A review of the health and economic implications of patent protection, with a specific focus on Thailand

Inthira Yamabhai1,2* and Richard D Smith2

Abstract

Background: Although it has been two decades since the Thai Patent Act was amended to comply with the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), there has been little emphasis given to assessing the implications of this amendment. The purpose of this review is to summarize the health and economic impact of patent protection, with a focus on the experience of Thailand.

Methods: A review of national and international empirical evidence on the health and economic implications of patents from 1980 to 2009 was undertaken.

Results: The findings illustrate the role of patent protection in four areas: price, present access, future access, and international trade and investment. Forty-three empirical studies were found, three of which were from Thai databases. Patenting does increase price, although the size of effect differs according to the methodology and country. Although weakening patent rights could increase present access, evidence suggests that strengthening patenting may benefit future access; although this is based on complex assumptions and estimations. Moreover, while patent protection appears to have a positive impact on trade flow, the implication for foreign direct investment (FDI) is equivocal.

Conclusions: Empirical studies in Thailand, and other similar countries, are rare, compromising the robustness and generalizability of conclusions. However, evidence does suggest that patenting presents a significant inter-temporal challenge in balancing aspects of current versus future access to technologies. This underlines the urgent need to prioritize health research resources to assess the wider implications of patent protection.

Introduction

Access to information that is generated through research and development (R&D) is a public good [1]. Because it is impossible to exclude people from using it, a price that reflects the actual cost of production cannot be charged. To address this, patents present a legal system that provides short-term exclusivity (or monopoly rights) over the production and sale of a specific product resulting from R&D. This allows the firm to sell at a price higher than would otherwise be the case, compensating the costs of R&D. However, there is some concern that the patent price is used to achieve 'super-normal' profits (profits in excess of those required to recoup R&D costs) at the detriment of wider access to patented products [2].

The implications of patenting spread further, as innovation, technology, and knowledge development are crucial drivers of economic development and technology transfer resulting from international trade and investment. The topic of patenting has found its way onto the global agenda due to the World Trade Organization (WTO)'s Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), which expanded the Western tradition of patenting to all members of the WTO. Under this Agreement, patent protection must be available for at least 20 years, must be without discrimination against the place of invention or origin of product, and must apply to both products and processes [3].

This has generated especially heated debate within the health community concerning the impact that patents...
may have on the price of and access to medicines, affecting both availability and affordability. However, arguments concerning patenting tend to take one of two sides: that patenting should be continually strengthened to encourage greater trade and investment, or that patenting should be weakened to ensure that medicines are as cheap as possible in the belief that this will ensure the greatest access for those in need. There is seldom, if ever, consideration of both sides when informing policy makers how to strike a balance between affordable medicines, both now and in the future, and trade and investment. For instance, whilst continually strengthening patenting will likely lead to higher prices, thus further reducing access, weakening patenting may stifle long-term access since pharmaceutical companies might be reluctant to introduce new medicines into the market, and foreign investors may look to invest in other countries where there is better protection of their products. In order to determine the appropriate balance in policy (such as the use of TRIPS-flexibilities), it is important to establish: (i) the impact that patent protection has on price; (ii) the impact that price has on current and future access; and (iii) the impact that patents have on innovation in national and international settings. This paper addresses these issues through a review of the literature concerning these areas, with a specific focus on Thailand.

**Patenting and Thailand**

Thailand is a lower-middle-income economy with a 2007 per capita Gross National Income of US$3,400 and a total population of 63.3 million [4]. Health services are provided by both public and private insurance schemes, with public insurance schemes covering 97% of the population. In 2007, 72% of national health expenditure was financed by public expenditure [5]. The prices of medicines in Thailand are set mainly by market competition, with no policy related to price regulation [6]. In 1979, Thailand’s Patent Act (B.E.2522) established the first legal protection for inventions in the country, although only process patents for pharmaceuticals were originally covered. This Act was revised in 1992 to introduce product patent protection for pharmaceutical products (13 years ahead of TRIPS compulsory compliance) [7].

The justification to amend the Thai patent law was to interest multinational companies to invest in Thailand. The other expected benefit of restricted patent protection in medicines is that this could increase domestic capability and strengthen the local pharmaceutical industry by the transfer of new technologies into the country [8], as the aim of a patent is to encourage technology transfer. Although technology diffusion can take place through a variety of channels that involve the transmission of ideas and new technologies—such as the imports of high-technology products, adoption of foreign technology and acquisition of human capital through various means—Foreign Direct Investment (FDI) was claimed as the most important channel for technology transfer [9,10].

This revision coincided with the rise of HIV/AIDS as a major health problem together with concern over the rising costs of anti-retrovirals (ARV). For instance, 200 mg (100 capsules) of original efavirenz sold in 2006 at 3,192 baht per bottle, while a generic equivalent was available at 1,292 baht [11]. A similar concern was expressed over other new medicines, which were not covered by the National Health Insurance system due to their high price [12]. The Sub-committee on selecting essential medicines under the National Health Insurance schemes therefore proposed compulsory licensing for seven patented medicines during 2006–2008 [13].

There were reactions from pharmaceutical companies. For instance, Abbott Laboratories withdrew its registration application for 10 new medicines in protest of the government use license on its product. These reactions were not confined to the pharmaceutical industry. In 2007 the Office of the United States Trade Representative elevated Thailand’s ranking from the Watch List to the Priority Watch List, indicating concerns over deficiencies in Intellectual Property Rights (IPR) protection and enforcement [14], and announcing that privileges under the Generalized System of Preferences would be removed for three Thai products: gold accessories jewellery, polyethylene terephthalate, and flat screen television sets [15].

From the experience of pharmaceutical patent protection and associated policies during 1992–2008, it is apparent that patent protection has both health and economic consequences. A conceptual framework illustrating the broad implications of patent protection is illustrated in Figure 1. Patent protection affects the price of pharmaceuticals whereby price is a component in determining affordability and therefore access to existing medicines and industry investment in introducing or developing new medicines. A higher price would hinder access, but stimulate the development of new medicines through a higher R&D budget enabling patients to benefit from access to new medicines in the future. Patent protection is also accompanied by foreign investment in domestic facilities for the production of pharmaceuticals. Finally, as indicated above, there are wider trade relationships that may be affected by patent decisions, and which are not related to medicines at all.

**Methods**

To ensure a manageable review, inclusion criteria covered the study scope and the type of study.
Study scope
Studies which assessed the implications resulting from patent protection for pharmaceutical products and/or processes, especially:

- the benefit and cost of patent protection for the pharmaceutical industry
- the interplay between patents and the affordability and availability of medicines
- the relationship between patents and new drug development
- the implications of patent protection on the wider economy, i.e. trade or foreign direct investment.

Types of studies
- Thai or English publications
- Research affecting any country
- Research articles, working papers or reports
- Research based on quantitative data (direct observation or experiment)

The databases searched covered both health and economic literature: Pubmed, Embase, Global health, International Bibliography of Social Sciences (IBSS), ABI/INFORM, and Econlit. The selected Thai databases were the Health System Research Institute database, Journal of Health Science, Thai thesis database, The Thailand Research Fund, Thai Journal Citation Index Center, and the Research Library of the National Research Council of Thailand. Given the specific case study setting of Thailand, the review of Thai literature also included unpublished (grey) literature such as research reports, Master's dissertations, or Ph.D. theses. The dates of the published studies (1980–2009) were set so as to ensure the inclusion of all work conducted when the requirement of global standard patent protection was needed as, since the 1980s, intellectual property has become an important business tool, and new internationally-agreed trade rules for intellectual property rights were seen as a way to cope with the international economic tension [16].

The keywords employed in search queries covered five areas of interest: (i) patent policy, (ii) health, (iii) price, (iv) access, and (v) economy. In each area, the related keywords are identified in Table 1.

Results
Initial searches resulted in 4,012 abstracts, of which 61 were from Thai databases. Of these, 43 passed the inclusion criteria, including only three from the Thai databases. Papers were categorised into: (i) role of patent on price, (ii) role of patented price on present access, (iii) role of patented price on future access, and (iv) role of patent on international trade and investment. Tables 2, 3, 4, 5, and 6 provide a brief summary of these empirical studies.

Role of patent on price
Twelve studies, including two Thai studies, looked at the effect of patents on price. Most of these studies focused on the patent expiration effect in the USA. Patent protection appears to increase price by around 26%-277% depending on which of the three estimation approaches is used.

Table 1 Keywords related to a research area

| Areas            | Keywords                                                                 |
|------------------|--------------------------------------------------------------------------|
| Patent policy    | Intellectual property rights, Patent protection, Patent TRIPS, TRIPS Plus, TRIP flexibility, Free trade agreement, Trade agreement |
| Health           | Public Health, Health, Drug, Pharmaceutical, Medicine                    |
| Price            | Price, Budget, Profit, Revenue                                            |
| Access           | Access, Afford/Affordability, Available/Availability                      |
| Innovation       | Innovation, Research and development/R&D, Incentive, New molecular entity, Invention |
| Economic growth  | Investment, Trade/International Trade, Foreign direct investment/FDI, Economic growth |
| Authors/ Ref. no. | Period | Setting (Country/medicines) | Objectives | Model | Method |
|------------------|--------|-----------------------------|------------|-------|--------|
| Watal (2000)/[17] | 1985-1992 | India, 22 patentable medicines in mailbox (varied in wide therapeutic areas) | The effect of product patents, price control and compulsory licensing on medicine prices and welfare. | Demand function estimation | Comparing effects from different demand functions—the constant elasticity demand and the linear demand function—and estimating price as a composite of the demand function. |
| Fink (2000)/[18] | 1992 | India, two therapeutic groups: quinolones and synthetic hypotensives | The impact of product patents on medicine price and pharmaceutical company’s profit | Demand function estimation | Modeling a demand function as a two-stage decision-making process (chemical entity and brands under that chemical entity). Then estimating price and profit under each substitution elasticity among chemical entities and among brands. |
| Boersma et. al. (2005)/[19] | 1996 to 2001 | The Netherlands, three medicines whose patents expired between 1996 and 2001 | To observe price and share prior to and after patent expiration | Observational study | Trend analysis of volumes and price (measured as defined daily doses (DDD) prior to and after patent expiries were calculated. |
| Suh et al. (2000)/[20] | 1984-1987 | USA, 35 chemical entities whose patents expired between 1984 and 1987 | The effect of generic medicine entry on price after patent expiration | Regression analysis | Collecting descriptive statistics of price after patent expiration and analysing the influential factors affecting price, which are number of multiple-source medicines, market growth, market size, profitability, severity of illness, duration of treatment, and number of years after patent expiration. |
| Magazzini et al. (2004)/[21] | July 1987-December 1998 (Quarterly data) | USA, UK, Germany, and France, all medicines whose patents expired within the study period | Price and determinant of price after patent expiry | Regression analysis | Collecting descriptive statistics of prices before and after patent expiration. Using regression of the price with control of market share of the patented products, market size, % of sales to the hospital segment, the average market growth, the number of brand names, ratio of the average price of original products, etc. |
| Grabowski and Vernon (1992)/[22] | 1983-1986 | USA, 18 expired patent medicines | The pricing and competitive behaviour after patent expiration | Regression analysis | Using descriptive statistics of price index of the overall market, original medicine, and generic medicine. Using regression of the determinant of generic entry. |
| Study Authors          | Study Period | Study Location | Study Overview                                                                 | Methodology            | Analysis Methodology                                                                 |
|-----------------------|--------------|----------------|---------------------------------------------------------------------------------|------------------------|-------------------------------------------------------------------------------------|
| Griliches and Cockburn (1994) [23] | 1987-1990    | USA, two anti-infective drugs: cephalaxin and cephradine | The pricing and competitive behaviour after patent expiration | Observational study     | Calculating the aggregate price indexes for a simple two-goods world where consumers buy either the brand or the generic version of a drug. |
| Borrell (2007) [26]    | 1995-2000    | 14 antiretroviral therapy medicines in 34 low and middle income countries | The impact of patents on medicine prices across developing countries | Regression analysis     | Developing a price function as a composite function of the number of medicines in patent and non-patent regimes, number of generics after patent expiration, number of doses per day, efficacy, adverse reactions, and number of years in the US market. |
| Supakankunti et al. (1999) [27] | 1987-1998    | Thailand, six therapeutic categories were chosen to represent the patented market | The effect of new patent law on price | Observational study     | There were no patented medicines so these medicines were selected by other criteria. Descriptive statistics were used to report the price movement or trend of the real price and nominal price of branded and generic medicines. |
| Limpananont et al. (2004) [28] | 2001-2004    | Thailand, antiretroviral therapy medicines | Price differences of patented and generic medicines | Observational study     | Comparing and calculating the price ratio of patented and generic DDD prices. |
| Jones et al. (2001) [29] | 1981-1994    | Canada, 82 medicines from the British Columbia Pharmacare Programme | The impact of the Canadian Patent Act in 1987 | Regression analysis     | Using descriptive statistics of prices before and after 1987 and log regression of generic market share, one factor, to predict market price. |
| Challu (1995) [30]     | 1987-        | Italy, 38 medicines | The impact of the 1978 patent law change | Observational study     | Comparing new drug prices in Italy before and after the 1978 patent law. Using US prices as a reference. |
The first approach uses elasticity of demand to calculate price. This has been used to estimate the likely effects of patents on the price of medicines not currently under patent protection, and to extrapolate to a situation of those medicines being under TRIPS obligations. Using this methodology, Watal (2000) showed that all patentable medicine prices in India would increase by a mean of 26% with linear demand and 242% with

Table 3 Empirical studies of the implications of patenting on present access

| Authors/Ref. no. | Period          | Setting (Country/medicines)                     | Objectives                                                                 | Model and Method                                                                 |
|------------------|-----------------|------------------------------------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| Akaleephan et al. (2009) [31] | 2000-2003       | Thailand, top 70 imported medicines.          | The implications of the TRIPS-Plus proposal, and extension of patent life on price and access | Regression analysis and Modelling It was assumed that the first medicine patent expired in 2003. Drug consumption and budget from using generic were estimated. This cost was then compared with increased cost from patent life extension. |
| Yamabhai et al. (2009) [32]      | 2006-2008       | Thailand, 7 government use licensed medicines in ARVs, heart disease and anti-cancer | The implications of Thailand's government use licenses on health and trade and foreign investment | Regression analysis and Markov model Estimating the increased no. of patients with access to government use license medicines from the current number of access and up to 5 years. The Markov model was used to simulate the heath impact. Trend analysis of export and foreign direct investment was employed. |
| Attaran (2004)/[33] | 2003            | 65 low and middle income countries, 319 WHO essential medicines | How many medicines are under patent in low and middle income countries?       | Survey Surveying pharmaceutical companies and their patent agents to determine where and how patentable medicines in the essential list of the WHO are now patented in developing countries |
| Borrell (2003)/[34] | 1995-1999       | 34 low and middle income countries, HIV/AIDS medicines | The impact of patent rights on medicine sales: reducing or increasing. | Modelling Developing two simultaneous relationships: (1) the relationship between the likely entry decision across drug-country-year triplets and patents; and (2) the relationship between market coverage (i.e. mean coverage of patients with a specific ARV drug) and patents conditional on drug entry decisions and patent regime. |

Table 4 Empirical studies of the implications of patenting on incentive to introduce medicine to market

| Authors/Ref.no. | Period          | Setting (Country/medicines)                     | Objectives                                                                 | Model | Method                                                      |
|-----------------|-----------------|------------------------------------------------|----------------------------------------------------------------------------|-------|-------------------------------------------------------------|
| Mansfield (1986)/[37] | 1981-1983       | 100 U.S. manufacturing firms from twelve industries including the pharmaceutical industry | The effect of patent protection on the rate of development and commercialization of inventions. | Survey | Surveying U.S. manufacturing firms in order to know the proportion of its inventions developed in 1981–83 that would not have been developed and or commercially introduced if it could not have obtained a patent. |
| Lanjouw (2005)/[39] | 1982-2002       | 68 countries at all income levels and including all medicine launches over the period of study. | How patent rights and price regulation affect whether new medicines are marketed in a country, and how quickly | Probit model | Using probit models of the probability that a new medicine is launched in a given country within either two years or ten years of the medicine’s first appearance in the global market and a log-logistic hazard model of the time path of country launches. |
constant price elasticity of demand [17]. Similarly, by accounting for different products through trademarks and advertising, Fink (2004) used this approach to estimate that prices would increase by 30–277% if these medicines came under patent protection [18].

This approach would be useful if the price elasticity of demand is known and correct. For the pharmaceutical market, the consumption decision commonly involves participation by a physician and a third party payer (government or hospital committee). The consumer may or may not play some part in the price payment, depending on a country’s specific regulatory and reimbursement regimes. The pharmaceutical market’s demand function is thus often distorted, and a model based on price elasticity of demand might not present a real world situation of the complexity of the pharmaceutical market.

Second, the observation of price before and after patent expiration is used to infer the price effect of patent protection. Boersma et al. (2005) illustrated that—when there is no patent protection—prices generally fall by 50–70% [19]. Suh et al. (2000) showed a decline to approximately 30% of the original price three years after patent expiration [20]. Also, Magazzini et al. (2004) showed that the price index decreased three years after patent expiration by approximately 20% in Germany and France while the UK price index was stable [21]. Conversely, two US studies by Grabowski and Vernon (1992) and Griliches and Cockburn (1994) showed that—following generic entry—an original product can have an increase in price of 7% and 11% after one year and two years respectively [22]. Another study showed a 60% price increase three years after expiration, while the generic price decreased by 30% [23]. These increases may reflect increased advertising intensity once the market protection of patenting has expired.

However, the effect in each country will differ since each nation has a different health system in terms of medical tradition, policy for financing and supporting generic entry, and brand royalty of physicians, pharmacists and customers. The marketing strategy also differs among pharmaceutical companies, who often spend more heavily on the intensity of advertising once the patent has expired, which could explain at least some of the post-patent price increase. It appears that medicine prices, in general, depend on several supply and demand factors. For example, therapeutic advantage and number of substitutes are both significant price determinants; as the number of substitutes increased in one study from one to two, there was an average 38% decline in the ratio of the new drug price to the average existing market price [24]. Kanavos and Vandoros (2011) also found that product age has a significant and negative effect on prices [25].

Third, studies perform regression analysis of factors influencing medicine prices, of which patent is one such factor. Borrell (2007) estimated patent impact on price

---

Table 5: Empirical studies of the implications of patenting on incentive to invent new medicine

| Authors/Ref.no. | Period | Setting (Country/medicines) | Objectives | Model | Method |
|----------------|--------|-----------------------------|------------|-------|--------|
| Grootendorst (2007)/[42] | 1988-2002 | Canada, prescription medicine expenditure | The implications of patent policies (Bills C-22 and C-91) on medicine expenditure and on R&D activity | Modelling | 1. Estimating the medicine expenditures as a function of year dummies and lagged public drug expenditures, while controlling for a vector of other covariates that could affect drug spending. 2. Estimating R&D expenditure whose patent policy changed as an influenced factor |
| Hughes et al. (2002)/[43] | 2001 | USA | The effect of patent termination on current and future patients | Modelling | From models developed by various scholars during 1987–2002, five step models were estimated: 1) the effect of patent termination on total revenue, 2) the effect of total revenue on R&D budget, 3) the effect of R&D budget on new medicine development, 4) the effect of new medicine on life year and 5) life year in monetary term |
| Giaccotto C. et al. (2005)/[44] | 1980-2001 | USA | The effect of price control policy on number of new drugs | Modelling | Estimating the decreased R&D budget as a function of five main items (price, GDP, foreign sales, dummy variables representing the years for which the Kefauver-Harris amendment and the Waxman-Hatch Act). The value of forgone R&D was then used to calculate the number of forgone drugs by dividing with $802 million (cost of R&D per drug) |
| Colleen (2003)/[45] | 1980-1990 | USA, six compulsory licensing (CL) medicines | The rate of innovation activities of pharmaceutical companies after CL | Observational study | Observing the rate of patenting and other measures of inventive activity five years before and after CL |
| Authors/Ref. no.         | Period     | Setting                        | Objectives                                                                                     | Model                                      | Method                                                                 |
|-------------------------|------------|--------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------|------------------------------------------------------------------------|
| TDRI (2003)/[47]        | 2003       | Thailand                       | The impact of Thai-US FTA on export and import                                                | Computable General Equilibrium (CGE)       | Estimating benefit from trade in goods and the benefit to the economy as a whole by matching the industries that have higher revealed comparative advantage (RCA) index |
| Ferrantino (1993)/[48]  | 1982       | U.S. firm, U.S. affiliated in 45 countries | The effect of IPR on trade and investment flows                                               | Gravity model                              | Using dummy (0/1) variables to reflect differences in national IPR protection schemes and control for economic risk (distance, phone, landlocked, colony and European countries), political risk (Paris Convention member, restriction to foreign firm, number of international memberships, duration of patent), labour costs, population and GDP, while dependent variables are total export, royalty fee, sales of affiliate |
| Markus and Penubarti (1995)/[49] | 1984 | 28 manufacturing sectors across 77 countries | The effect of IPR protection on trade flows                                                   | Regression                                 | Using an empirical model in which deviations of bilateral sectoral imports from anticipated levels are related to income, trade barriers, and patent laws |
| Braga and Fink (1999)/[53] | 1989 | 89 countries from developed to least developed countries | The effects of increased protection on intellectual property                                  | Gravity model                              | Using a gravity model of bilateral trade, foreign direct investment, and technology licensing and estimating the effects of increased protection on a cross-section of 89x88 countries. Using the index on national IPRs systems developed by Park and Ginarte (1996). Estimating the effects of explanatory variables (such as IPRs, GDP and population of both countries, geographical distance, a common border, language) |
| Pradhan (2007)/[51]     | 1970-2000  | India                          | The effect of patent protection on pharmaceutical exports                                     | Gravity model                              | Using a gravity model consisting of GDP of the importing country, distance, trading bloc dummy, price and exchange rate |

Table 6 Empirical studies of the implications of patenting on economic growth and/or foreign direct investment
| Study Reference | Time Period | Data Source | Methodology |
|-----------------|-------------|-------------|-------------|
| Kondo (1995)/[52] | 1976-1980   | U.S. outward FDI in 33 countries | Survey (for IPR index) and Multiple regression of FDI testing |
| Pfister and Deffain (2005)/[54] | 1994-1995 | The location choices of French firms in 17 developing countries | A conditional logit model |
| Fosfuri (2004)/[55] | four time periods: 1981–1983, 1984–1987, 1988–1991, 1992–1996 | 75 countries receiving investments in chemical plants during the period 1981–1996 | OLS, Tobit and GLS random effect |
| Nunnenkamp and Spatz (2004)/[56] | 1995 and 2000 | U.S. FDI and US FDI in industrial level in 166 countries | Finding FDI determinants through a regression of FDI on GDP per capita, population, distance to U.S., the cost of living abroad, average years of schooling and IPRs index using Ginarte-Park for the year 1995 and World Economic Freedom (WEF) index for the year 2000. Testing the industry characteristics by adding industry dummies in the previous independent variable set. |
| Reference | Year | Country | Methodology | Data | Findings |
|-----------|------|---------|-------------|------|----------|
| Lee and Mansfield (1996) [57] | 1991 | U.S. firms and investment in 14 developing countries | The effect of IPR protection level on U.S. firm’s FDI and the role of IPRs protection in chemical industry | 1. Survey for IPRs protection perception 2. OLS regression 3. Tobit model for chemical industry | Surveying perceived weakness of IPR protection from 94 US firms and developing two regression models to find the influence of IPR protection level for overall US FDI and level of technology transfer in the chemical industry. For OLS of overall US FDI, independent variables are weakness of IPR, size of market, with control for firm specific and country specific, IPR index, market size, dummy for Mexico, FDI in previous year, degree of industrialization, openness, and time dummy variables. For Tobit model from 14 US chemical industries, the independent variables are the percentage of firms that felt weakness of IPR protection, GDP, and dummy variables for firms, while the dependent variable is the percentage of firms that will invest in facilities for sales and distribution. |
| An et al. (2008) [58] | 1995 (for FDI or licensing) and 1994 (for exporting) | U.S. FDI in 52 manufacturing industries invested in 62 host countries | To examine the effect of strengthening IPR protection on the mode of technology transfer: exporting, FDI or licensing | A multinomial logit model of three mode of entry choices | The explanatory variables covering national characteristics, GDP, absorptive capacity, distance, cultural distance (English and index developed by authors), FDI fixed cost (economic freedom index), market capitalisation and investment cost index, and IPR index from Ginarte and Park 1990. The industry characteristics variables are industry R&D intensity and capital intensity (the ratio of total real capital stock to total industry sales). |
| Maskus (1998) [59] | 1989-1992 | U.S. FDI in 46 countries | The effect of patent protection on U.S. patent applications filed in host country, total sales of foreign affiliates of U.S. parents, U.S. exports shipped to affiliates and total assets, foreign affiliates of U.S. parents | Seemingly Unrelated Regression | Estimating a simultaneous set of equations to capture these joint impacts, controlling for market size, tariff protection, the level of local R&D by affiliates, distance from the US, investment incentives (proportion of affiliates receiving tax concession numbers in host country and in any of the countries) and disincentives (proportion of affiliates that employ a minimum amount of local personnel no. in host country and in any of the countries). |
| Study | Year | Sample | Methodology |
|-------|------|--------|-------------|
| Javorcik (2004)/[60] | 1995 | 1,405 global firms investing in Eastern European countries | Survey and Probit model |
| Du et al. (2008)/[61] | 1993-2001 | 6,288 US firms investing in various regions of China | Discrete choice model |

The impact of intellectual property protection on the volume of FDI was examined in Javorcik's study. A questionnaire of decision to invest in any country and mode of entry was developed. Using a Tobit regression of the decision and mode of entry on GDP per capita, population, corporate tax rate, legal effectiveness, corruption, privatization, openness, the overall progress in reform, effectiveness of the legal system, corruption level, privatization policies and openness to trade. For testing the mode of entry, the author included firm specific variables such as firm sales, R&D outlays as a percentage of net sales, selling, general & administrative expenses as a percentage of net sales, the number of four-digit SIC codes describing a firm's activities and a dummy variable of each investor's regional experience in the region before 1989.

The impacts of four economic institutions variables, including property rights protection, the degree of government intervention in business operations, the degree of government corruption and contract enforcement, on the location choice of foreign direct investment were examined in Du et al.'s study. A survey was conducted of private enterprises in China to create three indexes which are the degree of government intervention in business operations, the degree of government corruption, and contract enforcement. The other concerned variables are the agglomeration, dummy for presence of US Embassy or Consulates and dummy for government promotion policies, wages, infrastructures (length of highway per square kilometre in a region), and education (percent of higher education students in the region). IPR Index is the logarithm of the patent per capita approved number.
| Study          | Year Range | Sample Size | Study Description                                                                 | Methodology                                                                 |
|---------------|------------|-------------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Kawai (2009)  | 1998-2006  | 1,839       | The determinants of Japanese manufacturing firms’ location decisions in China      | A conditional logit model Empirical models were developed and tested. The dependent variable is choice of investment (1 = Yes, 0 = No). The independent variables are natural logarithms of the number of Special Economic Zones, IPRs index, natural logarithm of the share of total investment in fixed assets by state-owned units in relation to total investment, GDP, labour costs, road infrastructure and natural logarithm number of Japanese manufacturers All explanatory variables are lagged by one year. |
| Seyoum (2006) | 1990 and 1995 | 63         | The impact of patent protection on FDI                                            | The OLS regression Using the set of independent variables which include patent index by Ginarte and Park (1997) and controlling other variables such as market size, GDP growth, exchange rates, population, corruption, unemployment, trade/GDP, scientists and engineers, GDP growth |
| Lesser (2002) | 1998       | FDI in 44 developing countries | The effects of stronger IPR protection in the areas of imports and Foreign Direct Investment (FDI) | Multiple regression The variables includes income per capita, past FDI, exchange rates, tariffs, the proportion of previous year FDI to GNP of previous year, and the degree of industrialization. A new index was developed that uses membership in international treaties to measure the scope and efficiency of IPR. |
| Park and Ginarte (1997) | 1960-1990 | 60 countries from developed to least developed countries | The impact of IPR protection on economic growth (GDP growth) | Regression Creating an IPR index and estimating a system of equations to identify the effect of IPR protection and other national characteristics on economic growth such as R&D activity, investment, and education |
| Study | Period | Sample | Methodology | Findings |
|-------|--------|--------|-------------|----------|
| Athukorala and Kohpaiboon (2006)/[66] | 1990-2001 (three-year intervals) | 168 US-based MNEs that have invested internationally (42 countries) | The determinants of the international location of R&D activity by foreign affiliates of US-based MNEs | Regression analysis Included control variables are real GDP, distance, percentage of domestic sales to total affiliate sale turnover, technology intensity index, R&D personnel per million population, wages of technical personnel, tax incentives for firm-level R&D activities, intellectual property rights index (from World Economic Forum, Global Competitiveness Report), capital stock of US firms, an index of R&D potential of output mix, dummy variables for developing countries other than NICs, newly industrialized countries in East Asia, financial crisis dummy, and vector of time dummy variables |
| Blyde and Acea (2003)/[67] | 1985, 1990 and 1995 | The sources of FDI are 19 OECD countries and 40 countries as the recipients of FDI, 8 of which are from Latin America. | The inflows of foreign direct investment The gravity model of Latin America and developing countries after TRIPS | The independent variables are GDP per capita, population, dummy of common language, past colonial links and region, distance between countries, Ginarte-Park IPR index |
| Supakankunti et al. (2001)/[70] | 1988-1998 | Thailand | The impact of patent law change in 1992 on FDI in Thailand | Observation Providing the trend of FDI for industry in general and specifically for the chemical industry in Thailand |
in 14 ARV molecules in 34 low- and middle-income countries which have different patent regimes, where patent was eligible or ineligible between 1995 and mid-2000. This showed that combination therapy containing at least one patented medicine is on average priced 70% higher than combination therapy containing only generic alternatives. Combination therapy containing at least one original medicine is priced 16% higher than local copies even when it is introduced in no-patent regimes [26].

In Thailand, the introduction of product patent protection in 1992 seems to have had no effect on the price of patentable medicines that were in the market before 1992 [27]. Rather, the effect appears to concern only those patented medicines which were introduced subsequently. For example, one study compared the price of patented and generic HIV/AIDS medicines from 2001–4 and found that the patented price was approximately 1.5–3 times higher than the generic price in 2001 [28].

The experiences in Canada and Italy reflect the situation in Thailand. A study of the impact of the 1987 Canadian Patent Act, which extended the period of protection from seven to ten years while also allowing the generic industry to implement compulsory licensing, found that after 1987, medicine prices increased relative to pre-1987 prices [29]. Similarly, after a patent law in Italy came into effect in 1978, new medicine prices were 163% higher than new drug prices before 1978 [30].

Role of patented price on present access
Empirical evidence directly linking patented price and access is rare. Most studies describe how patenting increases prices (as above) and then assume that price affects access, but there is a lack of direct association between the extent of price increase and the extent of changes in access, controlling for other influence factors. As shown in Table 3, there were four studies found concerning this issue, two of which are in the Thai setting.

Akaleephan et al. (2009) examined the effect of patent life extension from a TRIPS-Plus proposal on access to medicines. They illustrated the drawbacks of extending the period of protection by showing that the availability of generics would help to save 105% of actual government expenditure, and accessibility would increase by 54% [31]. In addition, after compulsory license introduction in Thailand, the price of generic medicines was about 3–38% of their original price. As a result, there were approximately 8,000 extra patients utilizing EFV, and it is estimated that the increased number of patients with access to EFV will be 17,959 in five years [32].

Conversely, Attaran (2004) suggested that the main obstacles are associated with the country’s socio-economic status, such as the lack of manufacturing capacity or poor health care systems [33]. His survey results show that only 17 from a total of 319 medicines on the WHO Essential Medicines List are protected by patents. In addition, Borrell and Watal (2003) showed that switching all medicines under a patent regime to a no patent regime globally would have increased the percentage of AIDS patients with access to new medicines from 0.88% to 1.18% [34]. However, with reference to individual countries, the findings suggested different magnitudes of impact. For example, in Thailand where most of the relevant medicines were under patent, it was estimated that around 10,000 additional prescriptions would be prescribed if all patents were waived, generating an increase in access of some 50%.

Role of patented price on future access

Incentive to introduce medicine to market
Pharmaceutical companies may refuse to market new medicines in response to weak national patent policy [35,36]. Mansfield (1986) estimated that 65% of products would not have been introduced if patent protection could not have been obtained [37]. While patents make local markets more attractive, multinationals may delay or avoid launching medicines in lower-priced countries because they are concerned about the implications for pricing in other markets [38]. For instance, Lanjouw (2005) determined the effects of patent policy and price control policy on market entry, and showed that extensive price control and process-only patent protection lowers the probability of having a new medicine in lower-income countries by 30% [39]. A brief summary of these two studies is shown in Table 4.

The model employed in these two studies was multi-country, from high-income to low-income countries. Although the results are more generalized, they sometimes mislead. Under some circumstances and model assumptions, patent protection has a positive effect for some countries, while under other circumstances it has a negative effect. Single country studies are particularly effective at maximizing their explanatory leverage by exploiting the availability of comparable units of analysis, whether over market or medicine characteristic variations within a country [40].

Incentive to invent new medicine
One implication of removing patent protection to gain increased current access is that this might result in patients foregoing the opportunity to receive a new medicine in the future, as it would not be discovered or developed [41]. There were four studies looking at this possibility, as shown in Table 5. Grootendorst (2007) illustrated that this clearly generates trade-offs between benefits now and in the future [42]. Indeed, heavily depending on assumptions, Hughes et al. (2002) estimated that for every dollar in consumer benefit realized from providing
greater access to current medicines, future consumers would be harmed at a rate of three dollars in present value terms from reduced future innovation [43].

Giaccotto C. et al. (2005) investigated the role of price control on new medicine development, showing that price control policy in the USA during the 1980s resulted in forgone R&D investment of US$264-293 million, translating into 330–365 fewer new medicines, which is equal to one-third of all actual new medicines launched on the global market during that time period [44]. However, such studies lack a direct link between profitability and actual investment in R&D. They illustrate the effect of patents on profit and assume that this translates directly into R&D. Conversely, an observation of the innovation activities of pharmaceutical companies affected by compulsory licensing found that there was no uniform decline in the rate of medicine patenting (MNEs) were found. The results show that the strength of IPR protection has a significant positive impact on the U.S. FDI [56]. For example, a one percent rise in the perceived weakness of IPR protection would decrease the U.S. FDI in that country by 14%. In a sample of chemical firms, it was found that firms are likely to allocate their investment to sales and distributions and simple production activities rather than to manufacturing final products or to R&D facilities [57]. This is confirmed in another study [58], in which it was suggested that a one percent rise in the extent of patent protection would increase the U.S. investment in that country by 0.45% [59].

Javorick (2004) indicated that weak protection of intellectual property rights deters foreign investors in four technology-intensive sectors: (1) drugs, cosmetics and health care products; (2) chemicals; (3) machinery and equipment; and (4) electrical equipment. In addition, foreign investors, in all industries, tend to set up distribution facilities rather than engaging in local production in a country with weak IPR protection [60]. Four studies confirmed that MNEs prefer investing in the regions that have better intellectual property rights protection [61-63]. For example, a one point increase in IPR index would boost FDI by $1.5 billion [64].

Three studies using regression analysis yielded inconclusive results when analyzed in subgroups. Two studies showed the positive impact of strong national patent laws in developed countries, but showed a negative impact in developing countries [65,66] while another study revealed the converse results [67].

In terms of the pharmaceutical industry specifically, a strong patent system was found to have caused a considerable flow of investment into the American pharmaceutical industry [68]. However, some studies show a negative correlation between the levels of protection and foreign investment. This is supported by conclusions elsewhere that the exclusion of pharmaceuticals from patent protection was a significant factor leading Italy to
become a base for the export-oriented production of
generic medicines [69]. Supakankunti (2001) showed
that in Thailand there has been little foreign investment
in the pharmaceutical sector since the introduction of
the strengthened patent law in 1992 [70]. It has been
suggested that this is because foreign investors consider
Thailand an unsuitable destination due to the insuffi-
ciency of well-trained human resources, technology, and
equipment, as well as the inadequacy of the registration
system for new medicines [8] Table 6.

In conclusion, there are a number of empirical investi-
gations pointing to an uncertain relationship between
patent and FDI distribution, which depends on the polit-
cal and business risks of the country included, FDI
sources, data from opinion surveys or secondary data,
and the approach used to calculate the level of patent
protection scale. The question of just how important
patent protection is for FDI is still unsettled. Some
evidence indicates that patents have had a positive
impact on FDI overall and the pharmaceutical industry
in particular, while other evidence suggests that weak
patent protection of pharmaceuticals was the main
factor in making the country a manufacturing base for
these pharmaceutical companies. As both country-
specific and regional factors influence the effect of
patents on FDI, more regional and country–specific
studies should be conducted in order to validate the
findings of this study. As noted by Lesser (2002), the
effect of IPR on FDI may only be possible on a country-
by-country basis.

Conclusions
The empirical literature provides answers to some im-
portant questions related to the impact of patents, al-
though evidence remains largely inconclusive. With
respect to patent impact on price, both Thai and inter-
national evidence confirm that patenting shifts prices up
and has an effect on the price of the new registration
of medicines. In terms of present access, international
empirical evidence demonstrates that patent protection
does not always impede access, whereas a Thai study
suggested that implementing a limited patent life may
actually increase access. As for future access, evidence
suggests that strengthening patent policy in a given
nation may speed up the time required for entry into the
pharmaceutical market. Empirical models estimate that
higher profits, from patents, would increase the number
of new medicines to market through higher R&D bud-
gets, enabling patients to benefit from access to new
medicines in the future. Conversely, one observational
study revealed that withdrawing exclusive rights by com-
pulsory licensing might not have an effect on innovation
in the future.

The evidence found from this review confirms that
policy stimulating patent protection does have a positive
impact on trade flows. In terms of FDI, evidence pro-
vides inconclusive results, both generally and specific to
the pharmaceutical industry. Figure 2 summarizes exist-
ing evidence and the remaining gap, with an indication
of the relationship found from this review.

The review revealed that little empirical research has
been undertaken on the extent to which patent rights
affect health and economic factors. With respect to
health, the settings of the studies are very mixed across
therapeutic areas and medicines. The literature generally
shows that the size of impact varies wildly, depending
on which methods are employed in the studies. Current
evidence therefore makes it difficult for a country, such
as Thailand, to come to a conclusion on advice to
national policy makers who are to make decisions which
trade off health or access impacts with wider economic
issues. The high price of medicines may not be related
to patent rights. Furthermore, price may not be related
to access, either.

Recommendations
The trade-offs between patent protection, current and
future access to medicines, and related aspects of trade
and investment, are still subject to debate, since empirical studies are relatively rare, especially in countries such as Thailand. This underlines the urgent need to prioritize health research resources to assess the implications of patent protection.

It is clear that evidence on the role of patent/price on access, especially with respect to non-communicable diseases, is scarce, inconclusive, and problematic. This suggests a more holistic assessment is required which takes into account a country’s socio-economic status and health care system when estimating patent impact on access to medicine. The estimation of patent impact on technology transfer through FDI should be conducted on a country basis. In order to try and assess whether, on balance, a country is better off with patent policy related to health or not will require evaluating the implications for current and future access to medicines, and the wider national economy.

Competing interest
We declare that we have no competing interest.

Authors’ contributions
IY designed the research methodologies and carried out the study. RD co-designed the methodologies, participated in discussions, and provided interpretations. The manuscript was written by IY and RS. All authors have contributed to, reviewed, and approved the final manuscript.

Funding sources
These findings are the result of work conducted during a WHO fellowship. The views expressed in this paper are those of the authors, and no official endorsement by the World Health Organization is intended or should be inferred.

Acknowledgement
We are grateful for the joint financial support to the Health Intervention and Technology Assessment Program (HITAP) by the Thai Health Promotion Foundation, Health System Research Institute, Bureau of Health Policy and Strategy, Ministry of Public Health, and the Thai Health-Global Link Initiative Project (TGILIP).

Received: 16 October 2011 Accepted: 3 July 2012
Published: 1 August 2012

References
1. Smith RD, MacKellar L: Global public goods and the global health agenda: problems, priorities and potential. Glob Heal 2007, 3(1):19.
2. Woodward D, Smith RD: Global Public Goods for health: concepts and issues. In Global Public Goods for Health: a health economic and public health perspective. Edited by Smith RD, Beaglehole R, Woodward D, Drager N. Oxford: Oxford University Press; 2003.
3. Smith RD, Correa C, Oh C: Trade, TRIPS, and pharmaceuticals. Lancet 2009, 373(9664):684–691.
4. Thailand Overview. http://www.worldbank.org/en/country/thailand/overview.
5. Wibulpolprasert S (Ed): Thailand Health Profile 2005–2007. Nonthaburi: Ministry of Public Health; 2007.
6. Sookriwong C, Yoongthong W, Suwattanapreeda S, Chanjaruporn F: Medicine prices in Thailand: A result of no medicine pricing policy. Southern Med Review 2009, 2(2):10–14.
7. Ford N, Wilson D, Chaves GC, Lotrowska M, Kittiwatchakul K: Sustaining access to antiretroviral therapy in the less-developed world: lessons from Brazil and Thailand. AIDS 2007, 21:521–529.
8. Kuanpoth J: Intellectual property rights and pharmaceuticals: a Thai perspective on prices and technological capability. Intellect Prop Q 2007, 2186–215.
9. Wang J-Y, Bliomstrom M: Foreign investment and technology transfer: A simple model. Eur Econ Rev 1992, 36(1):137–155.
10. Borenstein E, De Gregorio J, Lee JW: How does foreign direct investment affect economic growth? J Int Econ 1998, 45(1):115–135.
11. Medecins Sans Frontieres: Untangling the web of price reductions: a pricing guide for the purchase of ARVs for developing countries. 9th edition. Geneva: Medecins Sans Frontieres; 2006.
12. Ministry of Public Health, National Health Security Office: Facts and evidences on the 10 burning issues related to the Government Use of patents on three patented essential drugs in Thailand. Nonthaburi: Ministry of Public Health, National Health Security Office; 2008.
13. Ministry of Public Health, National Health Security Office: The 10 burning questions regarding the Government Use of patents on the four anti-cancer drugs in Thailand. Nonthaburi: Ministry of Public Health, National Health Security Office; 2008.
14. Special 301 Report. 2007. http://www.ustr.gov/about-us/press-office/reports-and-publications/archives/2007/2007-special-301-report.
15. U.S. Removes Certain Indian/Thai Jewellery from GSP Programme, Chinese Producers Pooled to Take Advantage. http://info.ustr.gov/alert/ue0715.htm.
16. Intellectual property: protection and enforcement. https://www.wto.org/ english/trademark_e/whatis_e/tfa_e/agmt7_e.html.
17. Watal J: Pharmaceutical patents, prices and welfare losses: Policy options for India under the WTO TRIPS agreement. World Economy 2000, 23(5):733.
18. Fink C: How stronger patent protection in India might affect the behavior of transnational pharmaceutical industries. Washington, DC: World Bank; 2003.
19. Boersma C, Klok RM, Bos JM, Naunton M, van den Berg PB, de Jong-van den Berg LTW, Postma MJ: Drug cost developments after patent expiry of Enalapril, Fluoxetine and Ranitidine: a study conducted for the Netherlands. Appl Health Econ Health Policy 2005, 4(3):191–196.
20. Suh DC, Manning WG Jr, Schondelmeyer S, Hadsall RS: Effect of multiple-source entry on price competition after patent expiration in the pharmaceutical industry. Health Serv Res 2003, 35(2):529–547.
21. Magazini L, Paramolli F, Riccaboni M: Dynamic competition in pharmaceuticals: patent expiry, generic penetration, and industry structure. Eur J Health Econ 2004, 5(2):175–182.
22. Grabowski HG, Vernon JM: Brand loyalty, entry, and price competition in pharmaceuticals after the 1984 Drug Act. J Law Econ 1992, 35(2):331–350.
23. Griliches Z, Cockburn I: Generics and new goods in pharmaceutical price indexes. Am Econ Rev 1994, 84:1213–1232.
24. Lu ZJ, Comarow WS: Strategic pricing of new pharmaceuticals. Rev Econ Stat 1998, 80(1):108–118.
25. Kanavos PG, Vardaros S: Determinants of prescribed brand medicine prices in OECD countries. Health Econ Policy Law 2011, 6:337–367.
26. Joan-Ramon B: Pricing and patents of HIV/AIDS drugs in developing countries. Appl Econ 2007, 39(4):505.
27. Supakankunt S, Janjaroen WS, Tangphao O, Ratanawijitrasm S, Kraipornpak P, Praditthanavaj P: Study of the implications of the WTO TRIPS Agreement for the pharmaceutical industry in Thailand. New Delhi: WHO Regional Office for South-East Asia; 1999.
28. Limpananont L, Nilwatchararung D, Kulsoomboon Y, Maleewong U: Impact of U.S.-Thailand FTA on access to medicine in Thailand. Bangkok: Social Pharmacy Research Unit, Faculty of Pharmaceutical Sciences, Chulalongkorn University; 2004.
29. Jones JCH, Potashnik T, Zhang A: Patents, brand-generic competition and the pricing of ethical drugs in Canada: some empirical evidence from British Columbia, 1981–1994. Appl Econ 2001, 33(7):947–956.
30. Chullu PM: Effects of the monopolistic patenting of medicine in Italy since 1978. Int J Technol Manag 1995, 10:237–250.
31. Akaleephan C, Wibulpolprasert S, Sakubumrungruj R, Luangruangrong P, Jittraknatee A, Aeksanogri S, Udomakorn S, Thangcharoenathien V, Tantivess S: Extension of market exclusivity and its impact on the accessibility to essential medicines, and drug expense in Thailand: analysis of the TRIPS-Plus proposal. Health Policy 2009, 91:2174–182.
32. Yamabhai I, Mohara A, Kitchanan V, Chaisiri K, Tantivess S, Teerawattananon Y: Assessing the implications of Thailand’s Government Use Licenses, issued in
2006–2008: Health Intervention and Technology Assessment Program; 2009.

33. Attaran A: How do patents and economic policies affect access to essential medicines in developing countries? Health Aff 2004, 23(3):155–166.

34. Borrell JR, Watal J: Impact of patents on access to HIV/AIDS drugs in developing countries. Center for International Development at Harvard University; 2005.

35. Boehringer refuses to register Tipranavir in Brazil because of patent law. http://www.aidsaccess.org/09/index.php?option=com_content&task=view&ItemId=2.

36. Doubts over Abbott's latest AIDS drug claim. http://eng.moph.go.th/ContentDetail.php?ItemID=16014&strOrgID=001000202.

37. Mansfield E: Patents and innovation: an empirical study. Manag Sci 1986, 32(7):171–181.

38. Danzon PM, Wang YR, Wang L: The impact of price regulation on the launch delay of new drugs-evidence from twenty-five major markets in the 1990s. Health Econ 2005, 14(3):269–292.

39. Lanjouw JO: Patents, price controls, and access to new drugs: how policy affects global market entry. National Bureau of Economic Research; 2005.

40. Culppepper PD: Single Country Studies and Comparative Politics. Italian Politics & Society 2005, 60:2–5.

41. NGOUÉS JJ: Social costs and benefits of introducing patent protection for pharmaceutical drugs in developing countries. Dev Econ 1993, 31(1):24–53.

42. Grootendorst P, Matteo LD: The effect of pharmaceutical patent term length on research and development and drug expenditures in Canada. Healthcare Policy 2007, 23(1):33–84.

43. Hughes JW, Moore MU, Snyder EA: ‘Rapstéring’ pharmaceuticals: Access, innovation, and consumer welfare. National Bureau of Economic Research; 2002.

44. Giaccotto C, Santerre R, Vernon JA: Drug prices and research and development investment behavior in the pharmaceutical industry. J Law Econ 2003, 48(1):195–214.

45. ColleeM C: Cheap drugs at what price to innovation: does the compulsory licensing of pharmaceuticals hurt innovation? Berkeley Technology Law Journal 2003, 18(3):853–908.

46. FTA Watch: Thailand’s Free Trade Agreements and Human Rights Obligations. http://www.docstoc.com/docs/37091812/Thailands-Free-Trade-Agreements-negotiations-and-Human-Rights.

47. Thailand Development Research Institute: A study on the impact of Thailand-US Free Trade Agreement. Thailand-US Business Council (American Chamber of Commerce and the US-ASEAN Business Council); 2003.

48. Ferrantino MJ: The effect of intellectual property rights on international trade and investment. Rev World Econ 1993, 129(2):300–331.

49. Maskus KE, Penubarti M: How trade-related are intellectual property rights? J Int Econ 1995, 39(3–4):227–248.

50. Fink C, Braga CAP: Intellectual Property rights in a Gravity Model of International Trade Flows. In Policy research working Paper No 2051. The World Bank; 1999.

51. Pradhan JP: Strengthening intellectual property rights globally: impact on India’s pharmaceutical exports. Singap Econ Rev 2007, 52(2):235–250.

52. Kondo EK: The effect of patent protection on foreign direct investment. Journal of World Trade 1995, 29(6):97–122.

53. Braga CP, Fink C: How stronger protection of intellectual property rights affects international trade flows. Washington, DC: World Bank; 1999.

54. Pfister E, Defains B: Patent protection, strategic FDI and location choices: empirical evidence from French subsidiaries’ location choices in emerging economies. Int J Econ Bus 2005, 12(3):329–346.

55. Faduri A: Determinants of international activity: evidence from the chemical industry. CEPR Discussion Papers: 4601. 2004.

56. Nunnenkamp P, Spatz J: Intellectual property rights and foreign direct investment: a disaggregated analysis. Review of World Economics/ Weltwirtschaftliches Archiv 2004, 140(3):393–414.

57. Lee J-Y, Mansfield E: Intellectual property protection and U.S. foreign direct investment. Rev Econ Stat 1996, 78(2):181–186.

58. MacGregor KE, Puttanan T: Duration of rent extraction and the entry mode decision of multinational enterprises. Rev Dev Econ 2008, 12(4):861–876.

59. Maskus KE: The international regulation of intellectual property. Review of World Economics (Weltwirtschaftliches Archiv) 1998, 134(2):186–208.

60. Javoric B: The composition of foreign direct investment and protection of intellectual property rights: evidence from transition economies. Eur Econ Rev 2004, 48(3):39–62.

61. Du J, Lu Y, Tao Z: Economic institutions and FDI location choice: evidence from US multinationals in China. J Comp Econ 2008, 36(3):412–429.

62. Kawah N: Location strategies of foreign investors in China: evidence from Japanese manufacturing multinationals. Glob Econ Rev 2009, 38(2):117–141.

63. Seyoum B: Patent protection and foreign direct investment. Thunderbird International Business Review 2006, 48(3):389–404.

64. Lesser W: The effects of intellectual property rights on foreign direct investment and imports into developing countries in the post TRIPs era. IP Strategy Today 2002, 51–15.

65. Park WG, Ginarte JC: Intellectual property rights and economic growth. Contemp Econ Policy 1997, 15(3):51–61.

66. Athukorala P, Kohpalboon A: multinational enterprises and globalisation of R&D: a study of U.S-based firms: Australian National University, Economics RAS, Departmental Working Papers; 2006:38.

67. Wilde JS, Acra C: How does intellectual property affect foreign direct investment in Latin America? Integration and Trade 2003, 71(9):135–152.

68. Lehman B: The pharmaceutical industry and the patent system: International Intellectual Property Institute; 2003.

69. Scherer FM, Wetzourt S: Economic Effects of Strengthening Pharmaceutical Patent Protection in Italy. International Review of Industrial Property and Copyright Law 1995, 26:1009–1024.

70. Supakankunti S, Janjaroen WS, Tangphao O, Ratanawijittrin S, Kraipornak P, Pratdhanavij P: Impact of the World Trade Organization TRIPS agreement on the pharmaceutical industry in Thailand. Bull World Health Organ 2001, 79(5):461–470.

Cite this article as: Yamabhai and Smith: A review of the health and economic implications of patent protection, with a specific focus on Thailand. Health Research Policy and Systems 2012 10:24.