

**PATENT FILING STRATEGIES FOR PHARMACEUTICAL PRODUCTS: A
SIMPLE COST-BENEFIT ANALYSIS BASED ON FILING COSTS AND
PHARMACEUTICAL SALES**

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I. INTRODUCTION

Global patent filing strategies to protect pharmaceutical products are generally shaped by two basic considerations: the need to protect a broad geographic market and the long development time prior to commercialization. For most pharmaceutical products there are potential sales in almost every country. Though market size will differ depending on the country and the nature of the disease, therapeutic products are sold virtually everywhere. Consequently, patent protection for pharmaceutical products is typically sought in a relatively large number of countries. Second, there is a long development and clinical testing period required for regulatory approval. According to the Pharmaceutical Research and Manufacturer's Association, only one in five compounds that enter Phase I clinical trials ultimately obtain FDA approval, and the average time to discover and develop a new drug is twelve to fifteen years.¹ As a result, one or more patents covering a pharmaceutical product are usually granted well before the product reaches the market. In fact, patents often issue even before it is known whether there will be FDA or other regulatory approval.

Because of the long delay and uncertainty in getting to the market, it is advantageous to defer, as long as possible without risking any loss of rights, patent filing decisions and patent prosecution.² Over time, the prospects of success may become clearer, and better informed decisions can be made on whether to incur or continue to incur patent expenses. Unfortunately, inventors in highly competitive pharmaceutical research do not have the luxury of waiting too long to file for patent protection. Most applicants strive to file a priority application early, usually before a drug candidate has even entered pre-clinical testing. This means that costly global filing decisions usually need to be made at a fairly early stage in a drug's development, well before commercialization is certain. In terms of geographical coverage and expense, the two biggest decisions occur at the national stage of the Patent Cooperation Treaty ("PCT") and at the validation phase after the grant of a European patent.

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- ¹ PHARMACEUTICAL RESEARCH & MANUFACTURERS OF AMERICA, *WHY DO PRESCRIPTION DRUGS COST SO MUCH?*, at <http://www.phrma.org/publications/publications/brochure/questions/questions.pdf> (Mar. 1, 2001).
 - ² Notable exceptions to this rule of thumb include patents relating to products that are either already on the market or close to regulatory approval. Examples include patents for a new use or process improvement.

The PCT is designed to serve those who seek broad protection early while wishing to defer most of the global patent procurement expense until a later time.³ A PCT application is an international application, making it possible to simultaneously protect an invention in as many as 125 PCT contracting states.⁴ The 125 PCT member countries account for almost 98 percent of the world pharmaceutical market.⁵ Notable non-PCT countries are Argentina, Pakistan, and Taiwan.

In addition to providing early and broad coverage, the PCT also provides a mechanism for deferring expensive global filing decisions. Under the PCT, the procedure for seeking national (or regional) patents may be postponed up to thirty months from the first priority date claimed.⁶ Pharmaceutical companies typically take advantage of the full thirty-month period before entering the PCT national stage.⁷ Usually the PCT application claims priority to a national application filed one year earlier, such as a U.S. provisional patent application, so the deadline for entering the PCT national stage is eighteen months after filing the PCT application. The national procedure requires

³ *Yearly Review of the PCT: 2003 1*, World Intellectual Property Organization (WIPO) Pub. No. 901(E) (2004), available at http://www.wipo.int/pct/en/activity/pct_2003.pdf.

⁴ One hundred and twenty-five states had acceded to the PCT as of January 3, 2005. *Id.*

⁵ See *infra* Table 1.

⁶ Patent Cooperation Treaty, done June 19, 1970, art. 39, 40 (as in effect in 1970) (amended to include a 30 month time limit on Apr. 1, 2002), 28 U.S.T. 7645, 7685-86, available at <http://www.wipo.int/pct/en/texts/pdf/pct.pdf> [hereinafter PCT].

⁷ *Id.* Note that a PCT application can enter the European phase within thirty-one months from the priority date under the Convention on the Grant of European Patents (European Patent Convention) and the Implementing Regulations to the Convention on the Grant of European Patents. Convention on the Grant of European Patents, done Oct. 5, 1973, art. 150, 1065 U.N.T.S. 199, 298, available at <http://www.european-patent-office.org/legal/epc/e/ar150.html> [hereinafter European Patent Convention]; Implementing Regulations on the Convention on the Grant of European Patents, done Oct. 5, 1973, rule 107 (last amended June 18, 2001), at <http://www.european-patent-office.org/legal/epc/e/r107.html>.

furnishing a translation, where necessary, of the application into the official language of the designated national patent office and paying to it the usual fees.⁸

While designating many countries in a PCT filing is a nominal expense, perfecting the filing in numerous individual countries at the PCT national stage becomes a large expense for the patent applicant. For a pharmaceutical patent application of one hundred pages and twenty-five claims, it would cost over \$400,000 to file national applications in all 125 PCT countries.⁹ This dollar figure assumes that translation efficiencies will be employed by using a single translation, such as Spanish, for countries requiring the same language. It also assumes that filings will be made in regional patent offices, such as the European Patent Office, rather than in each of the individual countries that are part of the regional convention.

With the high number of PCT applications that a pharmaceutical company files each year,¹⁰ it is not economically feasible to perfect filing in all of the PCT countries at the national stage. Nevertheless, if the application covers a potential commercial pharmaceutical product, a broad PCT national stage list

⁸ *Basic Facts about the Patent Cooperation Treaty* 6-7, WIPO Pub. No. 433(E) (Apr. 2002), available at http://www.wipo.int/pct/en/basic_facts/basic_facts.pdf.

⁹ There are no typical page and claim numbers; they vary greatly. The numbers used for this study were based on a random selection of PCT applications with claims to small molecule composition of matter (n = 100, median number of pages = 91, median number of claims = 25).

¹⁰ Pharmaceutical companies were listed among the most frequent PCT users based on the number of PCT applications published in 2003. Merck was the first named applicant on 197 PCT applications published in 2003, followed by AstraZeneca (193); Novartis (187); Glaxo Group Limited (178); Bristol-Myers Squibb (143); Isis Pharmaceuticals (130); Eli Lilly (113); Pfizer (113); Pharmacia (100); Smithkline Beecham Corp. (99); Wyeth (96); F. Hoffmann-LaRoche (94); Abbott (91); Boehringer Ingelheim (87); Pharmacia & Upjohn (84); Aventis (77); Millennium Pharmaceuticals (74); Incyte (72); Schering (70); Smithkline Beecham Plc. (58); and Warner-Lambert (57). For some companies the number of PCT publications is actually higher because their affiliates or acquired companies are listed separately on the Most Frequent PCT Users list. *Most Frequent PCT Users*, 7-12, PCT NEWSLETTER (WIPO), NO. 06, June 2004, at 7-12, available at http://www.wipo.int/edocs/pctndocs/en/2004/pct_news_2004_6.pdf.

will typically cover about fifty to seventy countries.¹¹ While the cost will vary depending mostly on the countries selected, the size of the application, and the number of claims, the PCT national stage will be one of the largest single expenses the applicant incurs. Furthermore, the applicant still faces future expenses associated with patent prosecution, issue fees, and annuities as well as a large expense to validate national patents in Europe after the European patent is granted.

If it is not feasible to seek patent protection in all countries, how much of the pharmaceutical market should be protected, and what countries should comprise the protected market? To answer this question, we adapted methodology used in a 1995 study by Michael Bednarik,¹² and focused our attention first on the PCT national stage, where one of the largest single expenses is incurred. The Bednarik study was not specific to pharmaceutical patents. There, the value of a patent was measured in two ways: by the country's population and by its gross domestic product.¹³ The value was then compared to the cost of getting a patent to reveal which national patents provided the most "bang for the buck."¹⁴

II. RETURN VALUE SCORE ("RVS") METHODOLOGY

In this study, we calculated a measure called the "Return Value Score" ("RVS"), which is the return on the dollars spent to file a patent application in a country based on the country's total annual pharmaceutical sales. We used 2002 and 2003 sales figures provided by IMS Health Services.¹⁵ Patent costs for filings in non-PCT countries and at the PCT national stage were calculated using Global IP Estimator software, based on a one-hundred-page application having twenty-

¹¹ Based on private communications with patent departments at pharmaceutical companies.

¹² Michael K. Bednarik, *Planning a Global Patent Strategy to Maximize Value: Where to Get the Most "Bang for Your Buck,"* 77 J. PAT. & TRADEMARK OFF. SOC'Y 381 (May 1995).

¹³ *Id.* at 382.

¹⁴ *Id.* In the Bednarik study, the top ten countries providing the best values for patent protection were the United States, India, United Kingdom, Canada, Japan, Germany, Brazil, France, South Africa, and Australia. *Id.* at 387.

¹⁵ Available from IMS Health, 660 West Germantown Pike, Plymouth Meeting, PA 19462-0905 (U.S.), and IMS Health, 7 Harewood Avenue, London, NW1 6JB, U.K. (worldwide).

five claims and two drawings.¹⁶ It assumes that the original PCT application was filed in English and includes the cost of translation and fees for the patent office and foreign agent. The cost of a Spanish translation was only included once, for a filing in Mexico.¹⁷

III. PHARMACEUTICAL SALES AND FILING COSTS

Table 1 shows the ranking of countries based on the size of their pharmaceutical markets. For this calculation, the total pharmaceutical sales in a country were taken as a percentage of 2002 total worldwide sales of approximately \$417 billion.¹⁸ Member countries of the European Patent Organization (“EPO”) and the extension states were grouped together.¹⁹ Filing in the EPO rather than in separate European countries is an option that is almost always selected by pharmaceutical companies desiring to cover Europe at the PCT national stage. Note that a separate analysis for the validation phase after the grant of a European patent is discussed below. Table 1 also includes the market-size rankings for non-PCT countries. The non-PCT filings, if any, would

¹⁶ Available from Global I.P. Net, 564 Kaiola Street, Kihea, Hawaii, 96753 (U.S.), and Global I.P. Net Europe, 363, Rue de l’Eolienne, 83260 La Crau, France (worldwide).

¹⁷ The practitioner should not assume that the use of a Spanish translation that was prepared for an equivalent Mexican application will be acceptable automatically in another country requiring a Spanish translation. For example, the Spanish Patent and Trademark Office requires that the translation be prepared by a Spanish patent attorney or a sworn interpreter appointed by the Spanish government. Nevertheless, it should be expected that the prior translation will help to greatly reduce costs.

¹⁸ Available from IMS Health, *supra* note 15. In 2003, total worldwide sales were about \$464 billion. *Id.*

¹⁹ As of December, 2004, the European Patent Convention consisted of the following contracting states: Austria, Belgium, Bulgaria, Switzerland, Cyprus, Czech Republic, Germany, Denmark, Estonia, Spain, Finland, France, United Kingdom, Hellenic Republic (Greece), Hungary, Iceland, Ireland, Italy, Liechtenstein, Lithuania, Luxembourg, Monaco, Netherlands, Poland, Portugal, Romania, Sweden, Slovenia, Slovakia, and Turkey. EUROPEAN PATENT OFFICE, EPO MEMBER STATES, at <http://www.european-patent-office.org/epo/members.htm> (last updated Dec. 1, 2004). Extension states include Albania, Bosnia and Herzegovina, Croatia, Latvia, the former Yugoslav Republic of Macedonia, and Serbia and Montenegro (formerly known as the Federal Republic of Yugoslavia). *Id.*

be made in accordance with the Paris Convention, within one year after the priority application was filed and usually eighteen months before the PCT national stage. An interesting observation is that the U.S., Europe, Japan, and the other top seven countries alone account for greater than 92 percent of the world pharmaceutical market.²⁰

Table 1 also shows the cost of filing a national patent application at the PCT national stage or earlier for the non-PCT countries. From the side-by-side comparison of market share versus cost, it becomes readily apparent that some countries (e.g., Norway) are disproportionately expensive. The last column of Table 1 shows the cost of translation as a percentage of the PCT national stage cost in the previous column. The variability of translation costs and their significance in the cost-benefit analysis are discussed below.

Table 1
Ranking of Countries Based on 2002 Pharmaceutical Sales

Rank	Country	Percent of World Market	PCT National Stage Cost (USD)	Translation Costs ²¹ (percentage)
1	USA	45.83	3,287	0
2	EPO (+ Extension States)	25.05	13,623	0
3	Japan	12.35	17,382	66
4	Canada	1.87	2,440	0
5	Mexico	1.76	7,351	57
6	China	1.44	8,032	64
7	Brazil	1.18	4,842	48
8	South Korea	1.11	12,386	65
9	India	0.92	1,963	0
10	Australia	0.87	3,006	0
11	Taiwan (non-PCT)	0.61	6,932	66
12	Saudi Arabia (non-PCT)	0.36	10,974	51
13	Venezuela (non-PCT)	0.35	2,650	*

²⁰ See *infra* Table 1.

²¹ An asterisk indicates a translation efficiency due to multiple countries requiring the same language. In such cases, translation costs are not included in the calculation of PCT national stage costs or in the calculation of filing costs for non-PCT countries.

Rank	Country	Percent of World Market	PCT National Stage Cost (USD)	Translation Costs ²¹ (percentage)
14	Russia	0.34	7,895	55
15	Indonesia	0.33	5,942	46
16	Argentina (non-PCT)	0.32	3,160	*
17	Colombia	0.29	5,417	*
18	Philippines	0.27	2,252	0
19	Norway	0.26	19,088	55
20	Pakistan (non-PCT)	0.23	2,350	0
21	Thailand (non-PCT)	0.21	7,735	68
22	Egypt	0.20	6,185	47
23	South Africa	0.19	2,014	0
24	Israel	0.17	2,208	0
25	Chile (non-PCT)	0.15	2,962	*
26	Ecuador	0.12	4,427	*
27	Morocco	0.11	9,976	72
28	New Zealand	0.10	1,972	0
29	Hong Kong (non-PCT)	0.10	2,687	*
30	Bangladesh (non-PCT)	0.10	1,596	0
31	Peru (non-PCT)	0.09	5,548	*
32	Malaysia (non-PCT)	0.08	2,362	0
33	Dominican Rep. (non-PCT)	0.07	2,912	*
34	UAE	0.07	5,227	*
35	Lebanon (non-PCT)	0.06	2,336	*
36	Ukraine	0.06	7,023	*
37	Singapore	0.06	1,684	0
38	Tunisia	0.05	3,505	*
39	Uruguay (non-PCT)	0.05	3,496	*
40	Belarus	0.04	5,932	*
41	Kuwait (non-PCT)	0.03	2,066	*
42	Jordan (non-PCT)	0.02	18,229	*
43	Paraguay (non-PCT)	0.01	3,276	*
44	Bolivia (non-PCT)	0.01	3,419	*

IV. RELATIVE COST-BENEFIT ANALYSIS AT THE PCT NATIONAL STAGE

For a cost-benefit comparison at the PCT national stage, each country was scored based on the size of the pharmaceutical market covered per dollar-patent cost. A raw score for each country was calculated by dividing its pharmaceutical sales by its filing cost (for non-PCT applications or at the PCT national stage). The raw scores were then normalized based on Japan having an RVS of one hundred. Table 2 shows the normalized RVS for each country.²²

Table 2
Value of Patent Spending per Country at PCT National Stage Based on
Size of Pharmaceutical Market

Rank	Country	Return Value Score (normalized)	Rank	Country	Return Value Score (normalized)
1	USA	1963	12	Argentina	14.1
2	EPO ²³	250	13	Pakistan	13.9
3	Canada	108	14	South Africa	13.3
4	Japan	100	15	South Korea	12.6
5	India	65.6	16	Taiwan	12.5
6	Australia	40.7	17	Israel	11.1
7	Brazil	34.2	18	Bangladesh	8.4
8	Mexico	33.7	19	Indonesia	7.8
9	China	25.2	20	Colombia	7.6
10	Venezuela	18.5	21	New Zealand	7.3
11	Philippines	16.8	22	Chile	7.0

²² Return Value Scores may be normalized based on any country without altering the results of the analysis. Normalization based on Japan provided numbers that were relatively easy to compare.

²³ Includes extension states.

Rank	Country	Return Value Score (normalized)	Rank	Country	Return Value Score (normalized)
23	Russia ²⁴	6.1	29	Lebanon	4.3
24	Hong Kong	5.0	30	Thailand	3.9
25	Singapore	4.9	31	Ecuador	3.8
26	Malaysia	4.8	32	Dominican Rep.	3.7
27	Saudi Arabia ²⁵	4.6	33	Tunisia	2.5
28	Egypt	4.6	34	Peru	2.4

²⁴ The Eurasian Patent Organization (“EAPO”) is a regional patent system which comprises Russia, Azerbaijan, Armenia, Belarus, Georgia, Kazakstan, Kyrgyz, Moldova, Ukraine, Turkmenistan, Belarus, and Tajikistan. EURASIAN PATENT ORGANIZATION, STATES PARTY TO THE CONVENTION, *at* www.eapo.org/eng/information/about.html (last visited Mar. 20, 2005). Comparative world pharmaceutical sales figures were only available for Russia, Ukraine and Belarus. A Eurasian patent may be granted on the basis of an international application filed in accordance with the PCT. *See* Eurasian Patent Convention, *done* Sept. 9, 1994, art. 20, *at* <http://www.eapo.org/eng/documents/konvenci.html> (last visited Mar. 20, 2005). At the PCT national stage, the filing of a one hundred page EAPO patent application costs \$13,980, about 46 percent of which is due to the cost of a Russian translation. Using the Global IP Estimator software, *see supra* note 16 and accompanying text.

²⁵ The Gulf Cooperation Council (“GCC”) has a regional patent system which comprises United Arab Emirates, Kingdom of Bahrain, Kingdom of Saudi Arabia, Sultanate of Oman, State of Qatar, and State of Kuwait. PATENT OFFICE OF THE COOPERATION COUNCIL FOR THE ARAB STATES OF THE GULF, ABOUT GCC PATENT OFFICE, *at* www.gulf-patent-office.org.sa/about_GC.htm (last visited Feb. 12, 2005). The GCC requires documents in the Arabic language. PATENT OFFICE OF THE COOPERATION COUNCIL FOR THE ARAB STATES OF THE GULF, GUIDELINES FOR FILLING OUT A PATENT REQUEST FORM, *at* <http://www.gulf-patent-office.org/sa/directions.htm> (last visited Feb. 12, 2005). Comparative world pharmaceutical sales were only available for Saudi Arabia, UAE, and Kuwait. The patent cost for each of these countries was based on a direct filing in the national patent office. The filing of a one-hundred-page GCC patent application costs \$15,573, about 50 percent of which is due to the cost of an Arabic translation. Using the Global IP Estimator software, *see supra* note 16 and accompanying text.

Rank	Country	Return Value Score (normalized)	Rank	Country	Return Value Score (normalized)
35	Uruguay	2.1	40	Kuwait ²⁶	1.1
36	UAE ²⁷	2.0	41	Belarus ²⁸	0.8
37	Norway	1.9	42	Paraguay	0.6
38	Morocco	1.6	43	Bolivia	0.3
39	Ukraine ²⁹	1.3	44	Jordan	0.2

Table 2 shows the relative benefit of spending a patent dollar to protect a pharmaceutical product in various countries based on filing costs up to the PCT national stage. In other words, it shows the “bang-for-the-buck” comparison. For example, it is not surprising that the United States would rank number one, but the scores reveal how much more value United States patent spending provides at this stage. The U.S. score is almost eight times greater than for Europe and twenty times greater than for Japan. The disparity between the U.S. and Europe, in the value of patent dollars spent, will be even greater down the road. As discussed below, this is because validation in individual European countries will require costly translations after the European patent is granted.

As expected, countries that accept patent applications in English and do not require translations generally score well. India, Australia, Philippines, Pakistan, and Israel all accept English translations and rank higher in Table 2 than they do in Table 1. In fact, the rankings of India (score = 65.6) and Pakistan (13.9) were surprisingly high.³⁰ On the other hand, Russia (6.1) and particularly Norway (1.9) notably were on the low end.

²⁶ See *supra* note 25.

²⁷ See *supra* note 25.

²⁸ See *supra* note 24.

²⁹ See *supra* note 24.

³⁰ Pakistan became a member of the Paris Union on July 22, 2004. Paris Convention for the Protection of Industrial Property, *done* Mar. 20, 1883, Paris Notification No. 211 (entered into force on July 22, 2004), at http://www.wipo.int/edocs/notdocs/en/paris/treaty_paris_211.html (notification occurred Apr. 22, 2004).

V. COMPARISON OF FILING STRATEGIES

The cost-benefit analysis can be used to develop and evaluate various global patent filing strategies. The data in Tables 1 and 2 can be employed to evaluate a potential filing in any grouping of the countries. By taking the percentage of the world market and filings costs for the entire group, an RVS can be calculated for the group in the same manner as described above for the individual countries. Using an Excel spreadsheet, we were able to evaluate a number of scenarios representing different countries for patent filings. The following examples illustrate how various filing strategies compare using this analysis.

Option A. All Countries in Table 2

A filing in all of the countries in Table 2 would cost an estimated \$283,000 and would cover countries that represent about 99 percent of the pharmaceutical market, based on 2002 sales figures. The Option A group has an RVS of 1.6.

Option B. All Countries with a score of 10 or better

From Table 2, the EPO and sixteen other countries have a score of ten or better: United States, EPO (and Extension States), Canada, Japan, India, Australia, Brazil, Mexico, China, Philippines, South Africa, South Korea, and Israel (at the PCT national stage), and the non-PCT countries Argentina, Taiwan, Venezuela, and Pakistan. These countries represent almost 95 percent of the world pharmaceutical market. At an estimated filing cost of \$96,000, this group would cost about 34 percent of the cost of filing in all the Table 2 countries. The Option B group has an RVS of 138.

Option C. PCT Countries with a score of 10 or better

This group includes the same countries as in Option B, but without the four non-PCT countries. The Option C countries represent about 93 percent of the world pharmaceutical market. At an estimated filing cost of \$81,000, this group would cost an estimated 29 percent of the cost of filing in all the Table 2 countries. The Option C group has an RVS of 161.

Option D. All Countries with a score of 20 or better

The countries that have a score of 20 or higher include the United States, EPO (and Extension States), Canada, Japan, India, Australia, Brazil, Mexico, and China. These are all PCT countries that represent about 91 percent of the world

pharmaceutical market, at about 22 percent of the cost of filing in all the Table 2 countries. The cost for this group is an estimated \$62,000. The Option D group has an RVS of 206. By selecting Option D over Option B, the applicant sacrifices exclusivity in 4 percent of the world market, but the filing costs decrease by about 35 percent.

Chart 1 illustrates how sharply costs increase when coverage of the world pharmaceutical market increases only a few percentage points above 90 percent. The country groups comprise the countries described above for Options A through D. When above 90 percent, the slope for the cost line is much steeper than the slope for the percentage of market coverage line. The cost line slope increases dramatically when market coverage gets above 95 percent.

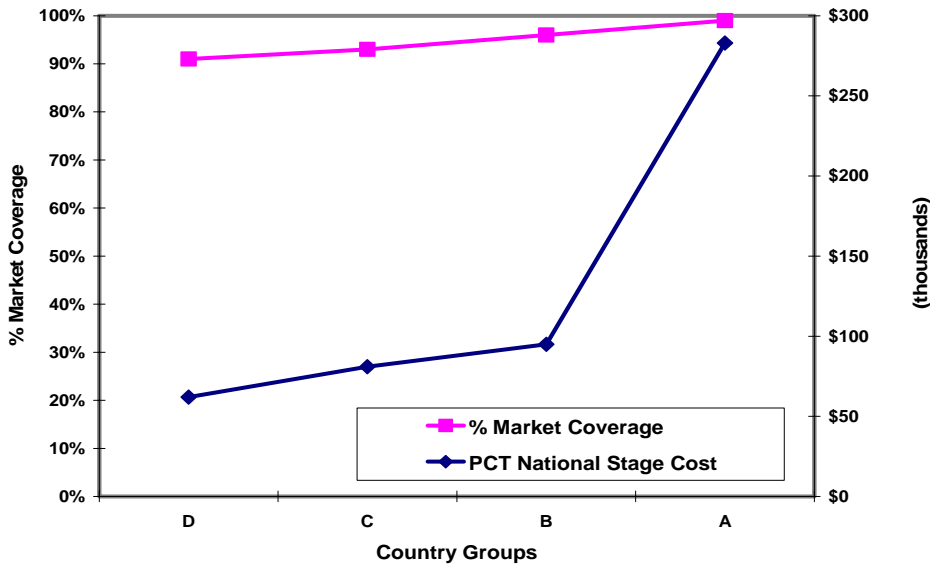


Chart 1

Percent Pharmaceutical Market Coverage versus PCT National Stage Cost

VI. IMPACT OF TRANSLATION COSTS

As expected, a significant cost component at the PCT national stage is the cost of translation. This cost is shown in the last column of Table 1 and ranges from about 46 percent to 72 percent of the total cost for the translation of one hundred pages. As a percentage of the total cost, the cost of translation will go up or down in a manner that is roughly proportional to the number of pages. In

practice, reducing the number of pages in the specification or negotiating a lower fee for the translation service or both will lower the cost. However, an interesting finding is that the translation cost is not likely to matter when the RVS is well below the minimum RVS that is selected as the basis for foreign filing.

To illustrate this point, consider a strategy to file in all countries that have an RVS of ten or better. Those countries would represent 94.5 percent of the world pharmaceutical market. Would it matter if one were able to obtain large savings on translation costs for countries that have an RVS of five or less? The answer is no, as shown using the calculations for Thailand and Norway. If the translation for a Thailand application could be obtained for only \$2,500, which is less than half of the estimated cost, the RVS would only improve from 4.5 to 6.8. Likewise, a 50 percent cost savings on a Norwegian application puts that translation cost in line with a French or German translation, but only improves the RVS from 2.2 to 3.1. The large cost savings in each of these examples would have little impact on the RVS scores, which remain well below ten. This finding makes sense when one considers that Thailand and Norway each represent only less than 0.3 percent of the world market. Generally, a translation cost savings does not matter when the RVS (and market size) drops well below the desired cut-off.

VII. RELATIVE COST-BENEFIT ANALYSIS FOR VALIDATION OF EUROPEAN PATENT

The EPO is a centralized patent grant system that was established in 1973 as a result of the European Patent Convention ("EPC"). It consists of thirty contracting states and six extension states.³¹ Under the EPC, a European patent can be obtained by filing a single patent application in French, German, or English.³² The European patent application then undergoes substantive examination in a unitary procedure that is binding on all the member states.³³ When the European patent is granted, it still must be validated in each

³¹ EUROPEAN PATENT OFFICE, *supra* note 19.

³² European Patent Convention, *supra* note 7, at art. 14(1), 1065 U.N.T.S. at 262, available at <http://www.european-patent-office.org/legal/epc/e/ar14.html>.

³³ *Id.* at art. 2(2), 1065 U.N.T.S. at 259, available at <http://www.european-patent-office.org/legal/epc/e/ar2.html>.

designated state for which patent protection is sought.³⁴ Under EPC article 65, any member state can require a translation, which has to be provided within three months after the European grant as part of the validation process.³⁵ Only Luxembourg and Monaco do not require translations.

The EPO Web site touts the European patent application as “[a] cost-effective and time-saving way of *applying for* patent protection in several different countries.”³⁶ The emphasis is added because the efficiency and cost savings pertain only to the European application and examination process. Broad European patent protection still requires a large expense after the European patent is granted. With the EPC countries using twenty separate official languages, most of the expense is in translation. Cost is particularly an issue in the pharmaceutical field, where a typical product patent tends to be much lengthier than average, requiring more pages of translation. For a patent containing twenty-five claims and requiring one hundred pages of translation, validation of the patent in all thirty-five European countries, including the extension countries, would cost an estimated \$180,000.³⁷

The EPO and the European Union (“EU”) have recently expanded to include several countries that are very small markets. The pharmaceutical market in Spain is larger than that of the eleven Central and Eastern European countries (“CEE”) combined.³⁸ In descending order of 2003 market size, the CEE countries are Poland, Hungary, Czech Republic, Slovakia, Slovenia, Bulgaria, Ukraine, Lithuania, Belarus, Latvia, and Estonia.³⁹ Eight of these countries, along

³⁴ See *id.* at art. 67, 1065 U.N.T.S. at 275, available at <http://www.european-patent-office.org/legal/epc/e/ar67.html>.

³⁵ *Id.* at art. 65, 1065 U.N.T.S. at 274-75, available at <http://www.european-patent-office.org/legal/epc/e/ar65.html>.

³⁶ EUROPEAN PATENT OFFICE, THE ADVANTAGES OF A EUROPEAN PATENT, at http://www.european-patent-office.org/gr_index.htm (last updated Sept. 1, 2003) (emphasis added).

³⁷ Using the Global IP Estimator software, see *supra* note 16 and accompanying text.

³⁸ See *infra* Table 3.

³⁹ *Id.*

with Malta and Cyprus, joined the EU on May 1, 2004.⁴⁰ Bulgaria, Ukraine, and Belarus are not yet members, although Bulgaria along with Croatia, Romania, and Turkey are candidates to join the EU.⁴¹ With this expansion and the increase in patent cost for covering the EU, a somewhat selective patent strategy would seem to make sense. However, a simple cost benefit analysis, as described above for the PCT national stage, does not account for the economic dynamics of the EU as a whole. A suitable strategy for obtaining adequate patent protection at a reasonable cost should consider not only the individual European countries, but also the interplay of markets within Europe. Individual markets within Europe are interdependent due to the free movement of goods (or parallel imports) and the price disparity among the countries. Because of this interdependence, a patent decision in one EU country may affect the return on a patent investment in another EU country.

In addition to the market complexities within Europe, another important consideration is that the CEE countries represent emerging markets that may grow at a faster rate than the pre-expansion EU market.⁴² In light of these factors, most pharmaceutical companies probably would take a conservative approach and seek patent protection in all of the EU countries for a promising development candidate. While broad coverage might make sense for one or perhaps two patents that protect a product, it might not be cost effective for additional patents on the product. Patents that cover various formulations, polymorphs, particular uses, or processes for making the product, especially when they do not extend in time beyond a base patent, would probably only require a more selective or "European-lite" strategy. In devising a European-lite strategy, applying the cost-benefit methodology described above to the European countries would be useful.

⁴⁰ EUROPEAN UNION, THE HISTORY OF THE EUROPEAN UNION, at http://europa.eu.int/abc/history/2004/index_en.htm (last visited Mar. 20, 2005).

⁴¹ EUROPEAN UNION, THE MEMBER STATES, at <http://www.eurunion.org/states/home.htm> (last visited Mar. 20, 2005).

⁴² See *Enhancing Income Convergence in Central Europe after EU Accession 81*, compiled in OECD ECONOMIC OUTLOOK NO. 74, Organisation for Economic Co-operation and Development (OECD) (June 2004), at <http://www.oecd.org/dataoecd/5/16/31920392.pdf> (last visited Mar. 20, 2005). The OECD monitors economic growth patterns on a regular basis. See OECD Economic Projections at <http://www.oecd.org>.

Table 3 shows the RVS for each of the European countries, their percent of the 2003 world pharmaceutical market, and European patent validation cost. The translation cost as a percent of the European patent validation cost and the non-translation component of the European patent validation cost are also shown. The asterisks show countries where efficiency in the translation is possible. For example, a French translation can also be filed in Belgium and Switzerland; a German translation is acceptable in Austria and Switzerland; an Italian translation is acceptable in Switzerland; a Greek translation can be used for both Greece and Cyprus; and a Czech translation can be used for both the Slovak and Czech Republics. Where the asterisk appears, the European patent validation cost was adjusted lower to account for the translation savings.

Table 3

Ranking of European Countries Based on Return Value Score⁴³

Country	Percent of World Market	EP Validation Cost (USD)	Translation Cost Percentage	Non-Translation Cost (USD)	Return Value Score (Normalized)
US	47.3	-	-	-	2229
UK	3.54	1,012	0	1012	610
Germany	5.67	9,065	84	1464	109
France	5.21	8,395	84	1337	108
Japan	11.3	-	-	-	100
Belgium	0.80	1,491	*	1211	94.1
Italy	3.56	8,279	85	1276	75.0
Switzerland	0.61	2,274	*	1274	47.1
Spain	2.51	9,854	73	2615	44.5
Ireland	0.20	1,349	0	1349	26.1
Turkey	0.80	6,766	78	1456	20.6
Greece	0.53	5,892	71	1692	15.8
Austria	0.53	5,873	*	4873	15.6
Poland	0.74	11,035	0	1035	11.6
Netherlands	0.74	11,140	91	1005	11.6
Slovak Rep.	0.11	2,060	*	1060	9.7
Slovenia	0.09	1,695	35	1095	9.5
Portugal	0.49	9,147	77	2147	9.3

⁴³ The countries shown are those for which pharmaceutical sales data are available.

Country	Percent of World Market	EP Validation Cost (USD)	Translation Cost Percentage	Non-Translation Cost (USD)	Return Value Score (Normalized)
Czech Rep.	0.25	5,705	81	1105	7.6
Bulgaria	0.07	1,921	41	1141	6.7
Luxembourg	0.03	902	0	902	6.0
Hungary	0.35	11,185	70	3342	5.5
Lithuania	0.06	1,851	19	735	5.5
Finland	0.34	14,331	67	4678	4.2
Latvia	0.02	1,451	41	861	2.8
Estonia	0.02	7,942	87	1065	0.5
Sweden	0.49	15,631	70	4650	5.5
Denmark	0.24	13,954	78	3001	3.0

The European countries listed in Table 3 represent over 27 percent of the world pharmaceutical market based on 2003 retail and hospital sales figures. The United States and Japan are included for comparison. The five major European markets are Germany, France, Italy, United Kingdom, and Spain. Together, these five countries represent 73 percent of the European market, at only 22 percent of the overall cost. As previously described, the RVS can be used as a guide to select and evaluate groups of countries. For example, a grouping consisting of Ireland (RVS = 26) and the seven countries with a higher RVS would represent nearly 79 percent of the European market, at 25 percent of the total cost. A grouping consisting of Portugal (RVS = 9.3) and the fifteen higher countries would represent 93 percent of the European market at a little more than 50 percent of the total cost. The problem countries for the patent owner are Sweden, Denmark, Hungary, and Finland. These four countries together represent only 5 percent of the European market, yet because of the translation requirement they account for almost one-third of the total cost of validation. Therefore, omission of these four countries might make sense in a European-lite strategy.

VIII. NET PRESENT VALUE ("NPV") OF PATENT PROTECTION

The cost-benefit analysis described above is useful for comparing the various countries and country groups in a relative sense. The Return Value Scores show, for example, that a patent dollar spent at the PCT national stage in Australia will protect three times more pharmaceutical sales than a patent dollar

spent in Taiwan, and will protect twenty times more sales than a dollar spent in Norway. The IMS Health pharmaceutical-sales data in combination with the IP Global Estimator cost data can also be used to show patent costs for various scenarios of market coverage. By selecting countries with the highest Return Value Scores, one can readily identify groups of countries that provide the greatest market coverage for the patent dollar spent.

This comparative analysis is a useful tool, but it only provides a relative cost-benefit evaluation. It tells us that a patent dollar in some countries has greater or lesser value than in other countries, but it does not tell us if we should actually spend the patent dollar anywhere. For example, consider two hypothetical countries: In the first country, patent protection is worth \$100 for every dollar spent; in the second country, the return is two to one. In relative terms, a patent dollar spent in the first country provides fifty times more bang for the buck. In absolute terms, however, the second country still may be a good investment. To know whether patent protection is worth the investment, we need to know how the cost compares to the present value of the expected future revenues that result from patent protection. Present value ("PV") is the discounted value of future cash flows that can be attributed to patent protection.⁴⁴ Net present value ("NPV") is the discounted value minus the patent cost.⁴⁵

What follows is our initial effort to estimate the value of patent protection in various countries. Attention was first directed to the smaller markets of the expanded EU, especially the CEE countries. Before EU and EPO expansion, we considered all of the EPO countries to be priority countries for the patent protection of a promising compound. This is consistent with the general consensus that such protection is desirable. However, should this assumption hold after EU expansion? Is it desirable to spend patent dollars in the new EU member states where the cost is relatively high and the market is relatively small? To address this question, we were aided in our analysis by the fact that there is or will be patent and regulatory uniformity within the EU, as discussed more fully below.

The key valuation component to be determined is the future revenue (or more specifically, profit) that results from patent protection. Where a patent

⁴⁴ RICHARD A. BREARLEY AND STEWART C. MYERS, PRINCIPLES OF CORPORATE FINANCE 14-15 (7th ed. 2003).

⁴⁵ *Id.* at 15.

exists, not all revenue can be attributed to patent protection. Even in the presence of generic competition some revenue will be realized, and this portion is not included in the NPV calculation. Also, revenue is not attributed to patent protection during periods of data or market exclusivity. Data exclusivity prevents regulatory authorities from accepting applications for generic drugs during the period of exclusivity. The five year data exclusivity period in the United States is relatively short compared to the EU.⁴⁶ New EU pharmaceutical legislation, enacted in 2004, applies the so-called 8+2+1 formula for new chemical entities (“NCEs”).⁴⁷ Under this formula, a generic application cannot be submitted until eight years after marketing authorization of the NCE, and the generic drug cannot be marketed for another two years.⁴⁸ This effective ten-year market exclusivity can be extended by an additional year if the innovator company obtains authorization for a significant new therapeutic indication during the first eight years.⁴⁹ If one adds the ten-year period of market exclusivity to the average of ten or more years it takes to get European marketing authorization after the PCT application is filed, a twenty-year patent term would not provide any additional exclusivity with respect to generic competition in Europe. Therefore, for the most part, revenue attributable to a European patent generally is produced during the period of a Supplementary Protection Certificate (“SPC”).

⁴⁶ Federal Food, Drug, and Cosmetic Act §§ 505(c)(3)(D)(ii), 355(j)(4)(D)(ii), 21 U.S.C. §§ 355(c)(3)(E)(ii), 355(j)(5)(F)(ii) (2004). Pursuant to the Act, no § 355(b)(2) application (Abbreviated New Drug Application, hereinafter ANDA) may be submitted by a generic manufacturer during the five-year exclusivity period which is granted to new drug applications for products containing chemical entities, except that an ANDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

⁴⁷ See generally Commission Regulation 726/2004 of 31 Mar. 2004 Laying Down Community Procedures for Authorization and Supervision of Medicinal Products for Human and Veterinary Use and Establishing a European Medicines Agency, art. 14(11), 2004 O.J. (L 136) 1, 10; see also EUROPEAN GENERIC MED. ASSOC., DATA EXCLUSIVITY, at <http://www.egagenerics.com/gen-dataex.htm> (last visited Mar. 20, 2005).

⁴⁸ Commission Regulation 726/2004, *supra* note 47.

⁴⁹ *Id.*

The SPC is a legal title that extends the duration of the exclusive patent right with respect to the drug.⁵⁰ The purpose of the SPC is to compensate for the patent term that is lost while the drug is under regulatory review before marketing authorization.⁵¹ The SPC is analogous to a patent term extension in the U.S. under the Hatch-Waxman Act, though there are some important differences.⁵² An SPC lasts for a maximum of five years after the basic twenty-year patent term expires, and up to fifteen years after the product is authorized to be placed on the market.⁵³ Therefore, for the NPV calculation in a country where there is an SPC and a ten-year marketing exclusivity period, we need only consider the revenues that are realized in years twenty-one to twenty-five after the PCT application is filed. This approximate window of time when product revenue can be attributed to patent protection corresponds approximately to years fifteen to nineteen after the European patent is granted.⁵⁴

Calculating the revenue due to patent protection requires the following inputs: (a) the amount of drug sales during the window of patent-only exclusivity; (b) the royalty (or margin) derived from the drug sales; (c) the probability of success, which is based on the likelihood that the European patent

⁵⁰ Council Regulation 1768/92 of 18 June 1992 Concerning the Creation of a Supplementary Protection Certificate of Medicinal Products, art. 4, 1992 O.J. (L 182) 1; Commission Regulation 1610/96 of 23 July 1996 Concerning the Creation of a Supplementary Protection Certificate for Plant Protection Products, art. 4, 1996 O.J. (L 198) 30.

⁵¹ See Council Regulation 1768/92, *supra* note 50; Commission Regulation 1610/96, *supra* note 50.

⁵² Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified in scattered sections of 15, 21, 28, and 35 of U.S.C.) [hereinafter Hatch-Waxman Act]. For the calculation of a patent term extension, see 37 C.F.R. § 1.775 (2004). Under the Hatch-Waxman Act, a patent term extension is equal to one-half of the time of the investigational new drug (IND) period, IND approval to the filing of a new drug application (NDA), plus the NDA period, the period during the NDA review. The maximum extension is five years and the total market exclusivity time cannot exceed fourteen years.

⁵³ See Council Regulation 1768/92, *supra* note 50, at art. 13, preamble; see also Commission Regulation 1610/96, *supra* note 50, at art. 13, preamble.

⁵⁴ The actual window may be slightly greater or less than five years, but five years is a reasonably conservative estimate that errs on the side of obtaining patent protection.

will protect a drug that makes it to the market; and (d) the percent loss in drug sales due to generic competition. The window of patent-only exclusivity (input (a)) extends from the end of marketing or data exclusivity to the end of the patent term, including any extension or supplemental protection. From the expected future revenue, during patent-only exclusivity, the PV can be calculated using a standard discount rate, which in turn can be obtained from the company's finance department. The NPV calculation can be illustrated using various European countries that have a low RVS value. To start, let's assume the following: (a) a drug with \$1 billion in annual worldwide sales; (b) a 20 percent royalty on sales of the drug in each of the countries;⁵⁵ (c) a 3 percent probability of success; (d) an 80 percent loss in sales due to generic competition; and (e) a 12 percent discount rate.⁵⁶ Based on these assumptions, the NPV of patent protection at the European patent validation phase was determined for various countries for a drug with worldwide sales of \$1 billion. The NPV was calculated based on revenues earned in the five-year period starting in year fifteen after the European patent validation phase.⁵⁷ The results are shown in Chart 2. Under this scenario, Denmark, Finland, Slovakia, Latvia, and especially Estonia have a negative NPV.

⁵⁵ A 20 percent royalty rate is a reasonable approximation for a company that expects to license its rights in the product. The margin may be higher for a company that markets its own product.

⁵⁶ A drug that averages \$1 billion in annual worldwide sales, five to ten years after the first commercial sales, would be a blockbuster. The average pioneer drug has a total life-cycle of fourteen to sixteen years, with significant sales-decay during the last six to nine years. See Hans H. Bauer & Marc Fisher, *Product Life Cycle Patterns for Pharmaceuticals and Their Impact on R&D Profitability of Late Mover Products*, 9 INT'L BUS. REV. 703, 709 (2000).

⁵⁷ All EU accession countries must comply with the entire body of EU pharmaceutical legislation; however, some countries are given limited time to bring their national legislation into compliance under transitional arrangements or derogations. See EUROPEAN COMMISSION, CHAPTER 1 – FREE MOVEMENT OF GOODS, at <http://europa.eu.int/comm/enlargement/negotiations/chapters/chap1/index.htm> (last updated Dec. 17, 2004). With respect to marketing exclusivity, the NPV analysis assumes that there will be harmonization by the time revenue is realized from an EP patent that is granted today.

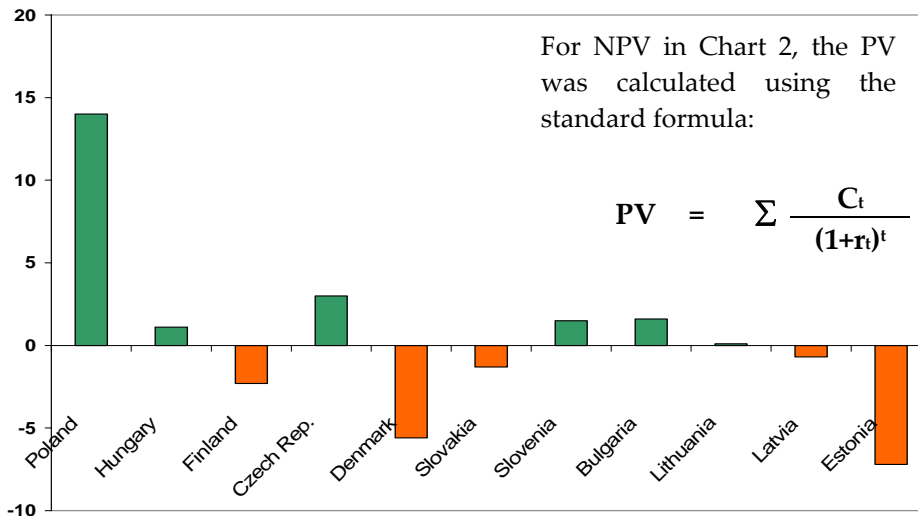


Chart 2

Net Present Value (in \$ Thousands) of Patent Investment at the EP Validation Phase for a Worldwide Billion-Dollar Drug⁵⁸

where PV is present value, C_t is the cash flow in year t , and r_t is the discount rate for year t . In other words, PV is equal to the sum of the discounted cash flows. Referring to the inputs for Chart 2, PV can be readily approximated using an Excel spreadsheet as follows: (Expected 5-YR Revenue)*(1.12)⁻¹⁷, where 1.12 is 1.0 plus the discount rate, and 17 is the average of the years 15 through 19, which corresponds to the window of patent-only exclusivity when the revenues from patent protection are being realized.⁵⁹ Note that the 17 is preceded by a minus sign because the $(1+r_t)$ term is in the denominator. The expected five-year revenue in a country is equal to 5 x (average annual sales) x (probability of success) x (percentage of royalty on sales) x (percentage loss in market share from generic competition). The NPV for a country is the PV for the country minus the cost of European patent validation. Note that this scenario is

⁵⁸ Key inputs are a five-year window of patent-only exclusivity starting at year fifteen; a 3 percent probability of success; and a 20 percent royalty of sales.

⁵⁹ The PV value is an "approximation," because 17 is used as the average of years 15 through 19. This average would be accurate if revenue over the time period is linear. However, there is usually a non-linear decay in sales over the time period. See Bauer & Fisher, *supra* note 56, at 709. The "[^]" symbol is used in an Excel spreadsheet to indicate an exponential term.

conservative in the sense that it is based on a blockbuster drug.⁶⁰ By the time patent-only exclusivity in Europe commences, the product is probably more than halfway through its product life-cycle, which averages fourteen to sixteen years. At this point, sales are beginning to decay from the competition of new drugs.⁶¹ Thus, sales tend to be in substantial decline throughout the period of patent-only exclusivity.

IX. SENSITIVITY ANALYSIS

Using the above PV formula, the inputs can be varied, and one can determine how sensitive the NPV calculation is to changes in our assumptions. For example, one can arrive at a more conservative scenario that would favor broader patent protection by making the following adjustments: (a) greater worldwide sales; (b) a higher probability of success in bringing the drug to the market; (c) a higher royalty or margin on sales; (d) a greater loss due to generic competition; (e) a lower discount rate; (f) a greater period of patent-protected revenue; and (g) a shorter time period between patent expense and market authorization. Because Slovakia is a country that had a slightly unfavorable NPV in Chart 2, it is good for illustrating the effect on NPV when changing some of the inputs. Chart 3 shows what happens to the Slovakian NPV when we change the probability of success, royalty rate, and period of time variables for patent-protected revenue.

⁶⁰ Patent managers tend to be more comfortable with a conservative approach. For this reason, we exemplify the NPV for patent investments protecting a blockbuster drug. The methodology is equally applicable if one were to assume lower average sales.

⁶¹ See Marc Fisher, Michel Clement, & Venkatesh Shankar, *International Market Entry Strategy: A Source for Late Mover Advantage?* 11 (unpublished seminar paper), at http://www.gsb.stanford.edu/facseminars/events/marketing/pdfs/S2004_Mktg_Sem_Marc_Fischer.pdf (Mar. 2004).

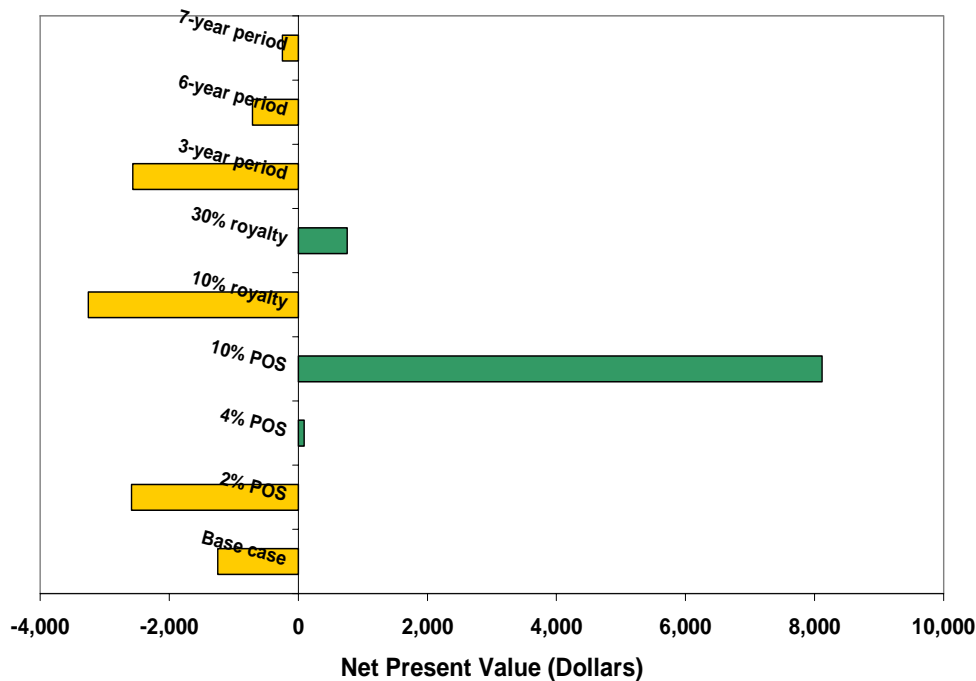


Chart 3

Sensitivity Analysis for Net Present Value of EP Patent in Slovakia⁶²

If a recently granted European patent protects a small molecular NCE that is in preclinical or clinical development, some of the inputs will be available as estimates from the company's project team manager. The project team for that NCE will have at least rough estimates of potential market size and the development timelines for the NCE and its estimated regulatory approval. From this information, the patent attorney can calculate the date that data and market exclusivity will end and how much patent exclusivity remains. Also, the project team manager can often provide a probability of success for the NCE. As can be seen in Chart 3, PV is very sensitive to probability of success. Among the inputs, probability of success is perhaps the least accurate of the estimates and depends

⁶² The base case for Slovakia assumed a 3 percent probability of success; a 20 percent royalty on sales; and a five-year period of patent-only exclusivity. With patent costs of \$5,260 at the EP validation phase, the NPV of the base case was a negative \$1,248. The chart shows the effect of changing the probability of success, royalty rate, and the period of patent-only exclusivity.

greatly on where the NCE is in development. Because of this sensitivity, a filing decision probably should not turn solely on whether an NPV is slightly negative or slightly positive.

When performing the NPV calculation for PCT countries outside the EU, it should be noted that most countries either have a shorter data- or marketing-exclusivity period or no data-exclusivity at all. For example, under the North American Free Trade Agreement, there is a minimum requirement of five years of data exclusivity that applies to the United States, Canada, and Mexico.⁶³ Iceland and Norway currently have a six-year period.⁶⁴ Other countries, including some that are members of the World Trade Organization (“WTO”), have no period of test data exclusivity.⁶⁵ This lack of data exclusivity runs counter to article 39(3) of the Trade-Related Aspects of Intellectual Property Rights (“TRIPs”) Agreement, which requires that the data be protected against unfair commercial use.⁶⁶ Some of the notable countries that provide for no or very limited test data exclusivity include Israel, India, Argentina, and Egypt.⁶⁷

⁶³ See North American Free Trade Agreement, Dec. 8-17, 1992, U.S.-Can.-Mex., art. 1711, para. 5, 6, 32 I.L.M. 605, 675.

⁶⁴ EUROPEAN GENERIC MED. ASSOC., *supra* note 47, at <http://www.egagenerics.com/gen-dataex.htm> (last visited Mar. 20, 2005).

⁶⁵ See U.S. TRADE REPRESENTATIVE, 2004 SPECIAL 301 REPORT (2004), at http://www.ustr.gov/assets/Document_Library/Reports_Publications/2004/2004_Special_301/asset_upload_file16_5995.pdf (last visited Mar. 20, 2005). [hereinafter 2004 SPECIAL 301 REPORT].

⁶⁶ The concept of data exclusivity is embodied in article 39(3): “Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use.” Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, LEGAL INSTRUMENTS—RESULTS OF THE URUGUAY ROUND vol. 31, 33 I.L.M. 81 (1994) [hereinafter TRIPs Agreement].

⁶⁷ Letter from L. Val Giddings, Vice President for Food and Agriculture, Biotechnology Industry Organization, to Mark Wu, Director for Intellectual Property, & Sybia Harrison, Staff Assistant to the Section 301 Committee, Office of the U.S. Trade Representative 2, 3, 6, 10, 11 (Feb. 13, 2004), at <http://www.bio.org/ip/action/3012004.pdf> (last visited Mar. 20, 2005).

A shorter period or no period of data exclusivity causes the window of patent-only exclusivity to shift to an earlier date. This shift is favorable to the NPV since the discount rate is applied over fewer years. In other words, the patent investment brings more value when it starts paying off earlier, and it pays off earlier when there is no other mechanism for exclusivity. There are other factors, however, that tend to make the NPV less favorable for many PCT countries outside the EPO. For one, patent investments at the PCT national stage occur earlier than at the European patent validation phase by about three to four years. In Norway, for example, a six-year period of marketing exclusivity does not improve the value of patent protection relative to the EPO countries. This is because the four fewer years of marketing exclusivity are offset by having to make the patent investment about four years earlier at the PCT national stage. Another factor to consider is that many countries do not provide for patent term extension beyond the typical twenty years. Countries where the patent term cannot be extended beyond twenty years include, among others, Thailand, Canada, China, Mexico, New Zealand, and Turkey.⁶⁸

Finally, the probability of success is likely to be lower at the PCT national stage than at the European patent validation phase for a pre-clinical or clinical candidate that is continuing to show promise. After entering the PCT national stage, another three to four years of preclinical and/or clinical information may result in a substantial change in probability of success for the compound, and consequently a substantial change in NPV.⁶⁹

As mentioned earlier, pharmaceutical companies tend to file patents claiming a promising product in about fifty to seventy countries. Some companies file in over ninety countries. This means that within the industry there are considerable differences regarding filing in at least fifteen to twenty countries. To determine whether it makes sense or is a good investment to seek patent protection in this group of lower priority countries, the NPV methodology described above can be useful.

⁶⁸ WORLD INTELLECTUAL PROP. ORG., HANDBOOK ON INDUSTRIAL PROPERTY INFORMATION AND DOCUMENTATION app. 3, at 3, 4, 10, 11, 15 (1996), at <http://www.wipo.int/scit/en/standards/pdf/03-09-02.pdf> (last visited Mar. 20, 2005).

⁶⁹ An interesting side note here is that there should be no rush to get a quick allowance of the European patent application during examination.

X. OTHER CONSIDERATIONS

While the cost-benefit analysis based on pharmaceutical sales and patent costs is a useful tool for designing a global filing strategy, there are other considerations that should be kept in mind. These considerations may impact the value of the patent or the desirability of seeking protection in a particular country. Some of these other considerations are discussed below.

A. *Projecting Future Sales*

The 2003 pharmaceutical sales figures may be a close approximation of sales in 2005, but today's patent filings cover new pharmaceutical products that will not reach the market for many years. What will the pharmaceutical markets look like far in the future when the product is first commercialized and during the subsequent years of the remaining patent term? Such projections can be estimated using IMS Health, as it provides sales trends for many countries.⁷⁰ With these numbers, it may be advisable to file in a country that has an RVS somewhat below the cut-off for the group that was selected, if robust sales growth for the country appears likely.

B. *Specific Disease Indications*

The pharmaceutical sales figures used above represent the total for all disease indications. However, market sizes will vary depending on the disease. For example, an obesity drug or cholesterol-lowering drug may not sell as well in Southeast Asia compared to a drug that treats infectious diseases. Also, the probability of success will differ depending on the disease. For example, the probability of success in going from the "IND" (investigation of a new drug) filing stage to market is about 28 percent for an anti-infective, but is roughly 15 percent for a central nervous system drug.⁷¹ The cost-benefit analysis can be refined by using sales figures and other inputs that are more applicable for

⁷⁰ Available from IMS Health, *supra* note 15. More information on the services IMS Health provides *available at* http://www.imshealth.com/ims/portal/front/indexC/0,2478,6599_1825,00.htm (last visited Mar. 20, 2005).

⁷¹ Troy Norris, Using Valuation for Real-World Decisions, Presentation before the 2004 Licensing Executive Society Annual Meeting in Boston (Oct. 17, 2004).

certain diseases or types of diseases. Annual pharmaceutical sales figures for selected diseases are usually available.⁷²

C. *Enforceability of a Patent*

Enforceability is difficult to factor into the analysis.⁷³ The cost-benefit analysis, above, does not consider whether a country's patent laws are strong or weak. There is a good argument to be made for simply ignoring this consideration. A country with weak patent protection today may have stronger patent laws in ten or twenty years. If globalization and an influential WTO fulfill their promise of strengthening weak economies, more robust patent protection may follow. Nonetheless, enforceability probably will not be a decisive factor unless the market size is small and other reasons for filing in the country are not that compelling.

D. *Parallel Trade in Europe*

How should parallel trade be factored into patenting decisions within the EU? Under EU law, parallel imports are permitted, so that a purchase of goods from the patent owner or licensee gives the buyer the right to import the goods into another EU country without the patent owner's permission.⁷⁴ For

⁷² Available from IMS Health, *supra* note 15.

⁷³ The World Economic Forum publishes two quantitative indexes that may be helpful for assessing whether a country has the stable political, legal, and social institutions necessary for patent protection. The indexes are the Growth Competitiveness Index, developed by Professors Jeffrey Sachs and John McArthur, and the Business Competitiveness Index, developed by Professor Michael Porter. For the 2004 indexes results, *see* http://www.weforum.org/pdf/Gcr/Executive_Summary_GCR_04 (last visited Mar. 20, 2005). An additional source is the U.S. Trade Representative (USTR). Pursuant to the Trade Act of 1974, as amended, the USTR issues an annual "Special 301 Report," which examines "in detail the adequacy and effectiveness of intellectual property protection in approximately 85 countries." For the 2004 SPECIAL 301 REPORT, *see supra* note 65.

⁷⁴ Commission Communication on Parallel Imports of Proprietary Medicinal Products for which Marketing Authorisations Have Already Been Granted, COM(03)839 final at 3, 6 [hereinafter Commission Communication]; *see also* Consolidated Version of the Treaty Establishing the European Community, Dec. 24, 2002, O.J. (C 325) 47, art. 28 (2002) [hereinafter EC Treaty].

example, drug prices are relatively low in Spain.⁷⁵ A portion of the drugs purchased from the patent owner or licensee in one of these countries can be resold at a higher price in England and Germany. Patent rights in England and Germany will not prevent parallel imports into these countries, because the principle of patent exhaustion applies throughout the EU; a patent owner exhausts his rights upon the first sale of goods anywhere within the EU.⁷⁶ It is important to keep in mind, however, that patent rights can be asserted against an importer who did not buy the drug from the patent owner or licensee.⁷⁷

Patent protection does not prevent parallel imports; such importation works to the detriment of the patent owner when the price is relatively low in a country of first sale, and there is enough supply of the low-priced drug to be moved elsewhere within the EU.⁷⁸ Price differentials and the volume of drug supply in the low-priced country are the main drivers of parallel trade.⁷⁹ This begs the question, whether the lack of a patent in a country of first sale will indirectly stimulate parallel imports. This could happen, for example, if the absence of a patent in one EU country invites competition and forces a lower price. The goods bought at this low price could be moved to a higher-priced country despite having patent protection there.

Because parallel imports depend largely on market factors that are unrelated to the patent situation in a low-priced country, it is not clear whether the absence of a patent in this country would cause an increase in parallel imports. An essential factor for parallel trade is having a sufficient volume of drug supply in the low-priced country.⁸⁰ In 2003, parallel trade growth slowed

⁷⁵ IMS HEALTH, PARALLEL TRADE – THE NUMBER ONE CONCERN IN EUROPE, at http://www.ims-global.com/insight/news_story/0210/news_story_021030.htm (Oct. 29, 2002).

⁷⁶ Commission Communication, *supra* note 74, at 10-11.

⁷⁷ See TRIPs Agreement, *supra* note 66, at art. 28.

⁷⁸ See Keith E. Maskus, Parallel Imports in Pharmaceuticals: Implications for Competition and Prices in Developing Countries 16, at http://www.wipo.int/about-ip/en/studies/pdf/ssa_maskus_pi.pdf (Apr. 2001) (final report to the World Intellectual Property Organization under terms of special service agreement).

⁷⁹ See *id.* at 11-12.

⁸⁰ See *id.*

considerably in both England and Germany after years of high growth.⁸¹ This has been attributed to more effective supply-chain management by pharmaceutical companies.⁸² Companies that can limit supplies flowing into countries like Spain can stem the tide of rising parallel trade.⁸³ In two recent European cases,⁸⁴ pharmaceutical companies withstood challenges by wholesalers who claimed that the companies' supply-management systems were anti-competitive.⁸⁵ At least for now, it appears that an effective supply-management system can mitigate substantially the loss in revenue due to parallel trade.

E. *Other Costs*

The cost-benefit analysis described above is based only on patent filing costs at the PCT national stage and the European validation phase. These are the largest expenses for the applicant who desires broad coverage of a

⁸¹ NEIL TURNER, IMS HEALTH, PRICING & REIMBURSEMENT REPORT: PRICING CLIMATE HEATS UP IN U.S. AND EUROPE 4, at http://www.imshealth.com/vgn/images/portal/cit_40000873/35/60/56695191PE_PriceClimateHeatsUp_Aug04.pdf (July 2004).

⁸² *Id.*

⁸³ Note, however, that article 81(1) of the EC Treaty prohibits agreements that have the purpose or effect of restricting competition. EC Treaty, *supra* note 74, at art. 81(1).

⁸⁴ Joined Cases C-2/01 P & C-3/01 P, Bundesverband der Arzneimittel-Importeure eV v. Bayer AG, [2004] 4 C.M.L.R. 13 (2004). The European Court of Justice (ECJ) dismissed an appeal by the European Commission from an earlier ruling that there was no abuse of dominant position by Bayer when it restricted the supply of its anti-hypertensive drug Adalat in Spain. *Id.* at para. 141. The European Commission had ruled that Bayer's practice was a violation of article 85(1) (now article 81(1)) and fined Bayer €3 million. *Id.* at para. 10, 12. The Court of First Instance annulled the fine. *Id.* at para. 16.

⁸⁵ *Id.* In a case before the French Competition Council, Phoenix Pharma, a pharmaceutical products wholesaler, alleged that ten pharmaceutical companies, including GlaxoSmithKline, Pfizer, and Eli Lilly, had a supply system designed to freeze market share and competition. The Council dismissed the challenge by Phoenix Pharma. *France: Abuse of Market Power*, EC Nat'l Competition Report (Cleary Gottlieb, Brussels), at 3, at http://www.cgsh.com/files/tbl_s47Details%5CFileUpload265%5C167%5CNational%20Competition%20Report%201Q%202004.pdf (Jan.-Mar. 2004).

pharmaceutical product, but they are not the only expenses. For example, maintenance fees in countries can vary quite a bit.⁸⁶ It should be noted that the analytical method presented here can be adapted to consider these costs as well.

F. *Additional Patent Protection*

The cost-benefit methods described above are applied to a single patent application covering a single pharmaceutical product; however, most promising pharmaceutical products are protected by more than one patent or application.⁸⁷ Typically, a company will build a patent estate around a product rather than rely on a single patent for protection. For example, the patent estate may include two applications covering the composition of matter for an NCE, where the first application claims the structure generically and the second claims it specifically. Furthermore, the method-of-use claims may or may not be in the same application as the composition-of-matter claims. The estate may also include patent applications that are directed, for example, to a particular polymorph, a manufacturing process, picket-fence chemistry, a combination therapy, a formulation, or a new use. Not only will a product usually be protected by different patents, but the patents may expire at different times. Obviously, not every patent or patent application in the patent estate will have the same value.

Since the RVS method compares countries and groups of countries in a relative sense, different patent applications covering the same product can be treated independently. This means that for a particular patent application, the RVS analysis itself will be unaffected by the presence of other applications in the patent estate. Consider, for example, a first application having generic claims to a product composition and a second application claiming the same product specifically. For each of these applications, the RVS analysis would be the same. There will always be more “bang for the buck” when countries are selected based

⁸⁶ *E.g.*, USPTO Fees and Payment of Money, 37 C.F.R. § 1.20(e)-(h) (2004); IP Australia, Patent Fees, at http://www.ipaustralia.gov.au/patents/fees_index.shtml#roughguide (2004); CANADIAN INTELLECTUAL PROPERTY OFFICE, COMPARISON OF FEES CHARGED BY CIPO FOR TRADEMARK AND PATENT ACTIVITIES IN COMPARISON TO OTHER JURISDICTIONS, at http://strategis.ic.gc.ca/sc_mrksv/cipo/con_dis/fee_review3-e.html (last modified Dec. 31, 2002).

⁸⁷ *See, e.g.*, Pfizer, Inc., Annual Report for the Fiscal Year Ending December 31, 2004, at 8-9 (Feb. 28, 2005), available at <http://www.sec.gov/Archives/edgar/data/78003/000095012305002379/y06124e10vk.htm#112>.

on having a higher RVS score.⁸⁸ This does not mean, however, that the same RVS threshold should be chosen for each application. Most likely, the RVS threshold for selecting countries will be chosen on a case-by-case basis, depending on the type of invention, the expiration date of the patent, and consideration of the overall patent estate.

The NPV of a patent application, on the other hand, may be affected by other patent applications that relate to the same product. However, the NPV analysis is simplified by assuming that the most important or key patent application accounts for almost all of the value of the patent estate. The key application is the one that provides the most protection against generic competition. This is usually the application that would be chosen for patent-term extension or supplementary protection, if available. Assigning almost all of the value of a patent estate to a single application is a conservative assumption that errs on the side of broad geographic coverage. This does not mean that the other patent applications have zero value, but they will probably be much less valuable than the one or two most important applications in the patent estate. Knowing the PV of the key application helps to put the value of the others into perspective. The PV analysis of the key patent application, together with a sense of the relative value of each of the remaining applications, is a useful guide for determining whether a particular patent cost is justified, in view of the other assets in the patent estate.

XI. CONCLUSION

Annual worldwide pharmaceutical sales figures and commercial software for estimating patent costs were used to develop a simple cost-benefit analysis tool. This cost-benefit analysis is useful for evaluating and developing global patent filing strategies for pharmaceutical products, enabling the applicant to maximize the value of the patent dollars it spends. What is most revealing from the analysis is the significant additional cost it requires to gain a few more percentage points of market coverage, beyond the countries that already represent about 91 percent to 95 percent of the world market. After about 90 percent of the market is protected by patent filings in the largest countries, incremental market coverage comes at a steep increase in cost. At Millennium Pharmaceuticals, we have used this type of analysis in devising our

⁸⁸ Pharmaceutical sales data in a particular country may not be relevant for some inventions, such as a manufacturing process. For example, this analysis does not address the value of a patent in a manufacturing country that is not the intended market for a product.

global patent filing strategy. We have also begun to model the value of patent protection in various countries where the RVS score is low, especially the smaller markets of the expanded EU. Future efforts will be directed toward refining the cost-benefit model by focusing on some of the considerations discussed above.