allow for index chaining using consecutive periods for goods entering of exiting the market. It may be pointed out that new goods previously unavailable are usually modelled as if their prices fell (for instance, from their reservation price –such that would have driven their demand to zero, etc.). The price changes for goods that continue in the basket is the fall in prices of patented products that lose protection each year. Conventional price indexes do not change when prices do not change.

COMMENTS BY JOAN ROVIRA OF THE REVIEW BY THE TEAM OF URUGUAY

I AGREE WITH MOST OF THE SUGGESTIONS YOU MAKE ON THE ROLE OF PRICES AND PRICE INDEXES IN THE MODEL.

THE SIMULATION MODEL IS ASSUMED TO PRODUCE EXPENDITURE FIGURES IN MONETARY VALUES AT CONSTANT PRICES OF THE INITIAL YEAR. THIS WAS INTENDED TO MEAN THAT CURRENT VALUES ARE DEFLATED BY A GENERAL PRICE CONSUMER INDEX, NOT BY A PHARMACEUTICAL PRICE INDEX. ONE CAN ASSUME THAT PHARMACEUTICAL PRICES VARY EXACTLY THE SAME WAY THAN GENERAL INFLATION; IN THIS CASE α WOULD BE THE GROWTH RATE OF CONSUMPTION/PRODUCTION IN UNITS, BUT THIS IS NOT NECESSARILY IMPLIED BY THE MODEL. IN FACT THE GROWTH OF MV CAN BE THE RESULT OF MANY COMBINATION OF GROWTH RATES OF P AND Q. THE MODEL DOES NOT TRY TO ADDRESS HOW P (PHARMACEUTICAL PRICES) AND CONSEQUENTLY Q (WHATEVER CONSUMPTION OF

PHARMACEUTICALS IN REAL TERMS, OR UNITS MIGHT MEAN) CHANGE OVER TIME. THIS ASSUMPTION WAS TAKEN FOR SEVERAL REASONS:

1. WE WANTED TO KEEP THE MODEL AS SIMPLE AS POSSIBLE. IT IS SUPPOSED TO BE AN AGGREGATE/MACROECONOMIC APPROACH. A DISAGGREGATE/MICROECONOMIC MODEL IS IN PROCESS OF DEVELOPMENT.

2. WE THINK THAT MOST COUNTRIES, ESPECIALLY DEVELOPING COUNTRIES, WOULD NOT HAVE RELIABLE PHARMACEUTICAL PRICE INDEXES AVAILABLE, ANYWAY. (BY THE WAY, WOULD THERE BE ANY FOR URUGUAY?)

3. WE THINK THAT AN EXPLICIT CONSIDERATION OF P AND Q EVOLUTION OVER TIME IN THE BASELINE SCENARIO IS NOT ESSENTIAL FOR THE MODEL PURPOSES

(THE MODEL IS AIMED AT EXPLAINING THE IMPACT OF IP CHANGES ON PRICES, EXPENDITURE AND ACCESS, IMPACT BEING DEFINED AS THE DIFFERENCE BETWEEN A BASELINE AND AN ALTERNATIVE SCENARIO)

AS YOU MENTION IN YOUR REPORT, THE MODEL IS NOT SOMETHING STATIC, BUT IT HAS BEEN CHANGING OVER TIME, MAINLY AS A RESPONSE TO REQUEST BY USERS. FOR INSTANCE, THE POSSIBILITY OF DIFFERENTIATING BETWEEN BRANDED AND UNBRANDED GENERICS, AS WELL AS, THE EFFECTS OF PATENT EXTENSION AND LINKAGE, WHERE ADDED TO THE INITIAL VERSION OF THE MODEL IN ORDER TO ACCOMMODATE SPECIFIC USER'S NEEDS. IN THAT LINE, IT WOULD BE CERTAINLY FEASIBLE TO DEVELOP A VERSION WHICH EXPLICITLY TAKES INTO ACCOUNT SEPARATELY P AND Q. THE QUESTION IS WHAT WOULD BE THE ADVANTAGE OF THAT SPECIFICATION AND WHETHER THERE ARE EMPIRICAL DATA THAT WOULD ALLOW A PRACTICAL USE OF IT.

I AGREE THAT THERE IS AN ASYMMETRY IN THE WAY EXPENDITURE IN THE BASELINE SCENARIO AND IN THE ALTERNATIVE SCENARIOS IS

DEFINED AND ESTIMATED. IN THE BASELINE SCENARIO EXPENDITURE FOR THE WHOLE TIME HORIZON IS BASED ON AN INITIAL VALUE AND A CONSTANT GROWTH RATE (BY THE WAY, WE ARE CONSIDERING A CHANGE IN THE LAST POINT IN ORDER TO ALLOW FOR DIFFERENT GROWTH RATES ALONG THE TIME HORIZON), WHEREAS THE CORRESPONDING ESTIMATES FOR THE ALTERNATIVE SCENARIOS ARE BASED ON THE EXPENDITURE OF THE BASELINE SCENARIO IN EACH YEAR, ADJUSTED FOR THE EFFECTS OF ESTIMATED PRICE DIFFERENCE (BETWEEN SCENARIOS, NOT YEARS) ON THE DEMAND CURVE.

REGARDING THE DEMAND CURVE, YOU SEEM TO IMPLY IN SOME PARTS OF THE REPORT THAT IT IS THE SAME ALONG TIME.

OUR VIEW IS THAT THE DEMAND CURVE IS DEFINED AS HAVING THE SAME FUNCTIONAL FORM (CONSTANT ELASTICITY) AND THE SAME ELASTICITY FOR ALL THE YEARS OF A GIVEN SCENARIO. THE DEMAND CURVE CAN BE MODELLED TO BE THE SAME FOR THE SAME YEAR IN DIFFERENT SCENARIOS BY INPUTTING THE SAME VALUE FOR THE ELASTICITY IN EACH SCENARIO. (THE MODEL ALLOWS THE USER TO SET DIFFERENT VALUES FOR THE ELASTICITY IN DIFFERENT SCENARIOS, BUT I AM NOT SURE WHETHER THIS OPTION IS TOTALLY CONSISTENT, OR ELASTICITY SHOULD BE CONSIDERED A FIXED PARAMETER). HOWEVER, THE DEMAND CURVE CHANGES, IN PRINCIPLE, FROM YEAR TO YEAR. FOR INSTANCE, IF ELASTICITY IS –1 AND MV BETWEEN TWO YEARS VARIES, IT IS OBVIOUS THAT THE DEMAND CURVE CANNOT BE THE SAME.

IN PAGE 8 YOU STATE: *THE ARGUMENT THAT THE COMPARISONS SHOULD BE VALID BETWEEN SCENARIOS FOR THE SAME PERIOD BUT NOT FOR DIFFERENT PERIODS UNDER THE SAME SCENARIO DOES NOT STAND, SINCE ANY DECOMPOSITION OF THE QUANTITY* $MV_t^x / MV_t = QI_t^x PI_t^x$ *SHOULD HOLD ALSO FOR DIFFERENT PERIODS. IF IT WORKS TO COMPARE SCENARIOS, IT MUST WORK ALSO TO COMPARE PERIODS WITHIN A SCENARIO. IF IT DOES NOT, IT WILL NOT WORK IN NEITHER OF THEM.*

I AM NOT CONVINCED OF THE JUSTIFICATION AND VALIDITY OF THIS STATEMENT. IN FACT YOU CAN HAVE A PHARMACEUTICAL PRICE INDEX FOR YEARS 2000 TO 2007 IN COUNTRY X AND A PRICE INDEX COMPARING THE PRICE LEVEL OF PHARMACEUTICALS IN SEVERAL COUNTRIES IN YEAR 2003. THE TWO PRICE INDEXES (LONGITUDINAL AND CROSS-SECTIONAL) MIGHT BE UNRELATED AND QUITE DIFFERENT AND STILL VALID FOR THEIR OWN DIFFERENT PURPOSES, NAMELY, ASSESSING PRICE VARIATION ALONG TIME IN COUNTRY X, AND ACROSS COUNTRIES IN 2003, RESPECTIVELY. THE PRICE INDEX IN THE MODEL IS SIMILAR TO THE CROSS SECTIONAL ONE OF THE EXAMPLE.

ON PAGE SECTION 2.5.2. PAGE 9 YOU CORRECTLY STATE THAT THE ASSUMPTION THAT ALL THE API (ACTIVE INGREDIENTS) HAVE THE SAME MARKET SHARE IS INCONSISTENT WITH OTHER MODEL ASSUMPTIONS.

I ASSUME THAT OUR STATEMENT COULD BE (AT LEAST, APPROXIMATELY) RIGHT FOR A PRICE ELASTICITY OF –1, BUT I AGREE THAT IT IS NOT APPLICABLE IN ALL CASES. I THINK THAT IT WOULD NOT BE INCONSISTENT TO STATE THAT ALL API UNDER EXCLUSIVITY HAVE THE SAME MARKET SHARE. THE SAME EQUALITY WOULD HOLD FOR ALL API UNDER GENERIC COMPETITION WITH THE SAME BRANDED/UNBRANDED RATIO.

IN SECTION 2.6. PAGE 10 YOU STATE THAT “ON THE OTHER HAND pd_t, THE PROPORTION OF UNBRANDED GENERICS TO ALL GENERICS WITHOUT EXCLUSIVITY, REMAINS A FIXED PARAMETER THROUGHOUT ALL THE BASELINE PERIOD (IN ALTERNATIVE SCENARIOS IT MIGHT BE A DIFFERENT CONSTANT)”.

IN FACT, YOU CAN CHANGE THE ANNUAL VALUES OF pd_t (AND OF ANY OF THE PARAMETERS OF THE FIRST FIVE COLUMNS IN THE SCENARIO TABLE) YEAR BY YEAR IF YOU WISH SO, OF PUT THE SAME VALUE FOR ALL YEARS.

IN PAGE SECTION 2.9. PAGE 11 YOU INDICATE THAT IT WOULD BE DESIRABLE TO HAVE AN INTERNATIONAL UNIFORM CLASSIFICATION OF APIS IN ORDER TO PRODUCE COMPARABLE RESULTS.

AS FAR AS I KNOW, THERE IS SUCH A CLASSIFICATION, THE ATC, (ANATOMIC-THERAPEUTIC CLASSIFICATION), BUT THE COMPARABILITY OF THE STUDIES ACROSS COUNTRIES WAS NOT A MAIN CONCERN OF THE MODEL SPONSORS, THEREFORE WE DID NOT IMPOSE ANY CLASSIFICATION THAT COULD INCREASE THE DIFFICULTIES OF DATA COLLECTION.

I THINK THAT YOUR MAIN CONCERN WITH THE MODEL IS THE WAY IT DEALS WITH (OR RATHER, IGNORES) THE VARIATION IN PHARMACEUTICAL PRICES OVER TIME, WHILE I DO NOT FIND THIS SIMPLIFYING ASSUMPTION TO POSE MAJOR PROBLEMS. BUT I WOULD BE HAPPY TO DISCUSS THIS POINT FURTHER WITH YOU.

MOREOVER, I THINK THAT THE MODEL SHOULD REFLECT THAT A CHANGE IN PRICE LEVEL OCCURS WHEN AN API CHANGES ITS IP/EXCLUSIVITY SITUATION. AS YOU INDICATE, “CONVENTIONAL PRICE INDEXES DO NOT CHANGE WHEN PRICES DO NOT CHANGE”. IF THIS IS THE CASE, WE MIGHT CONCLUDE THAT CONVENTIONAL PRICE INDEXES ARE NOT APPROPRIATE FOR THAT SITUATION, AND THAT AN ALTERNATIVE WAY OF ACKNOWLEDGING THE ACTUAL CHANGES SHOULD BE DESIGNED. (IN SPAIN – DUE TO THE PRODUCT PRICE CONTROL POLICY – OFFICIAL PRICE INDEXES PRACTICALLY DO NOT SHOW PRICE INCREASES. HOWEVER, PRICES GO ACTUALLY UP, BECAUSE THE OLD, LOW PRICE PRODUCTS ARE FREQUENTLY REPLACED BY NEWER VERSIONS, WHICH DO NOT BRING MUCH THERAPEUTIC ADDED VALUE, BUT A SUBSTANTIALLY HIGHER NEW PRICE)

AS I SAID BEFORE, THE PRESENT VERSION OF THE MODEL IS NOT NECESSARILY THE SINGLE FINAL VERSION. FROM THE BEGINNING WE THOUGHT OF A “FAMILY OF MODELS”. THERE MIGHT BE LOGICAL ERRORS THAT SHOULD BE FIXED, BUT ALSO ALTERNATIVE

SPECIFICATIONS, WHICH MIGHT BE MORE APPROPRIATE FOR PARTICULAR PURPOSES AND SITUATIONS. AS YOU RIGHTLY STATE, “PROPER PRICE INDEXES MIGHT BE CONSTRUCTED WITHOUT MAJOR DEVIATIONS OF THE MAIN ASSUMPTIONS OF THE MODEL”.

Review 3.

Dean Baker

(COMMENTS BY JOAN ROVIRA IN CAPITAL LETTERS)

This model is an extremely useful tool for providing a range of projections for the impact of TRIPS-plus agreements, or any other strengthening of intellectual property rules. Its great advantage is its flexibility and simplicity. The model imposes relatively few restrictions that cannot be circumvented by a sensitivity analysis that employs different assumption. In this way, almost any findings from existing or new research can be incorporated into the model.

For example, the model allows the user to select key parameters such as price differential between active ingredients subject to exclusivity and active ingredients subject to competition and the price elasticity of demand. The values selected for these parameters will be the primary determinants of the cost of stricter intellectual property rules. The flexibility of the model allows the user to conduct sensitivity analyses that apply the full range of plausible values for these parameters based on existing research and any new research that may subsequently be conducted.

The flexibility of the model also makes it possible to use sensitivity analyses to get around some of the assumptions that may not be strictly accurate. For example, the model effectively requires that the key parameters be held fixed through time and across drugs. This implicitly means that the elasticity of demand for drugs will not change over time and that it is the same across drugs. **However, it is certainly plausible that the elasticity of demand for drugs may get higher as more drugs enter the market, and a larger portion of the drugs developed are "lifestyle" drugs as opposed to drugs that are essential for life or health. The IPR-impact model can be used to approximate such a change by simply running a scenario with a higher elasticity parameter that could be consistent with a future period when demand elasticity is higher. The user can then take an average cost projection from a run of the model with an estimate of the current elasticity and the cost projected in the high elasticity case, or simply use the annual estimate of costs for later years from the**

second version, since presumably it would be in more distant years that we would expect the demand elasticity to be higher.

In the same vein, the assumption of a constant price differential between drugs subject to exclusivity and drugs in competition is also likely to be too restrictive. However, this assumption can be evaded in the same manner. Alternative scenarios can be run which use varying assumptions on price differentials, with the user taking an average of the projections as the best estimate of the cost of stricter IPR.

It is difficult to envision any finding on the impact of patent protection or data exclusivity that cannot be incorporated in the IPR impact model through some sort of sensitivity analysis of this type. In this way, it presents a very user friendly tool to get projections, which should give reasonable estimates of the impact of stricter IPR rules.

It would be helpful to less-skilled users to explicitly list some of the assumptions that may be overly strict, and to describe a set of sensitivity analyses that can be used to assess the impact of relaxing these assumptions. This may already exist in other material, but my short-list of overly strict assumptions would include the following:

1) the assumption that the elasticity for all drugs is the same and that it does not change through time;

2) the market for drugs has a constant rate of growth;

3) the ratio of the price of APIs subject to exclusivity to APIs subject to competition is constant through time;

4) the price of an API that loses exclusivity immediately falls to its competitive price.

I am sure that there are other assumptions that should be added to this list.

It would be very helpful to have a short 1-2 paragraph explanation as to why the assumption is not likely to be strictly accurate, how much difference the fact that it is not strictly accurate might make in the calculations, and then a simple method to

construct a sensitivity analysis that would show the range of outcomes that could be obtained by relaxing the assumption in question.

As a practical matter, it is likely to be difficult to get good data for many of the key parameters for many developing countries. For example, there is not likely to be good data on price elasticity for drugs for most countries. The evidence for the ratio of the price of APIs subject to exclusivity to drugs subject to competition may also be limited in countries in which patent protection or other forms of exclusivity for drugs is relatively new.

This need not pose much of an obstacle, since in general it should be possible to borrow data from similar countries. Here also, **it would be helpful to users if relevant research, including modeling exercises from other countries, were kept on a website where they could be easily downloaded.** This may be the current intention, but if not, I would strongly urge that a website be maintained for this purpose.

It is important to recognize that this model will not produce a comprehensive analysis of all the costs and benefits associated TRIPS and TRIP-Plus provisions. There clearly is some positive incentive for innovation if pharmaceutical companies can collect rents from their patents in a larger market. There also is a greater incentive to register drugs in a country if this registration is accompanied by a period of exclusivity. However, these benefits may be difficult to measure and furthermore, TRIPS and TRIPS plus agreements are not the only way to obtain these benefits. There are mechanisms other than patent protection that can be, and are, used to finance research. The registration of drugs, based on clinical trials that have already been completed, should be a relatively low cost process that does not require large rents as compensation.

In addition to the potential benefits that could result from stricter IPR there are also costs associated with rent-seeking in addition to the higher drug prices paid by patients and/or government health programs. The rents provide an incentive to market drugs in ways that may be misleading and may be bad for the health of patients. They also provide an incentive to give kickbacks of various forms to doctors in exchange for prescribing drugs. In addition, patents and other forms of market exclusivity can be an important source of political corruption as the drug industry fights for ever greater

protection or for having their drugs paid for by government health care programs. These forms of rent-seeking behavior have been an especially serious problem in the United States, the country in which patent rents are greatest.

In this context, it is probably also worth noting that stronger IPR protection can be a handicap for countries competing for the medical tourism market. This market already exceeds $10 billion annually by some estimates and it is growing very rapidly. Having access to low-cost drugs could be an important advantage to a country that is competing in this market.

This model does not attempt to quantify either, the potential gains that could result from greater innovation or greater access to drugs that have already been developed, nor the losses that countries could incur from rent-seeking behavior associated with stricter IPR rules. Both would be extremely hard to quantify and would require examining factors that are far removed from the immediate issues addressed in the model. It is therefore appropriate to exclude them from this sort of modeling exercise, although it is important that developing countries consider these factors in assessing the merits of TRIPS or TRIPS-Plus provisions. Just because they are difficult to quantify does not mean that they are not important. In particular, it is important that developing countries have mechanisms that ensure that pharmaceutical companies have an incentive to register drugs that have been approved elsewhere. A long period of data exclusivity is one such mechanism, but it is likely that less costly and inefficient mechanisms can also be used.

There is also a question as to whether this sort of model should be embedded in a general equilibrium framework. While this can be a useful exercise, given the enormous variation in the projections from general equilibrium models, general equilibrium modeling should not be the primary basis for calculating the cost of stricter IPR rules. The amount of error surrounding any specific calculation from a general equilibrium model dwarfs its usefulness as a more comprehensive measure of the impact of stricter IPR rules.

In conclusion, I consider this model to be an extremely useful tool for developing countries to calculate a range for the likely costs associated with the imposition of TRIPS or TRIPS-Plus rules. Having experimented with the model, I found it to be very

user-friendly. I am confident that a policy professional with even a minimal background in economics would be able to use the model with very little assistance. The model is sufficiently flexible that it can be easily adjusted to apply sensitivity analyses that cover almost any plausible scenario. It will be very helpful in informing policy decisions on IPR rules.

I AGREE WITH ALL THE COMMENTS AND SUGGESTIONS

Review 4

Joan Costa Font, Lecturer and Senior research Fellow at LSE

(COMMENTS BY JOAN ROVIRA IN CAPITAL LETTERS)

General assessment.

I think this is a useful tool for governments and agencies to predict the effects of changes in the IPR regime. The assumptions employed are adequate taking into account the data in hands of decision makers. The main advantage is that it is relatively simple so that it can be understood by policy makers and allows for several specific scenarios when regulation suffers changes, or when simply some country specific amendments are required. The main caveats lie in some few assumptions that might not always hold. I will however suggest some amendments that hope will improve the current version of the model. Generally, I think that some form of market structure for generics competitors could be introduced to account for different internist of generics competition across countries. **Once way to do that is by adding an aggregate measure of competition such as a Herfdahl index as a potential determinants of prices. This could be incorporated by simply gathering data on product market shares and aggregating it. DOES THIS MAKE SENSE IN AN AGGREGATE MODEL?** The data requirements are realistic and the model is feasible. Below I propose some improvements that could be added as sensitivity analysis.

Specific comments

Page 2, when discussing about monopoly power one should mention limit pricing and may be refer to some literature on market barriers. However, monopoly power has to be balanced out from benefits of economies of scale and scope that public agencies can obtain if they have enough monopsony power to negotiate down prices for drugs.

Page 3, when referring to quantifying effects one mist bear in mind that the full effects of UPR might not be quantifiable, such as externalities resulting from lower protection with the current modelling structure. In the same page the text refers to barriers resulting form prices only, but one might well think of some potential collusion between local generic producers, or the extension of so called quasi generics (originator

companies launching their own generic products) as potentially leading to price barriers besides IIPR.

Page 4 in reviewing the literature it must be acknowledged that is country specific so that the implementation of IPR might not be comparable in developing and developed countries. In fact one of the main inputs that this model requires is data form developing countries, especially econometric price elasticity estimates. **Suh (2000) is revised but no comments are included its results.** SUH (2000) REFERS TO THE US ONLY.

Page 5, authors argue that the effects of patent are only on static efficiency (competition and allocative efficiency) but **patents are assumed to have important dynamic effects as incentives to innovation. These effects are not covered in the model.** THEY CAN BE CONSIDERED BY INCREASING THE NUMBER OF NEW AI ENTRIES IN THE HIGHER IP SCENARIO. ANY SUGGESTION FOR A DIFFERENT MODELLING APPROACH?

Page 6, in discussing on potential methodologies to examining ex port change one might want to refer to the so called treatment effects modelling or difference in difference methodologies which are specially appropriate to build up counterfactuals and compare price patterns. A MORE PRECISE INDICATION WOULD BE WELCOME.

In page 8 discussions of the variables. In is important to discuss the meaning of social welfare. One way to make it operational is by assuming that is results from the addition of consumer and producer surplus, which implies measuring not only the effect of IPR on prices but on company's profit and welfare loss. USING AN INDICATOR OF SOCIAL WELFARE TO QUNTIFY THE IMPACT OF IP CHANGES, AS SOME PREVIOUS STUDIES HAVE DONE, WS NOT INITIALLY CONSIDERED IN THE MODEL. IT WOULD BE USEFUL TO CONSIDER 1) WHICH INDICATOR OF WELFARE SHOULD BE USED 2) WHO WOULD BENEFIT FROM THE NEW INDICATOR, AND 3) WHETHER SUCH AN INDICATOR MAKES SENSE WITHIN AN AGGREGATE MODEL.

In the point one, it is argued that the extent of competition will be measured as well as the effect on prices, however, it is not clarified the nature of competition. Is it

assumed that a Stackelberg model defines the extent of competition, so the first entrant in the market is accounted for? THE MODEL IS NOT TOTALLY EXPLICIT ON THE STRUCTURE OF THE MODELLED MARKETS, BUT THE CLOSEST PICTURE IS THAT UNDER EXCLUSIVITY THE ORIGINATOR HAS A MONOPOLY AND UNDER GENERIC COMPETITION WE HAVE PERFECT COMPETITION. COULD AN EXPLICIT STACKELBERG MODEL BE USED IN AN AGGREGATE APPROACH? IF SO, PLEASE ADVICE? Does the competition model assume a certain level of product homogeneity? YES, TOTAL HOMOGENEITY. I think that some scenarios can be designed so as to account for difference sin competition. OF COURSE IT IS ACKNOWLEDGED THAT IN THE REAL WORLD THERE IS NOT SUCH A THINK AS A PERFECT MONOPOLY, PERFECT COMPETITION, SINGLE PRICE AND PRODUCT HOMOGENEITY. WHEN EMPIRICALLY ASSESSING PRICES WE WILL CERTAINLY FIND DIFFERENT PRICES FOR THE VARIOS PRODUCTS CONTAINING THE SAME AI. THE OPTION TAKEN IS TO TAKE THE WEIGHTED AVERAGE OF THESE PRICES AS THE SINGLE PRICE THAT WOULD PREVAIL IN A COMPETITIVE MARKET.

In point two, in discussing effects on expenditure it is essential to discuss the effects on quantity as well as those on price. Besides that, may be it could be included the extent of monopsony power by insurance agencies. I would expect that prices in the developed word would be lower that in some developing countries due to the fragmentation of the health system in the latter. MY IDEA IS THAT THE PRICE DIFFERENTIAL BETWEEN EXCLUSIVITY AND COMPETITION SHOULD BE EMPIRICALLY ESTIMATED FROM A LARGE SAMPLE OF COUNTRIES. THE PRICE DIFFERENTIAL SHOULD BE A FUNCTION OF COUNTRY AND PRODUCT CHARACTERISTICS.

As for point three I do have some concerns when it comes to arguing that IPR protection impact on the competitiveness of the economy as the effects of IPR is not to protect the country but to allow a better diffusion of innovations and foster further technology change. Local companies are not necessarily producing at significantly cheaper prices. THIS IS AN EMPIRICAL QUESTION TO BE RESEARCHED. THE WHO-HAI STUDIES ON PRICES OF MEDICINES SUGGESTS THAT IT IS USUALLY SO. Furthermore, is the counterfactual that of local companies copying systematically new products? GENERICS MIGHT BE ALSO IMPORTED. I think that

the effect on then allocation of production should be generally secondary and largely irrelevant. Finally, the concept of a generic in developing countries might deserve some discussion, especially when countries do not ensure bioequivalence. QUALITY GOES BEYOND THE SCOPE OF THIS AGGREGATE MODEL. IT MIGHT HOWEVER MAKE SENSE TO TAKE ONLY BIOEQUIVALENT GENERICS WHEN COMPUTING THE PRICE THAT CHARACTERISES COMPETITION.

Page 10, a way to improve the structure is by creating a specific scenario where two types of consumers are define, one with high loyalty and low price elasticity and conversely another one with low brand loyalty, possibly less affluent individuals, which exhibit larger elasticity estimates. THIS SEEMS TO MAKE SENSE IN A MICROECONOMOC MODEL. HOWEVER, THIS COULS BE ADDRESSES BY THE IPRIA MODEL BY CONSIDERING THAT THERE ARE TWO MARKETS, ONE FOR EACH TYPE OF CONSUMER WITH A DIFFERENT DEMAND ELASTICITY, AND BY RUNNING THE TWO MODELS IN PARALLEL.

Page 13, in determining drug prices it could be possible to introduce the extent and type of competition by assuming some for of oligopolistic market structure, such that market power (lerner index) resulting form exclusivity can be derived by calculating the inverse of price elasticity and the inverse of the number of competitors. THIS SEEMS AGAIN MORE RELEVANT FOR A MICROECONOMIC MODELLING APPROACH.

May be in designing elasticity assumptions the model could ass the metaregression estimates from Gemmill et al 2006 in Health Economics. TO BE CHECKED

Minor issues

I guess that the model assumed that there will be no parallel trade to other countries if there are differences in IPR across countries. PARALLEL TRADE IS NOT EXPLICITLY CONSIDERED.

Some types in page 2 line 7 “but” is not needed and page 11 last sentence “lost” should replace “lose”.

Review 5.

Marcelo Olarreaga[8], University of Geneva

(COMMENTS BY JOAN ROVIRA IN CAPITAL LETTERS)

General evaluation

The objective of the paper is to present an excel-based simulation model that can assess the impact of TRIPS+ provisions on medicine prices and expenditure. One has to commend the author of the study for being among the firsts in this important but neglected field (Chaudhuri et al also provide an interesting model). It is a first step and, as such, very valuable.

One of the main advantages of the model is its simplicity. But this is also its main disadvantage as many interesting economic questions are left aside. This would not be too important if these other economic impacts were of second order, but I do not think this is the case. Economic agents generally respond to incentives, and adjust their behavior accordingly. This is not the case here, where behavior is largely exogenous. Neglecting adjustment can lead the authors of the country studies to either under- or over-estimate the costs/gains from adopting TRIPS+ provisions, which wouldn't be a big deal if this was a purely academic exercise.

However, these studies are intended for policy advice, and getting it wrong can, therefore, be very costly. It is probably not a coincidence that those complaining about TRIPS+ provisions in bilateral agreements and the costs they will impose to consumers and local producers, are generally not the local consumers or producers of these goods, but those who for ideological reasons see trade agreements with developed countries as a continuation of colonial ties and imperialism. I was in Uruguay in 2006 when the possibility of signing a bilateral agreement with the United States was discussed. The left parties in parliament and in government were very vocal against TRIPS+ provision, but not the national pharmaceutical companies. When asked why, they would answer that they did not expect much of an impact on their sales from TRIPS+ provisions, as

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most of their revenue was coming from the production of generics for which patents have expired a long time ago. Were they wrong? Maybe, and I think one of the case studies is based on the Uruguayan experience and can help shed some light on this. The point is that it is important to get the modeling assumptions as close to reality as possible for the policy advice to be valuable.

And, **it will be difficult to achieve this with a one-size fit all simulation model**. THE AUTHORS CERTAINLY AGREE WITH THAT STATEMENT. HOWEVER, THIS WAS PRECISELY THE PURPOSE OF THE INITIAL PROJECT, TO DEVELOP A USER FRIENDLY MODEL THAT COULD BE USED AND APPLIED BY LOCAL TEAMS TO ANY COUNTRY. WHEN COUNTRY TEAMS HAVE COMPLAINED ABOUT THE LIMITATIONS OF THE MODEL WE HAVE, EITHER INTRODUCED MODIFICATIONS TO MAKE IT FIT LOCAL CONDITIONS, OR ENCOURAGED LOCAL TEAMS TO DO SO. In India, where local pharmaceuticals were actively involved in reverse-engineering of patented products, the adoption of TRIPS may have been very costly (see Chaudhuri et al. 2003), but in other countries where local pharmaceutical firms had most of their revenue coming from sales of products that lost their patent protection a long time ago, the adoption of TRIPS may have been more benign. IN THIS TYPE OF COUNTRIES HIGH IP STANDARDS MIGHT NOT SIGNIFICANTLY AFFECT THE DOMESTIC INDUSTRY SITUATION, BUT THEY ARE STILL LIKELY TO AFFECT PRICES AND ACCESS, AS THE COUNTRIES WILL NOT BE ABLE TO IMPORT CHEAP GENERICS FROM INDIA AND ELSEWHERE, BUT WILL HAVE TO BUY THE ORIGINATOR PRODUCT AT HIGHER PRICES.

<u>Some problems with the modeling of the introduction of TRIPS+ provisions</u>

According to the assumptions in the model, the only thing that changes when there are changes to the length of the patent term, the introduction of the bolar exception, restrictions on test data, or restrictions on the use of compulsory licenses is that the length of time for the innovator to benefit from market exclusivity increases. And all the results will be driven by an exogenously calculated price-wedge between products subject to exclusivity and those for which patents have expired, that will now apply for a longer period of time.

These are very big assumptions. Economic agents generally respond to incentives and here are some reasons why other variables should not be kept exogenous:

1) **It is not difficult to imagine that as the threat of entry and the market contestability in the near future decreases, this will allow patent holders to price higher than they are currently doing. Thus the price-wedge is in fact endogenous to TRIPS+ modifications, and will likely vary depending on the time left for patent protection.** (AS IP CHANGES ARE USUALLY NOT RETROSPECTIVE AND AFFECTS ONLY NEW PRODUCTS, THE TIME LEFT FOR PATENT PROTECTION WILL NOT VARY. IN ANY CASE, SUCH AN ISSUE COULD BE EASILY CONSIDERED IN A MORE MANUAL VERSION OF THE PROGRAM. MOREOVER, THE FACT THAT THE PRICE-WEDGE DEPENDS ON IP PROTECTION CHANGES AND SHOULD BE CONSIDERED, DOES NOT IMPLY, IN MY OPINION, THAT IT MUST BE NECESSARILY MODELLED AS AN ENDOGENOUS VARIABLE) Whether excluding these effects biased upwards or downwards the impact on the medicine price index will depend on the average time left on the patents when calculating the exogenous price-wedge. If there is only a couple of months left on average, it is likely that the current modeling will under-estimate the cost of TRIPS+provisions, whereas if there is 20 years left on averages, the current modeling is probably over-estimating costs. The price wedge will also clearly depend on product specific demand and supply elasticities, but one has to recognize that these are difficult to measure before the introduction of the new product, and therefore to look at past experiences is as close as one can get. However, it would make sense to look at the variance in those price-wedges when doing a sensibility analysis to capture the importance of different market conditions. From some of the case studies I reviewed, it seemed like these price-wedges had a very large variance and therefore were probably hiding some very different demand and supply conditions.

2) It is assumed that domestic R&D is not affected by these changes. I have problems with this assumption. It will most likely depend on what the local pharmaceutical sector was doing prior to the introduction of these changes. I don't think there is any solid evidence on this, and the review of the literature presented by the authors is ambiguous: Scherer and Weisburst (1995) found no

evidence in Italy, but Nicol and Nielsen found that Australian biotechnology firms were expecting large benefits in Australia. Also stronger patents should have the effect of lowering contracting costs between foreign multinational and local subsidiaries (Arora, 1996 or Javorcik, 2004), which will probably make know-how transfers more likely. We probably do not have the answer to where this is more likely to occur, but to completely ignore it is troubling. (WE AGREE THAT THERE MIGHT BE SOME EFFECTS ON LOCAL R&D AND ON TECHNOLOGY TRANSFER TO THE COUNTRY, ALTHOUGH THERE IS LITTLE EVIDENCE FOR OR AGAINST THAT ASSUMPTION. THIS MIGHT HOWEVER BE CONSIDERED IN THE MODEL BY ALLOWING A HIGHER SHARE OF THE DOMESTIC INDUSTRY IN THE EXCLUSIVITY MARKET)

3) **Multinational R&D is assumed to be constant, and the number of innovations is exogenously given and unaffected by TRIPS+ provisions. Lanjouw (1998) estimates a 25 percent increase in global spending associated with the adoption of TRIPS by developing countries.** (LANJOUW'S HYPOTHESIS COULD BE REFLECTED IN THE NUMBER OF NEW PRODUCTS ENTERING THE MARKET IN THE BASELINE SCENARIO. IF YOU FURTHER ASSUME THAT THE IP STATUS IN THE COUNTRY MODELLED WILL ALSO HAVE AN INFLUENCE ON THE GLOBAL R&D AND INNOVATION RATE, YOU CAN INCREASE THE NUMBER OF NEW AI ENTRIES IN THE ALTERNATIVE SCENARIOS) This needs to change incentives to innovate at least in some countries. As TRIPS+ provisions are adopted it is likely that incentives for foreign companies to innovate will increase. **Thus the assumption that the number of new products proposed by innovators remains constant is a strong assumption. It is more likely that the number of new products offered to the market will significantly increase, and the gains for consumers of these new products are likely to be very large, as they have no substitutes.** (THE MODEL DOES NOT IMPOSE THAT ASSUMPTION, THIS IS UP TO THE USER TO DECIDE) A simulation model that incorporates "love for variety" features (vertical or horizontal) would probably find some large gains associated with the introduction of these new products. I WOULD BE INTERESTED IN

DISCUSSING HOW COULD LOVE FOR VARIETY BE INCORPORATED? DOES IT MAKE SENSE TO INTRODUCE LOVE FOR VARIETY IN THE PHARMACEUTICAL MARKET? **Moreover the introduction of these new products is also likely to put downward pressure on prices of other medicines as long as there is some substitution. So you can potentially get the result that by protecting patent holders for a longer period of time, you have lower prices of medicines after accounting for new entry. This would put the basic functioning of the model on its head. (IT CERTAINLY WOULD. I THINK THAT THERE IS A WIDESPREAD PERCEPTION THAT SIMILAR PRODUCTS (FOLLOW-ONS, ME-TOOS) DO NOT COMPETE IN PRICES, BUT IN CONSUMER PREFERENCES THROUGH MARKETING. HOWEVER, THIS ASSUMPTION DESERVES/REQUIRES SERIOUS EMPIRIC RESEARCH AND A MICROECONOMIC MODELLING. WITHIN THE PRESENT IPRIA MODEL, THIS COULD BE CONSIDERED BY CALCULATING THE PRICE DIFFERENTIAL EXCLUSIVITY-COMPETITION USING THE ORIGINATORS PRICE NOT AT LAUNCH, BUT AS THE AVERAGE OF THE PRICE WHILE ON EXCLUSIVITY)** I am not advocating that this should be the modeling, but rather that assuming that the impact of TRIPS+ is only to increase for a longer period of time the prices of drugs that were anyway going to be invented is a very strong assumption that no doubt biases the results towards finding a large negative impact.

Some problems with the measuring of the price-wedge

As mentioned above, **one would not expect the price-wedge for a particular product to be exogenous to TRIPS+ modifications, but rather a consequences of changes in a structural model where market contestability is further away, and producers and consumers adjust.** That said, taking it as exogenous clearly simplifies life. But the question is then **how to measure the price-wedge? And the paper provides very little guidance here**. On page 13, it reads that "the index for an alternative scenario in a given year reflects the weighted price differentials between API with and without

exclusivity...” On page 20 it reads that: “the price differential between the average price of an API under market exclusivity and that under competition?”

(THE BEST OPTION FOR MEASURING THIS DIFFERENTIAL WOULD PROBABLY BE TO SELECT A SAMPLE OF AI THAT HAVE LOST EXCLUSIVITY IN THE COUNTRY AND MEASURE THE DIFFERENCE BETWEEN THE PRICE OF THE ORIGINATOR UNDER EXCLUSIVITY AND THE WEIGHTED AVERAGE PRICE OF ALL VERSIONS OF THE AI - ORIGINATORS AND GENERICS - SEVERAL YEARS AFTER EXCLUSIVITY EXPIRED. IF WE HAD A PERFECTLY COMPETITIVE MARKET – NO PRODUCT DIFFERENTIATION NOR REAL QUALITY DIFFERENCES, I.E. PROVEN BIOEQUIVALENCE – ALL VERSIONS OF THE AI WOULD HAVE THE SAME PRICE)

I am lost. What are we comparing? Average over what? Ideally you need a before and after comparison of the same product after the expiration of the patent. That is the price while under market exclusivity with the weighted average of prices for this product once the patent has expired. A diff in diff type regression could do this quite nicely if the data was available, where the control group is products that have once been subject to a patent holder. But the text does not read that way, and **from the country studies I read, authors were using price differentials between the innovator and generic producers after the patent has expired to measure the price-wedge** (PROBABLY BECAUSE NO OTHER TYPES OF DATA WERE AVAILABLE.) So the price-wedge was actually capturing whether the company has been an innovator and not whether the company was still benefiting from market exclusivity which is what the model calls for.

If the patent has expired and there is a price differential this may suggest that looking at price differentials between generics and innovators may be problematic, as consumers do not seem to think that they are perfect substitutes. Otherwise a higher price for the innovator after the expiration of the patent is not sustainable. This calls for a more sophisticated demand system where there is some substitutability between innovators and generic drugs. CERTAINLY, THIS WOULD REQUIRE MICROECONOMIC-DISAGGREGATE MODELLING. WITH THE PRESENT AGGREGATE STRUCTURE THIS COULD BE CAPTURED BY A SMALLER PRICE DIFFERENTIAL BETWEEN THE AI UNDER EXCLUSIVITYAND THE AI

UNDER COPETITION. My suspicion is that these price differentials, after patent expiration, are more pronounce in the poorest countries where local producers may not be very sophisticated and local regulation are quite lax. Thus, it is in these countries that you would be measuring the largest losses associated with TRIPS+ provisions, when in reality they are likely to be the smallest because products produced by generic producers and innovators are seen as very different products by consumers.

Moving forward

I would like to see a lot more econometric evidence regarding the impact of TRIPS and TRIPS+ provisions on medicine prices in developing countries. **(ME TOO)** This project has led to an important data collection effort and could, therefore, be the basis for such a study. Ideally, these have to be country-specific studies as the functioning of private and public medicine markets is likely to vary across countries. But one could also envisage a cross country study. (YES, BECAUSE MANY COUNTRIES FOR WHICH SUCH AN IMPACT MODEL MIGHT BE APPLIED, STILL HAVE NO EXPERIENCE IN PRODUCTS LOOSING EXCLUSIVITY STATUS AND HAVE THEREFORE TO USE THE EXPERIENCE OF SIMILAR COUNTRIES)

Once the impact has been measured, I would suggest trying to explain the differences observed across countries with market variables such as market concentration, barriers to entry, exit, capacity to innovate, etc. These results could then help model a new version of the model (THIS COULD BE USED IN THE PRESENT IPRIA MODEL) with a more sophisticated demand and production structure where consumers and producers respond to incentives, and their responses vary depending on market conditions and other country characteristics (THIS POINTS TO A DESAGGREGATED MICRO MODEL, WHERE AI ARE SINGLED OUT)

Thus, a combination of partial equilibrium modeling and econometric work can probably get us a long way in terms of understanding the heterogeneity of the impact of TRIPS+ provisions on prices.

<u>Some minor comments</u>

a) It would be nice to have a small description of the functioning of the models in the papers mentioned at the bottom of page 5. Are we improving on these papers? OK

b) The discussion of ex-ante and ex-post analysis on page 6 is a bit misleading. I see ex-post analysis as trying to explain what happened using available data on past events. That's not what this is doing, regardless of whether the exercise is undertaken before and after TRIPS+ provisions are introduced. OK, WE´LL CHECK THIS.

c) On page 6, it is suggested that the model could be used to evaluate the "introduction of product patents". I don't see how this can be done if you do not have any information on patent applications, delays, and price-wedges before the introduction of a patent. You would need to make up the data completely. And it contradicts the first sentence 0n page 10 "The model is limited to assessing the impact of changes in conditions of market exclusivity in the drugs markets for which empirical evidence exists." (I DO NOT FULLY UNDERSTAND THIS COMMENT)

d) The discussion of inelastic and elastic demands is quite long and unnecessary for any reader with some basic economics (THE MODEL AND GUIDE IS MAINLY INTENDED FOR USERS WITH A LIMITED LEVEL OF ECONOMICS)). Without any good estimates of demand elasticities or a methodology to estimate them, the sensitivity analysis that it is proposed is not very useful. (HOWEVER, DECISION MAKERS MUST OFTEN MAKE CHOICES WITH LIMITED OR NO INFORMATION ON SOME ISSUES. THEY CANNOT DELAY DECISIONS (E.G. ON A TRADE AGREEMENT) UNTIL SOMEONE HAS ESTIMATED THE RELEVANT PRICE ELASTICITIES)

e) INN? (= INTERNATIONAL NON PROPRIETARY NAME = GENERIC NAME = SCIENTIFIC NAME) What is this? Need to define these things for non specialists if this is to stand as a paper by itself. Same with bolar exception, test data protection, compulsory licenses, etc.... OK, THE TYPICAL USER OF

THE MODEL WAS EXPECTED TO KNOW THESE TERMS, BUT WE CAN PROVIDE A GLOSSARY, JUST IN CASE.

f) There are a few typos. For example: Page 3, 3rd paragraph, “conductthese”; page 7: “from a multiple sources of information”; page 13: “..calculate the impact that of an increase in priceon the quantities demanded and on expenditure”, page 13: “the consumption will remain the unchanged”. OK, THANKS

References

Arora, Ashish (1996), “Contracting for tacit knowledge: the provision of technical services in technology licensing contracts”, Journal of Development Economics 50, 233-256.

Javorcik, Smarzynska Beata (2004), “The composition of foreign direct investment and protection of intellectual property rights: Evidence from transition economies “, European Economic Review 48(1), 39-62.

Lanjouw, Jean (1998), “The introduction of pharmaceutical product patents in India: heartless exploitation of the poor and suffering?” National Bureau of Economic Research WP #6366.

Appendix 6. Range of values of the main parameters

The values of the parameters for a country application of the model should in principle derive from empirical data in the country concerned. If the country has not experienced the policies which impacts the final user wants to simulate with the model, the analist has to rely on data from countries where the said policy has already been applied. This type of data might not be available, but the analyst might still want to obtain plausible data from other sources, at least for a preliminary application of the model. We therefore provide a summary of the values of the model parameters used in a subset of the country applications of the IPRIA carried out so far and suggest in other cases relevant published studies. Of course, this information is only for illustrative purposes and should not be assumed to provide reliable and valid results for a given country.

We provide no values for study-specific parameters - i.e. those which are directly dependent on the purposes of the analysis, such as the initial year of the simulation. We do not either provide information for country-specific parameters which are usually stated in regulatory documents or that, in case of lack of local data, should be estimated from expert opinion, rather than extrapolated from other countries, such as total sales in the initial year, annual rate of growth of the market, etc,

Table 1

Fixed parameters

Time horizon: YL-YI (YL: Last year of simulation period; YI: Initial year of simulation period)

TAPY1: Number of drugs in the market in the beginning of the initial year

d: Discount rate

Scenario dependent parameters

DT: Time from patent filling to market registration of a drug

PDE: Extension of patent duration due to delay in patent approval

PPDE: Proportion of drugs with extension of patent duration

TTC: Time from patent expiration to generic entry in absence of Bolar provision

DGE: Delay in generics entry due to linkage patent-registration

PDGE: Proportion of products with delay in generics entry due to linkage

RPec: Relative weighted average price of a drug under exclusivity (APe)

vs. its price under competition (APc)

RPbd: Relative weighted average price between original and generics products

E: Price elasticity

Review articles on the elasticity of demand of medicines

There are several review articles on the demand of medicines which might also provide a range of plausible values for a country for which no information on this variable is available.

Hughes and McGuire (1995), reviewed the price elasticity of the demand for drugs in the UK's NHS and did their own analysis. Demand elasticities ranged from –0.01 to –0.02 in an early study by Lavers (1983) up to –0.37 in their own study. All studies showed reductions in consumption and in expenditure on pharmaceuticals, but they did not analyse the potential effects on overall health expenditure and on health.

Lexchin and Grootendorst (2004) reviewed studies from 1-1-1977 to 31-12-1999 in OECD countriesthat assessed changes in prescribing behaviour, drug cost utilization, overall health care costs or utilization or changes in health status. 59 studies were initially selected, but 5 were later excluded because of lack of controls (3), extremely small groups (1) and post-only time series (1). Of the remaining 54 papers, 43 referred to the US or Canada, 7 to the UK and 6 to other EU countries. It is worth noting the apparently limited amount of research done on this topic in the EU, although this might be partially due to language bias and the disregard of grey literature.

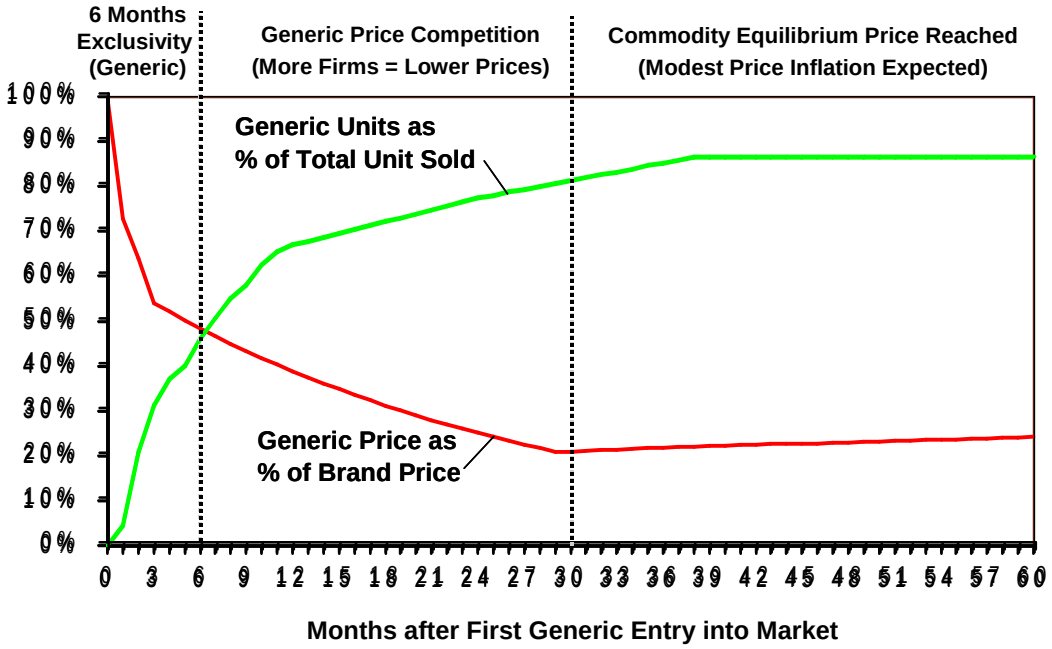
The most recent comprehensive review on the effects of prescription drug cost sharing is Gibson et al (2005), although it was were restricted to studies in English on populations from the US and Canada. The authors identified 30 studies, of which, according to the authors, eleven had not been addressed in previous reviews. Their results point to the fact that besides confirming the conclusions of previous reviews that cost-sharing usually reduces consumption of prescription drugs and induces a switch to generics, high levels of cost-sharing have other troublesome, although not consistently reported, unintended effects, namely, treatment disruptions such as lower levels of treatment adherence, continuation and initiation

A forthcoming study might provide some more appropriate information for the scop of the IPRIA as they refer to developing countries. Preliminary results were presented at the 2008 ECHE Conference. They conclude that price elasticities for different therapeutic products and countries range from between -1 to -2. These estimates seem to be in line with previous studies and normally higher than in high income. For instance, two studies on the demand of malaria treatment (Dzator and Asafu-Adjaye, 2004and Laxminarayan et al, 2006) found elasticities of -0.04 in Ghana and -0.49 to -2.23 in Sub-Saharan Africa,

respectively. Sauerhborn et al (1994) estimated a value of -0.79 for the elasticity to drug and travel costs in Burkina Faso.

Probably one of the most feasible and adequate ways of assessing the relative price difference(Pm – Pc) / Pc, is by looking at the average price of a sample of medicines on exclusivity and once they have lost it (Figure 1).

Fig 1. Generic Penetration of Brand Market: Units Sales and Price per Unit



SOURCE: Compiled by the PRIME Institute, University of Minnesota from data found in Kidder, Peabody

This is not be a feasible approach in countries that only recently introduced (product) patent for pharmaceuticals, as there might not be a large enough set of drugs that have gone from exclusivity to generic competition. The price differential between exclusivity and competition might be empirically estimated from another country or from a sample of countries. In the later case, the price differential might be expressed as a function of country and product characteristics.

References

Dzator, J. and J. Asafu-Adjaye (2004). "A study of malaria care provider choice in Ghana." Health Policy 69(3): 389-401.

Gibson TB, Ozminkowski RJ, Goetzel RZ. The effects of prescription drug cost sharing: a review of the evidence. Am J Manag Care 2005; 11(11):730-740.

Hughes D, McGuire A. Patient charges and the utilisation of NHS prescription medicines: some estimates using a cointegration procedure. Health Econ. 1995;4(3):213-20.

Laxminarayan, R., I. W. H. Parry, et al. (2006). Should New Anti-Malarial Drugs be Subsidized? Resources For the Future, Discussion Papers.

Lexchin J, Grootendorst P. Effects of prescription drug user fees on drug and health services use and on health status in vulnerable populations: a systematic review of the evidence. Int J Health Serv 2004; 34(1):101-122.

Oxfam International (2007). All costs, no benefits: How TRIPS-plus intellectual property rules in the US-Jordan FTA affect access to medicines, Oxfam Briefing Paper, March 2007

Sauerborn, R., A. Nougtata, et al. (1994). "The elasticity of demand for health care in Burkina Faso: differences across age and income groups." Health Policy and Planning 9(2): 185-192

Shaffer ER and Brenner JE (2009).A Trade Agreement's Impact On Access To Generic Drugs. Health Affairs, 28, no. 5: w957-w968Suh, D., W. Manning, et al. (2000). "Effect of Multiple-Source Entry of Price Competition After Patent Expiration in the Pharmaceutical Industry." HSR: Health Services Research 35(2): 529-537.

Srivastava D, McGuire A. Are developing countries responsive to the prices of medicines? Presentation at the 7th European Conference on Health Economics, Rome, Italy, July 23-26 2008.

Appendix 7. Pilot Country Studies: Colombia, Costa Rica and Guatemala

(File to be attached)

Appendix 8. Summary review and description of IPR impact studies in LA countries (in Spanish)

Autor/ Fecha / Titulo	Objetivo	Metodología	Principales Resultados
Ministerio de Salud del Perú, 2005 *EVALUACION DE LOS POTENCIALES* *EFECTOS SOBRE ACCESO A* *MEDICAMENTOS DEL TRATADO DE LIBRE* *COMERCIO QUE SE NEGOCIA CON LOS* *ESTADOS UNIDOS DE AMERICA*	Evaluar el probable impacto de los cambios en materia de propiedad intelectual, que se vienen negociando en el TLC con los EEUU, sobre: - Los precios de los medicamentos. - El acceso a los medicamentos. - El costo del tratamiento de un grupo de enfermedades con crecimiento acelerado en la carga de morbilidad (cáncer, VIH/SIDA, diabetes, hipertensión arterial, malaria, TBC multidrogoresistente y enfermedades mentales). - Los cambios en el gasto de bolsillo y en los presupuestos institucionales del Ministerio de Salud y ESSALUD. El estudio se enfoca en la protección con exclusividad a los datos de prueba.	El estudio tiene tres componentes: clínico-epidemiológico, fármacoepidemiológico y económico. Los dos primeros dan la estructura básica para estimar el impacto económico de las modificaciones de los derechos de propiedad intelectual sobre el mercado de medicamentos. El componente económico consiste en un análisis contrafactual, consistente en observar la cantidad de nuevas moléculas que en los últimos 5 años solicitaron registro sanitario, pero no patente y tienen copias genéricas en el mercado, esto permite una aproximación a la probable velocidad con que disminuirá la importancia relativa de los genéricos de marca en el mercado dada la patente o protección de los datos de prueba. Esta disminución llevará a que los precios de los productos en el mercado aumenten en una magnitud que dependerá de sus elasticidades precio y cruzadas. Es de esperar que los productos protegidos por patente o datos de prueba capitalicen los mayores incrementos de precios, según sus elasticidades precio. El modelo utilizado es del tipo AIDS (Almost Ideal Demand System) desarrollado por Deaton & Muellbauer (1980).	La introducción de la medida de datos de prueba ocasionara: En el período más probable (2011 y 2017) los precios promedio aumentarán entre un 55% y un 100%. Con respecto al acceso a medicamentos, el efecto mayor se observará en los primeros cinco años, período en el que el consumo de medicamentos se reducirá entre 2.4% y 3.1%, lo que equivale a que entre 700,000 y 900,000 personas quedarán fuera de la atención de salud, si los presupuestos del MINSA y ESSALUD y el ingreso de los hogares más pobres no se incrementa. Si bien el impacto económico total del TLC podría llegar hasta los US$ 398 millones, lo más probable es una pérdida de bienestar en el rango de US$ 205 a 300 millones, entre los años 2011 y 2017, lo que significará principalmente mayores gastos de bolsillo, pero también mayores gastos en el MINSA y ESSALUD. El efecto atribuible a los datos de prueba (“efecto TLC”) oscilará entre US$ 130 millones y US$ 170 millones, siendo su efecto al primer año de US$ 34.4 millones para mantener los mismos niveles de cobertura y cuidados de la salud de los hogares.

Autor/ Fecha / Titulo	Objetivo	Metodología	Principales Resultados
APOYO Consultoría (Perú), 2005, Impacto de las negociaciones del TLC con EEUU en materia de propiedad intelectual en los mercados de medicamentos y plaguicidas	Evaluar los efectos de la adopción de posibles compromisos en materia de propiedad intelectual, sobre la salud y el sector agrícola. Se evalúa: Impacto directo en el bienestar de los consumidores nacionales. Impacto indirecto en el acceso de los consumidores al sistema de salud pública. Impacto sobre la industria nacional. El estudio se enfoca en la protección con exclusividad a los datos de prueba.	La estimación de los impactos de las medidas sobre el mercado farmacéutico se realiza usando un análisis contrafactual, con fecha de corte a diciembre del año 2003. Se evalúan los efectos que se habrían dado en el mercado peruano si las medidas se hubieran hecho efectivas cinco años antes (enero del año 1999). Es decir, se asume que entre 1999 y 2003 hubiera estado en vigencia un TLC con EEUU, con una protección de datos de prueba como la propuesta, y se compara dicha situación con la que efectivamente se observó en dichos años (con un sistema de patentes sin protección de datos de prueba).	Los precios promedio *de las moléculas afectadas (una muestra de moléculas para una muestra relevante de enfermedades)* habrían sido más altos con TLC (que en una situación de competencia o sin TLC) en un promedio de entre 95% y 116%. Los incrementos de precios reducen el bienestar de los consumidores. Si la medidas propuestas por EEUU vinculadas a proteger los datos de prueba se hubieran implementado cinco años antes, durante el año 2003 los consumidores peruanos habrían requerido una compensación potencial (variación compensatoria) de entre S/.5.4 y 18.2 millones anuales para mantener el nivel de bienestar que hubieran obtenido bajo una situación de competencia para las moléculas vinculadas a enfermedades principales. Las principales instituciones públicas del sector salud (Essalud e INEN), podrían comprar menos medicamentos si los precios suben y un grupo de personas con enfermedades graves, como VIH-SIDA y tuberculosis, podrían dejar de acceder a tratamiento. Si las medidas propuestas por EEUU vinculadas a proteger los datos de prueba se hubieran implementado cinco años antes, durante el año 2003, dichas instituciones habrían requerido un incremento en su presupuesto de alrededor de S/.4,6 millones anuales para poder brindar el mismo nivel de servicio que hubieran logrado bajo una situación como la vigente para las moléculas vinculadas a enfermedades principales. Dicho monto permitiría evitar que los tratamientos de los pacientes se vieran perjudicados a causa del TLC. Se estima que el impacto, en términos de transferencias al exterior por menores ventas de empresas locales, para las moléculas relevantes, hubiese ascendido al valor agregado localmente asociado a un monto de ventas de entre S/. 1.5 y S/. 4.0 millones anuales.

Autor/ Fecha / Titulo	Objetivo	Metodología	Principales Resultados
INDECOPI (Perú), 2005, ANÁLISIS DEL IMPACTO ECONÓMICO DE UN RÉGIMEN DE PROTECCIÓN DE DATOS DE PRUEBA EN EL MERCADO FARMACÉUTICO PERUANO	Estimar el impacto de la puesta en vigencia de un sistema de protección de datos de prueba en el procedimiento de registro sanitario de medicamentos en dos aspectos: i) Uno primero, relacionado con el impacto sobre la competencia en el mercado farmacéutico, y el consiguiente efecto en precios y cantidades de equilibrio para cada clase terapéutica analizada, así como el efecto en el bienestar, y; ii) Uno segundo, relativo a los efectos esperados hacia futuro considerando el tamaño del mercado peruano y las moléculas que potencialmente podrían acogerse a la protección.	Un análisis contrafactual en el que se simula un escenario de monopolio para las marcas compuestas por los principios activos (monofármacos), que fueron registrados por primera vez en el país a partir del año 1998 hasta el 2003. Para la evaluación respectiva, se utiliza un modelo de equilibrio de mercado aplicado a la industria de medicamentos, el cual permite simular un estado de monopolio en la comercialización de un principio activo (molécula) en particular. Se utiliza el modelo empleado por Carsten Fink en su estudio realizado para la India, que evalúa el cambio en el comportamiento de las empresas farmacéuticas transnacionales, cuando se simula una situación en que empieza a regir patentes para medicamentos.	La simulación arroja resultados bastante diferentes para cada tipo de mercado (Grupos terapéuticos). Así, por ejemplo, considerando el escenario pesimista, los precios monopólicos estimados pueden llegar a situarse por encima de los precios de competencia registrados desde 0,16% para un mercado, y hasta 510,2% para otro. De igual forma, esto también se extiende para los montos hallados de pérdida de bienestar, en el que para un mercado ésta puede alcanzar el 0,02% del tamaño de mercado bajo condiciones de competencia; y para otro el 278,5%. La pérdida de bienestar calculada, hubiese ascendido al año 2003 a 12.1 millones de dólares, valor que habría representado el 28,1% del tamaño de mercado en condición de competencia durante el periodo evaluado.

Autor/ Fecha / Titulo	Objetivo	Metodología	Principales Resultados
Corporación de estudios para el desarrollo CORDES (Ecuador), 2005, Informe sobre el impacto económico sobre el sector farmacéutico y agroquímico ecuatoriano de la adopción de un capítulo sobre protección de derechos de propiedad intelectual en el marco del tratado de libre comercio	Calcular el impacto que tendría sobre el mercado de medicinas (y agroquímicos), en el país, otorgar exclusividad a los datos de prueba y conceder compensaciones por demoras en la aprobación de patentes.	Datos de prueba: Análisis contrafactual comparando lo que paso en la realidad con lo que hubiese pasado si en el periodo 2000-2005 el mercado Ecuatoriano hubiera tenido protección a los datos de prueba de medicamentos. Compensación por demoras en patentes: Calcula el costo anual para 2004 de las patentes de medicinas para el consumidor Ecuatoriano. Extrapolar ese costo a largo plazo Calcular los rezagos que podrían tener las patentes en el futuro. Calcular el costo que podrían tener estos rezagos.	Datos de prueba: El incremento en el precio de los productos que obtendrían mercados monopólicos relativos al mercado real fue del 186%. La reducción en la cantidad demandada es del 77%. En un escenario de elasticidades reales la pérdida de bienestar para la sociedad durante los últimos 12 meses hasta abril del 2005 se estima en aproximadamente 2,6 millones de dólares. Durante un periodo de 5 años la perdida seria de alrededor de 13,1 millones de dólares. Patentes: La compensación por demoras en la aprobación de la patente implicaría, en el escenario más probable, un incremento de entre 75,2 y 150 millones de dólares.

Autor/ Fecha / Titulo	Objetivo	Metodología	Principales Resultados
Corporación Sisma Mujer / Fundación IFARMA / Proyecto Girasol ()Colombia), 2008, IMPACTO DEL TRATADO DE LIBRE COMERCIO FIRMADO ENTRE COLOMBIA Y ESTADOS UNIDOS SOBRE EL ACCESO A MEDICAMENTOS REQUERIDOS POR MUJERES VIVIENDO CON VIH O SIDA Y SU IMPLICACION SOBRE LA CALIDAD DE VIDA SENTIDA	Estimar el impacto del tratado de libre comercio firmado por Colombia y Estados Unidos sobre el acceso los medicamentos utilizados para el tratamiento del VIH y SIDA en las mujeres en Colombia, y sus implicaciones sobre la esperanza y sobre la calidad de vida sentida por las mujeres viviendo con VIH o SIDA.	El modelo usado en este trabajo es de carácter predictivo y se baso en 3 trabajos desarrollados con anterioridad: Modelo IPRIA: Guía para estimar el impacto sobre el acceso a los medicamentos de cambios en los DPI. Desarrollada para la Organización Mundial de la Salud, OMS, 2005. Modelo para evaluar el impacto del CAFTA (Tratado de libre comercio entre Centro América y la República Dominicana con los Estados Unidos) sobre los medicamentos ARV. Informe sin publicar presentado como resultado de una consultoría al Banco Interamericano de Desarrollo, BID. Modelo IPRIM: Micromodelo de impacto para medir el efecto de las provisiones ADPIC –Plus en tratados de libre comercio. OMS, Instituto del banco Mundial IBM e Internacional center for trade and sustainable development ICTSD.	Mientras el escenario de patentes podría incrementar el gasto en un 3% anual en promedio, con un máximo de 5% hacia el año 2017, la protección a los datos de prueba incrementará el gasto en un 11 % con un máximo de 17% en los años 2011- 2012. El costo promedio por paciente año en el escenario que suma las medidas de los dos escenarios construidos (patentes y exclusividad a la protección de datos) se incrementaría en un 12,5 % en promedio con respecto al escenario básico, con un máximo del 19% en el 2011.

Autor/ Fecha / Titulo	Objetivo	Metodología	Principales Resultados
LENZ Consultores (Chile), 2009, Efecto de las patentes de medicamentos en el costo del plan auge, Chile	Simular los efectos esperables de una aplicación más estricta de los capítulos de propiedad intelectual, asociadas al régimen de patentes sobre el mercado de los medicamentos. En particular, se espera que el estudio permita conocer el impacto esperado sobre el costo del plan AUGE.	El modelo de simulación se basa en determinar el nivel y estructura de gasto del Plan AUGE identificando aquellos elementos que están asociados al componente de medicamentos. Sobre esta matriz de gasto se identifican aquellos medicamentos respecto de los cuales los laboratorios de investigación reclaman patentes. Respecto de esta porción del gasto en medicamentos se simula el efecto del cumplimiento de la legislación de propiedad intelectual, en específico respecto de las patentes de medicamentos, con el propósito de determinar el impacto en el costo total que estos arreglos tendrían sobre el Plan AUGE y su impacto fiscal. Para desarrollar el análisis sobre el modelo, se han definido 2 escenarios: 1. Escenario Base para los medicamentos con protección de propiedad intelectual en Chile y E.E.U.U. 2. Escenario para medicamentos sin patentes. La diferencia entre ambos escenarios, corresponde al mayor gasto por la aplicación estricta del régimen de patentes.	Con los datos revisados y los supuestos efectuados, el impacto generado por la protección de patentes induciría un incremento marginal del gasto del Plan AUGE. Este incremento, a nivel del gasto total, representa un 2,54% y, a nivel del gasto en medicamentos del 7,28%.

Autor/ Fecha / Titulo	Objetivo	Metodología	Principales Resultados
Ellen R. Shaffer and Joseph E. Brenner (Guatemala), 2009, A Trade Agreement's Impact On Access To Generic DrugsThe Central America Free Trade Agreement has kept some generic drugs from Guatemala even though they're available in the United States.	Examinar el efecto de las provisiones de CAFTA RD, sobre el acceso a medicinas de bajo precio, incluyendo genéricos, en Guatemala. El estudio se enfoca en la exclusividad a los datos de prueba.	Comparación de los precios de medicinas con protección de datos y los de sus equivalentes terapéuticos (con nombre de marca y genéricos).	La exclusividad de datos de prueba y las reglas de patentes como son aplicadas en Guatemala están limitando el acceso a algunos medicamentos genéricos que serian sustitutos menos costosos que algunos nuevos medicamentos de marca. Los resultados dependen del medicamento y la alternativa terapéutica con la cual se compare. Los datos oscilan desde 166% que cuesta más el Lopinavir + Ritonavir (Kaletra, protegido con exclusividad a los datos de prueba por 15 años) ofrecido en Guatemala que la alternativa genérica ofrecida por la Organización Panamericana de la salud para este mismo medicamento; hasta 845.600% que cuesta más el Voriconazol (Vfend, protegido con exclusividad a los datos de prueba por 15 años) que una versión genérica de la nistatina considerada como alternativa terapéutica a este medicamento.