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INTRODUCTION

PhRMA 2003 Intellectual Property Protection Objectives

Strong intellectual property protection (IPP) remains critical to continuing progress in new drug development for the benefits of patients in the U.S. and abroad. The drug development process continues to be a long, expensive and risky process, and PhRMA members rely on strong USG advocacy to ensure adequate and effective IPP in our commercially important overseas markets.

PhRMA member companies greatly appreciate continuing USG advocacy efforts to promote full compliance with the World Trade Organization (WTO) Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS). Given the difficult external environment of the last year, we appreciate all the more the tangible progress towards overall TRIPS compliance that has occurred in the last twelve months. There have been some important positive developments in meeting and exceeding minimum international standards for intellectual property protection (IPP), including the conclusion of two bilateral Free Trade Agreements that provide for clarification and enhancement of IP standards. Nonetheless, much work remains. PhRMA's comments on issues in individual countries also set forth our overall IPP objectives for this year,[*] which this introduction seeks to underscore.

Our highest priority remains the adoption and implementation of patent and other IP laws, which embody clear and enforceable standards, in order to bring WTO members into compliance with their TRIPS obligations. Second, PhRMA members seek continued USG advocacy to achieve heightened commitments in all WTO members to provide effective protection for commercially sensitive and confidential clinical dossiers associated with applications for marketing approval (data exclusivity). Third, we believe that there should be greater emphasis on the value of trademarks, which provide tremendous benefits to consumers generally and to patients taking medicines in the developing world. In this area as well, there is a greater need for effective enforcement of TRIPS standards. Finally, the continuing thread running through all of the above is the critical need for the U.S. to continue and intensify its efforts to provide technical assistance and training for WTO developing countries and other trade partners.

[*] The following should be read in the context of the extended TRIPS deadline now of 1016 for Least Developed Countries, so that while we seek continued capacity building for LDCs to provide needed technical assistance and training, we have not submitted any comments on IP regimes in LDCs.

TRIPS Implementation

We are pleased to note, due in large part to the sustained efforts of U.S. trade negotiators and our diplomats based abroad, the passage of TRIPS-compatible legislation by WTO members in 2002 that is intended to bring them into conformity with the minimum international TRIPS standards. Egypt, Chile, China provide notable examples of countries that have taken significant steps in this regard. This reflects the growing awareness in developing countries of the importance of patent and related disciplines in promoting foreign direct investment and sustainable economic development. However, implementing regulations and actual enforcement of TRIPS systems always lag passage of legislation. We greatly appreciate the continuing efforts of USG officials to assist in this process. In 2003 we need to both intensify efforts to bring remaining outliers into alignment with their international TRIPS obligations and to bring a greater focus to enforcement issues relating to patent and other TRIPS elements.

Effective Data Exclusivity

Effective legal protection for undisclosed information - - the clinical dossiers lodged with health regulatory authorities in association with applications for marketing approval --- remains a critical priority for PhRMA members.[#] Again in this area, we would like to acknowledge the continuing and effective USG advocacy which has brought an increasing number of our trade partners closer to compliance with this important TRIPS obligation (TRIPS Article 39.3). Chile, China, and Colombia are among those WTO members who have adopted or implemented new regulations for protection of clinical data in recent months. But enactment of laws alone does not ensure effective data exclusivity. A number of our important trade partners, including Argentina, Hungary, and Poland, have adopted data exclusivity laws that do not meet minimum international standards. In other cases where WTO members have facially compliant legislation we have substantial enforcement problems, including in Canada and Mexico where there is good paper protection for undisclosed information. And there remains a very small but important subset of countries that deny the WTO TRIPS obligation altogether, and provide no effective protection for the commercially valuable and confidential data related to PhRMA members applications for marketing approval. Despite the growing number of WTO members that have taken positive steps to come into conformity with TRIPS Article 39.3, Israeli and Turkish officials have stated that they are not convinced, in the absence of a WTO panel holding, that there is an affirmative obligation. Taiwan has also lagged in implementing needed 39.3 protection. We appreciate continuing USTR leadership on this important issue in the coming year and urge consideration of a possible launch of a WTO dispute settlement case to define the obligation contained in TRIPS Article 39.3.

[#] See Appendix A.

Effective Trademark Protection

Trademark protection[+] has been incorporated into TRIPS laws of most WTO members. PhRMA members remain concerned, though, that developing country members and particularly least developed countries (LDCs) may lack the domestic resources to fully implement and enforce trademark protections. Without effective enforcement, protection on paper for PhRMA member trademarks amounts to little. In addition, it is in the LDCs that trademark protection is most needed to provide consumer protection against spurious, low quality medicines, especially for their most vulnerable populations. We ask the U.S. Government to devote more resources to trademark advocacy and enforcement training over the next year.

Capacity Building

Capacity-building is a critical factor in achieving the above PhRMA IPP priority areas. To that end, we rely on U.S. Executive Branch agencies to continue to play a strong role in ensuring adequate training and technical assistance to build the capacity for WTO aspirants to participate meaningfully in the WTO and to implement their trade commitments. Towards this end, we applaud the creation within USTR of the new position of Deputy Assistant U.S.T.R. for Capacity Building and appreciate as well the efforts of the interagency Training Coordination Group (TCG). Acting through bilateral programs as well as in combination with other international organizations and/or Non-Government Organizations, the USG should continue to offer up substantial assistance to build capacity for drafting and updating relevant IP legislation and regulations, enforcing IP standards (through, for instance, the training of judges, prosecutors, health regulatory officials, customs officers and investigators), granting patents and registering trademarks and assisting in the development of IP education and training curricula. Improvements in these areas will lead to a more stable and business-friendly environment for foreign and domestic goods and services providers. This should also help thwart the increasingly widespread practice in some countries of counterfeiting pharmaceutical products, which results in unsafe drugs, and help address continued government corruption and bribery.

PhRMA members hope that their efforts can complement stepped-up U.S. and international public assistance on capacity-building in developing countries. For example, PhRMA is working closely with the Government of Jordan to implement a best-practices model for effective data exclusivity and linkage between the industrial property and health regulatory authorities. This will also have the impact of automating and expediting the approval process for both generic and innovative pharmaceutical products in Jordan. PhRMA is also working with organizations based in China, India and South Africa on possible modalities for broader participation in WTO and/or other

[+] See Appendix B.

technical assistance and training programs to bring the benefits of globalization to these important markets.

PRIORITY FOREIGN COUNTRIES

ARGENTINA

Argentina has traditionally been the most serious violator of intellectual property rights in Latin America. During 2002, Argentina and the United States reached partial settlement on the World Trade Organization (WTO) case pending since 2000. However, the two most commercially significant issues – data protection and adding product patent claims to pending process patent applications – were not settled and continue to cause serious commercial damage to PhRMA members. We are also concerned that pending legislation to amend the patent law will effectively limit availability of preliminary injunctions. Also, a new law mandating generic-only prescriptions diverts sales from PhRMA members' trademarked products sales to products that infringe intellectual property rights and fail to meet minimum international standards under the WTO Agreement on Trade Related Intellectual Property (TRIPS). We remain convinced that Argentina will not institute full protection of our intellectual property until mandated to do so by the WTO. In current circumstances, PhRMA has no recourse but to continue to seek Priority Foreign Country (PFC) for Argentina in 2003.

Intellectual Property Protection

Argentina's 1996 patent law came into force in October 2000. Because of its numerous deficiencies, ambiguities and contradictions, the law does not adequately protect intellectual property, is not compliant with TRIPS, and formed the basis of a U.S. WTO case against Argentina, which has been partially settled. In June 2002, the Government of the United States of America and the Republic of Argentina notified the WTO Dispute Settlement Body (DSB) that they reached an agreement on the matters raised by the United States in document WT/DS171/1 (*Argentina – Patent Protection for Pharmaceuticals and Test Data Protection for Agricultural Chemicals*) dated May 6, 1999 and in document WT/DS196/1 (*Argentina – Certain Measures on the Protection of Patents and Test Data*) dated May 30, 2000. The agreement established solutions for the following issues: (a) product by process patent protection, (b) shifting of the burden of proof in process patent infringement cases, and (c) preliminary injunctions. However, the settlement depends on the passage by the Argentine National Congress of draft legislation sent to the Senate on October 22, 2002.

Patents and Data Exclusivity

Despite the improvements that this settlement represents, the situation remains extremely difficult for the research-based pharmaceutical industry. Negotiations between the U.S. and Argentina did not resolve the most commercially significant problem: the intellectual property protection of the confidential and proprietary data developed by the research-based pharmaceutical industry to demonstrate the efficacy and safety of new medicines. Argentine health regulatory authorities continue to rely

inappropriately on the originators' data to approve unauthorized copies of innovative medicines. Argentine law 24.766, which regulates the disclosure and protection of test data, allows any competitor to begin marketing the innovator's product no later than 120 days after a request to market a copy product is filed, without having to undertake the expense of proving that the product is safe and effective. This clearly violates Article 39.3 of TRIPS. Because the Argentine Government consistently has refused to settle this portion of the dispute with the U.S., we remain convinced that only a decision by the WTO dispute settlement panel will induce change in Argentina.

Although preliminary injunctions are provided for in the draft legislation before the Argentine National Congress, the necessary conditions for grant of an injunction according to the draft are much more onerous than the de facto conditions currently applied in the courts. We are concerned that the effect of this legislation will be to halt injunctions because: (a) a technical expert must be appointed to the court from an established list, and it is unlikely that the local expert will have the necessary expertise to analyze pharmaceutical patents; and (b) it must be shown that harm to the patentee exceeds harm to the alleged infringer. Arguments by the alleged infringer that local industry will be damaged are likely to hold sway.

There are other important deficiencies in Argentina's intellectual property regime:

- Although the industrial property office (INPI) began issuing pharmaceutical product patents – for the first time in Argentine history – on October 24, 2000, few of the patents issued thus far have been for commercially significant products. The backlog of patent applications in INPI has not been remedied in spite of industry's attempts to propose alternatives intended to provide relief for patent applicants who encounter difficulties in enforcing patent rights.

- Health regulatory authorities continue to register copy products without taking into account the existence of patent rights.

- INPI has issued a directive (Circular A.N.P. Nº 008/02) prohibiting the grant of patents for second uses of known compounds.

- Compulsory licensing provisions are overly broad, defining price-fixing inappropriately and characterizing it as a situation where there are supply offers in the market at significantly lower prices than the patentee's price for the patented product.

- The Argentine Supreme Court rejected the conversion of pending process patent applications into product patents, as well as the revalidation of foreign patents.

- Procedures related to border measures (TRIPS Section 4) have not been adopted.

- Argentina issued in September 2002 a new ruling (Circular A:N:P. no. 008/02) that "second medical use" claims of any kind are no longer patentable.

Trademarks

Law 25.649, adopted in 2002 by the Argentine Congress, creates a serious and unjustifiable restriction of the use of trademarks. This law orders medical doctors to use the generic name of the medicine in all prescriptions. This compulsory prescription by generic name discriminates against trademarked innovative products. The research-based industry recognizes the importance of generic products in the pharmaceutical marketplace. However, true generics do not exist in Argentina, because copy products are not required to demonstrate their bioequivalence or bioavailability (i.e. their interchangeability) with original products. According to the regulations to Law 25.649, the doctor may also include the trademark in his or her prescription, but pharmacists may offer a substitute. If the medical doctor does not want the prescription substituted at the pharmacy, reasons must be indicated on the prescription. The effect of this law is the diversion of sales from innovative medicines to TRIPS infringing copy products.

Damage Estimate

Substantial and continuing loss of market share is directly attributable to Argentina's defective intellectual property regime. A study conducted in 2001 by Charles River Associates estimates those losses at $260 million annually (please see Appendix B). The pharmaceutical market contracted significantly in 2002 due to the serious financial crisis in Argentina. However, the new restriction on trademarks will increase our losses in relative terms. Please see Appendix C for a broader CRA study which estimates total losses in Argentina conservatively more than $750 million dollars a year.

PAKISTAN

The commercial environment in Pakistan suffers deficiencies in intellectual property protection as well as from a broad range of market access barriers as indicated in prior submissions for the National Trade Estimate Report. With regard to intellectual property protection, serious concerns exist with amendments made effective to the new patent law in October 2002 that will cause grave injury to the U.S. research based pharmaceutical Industry. PhRMA and its member companies also remain concerned by TRIPS-inconsistent trademark policies and the failure to provide 39.3 data protection.

In the context of the Administration's renewed focus on South Asia, PhRMA supports allocation of foreign assistance resources towards capacity building in Pakistan to support technical assistance and training towards the adoption and/or implementation of TRIPS obligations. The Government of Pakistan would benefit greatly from technical assistance for capacity and administrative building in infrastructure needed to effectively administer a patent examination process and implement effective data exclusivity (by the Ministry of Health). Given renewed and expanded U.S. assistance to Pakistan and the need for Pakistan to receive assistance as a developing country WTO member, PhRMA believes that this should be a high priority use for U.S. assistance funds to Pakistan.

Due largely to the adoption of extreme changes to the Patent Act and continued failure to adopt required TRIPS consistent 39.3 protection, PhRMA requests that Pakistan be designated as a Priority Foreign Country in terms of the Special 301 cycle for 2003.

Intellectual Property Protection

Patents

In January 2001, a new patent ordinance was promulgated which made incomplete though promising strides towards recognizing TRIPS level obligations. To date no rules or regulations have been released on this legislation. More troubling than the non-issuance of underlying regulations are changes made to the Act in 2002 that drastically inhibit the ability of U.S. based pharmaceutical companies to enjoy effective and meaningful patent protection in Pakistan.

The new amendment to the patent act, effective from October 2002:

- Eliminates use patents;

- Restricts patent filings to single chemical entities for pharmaceutical and agrochemical inventions;

- Restricts protection for derivatives or salts;

- Introduces onerous barriers to patenting bio-technology based inventions;

- Allows for parallel importation by parties unrelated to the patentee, for example, a compulsory licensee; and

- Establishes a mechanism for compulsory licensing if an invention has not been worked in a manner that promotes the "transfer and dissemination of technology".

Together, these amendments seriously devalue intellectual property rights in Pakistan and are inconsistent with Pakistan's current and future TRIPS obligations in both terms of spirit and law.

Furthermore, the Ministry of Health continues to register generic copies of patented products of US and other multinational pharmaceutical companies. In all practical matters, current and expected patent protection in Pakistan remains inconsistent with WTO obligations and disadvantages U.S. based multinationals.

PhRMA seeks the timely issuance of appropriate and transparent rules and regulations that underlie the Patent Act and the immediate withdrawal on the newly implemented, TRIPS inconsistent patent law amendments.

Data Exclusivity

As no administrative or legal right exists, in contravention of Pakistan's WTO obligations, PhRMA seeks expeditious adoption of either regulatory or legislative provisions to provide effective data exclusivity per TRIPS Article 39.3. To date, Pakistan remains out of compliance in not providing protection against unfair commercial use of data provided to the Government of Pakistan as a condition for marketing approval of pharmaceutical products. Such protection should preclude direct and indirect reliance by the Ministry of Health on the data package used to support initial marketing approval of the originator product for a period not less than 5 years. Protection should extend to the data itself as well as to conclusions based on that data, so that an application not filed by the innovator could not be made until the full term of protection has expired unless such party generated its own supporting data.

Trademark Protection

By Pakistan Government notification dated August 24, 1994, the non-proprietary or generic name of the substance has to be printed "with at least equal prominence as that of the brand name." The Pakistan Government has carried this forward as policy. The addition of the generic name in equal prominence to the trademark constitutes an infringement of the proprietary rights of the originator. This is intended to dilute existing differences in quality, efficacy and safety, and incorrectly implies total interchangeability and equality of two different products. In fact, Pakistan has no effective bioequivalence or bioavailability regulation in place. In this context, erosion of trademark protections constitutes a public health threat to Pakistan's most vulnerable populations (See Appendix B). PhRMA asks the U.S. Government to note that these laws conflict directly with Pakistan's obligations under WTO TRIPS rules protecting trademarks (TRIPS Article 20, indicating that "[t]he use of a trademark shall not be unjustifiably encumbered by special requirements . . . "), and therefore should be amended to comply with TRIPS.

Local Manufacture Requirement

PhRMA member companies operating in Pakistan face additional hurdles that devalue or limit the right to enjoy intellectual property rights the Ministry of Health insists on local manufacture as a condition of registration. This violates Pakistan's WTO TRIPS obligations (Article 27.3) and is generally not possible. Often products are manufactured at only one site from where they are supplied to other markets and the quantities required for Pakistan are so low that local production is not feasible. The result, effectively, is that registration of new chemical entities is often denied.

Damage Estimate

The absence of adequate patent and data protection together with other market access barriers results in total losses for the research-based pharmaceutical industry of $50 to $100 million per year. These losses represent a significant threat to the industry's ability to continue operations in Pakistan, and, more importantly, do not reflect the inherent damage unacceptable amendments to the Patent Act may make in other markets that may follow Pakistan's precedent.

POLAND

Despite the concerted and continuing efforts of the U.S. Government to gain compliance with international treaty obligations, the Government of Poland continues to fall short of providing effective protection for patented pharmaceutical products, processes, and for protected data. PhRMA members remain seriously concerned by the decision of the Government of Poland to curtail the effective protection of confidential test data until Poland's accession to the EU. PhRMA members are also particularly concerned that health regulatory authorities have granted marketing authorization to at least one unauthorized copy of a product still protected by a valid product patent. This copy product could soon appear on the Polish market. In addition, PhRMA members attempting to do business in Poland continue to suffer from market access barriers, including a lack of transparency in the Government pricing and reimbursement system for pharmaceuticals. Unfortunately, little has changed in the last year and Poland is no closer to providing adequate and effective protection for intellectual property rights relating to pharmaceutical products. Because of the importance of data exclusivity to PhRMA members, the general erosion of patent and other IP protection in Poland and an increasing array of market access barriers, PhRMA requests that Poland be identified as a Priority Foreign Country through the 2003 annual "Special 301" review process.

Intellectual Property Protection

More than three years after Poland's deadline for implementation of the World Trade Organization (WTO) Agreement on Trade Related Intellectual Property (TRIPS), Poland has failed to meet minimum international requirements for the protection of intellectual property related to pharmaceutical products. This is true across the board for data exclusivity and patent rights.

Data Exclusivity

Article 39.3 TRIPS requires WTO members to protect against "unfair commercial use" of the costly and confidential test data submitted to Governments as a condition for obtaining marketing approval of pharmaceutical products. Data exclusivity is an independent form of intellectual property protection that may not be linked to the existence of a patent. In the absence of effective patent protection for in-line products, however, data protection is the only means to protect innovative products still under patent in the U.S. and Europe from being exposed to premature copies.

Data exclusivity is regulated through provisions governing drug registration. Polish law currently provides for three years of protection, but even this short period can be waived at the request of the second applicant. Reportedly, in some cases not even bio-equivalency data for infringing products is required by the regulatory authorities, which leaves open the risk that the copycat product could be harmful to the

patient.

PhRMA believes that this 3-year period does not meet acceptable minimum international standards for data exclusivity. In fact, under Poland's current data protection regime, copy products regularly appear on the market in Poland in under three years. Although the TRIPS Agreement does not specify a specific term of protection, Poland is the only country to provide less than five years. China's recently adopted regulation provides a period of six years, and the European Union members provide a period of six to ten years, while the U.S. provides five years for pharmaceutical products with an additional three years for new uses.

It would appear that the Polish Government has adopted an intentional policy to encourage the production and rapid registration of as many unauthorized copies of products as possible prior to EU accession. This would explain the steep increase in the number of infringing copycat products registered since 1999. There appear to be two reasons for this. First, the Government erroneously believes that weak IP protection is a valid and effective healthcare cost control mechanism. Second, the Government does not understand that IP protection is fully consistent with a thriving and competitive local industry, and so seeks to protect its domestic producers by providing very weak data exclusivity.

A new Pharmaceutical Law came into force October 1, 2002. In article 15 the Law provides for 6-year period of data exclusivity provided that a patent is still active. A 10-year (non-patent linked) period is provided for high-tech products registered through the centralized EU procedure. However, according to Article 2 of the Pharmaceutical Law Implementation Law these provisions will come into force only after Poland accedes to the EU. In Article 3, the Implementation Law also provides for a 3-year data exclusivity period until Poland is a member of the EU. However, this period commences from the first registration of the innovative product worldwide. The delay between this occurrence and registration in Poland erodes this 3-year period such that the effective data exclusivity period may be less than 2 years.

There are a number of additional matters for concern. First, although the law provides for six years for original products registered in the EU, after accession the term begins to run from the initial registration date in the EU, which could significantly shorten the effective period of data exclusivity given Polish regulatory delay. Second, under the new law, the data exclusivity period would end before the conclusion of the six-year data protection term if there is no valid patent for the chemical compound in the product, in violation of the TRIPS Agreement (where there is no linkage between patents and data protection).

<u>Patent Rights and Enforcement</u>

Poland's Industrial Property Law came into effect in September 2001.

Unfortunately, the new law introduces additional inconsistencies with Poland's international TRIPS obligations. PhRMA members remain particularly concerned by the provisions in the 2000 law as relating to use of an invention without the permission of the right holder (compulsory licensing). Article 31 TRIPS sets out a number of requirements with respect to compulsory licensing. Although several of these conditions appear to be incorporated into the patent law enacted in 2000, others are not. In particular:

- Article 82.4 of the new patent law states that a compulsory license can only be granted if the applicant can prove that he has applied for a license from the right holder in good faith, but does not specify that the applicant has provided a reasonable period of time and reasonable commercial terms, as required by Article 31(b) TRIPS.

- Article 84.2 of the law requires the Patent Office to define the scope and duration of the compulsory license. It does not, however, comply with the requirement in Article 31(c) TRIPS that the scope and duration must be limited to the purpose for which the use was authorized;

- Although Article 86 of the law provides that in certain circumstances there is a power to amend compulsory licenses, this does not comply with Article 31(g) TRIPS which provides that a compulsory license must be terminated if and when the circumstances which led to it being granted cease to exist and are unlikely to recur;

- The amount payable in respect of the compulsory license is to be based on "the market value of the license." This is at best ambiguous and possibly inconsistent with Article 31(h) TRIPS, which requires the amount payable to be adequate in the circumstances of the case: the economic value of the license being only one factor to be taken into account;

- In addition, the Industrial Property Law, at Article 68, prohibits the enforcement of patent rights in an abusive manner. The patent law also provides that the abusive enforcement of a patent right is grounds for a compulsory license. However, Article 68 does not appear in the chapter of the law that deals with compulsory licenses, suggesting that this article is intended to have further effects. If this is the case, two possibilities arise. The first is that a third party infringer of a patent can invoke Article 68 as a defense. This would contravene the exclusive rights conferred by a patent under Article 28 TRIPS, and cannot be justified under Article 30 TRIPS. Secondly, acts falling within Article 68 will mean that Poland's competition laws can be invoked against the patent owner.

TRIPS Article 41 et seq. requires Poland to provide for fair and equitable enforcement of intellectual property rights. The current patent law does not provide for

preliminary injunctions, without which a patent may lose much of its value to the patent holder due to the time it takes to litigate a patent action. In addition, intellectual property judicial proceedings are often delayed by as much as three years.

The Industrial Property Law provides for preliminary injunction, but only in terms of a generalized statement. The law states that the patent holder can apply to the court (and not the patent office) in cases of infringement. It is noteworthy that a patent section will be established in the Supreme Administrative Court, although the legislative framework for this has not yet been created. Article 71 of the law would allow a party who was in good faith using an invention at the time of a decision on patent precedence was being taken to continue to use the invention without charge even when patent precedence by another party is confirmed.

Current damages for intellectual property rights violations are not adequate to compensate for an infringement of an intellectual property right. The infringer is only rarely ordered to pay the right holder's expenses associated with the defense the right and the right holder is rarely permitted to recover profits. These practices fail to comply with TRIPS Article 45.

Supplementary Protection Certificates

Poland has declared its intention to introduce Supplementary Protection Certificates (SPC) after Poland joins the EU. The SPC provision that would be available for any patented product with marketing authorization after January 1, 2000. The draft SPC provision closely follows EU Directive 1768/92. However, there are two issues that require clarification. The law does not state that a SPC may be applied for when a patent is pending and secondly does not state that the right of the patent holder is a negative right to prevent others from using the invention in question.

Market Access Barriers

Discrimination and a Lack of Transparency

Registration and reimbursement and pricing systems lack transparency, and the frame-work in which they are conducted undermines competition and consistently penalize foreign products and manufacturers. Marketing authorization alone does not guarantee access to medicines for patients. Manufacturers of innovative products must wait for many years before these are included in the reimbursement system. No innovative products have been included in the reimbursement system for four years, while copies of U.S. products are added to the lists on a regular basis.

A new Price Law came into effect December 12, 2001. The provisions currently concern reimbursed drugs but there is a possibility that the system will be extended to hospital products. The intention is to treat both domestic and foreign products in the

same way but instead of freeing domestic prices both foreign and domestic products will be subject to the current administrative price fixing procedure. Prices are set by the Minister of Health (MoH) together with the Minister of Finance (MoF). Reimbursement is determined by the MoH based upon a recommendation from a Drug Management Team (whose membership is a secret) which includes three representatives from each of MoH, MoF, Ministry of Economy (MoE) and non-obligatory representation of the Health Insurance Funds. The membership of the Team is predominantly cost rather than health oriented and the role of the MoE is unclear. Under the law, the process cannot take longer than 90 days from a price submission or 180 days if both pricing and reimbursement submissions are made. Criteria proposed are non-transparent and the appeal system is inadequate.

The price criteria include: level of prices in countries with a similar per capita GDP; price competition; impact on direct health care costs; volume of achieved and declared sales; costs of production; proved effectiveness of the product; and the importance of the product in combating diseases of significant epidemiology.

The provisions of the Price Law enacted in 2001 are not transparent:

- Pricing and reimbursement criteria are not fully objective and verifiable.
- No explanation provided for negative price/reimbursement decision.
- Inadequate appeal procedure without second instance and appeal only to the same authority that made the original decision.
- Possibility for unsubstantiated prolongation of process for longer than 90/180 days by demanding "additional information".
- 90/180 days period limited to communication of decision solely not for effective reimbursement date.

Other non-transparent instruments of the system include a reference price system grouping similar products, which is applied inconsistently and in an arbitrary fashion. The Anatomical Therapeutic Chemical (ATC)/Defined Daily Dose (DDD) system, which was developed as an instrument to measure drug consumption, is used contrary to WHO guidelines. The Ministry of Health uses DDD as a reference dose for establishing reference price limit in therapeutic clusters. The drug with the cheapest DDD is taken as a price limit for reimbursement for other products in the cluster. This system assumes that DDDs reflects therapeutic equivalence, but the guidelines state that "DDDs are not necessarily designed to reflect therapeutically equivalent doses and are therefore not suitable for comparing drugs for reimbursement and pricing decisions". As said in the Guidelines for ATC classification and DDD assignment 2001,

"therapeutic reference pricing and other pricing decisions on ATC/DDD classification is a misuse of the system".

While the previous regulations imposed significant market barriers to the research-based pharmaceutical industry, the new law will make it even more difficult for the U.S. research-based pharmaceutical industry to operate in Poland. The provisions distort free trade and hamper open competition by continuing to impose a non-market-based approach to the purchase and consumption of pharmaceuticals. Since the U.S. research-based industry is the world leader in the development of new medicines, our members and their innovative products will invariably and disproportionately bear the brunt of these measures and will also be denied the opportunity to compete fairly in the market.

The Minister of Health has recently proposed and the Government approved a new category of reimbursement of selected products for patients over 65 years of age with 1 PLN (about 20 cents) co-payment solely for products manufactured in Poland. Following protests about discrimination of foreign manufacturers a few imported products were included on the list. PhRMA members remain concerned that the system will be used to discriminate against foreign manufacturers. The products most affected will be those manufactured by U.S. companies that have premature copies on the Polish market.

Restrictive Formularies

In mid 1999, the Office of the Government Plenipotentiary for implementation of Health Insurance produced a formulary for primary care physicians indicating which products could be prescribed directly by them and which only after a specialist initiated therapy. The formulary was more restrictive than the reimbursement lists and left out many innovative products. The individual Health Insurance Funds were to decide on whether to implement the formulary or not.

Subsequently, very restrictive local formularies appeared, which favor copied products. The formularies are non-transparent, discriminatory, and limit the autonomy of the physician. The Office for Health Insurance Supervision (OHIS), a regulatory body, has stated that these formularies are illegal. However, although physicians are no longer required to prescribe from the formulary, they are afraid not to do so in case their contracts with Health Insurance Funds are not renewed.

Customs/Margins

For the past year, the pharmaceutical industry has been subject to investigations over transfer pricing issues.

The Polish pricing law does not recognize the status of importer and assimilates

the separate activities of importers and wholesalers. Under the old law this led to, *inter alia*, importers and wholesalers – who operate at different levels of trade – being attributed the same maximum wholesale margin of 11%, out of which importers had to cover not only their wholesale expenses, but also the additional costs of importation. Obviously, this margin was not sufficient to cover the importers' operating expenses and in order to be able to stay in business their parent companies made financial contributions, often by issuing credits in one form or another, to their Polish affiliates. Although this practice was accepted by the Polish customs authorities for years, this changed in 2001, when the authorities took the position that such credits should be deducted from the customs value. Due to the customs value being lowered, the maximum wholesale margin was exceeded and the law infringed. This allowed Polish tax authorities to claim back from the companies significant amounts of excess margins plus fines.

The previous Polish pricing law discriminated against imported pharmaceuticals and violated Poland's commitments under GATT Art. 3 as well as the Europe Agreement (in particular with respect to the free movement of goods, the right of establishment and customs rules). The discriminatory character of the old law has now been acknowledged, as confirmed by the European Commission in its recent progress report on Poland[1].

The proceedings that were instigated under the previous discriminatory law continue and the companies remain exposed to huge financial penalties. For the future, the situation remains at best unclear, but discrimination against imported pharmaceuticals remains entirely possible. In fact, the premises of discriminatory treatment are already embedded in the law which still does not allow for the cost of the activities of the importers to be covered.

PhRMA believes that it is imperative that the Polish authorities:

1. Cease all proceedings linked to this case and refrain from issuing any claims for alleged violations of the maximum wholesale margin requirements for imported pharmaceuticals on the grounds mentioned above;

2. Ensure that the new pricing law is interpreted and applied in such a way as to refrain from violating Poland's international commitments either by the letter of the law or the practice of its implementation.

Corruption

Health services and markets are characterized by interdependence of supply and demand, asymmetric information, gatekeeper power, divergence between public

[1] 2002 Regular Report on Poland's progress toward accession (COM(2002)700 final).

and private interests and incentives, and other characteristics, which provide fertile ground for corruption. With respect to pharmaceuticals, a large part of this stems from the fact that there is an evident lack of transparency in both registration and reimbursement procedures. Patients are in a uniquely weak position to counter these difficulties, especially if they are poor. In Poland, the situation is further complicated by:

- The overhang of old practices – including frequent bribery, lack of financial discipline and an arrears habit – inherited from the previous regime.

- Unstable and changing health care institutions.

- Inadequate pay of doctors and other medical personnel.

A World Bank study (Corruption in Poland: Review of Priority Areas and Proposals for Action, The World Bank Warsaw Office, October 11, 1999), states that corruption in the health sector is so great that health reforms would not work. Even if the impact falls short of this, it seems clear that access to health services and their efficiency and effectiveness are compromised by corruption.

Damage Estimate

Poland's intellectual property regime, and in particular its inadequate protection of original filing data, and the considerable market access barriers for foreign pharmaceutical products have significant adverse impact on the research-based pharmaceutical industry. Preliminary estimates PhRMA member losses of $400 – $750 million per year.

CONTINUED MONITORING (SECTION 306)

CHINA

The Pharmaceutical Research and Manufacturers of America (PhRMA) and its member companies operating in China recognize the efforts of the Chinese Government to improve the operating environment, both as a result of membership in the World Trade Organization (WTO) and generally. PhRMA had long advocated for and supported China's membership in the WTO, as well as Congressional approval of Permanent Normal Trade Relations with China. To this end, our member companies, individually and collectively, worked with other U.S. businesses and organizations to help educate policy makers on the benefits of bringing China into the WTO.

In our view, China's accession to the WTO on December 11, 2001, was an extremely positive development that will help accelerate China's integration into the global economy, strengthen the rule of law and enforcement of intellectual property protection (IPP), lead to improved transparency and create a level playing field for member companies in China.

However, we continue to face many fundamental problems which need to be addressed in order for China to adequately fulfill its WTO commitments. PhRMA also takes note that inadequate enforcement of China's intellectual property laws can pose a serious public health risk, and also serves to undermine the competitive advantage that innovative companies gain from their substantial investments in research and development.

For these reasons, PhRMA requests that China be maintained in its current status subject to Section 306 monitoring and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved. PhRMA also urges the U.S. Government to implement a formal review of China's conformity to its WTO obligations. In moving forward with this review, the following is provided by Industry as an example of the number of changes required in order to bring China's statutes and practices in to line with normal WTO practices.

Intellectual Property Protection

Data Exclusivity

Consistent with its WTO obligations, China's State Council recently approved language to provide data exclusivity according to the following criteria: 1) protection of no less than 6 years commencing from the date of marketing approval in China; 2) protection that is independent of any other intellectual property right that the product might enjoy in the marketplace; 3) prohibits the unauthorized commercial use of data submitted to Government agencies; and 4) allows no reliance on data provided to authorities whether that data was generated in China or in other countries. PhRMA

applauds China's commitment on this matter and urges the United States Government to closely monitor the implementation of the data exclusivity law so that PhRMA member companies will be able to receive the full benefit intended by the commitment.[2]

Furthermore, PhRMA encourages the U.S. Government to engage the Chinese Government, and principally the Chinese State Drug Administration (SDA), in the establishment of training program for SDA personnel on data exclusivity.

Patent Linkage: A Necessity for the Protection of Patent Rights

Until recently, there had been no requirement under Chinese law that would bind regulatory agencies to respect patents issued by the State Intellectual Property Office or the Chinese courts. We are encouraged that the SDA recently included some "patent linkage" provisions in the Drug Registration Regulation. This appears to be a very positive development, and one that we hope signals the commitment of the SDA to playing a strong and positive role in helping the Chinese Government meet its obligations under the Trade Related Intellectual Property Agreement (TRIPS).

Patent Term Restoration

To redress the loss of patent life due to regulatory delay, many countries have adopted systems of patent term restoration, giving back to the patent owner some time lost to regulatory requirements. The U.S., Japan and the E.U. provide up to five years of restoration. No such term is available in China.

Counterfeit Pharmaceutical Products

PhRMA member companies are deeply concerned with the significant increase in counterfeit pharmaceutical products in many parts of the world, including China. This is primarily an issue of public safety, as it is very dangerous for Chinese patients faced with a high likelihood that products in the marketplace are illegitimate and/or dangerous to health. There are an increasing number of stories of the serious health risks posed by counterfeit products in China, including the loss of life. While it is difficult to estimate the economic damage of counterfeit pharmaceuticals in China, a

[2] In 1993, the United States and China signed a Memorandum of Understanding (MOU) to allow Administrative Protection (AP) in China for pharmaceutical patents granted elsewhere between 1986 and 1992. The Chinese Government then extended this MOU to include the European Union (EU) countries and Japan. The MOU provided seven and one-half years market exclusivity, or AP rights, in China. However, due to a number of policy initiatives put forward by the Chinese Government, industry has realized few of the benefits intended under the MOU. PhRMA Member Companies have lost significant revenue and market share in China from inadequately enforced AP rights. The contradictory policies implemented by China to meet the 1993 MOU raise legitimate concerns within the innovative pharmaceutical industry as to China's ability and willingness to adequately and effectively implement and enforce, *de facto* and *de jure*, all of it's commitments under the WTO.

conservative estimate is that the innovative pharmaceutical industry loses roughly 10 to 15% of annual revenue in China to counterfeit products. The growing presence of counterfeit products on the Chinese market should become a top priority for public health officials in China. Increasing indications that counterfeit Chinese product are being smuggled abroad only increase the urgency of the issue as citizens of other countries, too, face this health risk. In fact, the easy availability of counterfeit prescription drugs even in highly public areas such as national and international airports show how much needs to be done in this area. From an industry perspective, we note that legitimate producers of pharmaceutical products are doubly prejudiced by counterfeits – not only do they suffer the direct undermining of their market share by pirates, but find that even legitimate product in the market is compromised, if consumers lose confidence in the drug supply, and thus shy from it.

PhRMA has taken an active and cooperative approach in trying to reduce counterfeit pharmaceuticals in China. A number of companies are working with the Quality Brands Protection Committee and other organizations in which participant companies jointly conduct proactive market sampling and surveillance, as well as raids on suspected counterfeit manufacturers and distributors. Detection and enforcement, however, are expensive and difficult, and cannot be accomplished by Industry alone. We would like to work as a partner with the Chinese Government to eliminate counterfeit pharmaceuticals, and urge the Chinese Government to make this a high priority issue.

While the State Drug Administration has promulgated an administrative sanctions law and established an anti-counterfeiting office, a comprehensive effort must be implemented to reduce the amount and scope of counterfeit pharmaceuticals in China, including:

- The allocation of more resources to anti-counterfeit pharmaceutical initiatives;

- A commitment by SDA to random, unannounced searches of suspected counterfeit pharmaceutical operations; and

- Most importantly, enactment of mandatory criminal prosecution and incarceration for convicted counterfeiters. The lack of effective deterrent penalties on parties engaged in producing fake pharmaceuticals is the most important first step the Chinese Government could take to stem the tide of counterfeits.

Also important, the production and trading of a medication's active ingredient in bulk form needs to fall under the same regulations governing production and trading of pharmaceuticals. At this time, such coverage is obtained only through chemical regulations. This makes it extremely difficult to enforce action against the producers of bulk ingredients for a medication with a legal protection other then a product patent (i.e. use patent, process patent, administrative protection). There are instances of local

bulk active producers advertising product using the MNC brand name. These producers understand the penalties for such an offence, if applied, are low.

Where appropriate, PhRMA is prepared to support U.S. and Chinese Government initiatives designed to address the important issues of counterfeiting, data protection and patent linkage with resources and expertise. PhRMA and its member companies wish to work in partnership with all stakeholders in helping to ensure all parties benefit from a more rules based trading system.

Market Access Barriers

Treatment of Patented Products in Hospital Bidding

PhRMA is concerned that market access opportunities for pharmaceutical products reliant on intellectual property rights are diminished under the existing bidding system in China.

Hospital bidding began in China with pilot projects in 1999 –2000 and has rapidly expanded to where by the end of 2002, the goal of the Ministry of Health is to have 70% of public hospitals purchase 50% of the value of their pharmaceutical portfolio through bidding. As part of this process, the Ministry of Health established bidding categories for "patent", GMP (generic), and non-GMP products.

However, the regulation is unclear whether drugs still protected by international product patents (China only recognized product patents for pharmaceuticals beginning in 1993) will be placed in the "patent" category, or be placed in the GMP generic category. PhRMA believes that Chinese authorities should recognize a transition period in hospital bidding, as most of these products at best enjoyed partial exclusivity during the years they should have received exclusivity. Products still under international patent protection need to be placed in the "patent" category, as should other newer products during a transition period.

Damage Estimate

Today, there are 12 PhRMA member affiliates in China, which PhRMA estimates enjoy approximately a 12% share of the Chinese pharmaceutical market of U.S. $6 billion (for finished formulations of western medicines) or around U.S. $720 million in annual sales.

These PhRMA member companies in China estimate that a substantial part of the market still is dominated by pirated or counterfeit products, and that their market share could rise from 12% to 25%, or roughly double current sales, if intellectual property problems in China were rectified. It is thus estimated that lost sales are in excess of US $800 million.

PRIORITY WATCH LIST COUNTRIES

ASIA-PACIFIC

KOREA

The US research-based pharmaceutical industry welcomes the new Government of Korea, under the leadership of President Roh Moo-hyun and looks forward to developing a productive, collaborative working relationship with his new administration. While PhRMA recognizes that President Roh's transition team is evaluating and developing pharmaceutical and health care policies, the research-based industry continues to suffer from discriminatory policies imposed by the previous Government of Korea.

Despite regular, in-depth US Government communication and engagement with the Government of Korea significant pharmaceutical and health care policies have developed in 2002 that have a disproportionate, negative impact on the US research-based pharmaceutical industry. These policies clearly weaken the benefits afforded by intellectual property protection and provide no transparency and consultation with the research-based pharmaceutical industry. PhRMA maintains that meaningful, transparent consultation between the Korean Government, US industry, and other key stakeholders is necessary to promote comprehensive health care reform and attract investment in biomedical research and development.

The Korean Government has imposed policies that fail to meet full World Trade Organization (WTO) obligations and inhibit US research-based companies to be rewarded for investment in innovation during the patent period. While we look forward to working with President Roh and his administration to resolve these issues, PhRMA recommends designating Korea a "Priority Watch List" in the current "Special 301" cycle.

Intellectual Property Protection

Patent Linkage

The absence of any direct linkage between KFDA and Korean Industrial Patent Office (KIPO) is another area of concern. KFDA, while assuming responsibility for safety and efficacy review, apparently has abdicated any responsibility for ensuring that competitors do not market products covered by patents through linkage to KIPO. Thus, instead of taking the opportunity to prevent infringement during the marketing approval process, the Government of Korea forces patent owners to resort to the court system after infringement has occurred. This practice results in significant commercial impact and the Korean Government remains non-committal with respect to near term implementation of such a system.

Market Access

Reimbursement Restrictions

The HIRA (Health Insurance Review Agency) continues to unilaterally impose reimbursement guidelines for new classes of pharmaceuticals that diminish intellectual property rights and unduly restrict or unreasonably delay treatment with the most effective, appropriate medicine.

Such reimbursement guidelines do not reflect the innovation recognized by patent protection, accepted scientific or clinical guidelines. These policies weaken the benefits afforded by intellectual property protection, restrict market access for innovative medicines, and target US research-based pharmaceutical companies. These guidelines are developed and imposed in a non-transparent manner and occur without appropriate consultation with industry, the medical profession or consumer/patient associations. These guidelines:

- Limit research-based companies ability to gain the rewards afforded by intellectual property protection
- Discriminate against innovative medicines researched and developed by US and European pharmaceutical companies
- Deny manufacturers the ability to gain market access for product evaluated under the A-7 pricing regulation agreed to by the US and Korean Governments
- Ignore KFDA (Korean Food and Drug Administration) evaluation, scientific evidence, and medical expertise on the quality, safety, efficacy, and appropriate use of medicines during both initial guideline development and any subsequent discussion with companies or medical experts
- Prevent physicians' choice in prescribing the most appropriate medicine to treat a disease
- Deny patients access to lifesaving, innovative medicines that improve both overall health and quality of life.

PhRMA is deeply concerned that the MOHW and (HIRA) are implementing short-term cost containment measures that disproportionately impact innovative pharmaceuticals, rather than contributing to comprehensive health care reform. Any arbitrary or restrictive reimbursement guidelines used as a short-term cost containment mechanism at the expense of intellectual property rights and market access for innovative medicines researched and developed by US companies severely limits Korean patient choice for the best possible treatment.

Reference Pricing

On May 31,2001 the Ministry of Health and Welfare issued a National Health Insurance Stabilization Plan, which included a proposal for the implementation of therapeutic reference pricing. In 2002, the MOHW reform proposal communicated no details as to the scope and methodology of the proposed reference pricing system.

MOHW proposed a number of reference pricing schemes in 2002, all of which categorize both patented and off-patent products based on therapeutic effect. Therapeutic reference pricing, or any mechanism that groups patented and off-patent products violates the premise of intellectual property protection.

Reference pricing promotes anticompetitive practices that discriminate against innovative medicines, researched, developed and patented by US research-based pharmaceutical companies. In addition, by imposing a ceiling on pharmaceutical reimbursement for innovative medicines, reference pricing would violate Korea's commitment to A-7 pricing of innovative medicines agreed between the U.S. and Korea.

Reference pricing is not a solution to a structural health care financing reform. Rather, it penalizes new innovative medicines, prevents competition, and restricts the clinical freedom of physicians to prescribe the best medication for a serious disease or illness, and limits patient access to the most effective therapies.

PhRMA urges the current Government of Korea to abandon policy proposals that effectively violate intellectual property rights and disproportionately discriminate against the US research-based pharmaceutical industry.

Damage Estimate

PhRMA Members believe that the above barriers have had a substantial adverse commercial impact, with annual damages of between $500 million to $1 billion.

NEW ZEALAND

The Pharmaceutical Research and Manufacturers of America (PhRMA) and its member companies' affiliates in New Zealand believe that the policies of the New Zealand Government agencies that set the reimbursement price of medicines, are anti-competitive and seriously erode the intellectual property protection for pharmaceutical products within the market. These practices have been in place for a number of years now. Unfortunately, the New Zealand government now appears to be making policy changes that are making the environment worse as opposed to improving it. At the end of 2002, the New Zealand government rushed through a change to their patent law that would allow for "spring boarding," or the authority for a generic manufacturer to embark on trials to ensure its drug is given immediate regulatory approval when a patent ends. This provision will significantly shorten a patent holder's exclusivity and is clearly a signal of the government's intentions regarding the research-based pharmaceutical industry.

What has become even more troubling than the New Zealand government's negative acts toward the industry is the obvious decline in the quality of the New Zealand health care system and the problems it is creating for the New Zealand population. There are daily reports now of shortages in the supply system for pharmaceuticals. This is leading pharmacists to resort to illegally importing products that are not available. The alternative is that patients will do without drugs that treat any variety of illness. Clearly the government's short-term goals of cost containment are causing serious problems for its public at large.

Given the lack of progress or clearly any interest in addressing the pharmaceutical industry's and the New Zealand public's concerns with regard to intellectual property protections, PhRMA would once again request that New Zealand be designated a "Priority Watch List Country."

Background on New Zealand's System

Once regulatory approval has been obtained from the New Zealand Ministry of Health, market access is effectively determined by entry to the Government Pharmaceutical Schedule (PS). The Pharmaceutical Management Agency (PHARMAC) was established in 1993 as a limited liability company to manage the purchasing of pharmaceuticals for the national health care system.

PHARMAC administers a Pharmaceutical Schedule (PS) that lists medicines that attract a Government reimbursement for patients and specifies the reimbursement level that will be paid for each listed medicine. The schedule also defines the supply conditions by restricting prescriptions of a product when it decides to reimburse a product.

Due to PHARMAC's practices, and the nature of a socialized health insurance system, significant sales of most medicines in New Zealand are not possible unless the medicine is reimbursed on the Pharmaceutical Schedule. Moreover, all private medical insurers in New Zealand reimburse claims only for medicines that are included on the Pharmaceutical Schedule; this means that no one will underwrite a premium or co-payment for the cost of a medicine unless it is "acceptable" to PHARMAC. The absence of a PS listing also severely limits the in-hospital use of some medicines. The potential impact of PHARMACs' practices on the hospital pharmaceutical market has been extended following PHARMAC being directed by the New Zealand Government to share responsibility for the purchase of hospital medicines with twenty-one newly established district health boards.

- PHARMAC's monopsonistic power over the PS creates barriers to market access by denying or conditioning the listing of new medicines on the willingness of manufacturers to accept discriminatory pricing and reimbursement policies. PHARMAC applies its discriminatory policies in the following manner:

- Grouping together of patented products with generics for reference pricing - This policy differs significantly from reference pricing in other countries and it erodes the value of intellectual property accrued through innovation.

- Denying a PS listing when PHARMAC subjectively considers that "sufficient" products are available to meet patients' needs;

- Denying or conditioning PS listing of new drugs upon the manufacturer's acceptance of a reimbursement level that is less than or equal to the current PHARMAC-imposed reimbursement level of existing medicines;

- Denying or conditioning PS listing upon the manufacturers' agreement to set the introductory market price at the reimbursement level, in effect, imposing a maximum price control at the time of listing;

- Denying or conditioning PS listing upon the manufacturer's agreement to Government-mandated cross therapeutic reference pricing which requires a major price reduction on one or more of the company's other medicines, often in a completely unrelated therapeutic class;

- De-listing of medicines based on the award of a single tender or "preferred provider" status;

- Lack of transparency in reference pricing methodology - Clinical evidence and therapeutic differences, as well as the views of physicians are ignored in favor of products with lower reimbursement levels.

Intellectual Property Protection

In December of 2002, the Government of New Zealand enacted a change to their patent act to allow generic producers to conduct testing needed for regulatory approval of an approved drug before the end of the patent term in New Zealand. These changes were not accompanied by corresponding changes needed to reflect the balance of interests found in the U.S. Hatch-Waxman system. This means that New Zealand has failed to provide for patent term restoration to compensate patent holders for time lost in the regulatory approval process, even while allowing spring-boarding or early-working of the patent. PhRMA members urge the U.S. Government to seek changes to provide the corresponding balance through an authority for patent owners to receive an extension on the term of their patents to compensate for the loss of effective patent life prior to the approval of the drug in New Zealand.

Market Access Barriers

Of great concern to the industry is the burden of PHARMAC's policies and practices on the value of U.S. companies' intellectual property. The manner in which the pharmaceutical reimbursement system is implemented effectively erodes the value of patents for new, innovative, more-effective medicines. PHARMAC places patented products in therapeutic groups that are referenced for purposes of reimbursement with generic products and allot the same reimbursement price for both.

Without price differentiation between patented products and generics, the value of innovation for the patented product is not recognized. In addition, the lack of access for patented products to the New Zealand Pharmaceutical Schedule, and requirements to subsidize the product cost by lowering the price of another product in a different therapeutic subgroup further devalues patented products to the level of generics.

Through its control of the levels of reimbursement and application of its reference pricing policies and other initiatives such as tendering, PHARMAC's actions burden and restrict U.S. trade in pharmaceuticals, and negatively affect the value of the intellectual property on which these innovative medicines depend. This is because:

- The period over which a level of reimbursement is negotiated or denied shortens the effective patent life.

- Government-mandated cross therapeutic reference pricing by PHARMAC forces price reductions on patent-protected medicines, or can expose the manufacturer to significant volume losses. These, together with practices

that effectively deny market access reduce the opportunity to earn an expected return on medicines whose value is inherent within their intellectual property.

In order to achieve or maintain reasonable market share, research-based pharmaceutical companies are forced by PHARMAC to provide these medicines at the price of off-patent medicines or prices that prevail as a result of trade-offs for unrelated medicines. PhRMA believes that these practices by PHARMAC, which the New Zealand Government allows, seriously undermine the value of intellectual property and fail to give adequate recognition to the value of innovation.

PHARMAC Exemption from Commerce Act

PHARMAC has been able, since its establishment, to institute these policies through its broad statutory exemption from the restrictive trade practices provisions of the New Zealand Commerce Act. Thus, while normal commercial competition law binds pharmaceutical companies, a Government agency has the right to act in such a way as to lessen competition significantly in the market without legal redress by affected companies.

The New Zealand Government has chosen to retain the broad exemption from Part II of the NZ Commerce Act 1986, dealing with restrictive trade practices in favor of PHARMAC (NZPHD Act, Dec. 2000). This Act maintains the broad exemption from Part II of the NZ Commerce Act for any agreement to which PHARMAC is a party that relates to publicly reimbursed pharmaceuticals.

The reality of the broad exemption is PHARMAC continues to be insulated from quite proper challenges of misuse of market power. This is a crucial point of principle, as through the administration of the reimbursement regime, PHARMAC and the District Health Boards can dictate who enjoys market access. They have the ultimate market power in circumstances where they can restrict, deter or eliminate suppliers from the market place, something that would otherwise be in clear breach of s.36 of the New Zealand Commerce Act, if it were not for the exemption. The empirical evidence shows that if pharmaceutical suppliers do not have their medicines listed on the Pharmaceutical Schedule and thus reimbursed, their ability to access the market is extremely limited, if not impossible, in most cases.

There is only a need for a limited exemption. PhRMA believes that PHARMAC, in its own capacity, and as agent for the District Health Boards, should be required to comply with New Zealand's competition laws. If the "owner" of PHARMAC, the Ministry of Health, is expressly subject to the Act in relation to PHARMAC's activities, as is the Crown or Government when it acts "in trade," there is really no reason why PHARMAC should be fully exempt as it is.

PhRMA strongly urges a reduction in the current broad exemption from the New Zealand Commerce Act.

Unfair Government Procurement Policies: Sole Supply Tenders

PHARMAC has expanded its restrictive listing policies in efforts to further reduce Government expenditure on pharmaceuticals. It is now more likely to use Requests for Proposals for sole supply to reduce the number of companies competing in a market to one supplier.

PHARMAC already has successfully implemented a number of tenders between 1998 and 2002 for sole supply, which have included a number of products still on patent. Current proposals for the purchasing of hospital pharmaceuticals anticipate the use of sole supply tenders.

PHARMAC reduces reimbursement of products that are not part of the tender process through referencing the product's price to the level of the lowest priced sole supply product in the established therapeutic sub-group. Manufacturers that are not successful in the tender process would have their currently reimbursed products de-listed.

New generic entrants are encouraged to provide low cost tender applications, not only by the attractive sole or preferred status arrangements, but also (in some cases) through offers by PHARMAC that it will pay up front registration fees, should they win the tender. Such successful tendered products are therefore promised sole or preferred status before they are even registered for sale in New Zealand. There is no recognition of patents or innovation as this system is applied.

Damage Estimate

The current size of the New Zealand market is estimated to by US $330.5 million. Because New Zealand does not have a domestic industry, U.S. companies have a market share of around 30% and sales of US $99.2 million. While PhRMA does not currently have a damage estimate figure, it is important to note that several leading U.S. research-based companies have been forced out of New Zealand, and other are reconsidering their long-term presence in this market.

While New Zealand is a small market, the damages incurred by U.S. industry as a result of its punitive pharmaceutical policies are disproportionately high. New Zealand represents an extreme example of socialist, command-and-control health care policies that puts cost-containment, bureaucratic and budgetary consideration ahead of patient welfare or innovation. New Zealand's policies have contributed to patient

deaths and adverse therapeutic outcomes as patients have been forcibly switched by PHARMAC to cheaper, less effective medications. The Government's restrictive listing policy has severely limited treatment options patients and doctors, and forced some seriously-ill patients to take medications that are less effective or have greater side effects. At international conferences, senior PHARMAC officials urge other Governments to adopt the "New Zealand model," and boast of their approach to targeting U.S. and European pharmaceuticals for punitive price reductions. Obviously, the fact that New Zealand does not have a domestic research pharmaceutical industry makes it easier to implement punitive policies targeted at U.S. and European companies. However, the widespread adoption of the New Zealand model would call into serious question the viability of innovative pharmaceutical research and the future promise of the biotechnology and genomics revolutions in generating new life-saving treatments for disease and disability.

The New Zealand Government has expressed interest in concluding a Free Trade Agreement with the United States. The apparent purpose of such an FTA would be to expand access in the U.S. for New Zealand's agricultural exports. While PhRMA defers to U.S. farm interests on the benefits of agricultural trade liberalization, we are concerned that a U.S.-New Zealand FTA would not result in reciprocal improvements in U.S. market access and therefore would not be in the overall U.S. national economic interest. To date, our industry's experience suggests that New Zealand would use egregious regulatory barriers to restrict access in sectors where the U.S. has a comparative advantage and where the benefits of trade liberalization would normally be expected to accrue. Under these circumstances, PhRMA strongly opposes initiation of FTA negotiations with New Zealand until PHARMAC's abuses are eliminated and New Zealand patients are granted access to innovative life-saving medicines.

PHILIPPINES

PhRMA requests that the Philippines be included in the 2003 "Special 301" Priority Watch list due to serious concerns raised by increased counterfeiting related to parallel imports, absence of enforcement of current IP provisions available under Philippine law, and the lack of data exclusivity. We urge the U.S. Government to continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

Parallel Imports and Counterfeiting

The Government parallel imports medicines from sources outside the Philippines, notably India. Legitimate generic pharmaceutical products, i.e. products no longer protected by patent or subject to data exclusivity, and produced according to Good Manufacturing Practices (GMP) as regulated by the U.S. Food and Drug Administration (FDA), may be imported through parallel trade consistent with the TRIPS Agreement. The vast majority of products on the WHO list of essential medicines are available generically, consistent with the above.

The presence of counterfeit pharmaceutical products is escalating in the Philippine market, possibly exacerbated by the influx of parallel imported products which threaten the integrity of legitimate distribution channels. The implications on public health of counterfeit pharmaceuticals are of concern to the Philippine Government and the industry urges the Government to dedicate appropriate resources to fighting this problem.

Parallel importation violates intellectual property rights when the exclusive right to the use (including import and export) of a patented and/or trademarked good, provided to the owner of the intellectual property in the country of registration, is infringed upon. The industry is concerned about the increasingly common practice of importing generic copies of products with a valid patent in force.

Enforcement

Under the enforcement provisions of the TRIPS Agreement (Articles 41 - 61), WTO members are obligated to provide effective and timely remedies to ensure that products that infringe on a patent holder's rights are kept out of the stream of commerce, including provisional remedies, injunctive relief and border measures.

An effective patent system in the Philippines and elsewhere depends on the ability by the patent holder to control the distribution of its patented pharmaceuticals—a

system that would be greatly undermined in an environment described by unfettered parallel imports and the presence of counterfeits.

Data Exclusivity

The Philippines became obligated to provide protection of confidential test data under Article 39.3 of TRIPS on January 1, 2000. Compliance with TRIPS Article 39.3 will ensure that information provided by an innovator to regulatory authorities will not be disclosed to the public or to other manufacturers, or relied upon, directly or indirectly, for a fixed period of time.

This WTO obligation has not yet been implemented. In recognition of the significant cost, time and risk that is put into generation of this data, the industry respectfully urges the Government of the Philippines to immediately take steps to come into compliance with this obligation.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

TAIWAN

PhRMA members active in Taiwan face challenges relating to deficiencies in Taiwan's intellectual property protection for pharmaceutical products as well as a variety of market access barriers, which inhibit trade & investment in Taiwan. Serious concerns center on Taiwan's continued failure to provide data exclusivity, the lack of effective enforcement against counterfeit pharmaceuticals as required by its accession to the World Trade Organization (WTO), and its refusal to adhere to an agreement reached with the U.S. Department of Commerce to resolve validation requirements and its. Additional market access barriers to U.S. research based pharmaceutical companies, such as ongoing anticompetitive practices in Taiwan's drug distribution system, continue to discriminate against foreign innovative products.

Given Taiwan's apparent disregard of a formal commitment made to the U.S. Government as well as its failure to implement appropriate data exclusivity and anti-counterfeiting measures as required by the WTO, PhRMA recommends designating Taiwan a "Priority Watch List" in the current "Special 301" cycle in light of the seriousness of the issues involved.

Intellectual Property Protection

Data Exclusivity

While Taiwan was required to implement the of level protection of the Trade Related Intellectual Property Agreement (TRIPS) at the time of its WTO accession, it has not yet enacted legislation to implement the obligations contained in TRIPS Article 39.3 on data exclusivity. Article 39.3 requires Governments to prevent reliance, without the originator's consent, by regulatory authorities or third parties on the data submitted in the registration process, for the manufacturing and marketing copies of a drug during a period of exclusivity.

While Taiwanese officials have cited existing laws, such as the Government Official Service Act, the Trade Secret Act and Taiwan's criminal statutes, which provide for the non-disclosure of various types of confidential information and commercially-sensitive trade secrets, these only address Taiwan's TRIPS Article 39.2 obligations to protect trade secrets. Current Taiwanese statutes, however, do not fulfill Taiwan's separate and distinct obligation under TRIPS Article 39.3 to provide data exclusivity. Taiwan's current laws are not sufficient, since, TRIPS Article 39.3 requires Governments to enforce data exclusivity against "unfair commercial use," whereas the Trade Secrets Act leaves enforcement in the hands of the holder of the trade secret.

Patent protection and data exclusivity protection are two separate and distinct forms of intellectual property and under WTO rules require separate legal protections. There are two steps in bringing an innovative drug to market: (1) the discovery of the

new pharmaceutical compound and (2) the demonstration to regulatory authorities of the safety, quality and efficacy of the drug. Patent protection ensures that the first step—the discovery of the compound--occurs. Effective protection of the data ensures that the second step is completed by providing a period of exclusivity for data developed during clinical testing of the product's safety, quality, and efficacy.

The continuing absence of data exclusivity in Taiwan will have a chilling effect on industry investment in advanced research in Taiwan.

Counterfeiting

PhRMA member companies have noticed that the problem of counterfeiting of pharmaceuticals has dramatically escalated in Taiwan in the past year. Counterfeit products are manufactured in Taiwan, as well as imported from other markets, and are widely available. This problem poses a serious risk to public health in Taiwan unless it is more aggressively addressed by the Government of Taiwan. It also results in significant commercial harm to PhRMA members operating in Taiwan.

Market Access Barriers

Unfair Validation Requirements

In May 2001 the Taiwan DOH announced onerous requirements for the submission of complex proprietary manufacturing data for all products both currently marketed and to be registered. Specifically, this data, known as validation data, is generated as part of procedures conducted by a company to demonstrate that a product complies with current Good Manufacturing Processes (*c*GMP). The data is normally inspected at the manufacturing facility, and is never supplied to a regulatory authority except in brief summary format as a prerequisite to inspection.

In spite of significant challenges from PhRMA and other organizations, these requirements are currently undergoing implementation in Taiwan (since June 10, 2002). While the initial published requirements (in terms of volume of data) were reduced to a more acceptable level through dialogue with the DOH, implementation is still in its early stages, and the DOH is currently making requests to companies for significant additional quantities of data beyond that agreed. Given that the agreed reduced level of data still far exceeds any other international regulatory agency's data requests in this area, the supplemental requests on the part of the DOH are wholly unacceptable. PhRMA believes it is critical that (a) the implementation period during which companies cannot be penalized for non-compliance with the requirements be extended to allow for a formal dialogue on the requirements; (b) a formal dialogue mechanism be established between the DOH, PhRMA and other stakeholders to concretely establish data requirements for both manufacturing facilities and products; and (c) the DOH treat the foreign industry equally to the domestic industry by offering

facility inspections, in line with international practices, as an alternative to submission of validation data. Specifically concerning (b), PhRMA contends that the 'validation data templates' for both facility and product validation data, that were agreed with the DOH as acceptable quantities of information to fulfill these requirements, should continue to be accepted without amendment or addition by the DOH. Furthermore, the DOH should accept the 'validation data templates' for new products.

Most troubling of all is the apparent refusal of the Bureau of Pharmaceutical Affairs of the Department of Health to abide by an agreement reached with the U.S. Department of Commerce on a process to help resolve the burdensome, non-transparent and discriminatory requirements being faced by foreign pharmaceutical manufacturers in Taiwan.

PhRMA and its member companies are deeply troubled by the apparent disregard Taiwan places in a formal agreement made with the U.S. Government. It is more than disappointing that in addition to an agreement being reached and despite repeated assurances to senior U.S. trade officials, including Commerce Under Secretary Aldonas, that DOH continues to threaten the removal of U.S. pharmaceutical product from the market as well as a ban on future marketing of pharmaceutical products from U.S. innovative companies.

Violations of National Treatment in Reimbursement

Article 49 of the National Health Insurance law mandates reimbursement to healthcare providers at actual transaction costs. In practice, this is not enforced, thus allowing generics producers with little or no R&D costs to recover, the ability to offer significant and highly questionable discounts to the reimbursement rate. Industry supports strong enforcement of Article 49 by the Government, so that product bonuses, discounts and other forms of unrecorded promotions, do not misrepresent true reimbursement practices and levels.

Hospitals are permitted to claim the full reimbursement price, after negotiating deep discounts from some manufacturers. This results in a "*Black Hole*" (profit for hospitals), which is placing severe pressure on the BNHI healthcare budget, which concurrently is running at serious deficit. This skews the actual reimbursement payments by Government, may be influencing prescribing patterns in Taiwan (to local products with deep discounts) and creates pressure for continuing price cuts. The resolution of the "*Black Hole*" in Taiwan – more direct funding of doctors and hospitals and the separation of prescribing and dispensing of pharmaceuticals -- should lie at the core of any meaningful attempts to effect real reform of the reimbursement system.

In addition, PhRMA believes that DOH allows the *"Black Hole"* to persist, and the Bureau of National Health Insurance (BNHI) permits overpricing of local generics in general, as part of a national strategy to promote the development of a local biotech

industry, which does not yet fully exist. PhRMA believes that this form of subsidization of the local generic industry is illegal under WTO rules.

One additional subject, requiring monitoring, is the Government's implementation in 2002 of global budgeting for the hospital sector to remedy to deficits in the healthcare budget. PhRMA believes global budgeting will further exacerbate, rather than relieve, the distorting effects of the "*Black Hole.*"

Proposed changes to the pricing system in 2002, which emphasize mandated reductions in the price of pharmaceutical products, while failing to comprehensively address the *"Black Hole,"* are inappropriate and should be delayed accordingly. If the Black Hole is allowed to perpetuate itself, its distorting impact on the Taiwan market will only escalate.

PhRMA is also disappointed that the Government has failed to adopt legislation to clarify the intent of Article 49 that was introduced in the Legislative Yuan recently to address the "Black Hole."

Damage Estimate

The International Research-Based Pharmaceutical Manufacturers Association (IRPMA), an association of US, European and Japanese R&D-based pharmaceutical companies in Taiwan, estimates impact of the losses due to discriminatory reimbursement practices alone on PhRMA member companies as greater than $650 million annually.

EUROPE

CROATIA

Industry members continue to suffer from inadequate and ineffective intellectual property protection in Croatia, including the absence of protection for confidential test data. In addition, PhRMA' members attempting to do business in Croatia continue to suffer from market access barriers, including an extremely long registration process (3.5 times longer than that regulated by the Croatian drug law) and a lack of transparency in Government pricing and reimbursement procedures.

Intellectual Property Protection

Enforcement

The first patent protection law in Croatia was introduced in 1993. Under this law, only process patent protection is available for pharmaceutical products registered in Croatia before 1993. Therefore, many major foreign pharmaceutical products marketed in Croatia are protected only by a process patent and are therefore exposed to easy copying by local firms. Furthermore, there is no linkage between the national patent authority and the central health regulatory authority to ensure that the health regulatory authority does not provide marketing authorization for unauthorized copies of products subject to patent protection. Therefore, even for products registered after 1993, copies can be easily registered. This lack of protection has allowed and continues to allow local and other companies to routinely copy pharmaceuticals patented in the U.S. and EU.

Art. 41 Trade Related Intellectual Property Agreement (TRIPS) requires that World Trade Organization (WTO) Members ensure that their enforcement procedures permit "effective action" against intellectual property infringement acts and include "expeditious remedies to prevent infringements and remedies, which constitute a deterrent to further infringements." The Croatian legislation does not contain any specific provision that imposes an obligation upon the court to make either preliminary or final determinations, affirmative or negative, within certain time-limits, nor that the court must decide on certain subsidiary requests (such as a temporary injunction) before the decision on the merits. This has allowed judicial authorities to avoid making immediate decisions - especially temporary injunctions - in all types of proceedings (including patent infringement matters) using their discretionary right to make decision on such matters along with the final decision on the merits. In practice, this means that the manner in which a lawsuit is conducted and its final decision depend on the competence, authority and determination of the judge. This is not only contrary to the provisions of TRIPS but is also contrary to the provisions of domestic Croatian law which offer a number of effective means to protect the interests of right holders against infringements.

Data Exclusivity

Croatian legislation does not provide for an effective protection against unfair commercial use of confidential data submitted by the pharmaceutical companies seeking marketing authorization, as required by Art 39.3 of the WTO TRIPS agreement (Croatia has been a member of the WTO since November 2000). This has left the U.S. research-based pharmaceutical industry vulnerable to copying by domestic or foreign generic companies. As stated, domestic and foreign generic companies are using this opportunity very widely by using confidential test data of original product when registering their copy product.

There is a high probability that the regulatory agency in Croatia may continue to use undisclosed data for the support, clearance or review of other subsequent applications for marketing approval.

Market Access Barriers

Marketing Authorization

The Ministry of Health controls the drug registration process. The current registration procedure is not harmonized with EU directives and should last 270 days according to the current Croatian drug law. The process includes a technical review by the Institute for Drug Control, which reports to the Minister of Health. The registration commission of the Ministry of Health is responsible for reviewing and granting marketing authorization. In spite of the current drug law, the Institute of Drug Control is blocking registration efforts and keeping innovative products off the market for more than 900 days.

The Institute for Drug Control also analyzes every batch of drug that is shipped to Croatia for marketing; this step adds a month delay to all shipments.

Government Pricing and Reimbursement

PhRMA members are concerned about the recent developments regarding the regulations issued by the Croatian Government on the reimbursement and pricing of pharmaceuticals.

- The Review Process Lacks Transparency

The decision of the sick fund (HZZO) does not contain a statement of reasons based on objective and verifiable criteria and cannot be appealed to a judicial authority. In addition, there is no formal time frame for the Government to review applications for reimbursement.

The Croatian sick fund disregards the considerable R&D costs associated with innovative medicines.

Many innovative products that are still protected by patents in the U.S. or the EU are reimbursed in Croatia at levels that are not significantly different than the prices of local and Slovenian copies, therefore disregarding the high R&D costs of pharmaceutical innovation. Furthermore, foreign pharmaceutical producers have to absorb an import tax of 4.3% and import costs of 2% for products imported from the U.S. in order to be reimbursed at the reference wholesaler price of Croatian or Slovenian products (for EU origin products, import taxes are 2.6%, while for Slovenian products, including copies of patented US products the taxes are 0%). More than 73% of the products that reduced their prices are imported products.

- Pricing Regulation for Pharmaceutical Products

Products most affected by the current pricing regulation (that came in to force in November 2001) are innovative drugs. According to the policy, producers must adjust their prices for each product to an arbitrary 95% of the average wholesale price of the active substance in the comparative countries of France, Italy and Slovenia. Slovenia has already introduced an 85% adjustment factor to the average of wholesaler prices in France, Italy and Germany. In contrast, products (mainly domestic) that are currently priced below 70% of the same average of the wholesaler prices by active substance in the reference countries can increase their prices up to the 70% limit. In many cases, local or Slovenian copies are referenced at the price of a molecule that it is still covered by a valid patent in France or Italy. As a result copies or generics are priced up to an unreasonable 90% of the patented product or a branded product, while original products are required to sell at a loss versus reference countries. The price determination mechanism applies to domestically produced products, as well as to imported products, but in the case of the latter is also intended to cover the customs duty of 4.3% for US products and 2.6% for EU products and the customs processing fee of 2% (article 4). Therefore, the current policy discriminates in favor of Croatian and Slovenian producers (Croatia does not levy import taxes on medicines produced in Slovenia).

The policy disregards the high costs associated with the discovery, development, testing and introduction of innovative pharmaceuticals, thus creating a barrier to market access for innovative drugs in the Croatian market.

The price setting mechanism violates the international obligations of Croatia under the WTO and the U.S.-Croatian Treaty on the Encouragement and Reciprocal Protection of Investment.

- Conflict of Interest

The Croatian Institute for Health Insurance is the national authority responsible for decisions on the reimbursement process for pharmaceuticals and in the same time is a shareholder of the major pharmaceutical Croatian company, Pliva. At the end of 2001, the Croatian Institute for Health Insurance concluded a swap agreement with Pliva that received 7.94% of its shares outstanding, in exchange for its receivables from Croatian health institutions. Currently, The Croatian Institute for Health Insurance owns 1.13% of Pliva share capital that represents a conflict of interest potentially interfering with the reimbursement process.

Damage Estimate

Preliminary estimates suggest that potential increase in exports per annum if the trade barriers described were removed, would be $25–$50 million.

HUNGARY

Despite the concerted and continuing efforts of the U.S. Government to gain compliance with international treaty obligations, the Government of Hungary continues to fall short of providing effective protection for patented pharmaceutical products, processes, and for protected data. In addition, PhRMA members attempting to do business in Hungary continue to suffer from market access barriers including a lack of transparency in the Government pricing and reimbursement system for pharmaceuticals, despite U.S. Government efforts to seek changes in practices and policies of the Hungarian Government. Given these circumstances, PhRMA believes that Hungary should continue to be included in the 2003 "Special 301" Priority Watch List.

Intellectual Property Protection

Certain aspects of Hungary's patent protection regime are inconsistent with its obligations under the Trade Related Intellectual Property Agreement (TRIPS), which came into force on January 1, 2000, if not earlier, to the extent that Hungary did not invoke the transition period for developing countries found in Article 65.3 of TRIPS.

Data Exclusivity

As it takes 10 to 12 years to bring a new medicine to the market, the benefits of the 1994 Patent Act will not be felt before 2004-2006. Until then, data exclusivity is the only type of protection that may prevent early copying.

TRIPS Article 39.3 requires members of the World Trade Organization (WTO) members to protect against "unfair commercial use" of undisclosed test data and other confidential protected data submitted to Governments as a condition for obtaining marketing approval of pharmaceutical products utilizing new chemical entities. In most industrialized countries, a special legal regime provides that no person may, without the permission of the person who generated and originally submitted the costly and confidential data, rely on such undisclosed and proprietary test data in support of an application for product approval, not only while the originator's marketing application is pending before the regulatory authorities, but also for a specified period from the marketing approval date of the original product. However, current Hungarian law contains no restrictions on its regulatory agency with regard to reliance on the original filing data for any specific time period. In fact, the health regulatory authority has permitted registration of second filing applications, which rely on the original filing, without the originator's consent, even in cases where the time between the original filing and the second filing is less than five years and in some instances as little as a few months. The health regulatory authority has taken the position – stated, for example, in a recent reply to U.S. companies questioning the process – that in the

absence of such restrictions clearly prescribed by legislation, it would not deal with the issue.

The Hungarian Government has claimed that its Unfair Competition Law (UCL) of 1994 is sufficient to fulfill Hungary's obligations under Article 39.3. However, the Unfair Competition Law is not suited to fulfill these obligations, for several reasons. First, the UCL is not directed at the behavior of Governments, which is the intent of this paragraph of TRIPS, but at the actions of private parties. Second, the UCL is designed to allow for a civil action after the breach of confidentiality has occurred; it has no power to prevent the breach, which is the intent of Article 39.3. Third, confidentiality obligations imposed on Governments, including those of Article 39.3, would inhibit any data gathering process that would be necessary to pursue a case through the UCL. In other words, there is nothing in the UCL to prevent the Government from creating an anti-competitive situation as a result of not protecting the data of the original filer. Since this is the intent of TRIPS Article 39.3, the UCL is an insufficient means of fulfilling Hungary's obligations under that article. As long as Hungary does not have a specific regime in place to guarantee the protection of original filing data, it is in violation of TRIPS.

On April 12, 2001, Hungary issued a decree that will protect the confidential test data submitted by research-based pharmaceutical companies as a condition of marketing approval as of January 1, 2003. However, there remains a large portfolio of innovative products that are currently on the market or will be registered within the next year that remain exposed to easy copying.

In addition, the data exclusivity term would begin at the date of the first marketing authorization in the EU. Since Hungarian marketing authorizations are typically issued later than authorizations in the EU with its central and mutual recognition approval procedures, the Hungarian reference to a third country may considerably shorten the data exclusivity period. Furthermore, reference to third country marketing approval dates is not provided for nor is it in the spirit of Article 39.3 TRIPS. Moreover, despite a formal marketing authorization, a pharmaceutical company may not market the product before the price of the product approved by the Government is published in the Official Gazette. This requirement typically takes one year, but recently up to two years, thereby reducing a would-be six-year period correspondingly.

Finally, although the period of protection for confidential data is a maximum of six years, the data exclusivity period ends earlier than six years – possibly at zero years – if and when the patent expires earlier. This opens the possibility for unfair commercial use of the originator's data in violation of Article 39.3 TRIPS which does not provide for a linkage of data exclusivity to a patent.

The absence of any direct linkage between the Hungarian Regulatory Agency and the Patent Authority is another area of concern. The regulatory authority, while assuming responsibility for safety and efficacy review, apparently has abdicated any responsibility for ensuring that competitors do not market products covered by patents through linkage to the patent office. Thus, instead of taking the opportunity to prevent infringement during the marketing approval process, Hungary forces patent owners to resort to the court system after infringement has occurred. This results in significant commercial impact and Hungary remains non-committal with respect to implementation of such a system.

Enforcement

TRIPS Article 41 requires that WTO members ensure that their enforcement procedures permit "effective action" against intellectual property infringement acts and include "expeditious remedies to prevent infringements and remedies, which constitute a deterrent to further infringements." As such, it is not enough for a WTO Member to merely make available in their statutes the remedies that are enumerated in the TRIPS Agreement, such as preliminary injunctions and damages, but it must also ensure that these remedies are effectively and expeditiously applied by their judiciary in relevant cases.

Among the obstacles that U.S. patent holders, especially those holding pharmaceutical patents, are facing with respect to the enforcement in the Hungarian courts of their intellectual property rights, is the difficulty of obtaining preliminary injunctions against infringements of their process patents. This problem is especially exacerbated by the seeming unwillingness of the Hungarian judiciary to reverse the burden of proof in process patent infringement cases involving new products, as required by TRIPS Article 34. The unwillingness to order the defendant to demonstrate the actual process used in producing an identical product in a process patent infringement case involving a new product makes it very difficult, if not impossible, to enforce a process patent in the Hungarian courts. This is particularly true given the difficulty that process patent holders have in determining, through reasonable efforts, the process that was actually used by the defendant.

In addition, lax civil procedural practices by Hungarian courts unfairly allow a defendant to introduce new defenses at advanced stages of infringement cases – sometimes even during appeals that are pending in the second instance – resulting in protracted litigation from which the alleged infringer unfairly benefits. Furthermore, Hungarian courts fail to revoke the rights of defendants who fail to comply with requests to submit sufficient evidence.

Finally, current damages for intellectual property rights violations are not adequate to compensate for the injury the right holder has suffered because of an infringement of his intellectual property right. It is also rare that the infringer is ordered

to pay the right holder expenses associated with the defense of the right holder's intellectual property right, or ordered to recover profits. This is not in compliance with TRIPS Article 45.

Taken together, these current practices provide less-than-expeditious enforcement of intellectual property rights. As a result, the enforcement of patent rights that is envisaged by the TRIPS Agreement is rendered ineffective in Hungary.

Requirement of Local Working

Current Hungarian patent law does not explicitly recognize the importation of a patented product as meeting the "working the patent" requirements contained in the law. As such, Hungarian law should be amended to guard against the granting of a compulsory license when patented products have been imported. Local manufacture should not be necessary to satisfy the working requirement.

Failure to comply with U.S.-Hungary Bilateral Trade Agreement

By improperly defining the filing date of certain "pipeline" patent applications, Hungary has failed to implement the Agreement.

Market Access Barriers

The three-year pricing and reimbursement agreement between the Hungarian Government and pharmaceutical companies has been violated by Hungary. Under this agreement, pharmaceutical companies were supposed to receive regular price increases by the Government and obtain access to the reimbursement list. The Hungarian Government has unilaterally abrogated this agreement, and wishes to put in its place a new, four-year agreement.

PhRMA members are concerned that this agreement will not adequately guarantee access to the market for innovative pharmaceutical products. The new proposal states only that ministerial decrees will form the legal framework for market access of new products, but does not state any specifics regarding access of new products to the reimbursement lists or Government price increases.

In addition, the Government has implemented a price-volume system for certain product classes, as well as a therapeutic reference price system without any legal framework under which to do so. The Government has also implemented a policy of delisting products from reimbursement without consultation or notice. Under this system, only the two cheapest products (selected arbitrarily by the Government) within the same Anatomical Therapeutic Chemical (ATC) class will be reimbursed. As a result, Hungarian patients are being forced to change their usual therapy regimens.

There is a general lack of objective and verifiable criteria by which medicinal products are admitted to or removed from reimbursement lists. This is especially true in the case of products that receive 90%-100% reimbursement. For example, the Government has recently withdrawn reimbursement for an innovative product, without the recommendation of an expert committee as required under Hungarian law, while leaving 90% reimbursement for the copy product in place.

This lack of transparency is also evident in the case of the positive list for indigent patients (Közgyogy) affecting approximately six percent of the population but nearly 20% of total pharmaceutical demand. Indigent patients receive all medical care, including pharmaceuticals, free of charge. The list contains all categories on the general positive list, as well as additional categories that are not reimbursed through the general list.

The vast majority of the products on the Közgyogy list are locally produced products. Even when an imported product is available at equal or lower price, preference is given to the local one. Additional products – not reimbursed through the general list – are exclusively locally produced. Companies are not informed about the reasons for non-inclusion of their products and no appeal procedure is available.

Damage Estimate

PhRMA conservatively estimates that the industry loses between US$ 50 million and US$ 100 million annually because of the aforementioned trade barriers.

ITALY

The Italian Government has unilaterally and retroactively curtailed patent protection for pharmaceutical products by changing the terms and conditions relating to patent term restoration. Under the new regime adopted in 2002, Italy will now shorten the effective patent term, allow otherwise infringing activities during the last year of the patent term, and discriminate against foreign pharmaceutical producers. For these reasons, we ask that Italy be placed on the "Special 301" Priority Watch List for 2003.

Intellectual Property

Curtailment of Patent Restoration

Throughout the EU, as in the U.S., patents have a term of twenty years from the date of filing. To reinstate patent life lost during regulatory review, the EC enacted a law providing for an effective patent period of fifteen years. The mechanism to provide this additional protection is known as the Supplementary Protection Certificate, or SPC. (It is worth noting that the SPC only provides additional patent protection for the product for which marketing approval was sought, not for the entire scope of the patent.) This has not operated uniformly throughout the European Union, however. For example, the Italian Complementary Patent Certificate, or CPC, has provided up to eighteen years of supplementary protection for a maximum of 20 years effective patent life, and was available from November 19, 1991 to January 2, 1993. Products seeking CPC protection after January 2, 1993 were granted the same term as under the SPC, namely up to 5 years of extension for a total of 15 years.

In 2002, however, the Government of Italy acted to undermine the effect of the CPC system operating there in order to reach convergence with the system operating elsewhere in the European Union. Article 3(8) of the Italian Decree 63/32002 (converted into law 112/2002) (the "Decree") retroactively takes away the period of supplementary patent protection that has already been granted under Italian law for products that were able to take advantage of the CPC. The Decree reduces the CPC immediately by one year and then by two years for each calendar year thereafter. For example, the patent term protection that would expire under the CPC in December 2009 would expire in 2008 in the first year and then 2006 in the second year of the Decree. The retroactive reduction of patent protection in granted complementary protection periods is an expropriation of property, and hurts the commercial interests of PhRMA members operating in Italy. All CPCs that are valid beyond January 1, 2004 will be affected. While Italy has the right to change its system prospectively, the curtailment of patent terms already subject to patent term restoration under the CPC system results in a nullification and impairment of PhRMA members patent rights in Italy. Italy should amend its Decree to ensure that it operates only prospectively and does not curtail current patent rights.

Patent Infringement

In addition to the foregoing, Article 3(8) of the Italian Decree 63/32002 introduces an amendment to the rights of the patent holder during the period of protection under the CPC that permits infringing activities. More specifically, local pharmaceutical companies may now commence registration procedures for patented products one year in advance of the expiration of the Italian CPCs.

Further, the Chamber of Deputies has included an additional provision that allows third parties to make active ingredients which are otherwise prohibited during the complementary protection certificate period if the product is to be exported and the third parties obtain a so-called voluntary license. The law does specify that these products may be exported only if the period of patent and SPC protection has expired in the third country.

Violation of European Union Regulation and GATT 1994 National Treatment

There is a fundamental objection to the Decree under EU law, by virtue of its disproportionate and discriminatory effect on imported products. Italian CPCs that were granted prior to the EU Regulation applied predominantly to the products of non-Italian companies, namely those discovered and developed by the R&D based pharmaceutical companies outside Italy.

The Decree will therefore take away IP rights from groups based outside Italy, not from local Italian firms. PhRMA members believe that the Decree represents a clear violation of GATT 1994 Article III principles of non-discrimination. This also violates Article 28 of the EC Treaty as it will necessarily deprive of protection products coming from outside Italy rather than indigenous production.

Damage Estimate

The damage caused by the loss of both patent term and the infringing activities of local Italian companies now permitted to manufacture and export patented products in Italy is difficult to calculate at this time. The Italian precedent, however, represents the first OECD member country to incorporate into domestic law limitations on patent rights for purpose of encouraging exports during the period of patent protection, and represents a threat to the industry far beyond the borders of Italy. The damage caused to U.S. pharmaceutical manufacturers due to the deficiencies of the Italian patent regime thus potentially could harm U.S. commercial interests throughout the European Union and in other commercially important markets. PhRMA estimates the losses attributable to the new Italian decree to potentially reach $100 million in Italy alone.

MIDDLE EAST, AFRICA, SOUTH ASIA

INDIA

The Government of India has not provided patent protection for pharmaceutical products since 1970. In the absence of this and any other IP protection for medicines, PhRMA members face an extremely negative climate for bringing innovative products through the expensive research and development process and introducing them into the Indian market. In May of 2002, the Indian Government passed legislation intended to meet its international obligations under TRIPS, but we remain concerned that some provisions fall short of TRIPS requirements. In addition, implementing regulations have not yet been completed, so the law has not taken effect.[3] In May, then Minister of Commerce and Industry Maran explicitly confirmed India's intention to complete legislative action needed to provide full patent protection for pharmaceutical products in time for the TRIPS deadline of January 1, 2005.

Data Exclusivity provisions required by January 1, 2000 for all developing country members of the World Trade Organization (WTO) were not included in this legislation, though Indian Government officials have made statements in recent months that appear to acknowledge this obligation for India. PhRMA members also have seen limited progress in reducing market access barriers discriminating against the U.S. pharmaceutical industry. As noted during Under Secretary Larson's recent visit to India, India also lacks the intellectual property infrastructure and capacity to meet minimum international standards and badly needs technical assistance in this area.

In this context, the U.S. should both pursue a high-level dialogue to promote compliance with WTO disciplines across the board, including intellectual property, and at the same time expand international assistance opportunities for the training of patent examiners, among other urgently needed technical cooperation, to prepare India to meet its TRIPS 2005 obligations. In light of the passage of legislation intended to meet its immediate obligations under the World Trade Organization (WTO) Agreement on Trade Related Intellectual Property (TRIPS), and given the need for technical assistance and capacity building to support continuing regulatory reform, PhRMA is upgrading its assessment of India's intellectual property regime for pharmaceutical products. PhRMA members urge that India be included in 2003 "Special 301" Priority Watch List.

Intellectual Property Protection

While India has the right to delay product patent protection for pharmaceutical products until 2005, PhRMA remains concerned by ambiguities or inconsistencies in

[3] The Government of India has indicated willingness to clarify some of the ambiguities in the legislation though the rules process and to this end we have, along with other interested parties, submitted comments on the rules.

the Second Patent Amendments passed in May of 2002 which do not bring India within full compliance with its current TRIPS obligations. We also believe that the draft rules, as published, fail to clarify areas of ambiguity where the 2002 Act may fall short of TRIPS requirements, particularly in the areas relating to local working, other compulsory licensing provisions, and the definitions relating to patentability of inventions. We have sought clarification of the implementing rules, also known as the sub-legislation or secondary legislation, for the Second Patent Amendments Act.

India has also failed to introduce effective protection for the confidential and commercially valuable data associated with applications for marketing approval, also known as data exclusivity. TRIPS Article 65.4 delays the obligation to administer the formal system of patent examination and registration required by TRIPS Articles 27 - 34 for pharmaceutical and agro-chemical products. Only these TRIPS obligations, and no others, are affected. Accordingly, the Indian Government is bound by the January 1, 2000 deadline for requirements to respect the confidential protected data of originator firms, and formal protection for confidential data (39.3). While some positive statements are emerging from the GOI, the issue continues to be obfuscated by the local industry lobbies, which appear to confuse data exclusivity with patent term extensions and then link the issue to the TRIPS and public health debate. In addition, the Ministry of Health is completely unprepared for adoption and implementation of data protection, and requires technical assistance along the lines provided in Egypt by US AID under the Strengthening Intellectual Property Rights in Egypt (SIPRE) program. We are encouraged, though, by recent Government of India statements to the effect that India recognizes the data exclusivity obligation and has begun to discuss the issue at high levels within the cabinet. It is critical that the U.S. continue to press this issue towards a successful conclusion.

Finally, we continue to believe that India has not acted in good faith in implementing its obligation to provide Exclusive Marketing Rights (EMR) under TRIPS Articles 70.8 and 70.9. Using the excuse that it is examining the mailbox application with regard to patentability under the 1970 Act, a requirement not found in TRIPS, India is yet to approve a single application for EMR despite a number of qualified applicants. Both PhRMA members and Indian companies have unsuccessfully sought EMRs for facially qualified products. The process has been made so non-transparent and difficult that PhRMA members who have filed for EMRs now have little hope of ever receiving the rights to which they are entitled as a transitional measure pending full patent protection. The hurdles placed in front of international companies are higher than those applicable to domestic EMR applicants.

Non-Functional Patent Office, Lack of Other IP Infrastructure

In addition to the difficult situation posed by lack of patent exclusivity, PhRMA members are gravely concerned by the absence of needed resources to upgrade India's capacity in the patent area. India's Patents Office is essentially non-functional.

In anticipation of the improvements required by the TRIPS Agreement, there has been a surge in the filing of patent applications and many more are expected. The Indian Patents Office, based on its size, degree of modernization and past practices, is and will be unable to cope with these filings. Recent statistics indicate a backlog of over 30,000 unprocessed applications, which, measured against the average output of the collective Indian Patents Office, will not be examined or granted well into the latter part of the next decade.

While we appreciate India's current efforts to invest in upgrading existing facilities, underlying problems in India's patent law render effective patent administration impossible. The Government of India needs to follow-up its modernization efforts at the administrative and legislative level to make it possible to operate a modern patent office in India. The U.S. Government should provide needed assistance to India as a developing country WTO member for capacity and infrastructure in this area.

Market Access Barriers

In the area of Drug Pricing, India has recently announced the Drug Policy 2002, which tries to ostensibly reduce the span of control; it, however, retains some of the most stringent price controls and monitoring in the world under the rigid provisions of Drug Price Control Order (DPCO). Moreover, the new policy discriminates against drug discovery through foreign R & D by exempting for 15 years drugs discovered through indigenous R & D from coming under the purview of DPCO Drug Price Control Order (DPCO).

This pricing regime, combined with the lack of any meaningful patent or other intellectual property protection, makes India a less viable market for research-based companies from a commercial standpoint, particularly if those companies were to consider placing the latest and best innovative drugs on the Indian market. Even if the current impasse on the new DPCO were to be resolved soon, no major improvements can be expected in the pricing policy. This is because of structural & logical flaws in the criteria and bases for price-fixing that are and have been inherent in all past & present DPCO's. In fact, we do not expect a significant improvement from the new pricing policy that is underway in India. Our industry would urge any new Government in India to consider abolishing the DPCO. The DPCO is neither in the interest of the Indian economy nor of the Indian pharmaceutical industry, nor, and most important, in the interests of the Indian healthcare consumer. Despite the lowest prices in the world, 70% of the population still has no access to modern medicine.

<u>Import Policies</u>

PhRMA member companies operating in India face high 44% effective import duties for active ingredients and 66% for the finished products. The Government of

India has stated its intention to progressively lower import tariffs on pharmaceuticals, particularly with reference to essential medicines. Duty rates, however, remain unacceptably high, and are still very often being used as a discriminatory protectionist tool to promote domestic industrial policy. In 1996, tariffs were brought down to 85% with plans to further decrease rates to 25% by the end of 1999. Progress has been slow and tariff rates remain currently high. PhRMA urges U.S. negotiators to insist that tariffs be brought down to zero, the goal of many WTO signatories. As in many other areas, there is little confidence that enforcement of these new rules will be at the necessary and appropriate levels.

Standards, Testing, and Labeling

India has little or no regulatory framework for Clinical trials. Though the Government made a genuine attempt to bring in a radical reform in drug manufacturing practices in the country by adopting rules for Good Manufacturing Practices (GMP) last year, the non-transparent and labyrinthine procedures in the Drug Controller's Office do not inspire confidence.

In addition, discriminatory problems remain in the area of trademarks, most specifically with respect to regulations concerning the size and placement of the generic name on medicines in India. Finally, PhRMA member companies operating in India have reported arbitrary local FDA decisions.

Damage Estimate

Please see the Appendix for a Charles River Associates (CRA) study which conservatively estimates losses in India due to the absence of intellectual property protection at more than $1.7 billion dollars annually. Note also, however, that the damage caused by the inadequate protection of intellectual property rights in India reaches beyond direct losses caused by displaced sales in India. Indian bulk pharmaceutical companies aggressively export their products to third countries where intellectual property laws are similarly lax. The damage caused to U.S. pharmaceutical manufacturers due to the deficiencies of the Indian patent regime thus goes beyond displaced sales in the Indian market, and reaches to the ability of U.S. companies to compete in other significant markets, especially in the Asia-Pacific and Middle East regions.

ISRAEL

As noted previously, Israel's intellectual property protection for pharmaceutical products has deteriorated substantially over the past decade. The situation now contrasts sharply with that of industries relying primarily on copyright and trademark protection, where Israel offers a fairly strong legislative regime and reportedly has improved its enforcement record. With respect to the pharmaceutical sector which is highly dependent on protection of patents, and undisclosed information (data exclusivity) the Government of Israel actively undertakes policies that erode intellectual property protection, which include curtailing the effective patent term, limiting exclusive rights for patent holders, and denying data exclusivity as required under the World Trade Organization (WTO) Agreement on Trade Related Intellectual Property (TRIPS). PhRMA urges that Israel remain on the 2003 "Special 301" Priority Watch List.

Intellectual Property Protection

Data Exclusivity

Israel has failed to date to adopt protection for confidential data as required by the WTO TRIPS Article 39.3. Despite assurances to the contrary, the Government of Israel's Health Ministry does not protect the confidentiality of commercially valuable test data. In this area, Israel falls into the category of a country that provides no legislative or regulatory protection for undisclosed information submitted to the Ministry of Health. The cost of generating this information is estimated at $802 million. The absence of data exclusivity in Israel allows manufacturers other than the right holder (i.e. the Israeli generic companies) to rely on test data from drug marketing applications by innovator firms from the date that the innovators receive their marketing approval.

Not only is this legal posture a growing anomaly among leading U.S. trade partners, it exposes Israel to a potential WTO TRIPS dispute. PhRMA requests that the Government of Israel provide for an exclusivity period similar to the protection granted in OECD countries.

Patent Registration Delay

A patent is thoroughly examined by the patent examiners in the Patent Office who are experienced in the relevant art. After examination and acceptance of the application, it is published for possible oppositions in the Patent Gazette. If the application is opposed, the opposition proceedings may take years (3-5 years is a realistic and somewhat optimistic timetable) until there is a decision in the opposition proceedings. During the opposition proceedings the patent is not registered and not yet valid. Thus, and although the Patent Office thoroughly examined the application and approved it, a local generic manufacturer may block the registration of the patent for many years. It is worth emphasizing that the damages which may be incurred by

the patentee during this period of the opposition proceedings are enormous. Indeed, in most (if not all) OECD countries the opposition proceedings are conducted post registration (e.g. in the EPO) and it is not possible to block the registration of the patent (this is also the case in the U.S.).

Parallel Importation

In early 1999, the Government of Israel (GOI) passed into law amendments to the Pharmacists' Ordinance that would allow importation by non-right holders of patented pharmaceutical products registered in Israel. In early 2001, the Ministry of Health provided licenses to sick funds and other entities to import products currently under patent in Israel. To date, 22 parallel import licenses have been granted by the Ministry of Health, causing damage to American research based pharmaceutical companies.

Counterfeiting

PhRMA members also remain concerned by the failure of the GOI to provide adequate provisional and border measures required by TRIPS Articles 50 - 60 in order to deter infringement and counterfeiting activities related specifically to pharmaceutical products. The Israeli Customs authorities and Ministry of Justice officials need to aggressively investigate and prosecute the smugglers of counterfeit products. In one particular case, Israeli customs seized counterfeit Viagra over six times in the last 8 months alone, but smugglers have never been apprehended, arrested, or prosecuted. In addition, the authorities have not given Pfizer, the company producing the patented and trademarked product, any information about the couriers. The Israeli Minister of Health and the police also need to suspend the business of illegal medical operations that distribute counterfeit or unapproved diverted products.

Market Access Barriers

The Israeli Knesset has recently passed an amendment to the Pharmacists Ordinance that allows for fast-track registration of generic products based on FDA or European Medicine Evaluation Agency (EMEA) approval. Generic products approved by these authorities would be granted an automatic marketing authorization unless the Ministry of Health objects within 70 days. This amendment primarily benefits local generic producers thus violating GATT 1994 Article III National Treatment requirements.

Damage Estimate

Adoption by Israel of some of the patent-weakening measures currently being discussed in other countries and in the TRIPS Council would damage PhRMA members. Israel has a strong generic pharmaceutical industry that would benefit

commercially, at the expense of PhRMA members, from a change in law to allow unauthorized production for export of patented products. If this were to come to pass, damages to PhRMA members could easily exceed $100 million dollars from this alone, but the damage would be felt in other markets. Should the Government of Israel adopt a policy of compulsory licensing for export, other OECD countries would be able to parallel import from LDC's which imported generic versions of patented products from Israel, far exceeding the damages incurred in Israel alone). In addition, damage to the industry from lack of protection for confidential data, given that the threat of parallel importation on patented pharmaceutical products is not in place, is difficult to estimate. However, based on experiences in other markets, parallel importation could yet have a domino effect on the whole market and would not be limited to a specific product. Parallel importation could seriously damage the Israeli healthcare system, and the Israeli pharmaceutical and related sectors.

The Israeli pharmaceutical market totals some $690 million (1998). Sales of patented imported products were approximately $450 million (most sales are by the multinational pharmaceutical companies). Sick funds represent 90% of the market, i.e., $400 million in patented imported products.

Continued deterioration of the intellectual property environment in Israel will have an adverse impact on employment and investment at a time that the Israeli economy can ill afford it. Members of the research-based pharmaceutical industry in Israel currently employ 1000 people; many may lose their jobs. (Bristol Meyers Squibb has already pulled most of its activities out of Israel, reducing its staff from 80 to 20). Furthermore, international research-based firms invest $1000 million per annum in clinical trials conducted by Israeli medical institutions and physicians.

LEBANON

Although Lebanon has taken steps towards meeting minimum international standards for IP protection and affording market access for products relying on intellectual property, key outstanding implementation issues need urgent resolution before PhRMA members will benefit from an improving investment climate. These include clarification and enforcement of the data exclusivity provisions in the new patent law, linkage between health regulatory and industrial property officials, and a firm stance against parallel imports. PhRMA members are troubled by the continuing practice of registering unauthorized copies of innovative patented pharmaceutical products, despite passage of a new patent law, which has been further magnified by a mutual recognition agreement with Syria, a well known producer of unauthorized copies. In addition, the possibility that the Government of Lebanon may sanction large-scale pirate production of pharmaceutical products for export highlights the regional implications of Lebanese policy. In light of these issues, PhRMA recommends that Lebanon be included on the 2003 "Special 301" Priority Watch List.

In early 2002, senior executives from PhRMA member companies presented these concerns to the Lebanese Prime Minister, Minister of Health, Minister of Justice and Minister of Economy as part of a regional PhRMA meeting held in Beirut. Although personal assurances were given to address the deficiencies in the patent law and safety concerns regarding parallel imports, no concrete actions has been taken to date.

Intellectual Property Protection

In July 2000, the Lebanese passed a new industrial property law, which represents a major improvement over the 1924 law. It provides a basic level of product patent protection with a 20-year term of protection and will provide incentives for new foreign direct investment generally, as well as technology transfer specifically to the pharmaceutical sector. Most of the language is compliant with the World Trade Organization (WTO) Trade Related Intellectual Property Agreement (TRIPS) (including some level of data protection, limited compulsory licensing, increased penalties for infringement, and no phase in period for product protection for pharmaceutical products).

The new law provides a good basis for Lebanon's eventual WTO accession. PhRMA supports Lebanese efforts in advance of WTO membership to address longstanding trademark and patent issues. A number of amendments will be necessary in order to bring it into full compliance with TRIPS, but the industry views this bill as a major step forward.

However, in its present form, the patent law does not provide any tangible protection for the products of PhRMA members due to the requirement for a Lebanese patent and the lack of pipeline protection. In addition, the data exclusivity provisions as

they apply to commercially valuable pharmaceutical test data, are ambiguous and unenforceable. In an effort to address the deficiencies in the data protection provisions, local PhRMA members have provided the Ministry of Health a briefing paper outlining the industry's concerns and the basis for the data protection provision by the Ministry of Health. The submission was made on December 12, 2001, and remains under consideration by the Ministry of Health which had promised to review it and forward it to the Ministry of Justice for the latter's final opinion. As of today, it is unclear what the final position of the Lebanese authorities will be.

Although much work needs to be done, we note that credit is due to the first Government since independence to make significant efforts to modernize the copyright, trademark, and patent laws. PhRMA remains committed to supporting these efforts through continued dialogue with the Lebanese authorities and sponsorship of workshops.

Recent Registrations of Copy-Cat Products

PhRMA members continue to be concerned by the registration of unauthorized copies by the Ministry of Health. The registration of these copies is a direct result of the requirement for a Lebanese patent and the lack of effective and enforced data protection legislation. Many applications to register copies of PhRMA members' products were filed with the Ministry of Health by bogus applicants. Such applications are filed and processed by the Ministry of Health in compete secrecy. This secret procedure prevents PhRMA members from learning about any applications filed to register copies of their products. The owners of the original products only learn about the filing of such applications either fortuitously or once the application is approved and the product released. Because of such secrecy rule, many copies of PhRMA members' products were actually registered and released in the Lebanese market. However, in those cases where the filing of the bogus application was discovered before the registration was completed, PhRMA was able to prevent the registration of a small number of its members' copies through direct lobbying and the assistance of the U.S. Embassy.

On the judicial front, two PhRMA members have challenged the marketing of a pirate version of their product in court based on unfair competition with verdicts expected by end year. In addition, several infringing copies have been approved by the Ministry of Health in the past eighteen months.

A mutual recognition agreement with Syria ratified early this year provides for the immediate and automatic introduction of pharmaceutical products manufactured in Syria into Lebanon. As one of the primary manufacturers of pirate copies of patented pharmaceuticals, a flood of copycat products made in Syria is expected in the coming year. Lebanon's intentions to move away from recent progress in intellectual property

protection were clearly highlighted by recent Government tender awards to pirate copies of Syrian origin.

More troubling, PhRMA has received credible reports that the Government of Lebanon is considering approval of applications to build several pharmaceutical plants that would be dedicated to production of infringing copies both for the domestic and export markets. In this regard, PhRMA appreciates the continuing and effective advocacy efforts led by the American Embassy in Beirut to improve protection for intellectual property, including patented pharmaceutical products.

Parallel Importation

As a net importer of goods, new legislation passed by parliament in 2002 was designed to facilitate parallel importation thus circumventing local distributor agreements. First and foremost, parallel importation poses serious health and safety risks to Lebanese patients due to the porous supply chain outside the manufacturer's control and the known risks of spurious medicines to patients in Lebanon. It is clear that the legislation was adopted without the special nature of pharmaceuticals in mind or a proper analysis of the effect on drug supply safety. The importation of these products is justified as a "cost containment" measure, yet senior ministry of health officials privately acknowledge that parallel importation will fail to produce any savings on medicines for patients.

Parallel importers, distributors, wholesalers, and retail pharmacists do not customarily pass on any "savings" associated with exchange rate arbitrage. Senior health officials recognize that parallel importing puts the drug supply at risk, but have failed to stop the practice. Industry has argued that it is very hard to police the supply of medicines once the chain of supply from manufacturer to authorized importer is broken. Counterfeiting and/or poor quality goods easily enter the drug supply.

During meetings with senior officials, PhRMA members have received personal assurances that bureaucratic requirements will effectively make the parallel importation of pharmaceuticals unfeasible. However, member companies have reported a continuous stream of large volume purchase inquiries in Europe destined for Lebanon. It is clear that until legislation regulating the parallel import of pharmaceuticals is introduced, local importers will attempt to take advantage of legislation loopholes.

Market Access Barriers

Public Procurement

A serious trade barrier concerns public sector procurement. The Government procurement policy discriminates against foreign suppliers by allowing local manufacturers a 15% price advantage in public sector business. This discriminatory

practice contributes to higher costs for public sector procurement-ironic, considering Government efforts at cost containment-- and represents an added burden on taxpayers. It is also widely acknowledged that locally produced products have "priority standing" over imported products in Ministry of Health registration procedures, which translates into preferential waiting periods for obtaining marketing authorization.

Regulatory Barriers

Research-based companies are urging the Ministry of Health to develop a "fast track" approval process for New Chemical Entities (NCE) and their associated line extensions. This would speed the introduction of new, innovative and often life and/or cost- saving medicines to patients. Unfortunately, a lack of resources, outmoded regulatory requirements, and the lack of criteria for distinguishing between innovation and imitation, contribute to unnecessary delays to registering new products. Delays of up to two years are common, while in neighboring Cyprus, new products are often approved in as little as 90 days (based on prior "reference country" approvals, e.g., FDA or European agency approvals). To date, the Government has failed to take any action regarding industry proposals, meaning Lebanese patients often must travel abroad or rely on risky, uncontrolled "suitcase" importation to obtain the latest medicines on the black market.

In a positive move, a new draft registration law in line with international regulatory standards has been submitted by the Ministry of Health to cabinet for approval with a law expected to become effective by early 2003. This legislation should facilitate the registration of products by multinational pharmaceutical companies and address some of the bureaucratic delays experienced by U.S. industry in introducing innovative medicine.

Damage Estimate

The 2002 sales value of PhRMA member patented products in Lebanon is over $200 Million. Over 1,400 health care professionals are employed by multi-national companies in Lebanon with a 7% increase in new hires estimated over the course of the past year (2002). PhRMA is currently studying methodology that could be used to estimate losses in Lebanon due to the problems outlined above. Lebanon represents one of the faster growing pharmaceutical markets in the Middle East, and there is significant market support for innovative, branded pharmaceuticals.

MOROCCO

While PhRMA members strongly support the initiation of Free Trade Agreement (FTA) negotiations between the United States and Morocco, we remain concerned by the failure of Morocco to meet both current obligations under the World Trade Organization (WTO) Agreement on Trade Related Intellectual Property Rights (TRIPS), as well as basic GATT 1994 requirements such as national treatment. The key issues affecting U.S. research based pharmaceutical companies in Morocco can be grouped into 2 areas: (1) inadequate protection of intellectual property rights (IPR), and (2) industrial policy and legal Issues that form market access barriers to good reliant on intellectual property protection. Given the increasing gravity of some of these concerns and the opportunity posed by FTA talks to resolve the issues, PhRMA recommends that Morocco be included on the 2003 "Special 301" Priority Watch List. We urge U.S. FTA negotiators to ensure that Morocco not gain benefits in the FTA merely for meeting current obligations or remedying current IP or market access violations.

Intellectual Property Protection

PhRMA members still await implementation of Morocco's new patent law, published in March 2000. When implemented, this patent law should allow for the protection of pharmaceutical products in compliance with TRIPS. Unfortunately, more than two years later, implementing regulations have still not been issued and this new patent law is still not in force. Thus we face a situation where Morocco has not yet provided basic patent protection for pharmaceutical products. PhRMA recommends that, as a precondition for initiating FTA negotiations, the U.S. Government seek Morocco's publication of the patent law implementing regulations so that the Patent Law can enter into force and the Moroccan Patent Office (OMPIC) can start issuing patents for pharmaceutical products.

While the Government of Morocco provided de facto patent protection for PhRMA member products until recently, it has now implemented a policy to encourage the filing of marketing applications of patented products. As a result, a growing number of copy products is now appearing in the market. Again, PhRMA urges that as a precondition for initiating the FTA negotiations, Morocco should freeze or suspend marketing approval for any unauthorized copy products made in the interim period between announcement of intention to start FTA negotiations and the present.

In addition, PhRMA members are concerned by the absence of data exclusivity in Morocco, which means that there is no effective protection for the commercially valuable and proprietary undisclosed data associated with applications for marketing approval. The considerable effort that research-based pharmaceutical companies undertake to gain marketing registration of their innovative pharmaceutical products is recognized by the TRIPS Agreement, which requires its Member countries, including Morocco, to provide data exclusivity. TRIPS Article 39.3 requires WTO members to

provide a period of data exclusivity during which all proprietary information submitted to a regulatory body is to be protected from unfair commercial use. As with the patent law rules, Morocco should implement effective data exclusivity as a condition of FTA negotiations, and should not gain any additional benefit as a result of meeting current obligations.

Lack of Linkage between Regulatory and Industrial Property Officials

Another issue of concern is that health authorities often fail to coordinate with patent officials and inappropriately issue sanitary registrations for products already under patent, whose patent application is pending, or whose period of data exclusivity has not expired. The adoption of "linkage" regulations (i.e., establishing a formal link between health and patent authorities) would help to ameliorate this situation, requiring that "second applicants" (i.e., generic, or in some cases, "pirate" applicants) demonstrate that the product for which they are requesting market approval is not the subject of a valid patent or pending application. "Linkage" exists in the United States, Europe and Japan, and is crucial to maintaining the integrity of the intellectual property and patent system. U.S. negotiators should ensure that Morocco provides this linkage as part of its commitments under the pending FTA.

FTA Objectives

We strongly support inclusion of a chapter in the FTA that establishes adequate and effective standards for intellectual property protection, and which would facilitate the granting and enforcement of rights. The essential elements of such a chapter include measures that build upon and enhance the standards established by the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and recent bilateral agreements between the United States and other countries.

Of critical importance to such a chapter are:

- Measures that provide effective protection for test data that must be produced to support approval of pharmaceutical products. Such measures should ensure that copies of products may not be approved for marketing for at least ten years following an approval based on the test data provided to the Ministry of Health.

- Measures to prevent the granting of marketing approval of copies of pioneer pharmaceutical products before the expiration of applicable patents, and to remove from the stream of commerce current infringing products. This will ensure that regulatory procedures are not used in a way that undercut the legitimate interests of the patent owner.

- Measures that provide patent term restoration for products the marketing of which has been delayed by regulatory or patent granting procedures.

- Measures that will enhance protection for trademark rights, including by prohibiting restrictive or burdensome labeling requirements for regulated products (e.g., use of generic names for pharmaceutical products in a way that impedes the effective use of trademarks in such products), and which allow a PhRMA member to better control distribution of trademarked medicines, consistent with the public's interest in safe and authentic medicines.

- Measures that enhance the ability of patent owners to obtain preliminary injunctive relief in judicial proceedings where there is an ongoing infringement of rights.

The inclusion of a chapter that addresses these points is necessary to bring the intellectual property systems of Morocco up to levels that approximate the standards of protection available in the United States. We also note that Morocco still does not comply with the minimum standards established by the TRIPS Agreement. Negotiations with Morocco should be conducted in a manner that ensures that necessary changes to conform to the TRIPS requirements are made prior to the conclusion of a new agreement.

Beyond the intellectual property area, PhRMA members also confront two problems that appear rooted in industrial policy relating to local manufacturing or investment and local ownership legal requirements.

Market Access Barriers

Industrial Policy and Legal Issues:

- Local manufacturing site requirements

In order to become a pharmaceutical company in Morocco, a company must build a local manufacturing plant, regardless of the economics (small volumes means that one year consumption can be manufactured in one month) and the fact that local industry only utilize 30-40% of total current manufacturing capacity. This requirement is aimed at imposing on foreign pharmaceutical companies a local brick and mortar investment. This local manufacturing requirement fails to see (a) the over capacity problem that is plaguing the local industry and hurting the viability of local companies, and (b) the reality of the investment made by the research-based pharmaceutical industry in hiring and training hundreds of medical representatives to disseminate scientific information to the medical community. Medical representatives also represent a highly trained and well-paid work force that should be of greater value to Morocco than a few additional factory workers.

PhRMA requests that USTR seek the agreement of the Government of Morocco to amend the Law of 1960 in order to allow foreign companies to retain full ownership

of their local investment and be entitled to register their products under their name in Morocco regardless of (i) capital structure and (ii) local manufacturing capabilities[4]. Other countries like Jordan have shown that there are other and better ways to create a strong pharmaceutical industry and to ensure that pharmaceutical products are safely manufactured and marketed in the best interests of the public.

- Local ownership legal requirements

A second onerous condition of doing business as a pharmaceutical company in Morocco is the requirement that a majority interest in the company must be owned by an actual pharmacist. This also exacerbates the negative impact of current requirements of investment in bricks and mortar facilities.

Under Moroccan Law 1-59-367 of February 19, 1960 (the "Law"), only companies that are controlled and majority-owned by individual pharmacists (half of which must be licensed to practice in Morocco, i.e., Moroccan pharmacists) can be licensed to be "pharmaceutical companies" in Morocco. Failing to meet such criteria, a company (i) cannot manufacture, import and market pharmaceuticals; and (ii) cannot have any official contacts with health authorities, even about its own products that are sold by a local distributor.

As a result of this ownership requirement, an American company wanting to invest in Morocco has few good choices. The company can transfer 51% of its local investment to individual pharmacists (half of which have to be Moroccan pharmacists) in order to benefit from the rights granted to local pharmaceutical companies, or stop becoming a pharmaceutical company in Morocco, and register all its products through a third party owned local company. The local company would then enjoy quasi-ownership rights in Morocco over the U.S. company's products, and the local company would be deemed by the Ministry of Health to be the "owner" of the products.

This aspect of the Law of 1960 is also criticized by local companies, which are prevented from seeking capital infusions from outside investors (either companies or non-pharmacists). This greatly limits their expansion potential. Local pharmacists are also hurt because they are unable to transfer ownership of their company to their non-pharmacist heirs.

[4] Per the request of the Trade Policy Staff Committee (TPSC) PhRMA is evaluating draft legislation aimed at ammeding the law of 1960 and will provide this analysis as soon as possible. We have learned thus far that local manufacturers are now being encouraged by the Ministry of Health to launch their copies of major innovative products without permission or authorization by the right holder. Local company Galenica has launched a generic of Pfizer's Zithromax last month (November 2002), and at least three other local copy-cat versions of Zithromax are currently under regulatory review. At least two copies of Pfizer's Norvasc, an anti-hypertension treatment, are under regulatory review as well. Both Zithromax and Norvasc are protected by patent until 2007-2008 in major markets.

Accordingly, PhRMA requests that USTR seek Morocco's agreement to amend the definition of a pharmaceutical company in the Law of 1960 to modernize the Moroccan legal environment for the benefit of both local companies, which will be able to attract much needed capital, and foreign companies, which will be able to own 100% of their local investment.

Import License Restrictions

Only products that are specifically life saving, of small volume, or cannot be produced technically in Morocco, qualify technically as such for import licenses and this after considerable review. Furthermore, to import finished products, the Government requires a local production facility to be maintained. Although this is not a provision in the patent law itself, it has same effect. U.S. negotiators should ensure that Morocco dismantle this requirement.

Custom Duties

Custom duties applicable to U.S.-origin pharmaceutical products are much higher than those duties applicable to EU-origin pharmaceutical products. In addition, since March 2000, EU-origin products enjoy a progressive reduction of custom duties in the amount of 25% every year. As a result, EU products will be subjected to 0% duty as of April 2003, thus making comparable competitive U.S. products much more expensive to Moroccan patients.

It is therefore of utmost importance that a Free Trade Agreement provide for the removal of custom duties applicable to U.S.-origin pharmaceutical products, as such duties that currently deprive U.S. companies from competing on a level-playing field with EU companies.

Regulatory Delays

PhRMA is concerned that the processes for New Drug Registration require major work and clarification of key issues impacting the administrative process. These span from the lead times related to their completion and the costs involved in the application processes themselves, to the specific guidelines and requirements. It is hoped that the lead-times to registration can be effectively reduced.

Distribution Agreement

Moroccan law severely limits unilateral termination of distribution agreements. Termination of distribution agreements is only possible by mutual consent or through the award of unreasonable indemnification rights due to the subjective criteria specified by local distributors. Local distributors have no incentive to pursue aggressive

distribution of the goods they represent, since a poor performance on their part does not put at risk their distribution agreement.

The Law Regarding the Distribution of Shares

The Moroccan pharmaceutical law of 1960 is very restrictive and gives no flexibility for foreign investors.

Pharmaceutical Law / 1960

- The share capital of the pharmaceutical companies executing pharmaceuticals acts must belong for 51% to one or several pharmacists, and 26% at least to pharmacists authorized to practice in Morocco.

- In these same companies, the Chairman and half + 1 of the board members must be pharmacists.|

- The Responsible Pharmacist must be at the same time shareholder & Director of the Board.

Damage Estimate

We do not yet have an estimate of damages relating to the new practice of the Ministry of Health to approval locally manufactured copies of PhRMA member products patented in other markets. PhRMA members also suffer in Morocco from the absence of (i) formal implementation of the patent law, and (ii) data exclusivity. Both of these issues create a major risk to new, innovative products at a time when the health authorities in Morocco are shifting their priorities and are looking increasingly at the authorization of copies of still patented products.

SOUTH AFRICA

PhRMA member companies appreciate the good will and continuing statements of the Government of South Africa (SAG) that it intends to meet fully its multilateral obligations as spelled out in the World Trade Organization (WTO) Trade Related Intellectual Property Agreement (TRIPS). In April 2001, the Pharmaceutical Manufacturers Association of South Africa and the 39 companies involved in litigation against the South African Government reached a mutually beneficial settlement of litigation originally initiated by the industry in 1998. Under the terms of the settlement, the Government of South Africa reaffirmed its commitment to TRIPS and to implement the Medicines Act Amendments of 1997 in conformity with its international obligations and the South African Constitution. The Government and the industry also pledged to work together to ensure wider access to pharmaceutical products for pressing public-health crises, including infectious diseases such as HIV/AIDS, TB, and malaria.

The industry has worked cooperatively with the Government to assist in the development of regulations to ensure the consistency of the Medicines Act with TRIPS. Nonetheless, PhRMA members continue to be concerned regarding the implications for sustained development of innovative drugs and the erosion of patent protection through adoption of pre-expiration working that does not provide for data exclusivity or patent term restoration. In addition, we believe South Africa invites heightened public health risks through a parallel import regime, as contemplated by the Government of South Africa.[5] In addition to intellectual property concerns, PhRMA members have a number of other bilateral trade issues that would benefit from the advocacy of the United States Government (USG).

We also see the upcoming Free Trade Agreement negotiations between the U.S. and the Southern Africa Customs Union (SACU) as an important opportunity to address continuing concerns and to provide needed technical assistance and capacity building designed to improve South Africa's intellectual property regime and improve prospects for increased investment in its pharmaceutical production capacity. For these reasons, PhRMA requests that the U.S. Trade Representative include South Africa on the 2002 "Special 301" Priority Watch List.

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[5] PhRMA remains concerned by the policy of encouraging parallel importation. While we recognize that TRIPS does not provide dispute settlement for the patent exhaustion issue, the adoption of international exhaustion or implementation of parallel importation will not improve access to essential medicines, more than 95% of which are off patent. Both patent and trademark protection provide the benefit of consumer safety. Given the recognized upsurge in organized criminal enterprises focused on the smuggling of counterfeit or otherwise questionable pharmaceutical products worldwide, many experts urge caution in this area. HHS Secretary Thompson recently cited the insurmountable problems associated with sampling and testing of products to identify and remove counterfeit, adulterated or misbranded drugs that could enter the country in large commercial quantities in rejecting a re-importation program for the United States, even where the FDA would have been regulating the initial sale. The South African program goes beyond the scope of the contemplated U.S. system, which would introduce an even higher level of risk.

Intellectual Property Protection

New Developments

In recent years members of PhRMA operating in South Africa have experienced significant delays in the medicines approval process. This significantly shortens our effective patent term for new innovative products. Meeting the specific requirements of the South African dossier rather than being able to submit the common technical document (CTD) generally delays applications for registration by 3 to 6 months. The approval process at the South African Medicines Control Council (MCC) is significantly slower than the Food and Drug Authority (FDA) in the US and the Medicines Authority in Europe (18 to 24 month delays beyond approval in the U.S. and Europe are not uncommon).

In terms of Patent Term Restoration (PTR), to a certain extent, the Government of South Africa currently provides this informally, due to delays in the approval of generics. The recent amendment to the Patents Act introducing the Bolar-type provision and the accelerated approval process for generics remove this "balance." This adjustment is skewed to benefit the generic producers only, at the expense of reducing patent terms of innovative medicines. Usually, provisions of this nature are introduced as a package similar to the example in the United States, through Hatch Waxman.

In addition, South Africa has not yet implemented effective protection for the confidential and commercially valuable clinical data associated with applications for marketing approval. South Africa should demonstrate full compliance with this key TRIPS Obligation as a condition for FTA negotiations by establishing a minimum period of no less than five years from the approval of marketing of a pharmaceutical product for the South African market during which it will not accept a competing application for approval for a product (regardless of patent status) that lacks its own clinical dossier. This prevents not only the sharing of privileged and undisclosed information provided to health authorities as a requirement of marketing approval but also the unfair commercial use of this data, which would result in the enrichment of a commercial competitor through either direct or indirect reliance on the data.

Although the Government of South Africa has not yet fully disclosed the final regulations to implement the Medicine Act Amendments of 1997, it appears that the Government is intent upon implementing parallel trade, a policy that is fraught with risks. We continue to have both safety and intellectual property concerns. In the IP area, for example, concerns include the authority provided in the regulations that would potentially allow a third party to use an innovator's trademark, which undermines the fundamental purpose of trademarks as assurance of quality and traceability. Finally,

given the potential perception of a deteriorating investment climate in South Africa, it is important that the regulations support a commercial environment that will attract foreign direct investment across sectors.

PhRMA members continue to seek a cooperative relationship with the Government of South Africa to address the HIV/AIDS pandemic in Southern Africa. In particular, PhRMA members remain committed to assisting the SAG in establishing programs to halt the progress of the HIV pandemic. PhRMA members welcome the recent decisions of the SAG to accept offers from Pfizer, but are distressed by the delay in launching of a nationwide program of Mother to Child Therapy (MTCT). This is particularly problematic in light of the outstanding offer by PhRMA member Boehringer Ingleheim to provide an unlimited quantity of medicine needed for treatment of vertical transmission for at least five years.

PhRMA members are also concerned by reliable reports of smuggling into South Africa of unauthorized copies of PhRMA member products. Although this is clearly not state policy, it represents an increasing problem. By their failure to act, the South African Government has adopted a policy of inaction that is harmful both to the people of South Africa and PhRMA members.

Prevention of diversion of State-purchased medical supplies remains another high priority for PhRMA members operating in South Africa. PhRMA member companies continue to work closely with a number of South African agencies and ministries to help combat theft of medicines. In South Africa, where at least 50% of all State drugs are stolen or lost through poor management, parallel imports would exacerbate the entry into the market of counterfeit goods.

In April 2000 police seized over R100m worth of stolen and counterfeit medicines, catching the perpetrators red-handed. Two years later, the matter remains unresolved, with the accused alleging that they were "gearing up for business under Section 15C of the Medicines Act". In an uphill battle, PhRMA companies have spent around R1m in the past year alone on legal counsel to assist the State's prosecution, who feel domestic pressure to look the other way, especially when people involved are linked to the Government. Government raids periodically have also uncovered potentially lethal products found in circulation but the perpetrators do not necessarily get prosecuted.

This lack of security in the State distribution chain renders the preferential prices given to the SA Government wasted. As such, leakage in the State sector amounts to the single major hindrance to medicine access in SA. It also eases the entry into the market of counterfeits, substandard and potentially harmful medicines.

PhRMA FTA Priorities

Given the foregoing, PhRMA members believe that there are important opportunities to use the upcoming FTA talks to improve standards available in South Africa for protection of intellectual property relating to pharmaceutical products. We hope that USG agencies can renew efforts to bring standards for IP protection into closer alignment with U.S. standards. PhRMA priorities include:

- Full Protection of Test Data: For effective protection of commercially valuable and confidential data, it is essential that South Africa explicitly prohibit not only the disclosure of the data, but the direct and indirect reliance on the data, within the definition of unfair commercial use. In addition, while the data must be protected from the time it is lodged with regulatory authorities, the period of non-reliance (5 years minimum) should commence from the date that marketing approval is granted.

- National Exhaustion of Patent Rights: Patents are national instruments, but the exclusive rights provided under the WTO TRIPS Agreement and the WIPO Paris Convention may be undermined by the Medicine Act Amendments of 1997. The absence of a standard of national exhaustion also undermines PhRMA member efforts to improve access to essential medicines, including HIV therapies, to vulnerable or underserved populations.

- Legitimate Government Use Provisions: The USG should seek to limit the scope of Government use authority to exclude the possibility of Government use for the purpose of export, or for sale to the general public. In short, "Government use" authority should be limited to those acts required to carry out a legitimate Governmental function.

- Linkage Between Industrial Property Offices, Regulatory Authorities and Enforcement Agencies: The enforcement of patent rights is difficult in most countries. Measures that are taken by a Government of a country that facilitate infringement run counter to the objectives of granting adequate and effective protection for intellectual property rights. For this reason, we urge the United States to ask South Africa to provide explicit provisions that will oblige the relevant Government authorities to ensure that their administrative activities do not facilitate the infringement of patent rights. In particular, we urge the United States to seek a prohibition on the granting of marketing approval by a health regulatory authority that will take effect during the term of the patent to a party other than the patent owner. This type of provision is included in the United States system and greatly facilitates the effective enforcement of patent rights by removing the possibility that generic copies

will be able to enter the market during the term of the patent.

- Enhanced Trademark Protection: There is a growing trend in measures that directly or indirectly undermine trademark rights. Measures include labeling requirements that foreclose use of the trademark in comparison to the generic name of a pharmaceutical product, which is necessary to ensure the strength of the mark. We encourage the United States to seek the full enjoyment of trademark rights in South Africa. Measures eroding trademark rights may include, for example, measures that require the use of a larger generic name than the trademark or which remove rights for use of a trademark instead of a generic name for a pharmaceutical product.

- Clarification of Compulsory Licensing Provisions: Use of Compulsory licensing, while included within the flexibilities of the WTO TRIPS Agreement, should be used in cases of true market failure. In the case of South Africa, where there have been a plethora of offers of donation, concessional sale, or voluntary licenses, there has been a clear demonstration of the ability of the market to address the access issue. Compulsory licensing has been a solution without a problem. More specifically, we seek limitation of the use of compulsory licenses to three circumstances (anti-trust; national emergency/ public non-commercial use and Paris Article 5(4) circumstances).

- Limitations on Pre-Expiry Activities: These are also known as "Bolar" pre-expiry activities. PhRMA believes that only those activities needed to gain marketing approval should be permitted. Export of product from South Africa should be limited only to those countries with "Bolar" provisions for marketing approval purposes. In addition, the patent owner should be notified of the identity of any third party making use of the existing patent during the term of the patent; and,

- Patent Term Restoration: PhRMA believes that time lost due to regulatory delay in the original country of application as well as in South Africa should be restored.

Background on the Medicine Act Amendments

A number of the issues that would benefit from advocacy arise out of the adoption by South Africa of the Medicine Act Amendments of 1997. Until November 23, 1997, South Africa had a relatively modern patent regime, providing full product patent protection for pharmaceuticals. Regrettably, on November 23, the Government adopted a new law, the "Medicines and Related Substances Control Act Amendments," that, if implemented, would seriously undermine the terms of intellectual property (IP) and patent protection for pharmaceuticals in South Africa. Specifically, Article 15C of the new law states:

The Minister may prescribe conditions for the supply of more affordable medicines in certain circumstances so as to protect the health of the public, and in particular may –

> (a) Notwithstanding anything to the contrary contained in the Patents Act, 1978 (Act No. 57 of 1978), determine that the rights (emphasis on all rights) with regard to any medicine under a patent granted in the Republic shall not extend to act in respect of such medicine which has been put onto the market by the owner of the medicine, or with his or her consent;

This clause, 15C(a), would appear to allow the Department of Health to revoke all pharmaceutical patents valid in the Republic of South Africa, "notwithstanding anything in the Patents Act," at ministerial discretion. Depending on implementation, this potentially would undermine both domestic South African law and South Africa's WTO TRIPS obligations. Furthermore, the new law, at 15C(b) allows for the parallel importation, a violation of the right holder's exclusive right to control importation of the product. PhRMA recognizes that TRIPS allows flexibility in this area, but widespread parallel importation would pose a serious threat to the viability of American pharmaceutical investment in South Africa. As stated, we have been working closely with the Government of South Africa on the related regulations to mitigate the impact of the changes in law.

Market Access Barriers

As the opportunity arises, PhRMA members also seek USG support to reduce or eliminate market access barriers that discriminate against products relying on intellectual property protection.

Price Controls

While PhRMA understands the natural desire of Governments to supply the best drugs to their citizens at a reasonable cost, the process of pharmaceutical discovery is very expensive, and the cost is growing every year. The most recent estimate is that more than $800 million is required to bring a drug to market, where only one product results from a pool of more than 5,000 patented molecules. Pharmaceutical research is fraught with uncertainty, because it will be 10 to 15 years before significant commercial products can be brought to market. Given this high risk, expensive research will only be pursued if there are reasonable prospects for return on investment capital.

The Medicines Control Amendment Act 90 of 1997 also makes provision for the implementation of price controls and or reference pricing at the discretion of the Minister acting on the advice of a pricing committee. While the Act is not yet in force, it's wording (contained in Section 22):

- Provides for the prescribing and publishing of prices,

- Stipulates that there shall be only one price – this does not apply to the State, which is the purchaser of up to 80% of all pharmaceuticals in SA.

- Provides for the implementation of a "professional fee" at retail that can only be reasonably computed if the manufacturers sell their goods according to a reference-based pricing system. Such pricing proposals would punish innovative products by allowing relatively higher prices for older products and capping compensation for newer, more costly and more beneficial therapies. The general practice threatens U.S. global leadership in biomedical innovation.

Accordingly, we urge the USG to seek opportunities to raise the issue with the Government of South Africa to gain relief for the industry, as follows:

Recognition of Innovation

The South African Government should recognize the value of innovation of pharmaceuticals in the formulation of health care policies and health care measures, so as not to impede the introduction of innovative products, which bring more effective and more cost-effective treatments to patients.

Pricing and Reimbursement Principles

As set forth in the negotiating priorities of the TPR legislation, we ask that the USG address non-market based Government interventions which restrict patient access to innovative U.S. medicines, abusive price controls, reference pricing, monopsonistic purchasing practices, state-trading monopolies, unreasonable restrictions on listings in Government-established formularies, Government toleration of illegal discounts, financial incentives, or practices, that disadvantage innovative U.S. medicines and/or represent a WTO-illegal subsidy to local manufacturers, and other non-market-based practices or measures which have the effect of distorting trade.

Transparency

In other fora, the U.S. has recognized the fundamental importance of transparency in the formulation and consideration of health care policy and expanding access by patients to innovative U.S. medicines. Transparency gives U.S. stakeholders an opportunity to comment during the formulation of Government health care policies and regulations that affect trade and access to new medicines. PhRMA urges that the USG pursue greater transparency, ensure meaningful consultation, and

advance the rule of law should advocacy opportunities in South Africa arise, especially in the upcoming FTA negotiations with SACU.

Drug Regulatory Processes

Non-scientific regulatory processes represent a serious barrier to innovative U.S. medicines and a threat to patients suffering from life-threatening diseases. In South Africa, we have witnessed heated rhetoric that casts doubt on the effectiveness or safety of medical products without any scientific basis. Accordingly, the USG should seek a commitment from the Government of South Africa to pursue timely and transparent, science-based regulatory review and approval procedures; and prohibitions on unfair practices which may delay introduction of new medicines, *e.g.* duplicative or scientifically unjustified (local) clinical trials for product submission and registration; undue certificate of free sale requirements that delay either submission or product approval, local testing requirements for small molecule drugs, vaccines, and biologics; and undue regulatory delays. Such barriers distort trade, but more important put the lives and welfare of patients at risk by limiting access to advanced medical treatments.

There is a backlog of around 2000 applications for new chemical entities at the Medicines Control Council – the SA drug regulator. These applications have been delayed for up to three years.

The USG should advocate:

Drug Regulatory Procedures

Regulatory procedures for the approval of new medicines should be timely, transparent, and non-discriminatory, and based on generally accepted international scientific standards. New chemical entities take up to three years to register in SA while generics can take over a year.

Science-Based Drug Regulatory Requirements

Regulatory requirements should be consistent with global scientific standards, such as the International Conference on Harmonization (ICH), and decisions regarding product approvals should be based only on the assessment of quality, safety, and efficacy. We note with concern the powers given to the SA Minister of Health in the recently published National Health Bill (November2001 – Sections 81-85). These allow her to determine how research may be carried out on human subjects and empowers her or her appointees to determine the methodology, procedure, practice or standards for treatment or research. The only restraint on the Minister appears to be that these standards should be generally recognized as authoritative within a relevant profession.

Transparency of Drug Approval Regulations

Laws and regulations regarding drug approvals should be transparent and should be formulated through procedures that provide (1) for notice and comment by interested U.S. stakeholders, (2) timely and effective opportunity for U.S. stakeholders to submit comments, positions, and views for due consideration by the relevant authorities; and (3) timely and effective opportunity for U.S. stakeholders to consult with the relevant authorities and study groups regarding the formulation of health care regulations and laws.

Tariffs/Taxes

In general, PhRMA members oppose the policy of foreign Governments assessing Value Added Tax (VAT) on concessionary sales or donated pharmaceutical products, or charging high tariffs on finished goods or bulk active ingredients. South Africa follows the policy of assessing a 14% VAT on all pharmaceutical imports, irrespective of whether the sale is on commercial terms. We would appreciate U.S. Government advocacy to eliminate this shortsighted policy.

To its credit, the South Africa Department of Trade and Industry has fulfilled its GATT 1994 obligations to eliminate all tariffs for pharmaceuticals.

Damage Estimate

The South African market is estimated at approximately R12 billion a year, with research-based pharmaceutical firms accounting for around 80% of the industry and employing around 17,000 highly skilled people. The above-described policies would cause tremendous harm to the South African pharmaceutical sector, a sector where PhRMA members have spent approximately R500 million annually on social projects, clinical trials, and research and development in South Africa, in addition to significant contributions made to maintain high academic standards. South Africa PMA itself trains around 300 industry employees annually, enabling factory workers with little formal secondary qualifications to qualify as Pharmacist's Assistants. This course will, however, now be phased out within two years, given the closure of 34 factories over the past two years – a direct result of the hostile business environment and Government's ambivalence towards patents. In addition to harm to the local market, implementation of the threatened policies would cause untold damage elsewhere in markets in the developing world.

PhRMA is currently studying methodology for estimating the likely damage to U.S. industry from the continuing threat of broad-based compulsory licensing and parallel importation in South Africa. Given the continuing uncertainty in the South African market, South Africa's pharmaceutical industry may already have suffered substantial losses in terms of plant-siting and other decisions made on an ongoing

basis by multinational corporations, which now view the South African market as less stable for long-term investment.

U.S. investors in South Africa are further encumbered by the recent amendment of the SA Competition Act. In brief, this law no longer exempts from its scope intellectual property rights acquired through the country's IP laws. The Act now requires the holders of these rights to apply for exemptions to exercise these rights. Apart from the obvious logistical problems associated with such a requirement, the effect of this amendment is to create barriers to market entry for IP intensive industries and services.

TURKEY

While aspiring to membership in the European Union, Turkey continues to lag seriously behind other EU accession candidates and EU member states both in terms of the level and quality of intellectual property protection for patented products and other market access barriers, which impermissibly disadvantage the U.S. research-based pharmaceutical firms doing business in Turkey. We appreciate continuing USG advocacy efforts on the issue of data exclusivity, and ask that those efforts be intensified in 2003 to achieve for data exclusivity the level of protection required by the Trade Related Intellectual Property Agreement (TRIPS). We also urge the U.S. Government to promote more transparent, non-discriminatory pricing for both locally manufactured and imported products as part of the overall economic reforms that are ongoing in Turkey and to seek reversal of the current so-called "cheapest cost generic" reimbursement policy. The situation for PhRMA members doing business in Turkey is becoming increasingly worse. Thus, we seek urgent USG intervention on these issues with the new Government of Turkey and request that the country be placed in the 2003 "Special 301" Priority Watch List.

Intellectual Property Protection

The United States, the European Union and Turkey have been in negotiations over the improvement of Turkey's intellectual property regime for several years. With the conclusion of the Customs Union agreement between Turkey and the EU, Turkey implemented June 27, 1995 and September 22, 1995 through decree Nos. 551 and 566, a patent system intended to meet its obligations. These decrees provided for patent protection for pharmaceuticals effective on January 1, 1999 and authorized the acceptance of patent applications for products or processes made after January 1, 1995.

By virtue of Article No. 4 of Decree No. 551, Turkey placed the obligations contained in international treaties over and above the provisions of the decree. As a result, Turkey should comply with all of the patent protection obligations found in TRIPS Agreement. However, implementation of these decrees in Turkey was not done in a manner fully consistent with its obligations. Industry's highest intellectual property priority at this time, however, is data exclusivity – the commercially most significant intellectual property protection issue in Turkey.

Data Exclusivity

The Government of Turkey has failed to adopt any legal or administrative mechanism to protect the confidential and commercially valuable data associated with applications for marketing approval by the Ministry of Health in Turkey. In fact, Article 9 of the Pharmaceutical Product Registration Procedures of the Turkish Ministry of Health is totally non-compliant and contradictory to TRIPS Article 39.3 requirements as

interpreted both by the U.S. and the EU. The article requires the Ministry of Health to rely on the data of the prior registered product in order to demonstrate that the generic copy is equivalent to the originator's product for safety and efficacy. Furthermore, the article of the subject Procedures does not provide any period of exclusivity. The Turkish Ministry of Health has approved a considerable number of unauthorized infringing products on the basis of this Article, even after the TRIPS implementation deadline of January 1, 2000.

Article 9 of the Pharmaceutical Product Registration Procedures should be immediately amended by the addition of a period of non-reliance of 10 years, starting from the day of marketing approval of the registered drug. Furthermore, the data should be protected against disclosure or reliance from the day the data is submitted to the authorities.

Market Access Barriers

Import Price Discrimination

The Government of Turkey applies an unequal set of policies for the pricing of medicines, which has lead to discriminatory treatment against imported pharmaceutical products, as their treatment is under a more stringent set of policies than for the locally manufactured products. In particular the Government of Turkey should be urged to put an end to the discriminatory process that creates a significant price premium for locally manufactured copy products (without any process of lower price referencing) and, on the other hand, an arbitrary lower price reference for imported products. Since April 2001, the total impact on the U.S. and European R&D industry and a number of local Turkish companies, which import, has been over $200 million USD.

Anti-Innovation/Discriminatory Reimbursement

The Government of Turkey has implemented a so-called "cheapest cost generic" reimbursement system that discriminates against PhRMA members and exacerbates the harm caused by failure to implement data exclusivity. This program has already been implemented for two social security funds and the Government, having failed to realize expected cost containment, now may extend it to new institutions. This policy discriminates against PhRMA members and encourages use of poor quality, inadequately tested drugs that are neither bio-equivalent nor manufactured under good manufacturing practices. In addition, the research-based industry is concerned with the savings measures by the reimbursement systems of Turkey that have targeted innovative and critical care therapies (data exclusivity protected products, cancer treatment products). Meanwhile, significant reimbursement funds have continued to be allocated to the payment of non-innovative and less-critical therapies, such as Over-the-Counter drugs (OTC's include vitamins, pain killers, etc.), and to the payment for premium-priced generic copies of off-patent products.

Pressure to Locally Work Products

In addition, Ministry of Health practices aimed at limiting pharmaceutical import licenses benefit local industry while discriminating against foreign companies by requiring burdensome proof of the "necessity" of importing products in lieu of manufacturing locally.

Perhaps most discouraging about these newly announced policies is the fact that Turkey has previously professed its desire to liberalize its economy and allow for an open and transparent marketplace based on accepted principles of the World Trade Organization (WTO) and international trade norms.

Damage Estimate

According to IMS Health data, the market for pharmaceutical products in Turkey is one of the largest in the region, with sales well in excess of two billion dollars. PhRMA projects that the market could grow to approximately five billion dollars by 2006. U.S. companies represent twenty percent of the market at the end of 2001. PhRMA estimates that the potential damage from the problems outlined above could easily exceed one hundred million dollars, and that if unchecked, the damages over the next five years could grow to nearly 500 million dollars. Although we do not yet have econometric analysis of the data for Turkey, please see Appendices B and C for discussion of the general issue of methodology for calculation of losses due to inadequate protection of data and other forms of intellectual property protection for pharmaceutical products.

WESTERN HEMISPHERE

ANDEAN COMMUNITY

(Bolivia, Ecuador, Peru, Venezuela)

Two recent, problematic Andean Community rulings appear to violate provisons of the World Trade Organization (WTO) Agreement on Trade Related Intellectual Property Agreement (TRIPS): (1) the Andean Tribunal's September 28, 2001 invalidation of all use patents, and (2) the Andean Community Secretariat's October 22, 2001communique essentially abolishing data exclusivity. The intellectual property situation varies from country to country and each is addressed individually in this submission, but PhRMA wishes to express concern about the region-wide situation, given that all five countries adhere to a common intellectual property law, Andean Community Decision 486. Given these issues (discussed in detail below), PhRMA requests that the Andean Community be included on the 2003 "Special 301" Priority Watch List.

Decision 486 improved upon its predecessor, Decision 344, in several ways, including expanding the definition of patentability and eliminating restrictions like the exclusion of patentability of the World Health Organization (WHO) essential drug list. Article 266, which discusses data exclusivity, reproduces the language of Article 39.3 of the TRIPS agreement. The definition of "unfair commercial use" and determining the term for data exclusivity were left up to each member country to determine individually. To date, no Andean country has done so. In our view, the Andean Community should adopt a ten-year standard against the use of proprietary data submitted for registration purposes, as is the case in several EU countries.

A very troubling recent development took place on October 22, 2001, when the Andean Community Secretariat, in a memorandum to legal counsel representing the pharmaceutical industry in Colombia, declared that Governments are not obligated to provide data protection, flagrantly contravening Article 39.3 of TRIPS. The Secretariat incorrectly declared that the competent national authority has the right to use or in any way rely on the information provided to it by the first registrant in order to provide marketing approval to a third party. This flies in the face the TRIPS Article 39.3's main objective: preventing member states of the World Trade Organization (WTO) from allowing third parties to benefit unfairly from the originator's data. Moreover, the Secretariat's discussion of trade secret misappropriation suggests a complete misunderstanding of how Article 39.3 differs from Article 39.2, which governs trade secret misappropriation. The following are the key passages of this memorandum:

> "The 'exclusivity' of proprietary information and therefore the infringement thereof, may only be demanded within the scope of a horizontal nature market relation (that is, among competitors) but not within the scope of a vertical nature public law relation, as the one existing between the administrator and the public, since the authority has

> the right and obligation to access and use information in compliance with its attributions…For the above stated reasons, in our opinion, the competent national authorities are not prevented from using the information they possess, in the evaluation of other applications related to the same pharmaceutical products."

This denial of TRIPS Article 39.3 has inflicted significant commercial damage on PhRMA members in the Andean region. Infringing copies grab market share while rights holders are forced to expend resources and time (in Latin America, generally several years) seeking redress in local courts. Andean Community countries should implement and enforce provisions guarding against the unauthorized commercial use of company proprietary data, as per the principles outlined in TRIPS Article 39. Colombian Decree 2085, which provides a term of five years of data protection, could serve as a useful model for other Andean Community members. Pharmaceutical research and clinical trials represent an enormous investment, making the resulting safety and efficacy data extremely valuable. As is described in several other country sections in this submission, allowing the registration of products that use, or incorporate by reference, the company proprietary data of the innovator is an unfair trade practice that severely, and at times completely, undercuts intellectual property protection for pharmaceuticals.

Unfortunately, Decision 486 falls short of adequate pharmaceutical patent protection by placing unjustified restrictions on biotech inventions and by maintaining an ambiguously worded provision regarding use patents, leading to their recent invalidation by the Andean Tribunal Justice. The Andean Tribunal of Justice ruled against Peru in September 2001, disallowing use patents altogether. (The Tribunal is preparing to do so also regarding Ecuador and Venezuela.) This decision represents a serious blow to intellectual property protection throughout the Andean region. We believe that this clear TRIPS violation must be remedied either through a subsequent Andean Tribunal decision, or by the Andean Secretariat, or by member countries, given the conflict between this ruling and the pre-eminence of international treaties to which Andean Community countries are parties. If it is not corrected, there will be a substantial commercial impact on U.S. commercial interests and a clear violation of United States treaty rights.

Several important medical advances would not be available to patients around the world without the availability of second-use patents. These products are subject to the same review process as any other patent application, meaning they must be new, involve an inventive step, and be capable of industrial application. Second use patents are thus no different from any other patent. Patent laws of the U.S. and our major trading partners incorporate these standards, which are also enumerated in the WTO TRIPS Agreement (Article 27). Pharmaceutical research companies apply for patents on new molecules at the earliest possible opportunity. Additional, unforeseen medical indications may be discovered during the lengthy research phase that follows. The

results benefit patients and, if they meet the patentability criteria outlined above, deserve patent protection. The Andean Community, by outlawing these patents, is misinterpreting TRIPS and is out of step with most countries in the world.

Pharmaceutical companies have filed product patent applications since Decision 344 took effect in 1994, and products that are the subject of these applications are on the market. However, the risk of patent piracy remains high due to administrative and other delays in the approval process and inadequate enforcement against unfair commercial use of patented products. Moreover, health authorities have consistently failed to coordinate with patent officials and inappropriately issue sanitary registrations for products already under patent, whose patent application is pending, or whose period of data exclusivity has not expired. The adoption of "linkage" regulations (i.e., establishing a formal link between health and patent authorities) would help to ameliorate this situation, requiring that "second applicants" (i.e., generic, or in some cases, infringing applicants) demonstrate that the product for which they are requesting market approval is not the subject of a valid patent or pending application. "Linkage" exists in the United States and Japan and is crucial to maintaining the integrity of the intellectual property and patent system.

Ecuador

Copy registrations in violation of TRIPS article 39.3 and in contravention of other TRIPS principles increased in 2002. The Andean Tribunal ruled that Ecuador could not issue or recognize second use patents. A price freeze throughout 2002 caused commercial harm for PhRMA members.

Intellectual Property Protection

Although Ecuador has a good patent law, enforcement remains a significant problem. Third parties continue to profit at the expense of originator companies because the Government of Ecuador continues to allow the registration of copies of PhRMA company products with pending patent applications and provides sanitary registrations to copies of innovative products in violation of TRIPS Article 39.3 concerning data protection. The Andean Tribunal's ruling in 2002 against Ecuador's issuance of use patents will negatively affect patent applications in Ecuador and elsewhere in the Andean Community.

<u>Legislation on Medicines</u>

An Ecuadorian law promoting generic production and use appears to discriminate against innovative pharmaceuticals. Local manufacturers are given preferential treatment; at least 20% of generics must be locally made. Government institutions must only buy generics. These provisions violate several Constitutional

rights by granting competitive advantages and privileges to generics at the expense of free market principles.

Price Controls

A price freeze was imposed in January 2002 and subsequently renewed through the end of the year. This measure appears to violate Ecuador's Protocol for WTO Accession and the bilateral investment treaty between the U.S. and Ecuador. Such price controls are often *de facto* discriminatory. In the absence of a viable local industry, Governments impose a disproportionate share of cost containment burdens on innovative U.S. pharmaceutical firms. Such price controls threaten U.S. global leadership in biomedical innovation.

Health Registration

The generic drug law allows for homologizing of health registrations issued in selected countries through very simplified procedures only for generic products, thus creating a discriminatory practice against innovative pharmaceutical products. While all products of research-based companies comply with quality standards established in the law, copy products are allowed to be in the market even without Good Manufacturing Practice (GMP) certifications.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

PERU

Peru does not protect confidential data from unauthorized disclosure and unfair use. An Andean Tribunal ruling has forced it to stop issuing use patents. A discriminatory measure favors local producers in Government procurement.

Intellectual Property Protection

The Government of Peru continues to provide sanitary registrations to copies of innovative pharmaceutical products in violation of TRIPS Article 39.3, which requires Governments to prohibit the "unfair commercial use" of confidential test data. The Government of Peru could remedy these ongoing treaty violations by simply refraining from granting sanitary registrations to copies of innovative pharmaceutical products for a term of years unless such copies provided their own confidential test data.

The Government of Peru's ongoing TRIPS violation also represents a breach of the ATPDEA eligibility requirements. Because Peruvian companies are the direct beneficiaries of these intentional intellectual property violations by the Government of Peru, the Governmental acts approving copies of innovative pharmaceutical products amount to an expropriation of US intellectual property and therefore constitute "ineligibility" under multiple US trade and foreign assistance laws.

Discrimination in Public Procurement

The Government of Peru discriminates against foreign manufacturers by granting a 20% bonus or bidding preference to national manufacturers participating in a public "competitive" bidding process. This benefit, granted in favor of goods manufactured in the Peruvian territory, constitutes discriminatory treatment against foreign manufactures and also violates the Andean Trade Preference Act eligibility requirement concerning the "the application of transparent and non-discriminating policies in public purchasing".

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

Venezuela

Intellectual Property Protection

After several years of respecting confidential data, the Venezuelan Government announced in February 2002 that it would no longer do so, and registered over 20 copy products. These copy registrations are a clear violation of TRIPS Article 39.3. Data protection is also a component of the G-3 treaty, to which Venezuela is a party, and the Venezuelan Attorney General in 2001 issued a ruling mandating a five-year data protection term. The decision to register copy products is a very disappointing development, since intellectual property rights were previously protected by law and generally respected in practice in Venezuela.

Discriminatory Taxation

In August 2002, Venezuela imposed a 16% value added tax on imported pharmaceuticals. This clearly discriminatory measure appears to violate WTO rules, as well as the G-3 treaty, and is having a significant commercial impact on PhRMA member companies.

Government Procurement

A July 2002 "Buy Venezuelan" decree gives local producers advantages and preferences in bidding on Government contracts.

Price Controls

Although market reforms in the 1990s eliminated price controls for most sectors of the Venezuelan economy, the pharmaceutical industry remains subject to price controls. Only the prices of over-the-counter (OTC) medicines and products with more than four alternatives in the market have been liberated, while the prices for many products that are most significant for the research-based industry continue to be heavily controlled. In late 2002, it appeared as if the Government would limit price increases to 50% above 1998 prices, which would have a negative impact given even greater devaluation of the Venezuelan currency and high inflation during that same period.

Medicine Law (Ley de Medicamentos)

A medicine law passed in 2000 contains provisions of concern to the research-based pharmaceutical industry, including:

- language allowing the Government to regulate prices;
- a mandatory National Therapeutic Formulary at public institutions;
- a provision on prescription substitutions at the pharmacy level;
- a requirement that pharmaceutical companies produce individualized doses to meet the exact level required per patient; and
- a requirement that all medicine imported into the country be evaluated by clinical trials in Venezuela.

The law also may be unconstitutional because it calls for accumulated sanctions.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

BRAZIL

The environment in Brazil remains challenging for the research-based pharmaceutical industry. Despite a largely good patent law, in practice Brazil has issued very few pharmaceutical patents in recent years. Only two non-pipeline patents have been issued in 2002. This appears to be deliberate discrimination against our industry, particularly troubling in view of the millions of dollars PhRMA member companies pay in application fees (over $75 million since 1994). The health regulatory agency (ANVISA) has been tasked with approving pharmaceutical patents before they are issued, which appears to be a violation of the World Trade Organization (WTO) Trade Related Intellectual Property Agreement (TRIPS) (Articles 27 and 62.2) and seems to have contributed to the slowdown in processing. Unauthorized copies of pharmaceutical products have received sanitary registrations relying on undisclosed tests and other confidential data, in violation of TRIPS Article 39.3. During 2002, the Government proposed legislation and regulations that could negatively impact intellectual property and market access. They have not yet been adopted, however. A discriminatory price freeze continues to inflict serious commercial harm in a year in which the Brazilian currency has depreciated sharply. Although a Government formula exists to allow price increase prices based on inflation and other factors, it has not been implemented fully. The Brazilian pharmaceutical market continues to shrink and contracted about 7% in 2002, the third year of decline. In light of these concerns, PhRMA requests that Brazil be included in the 2003 "Special 301" Priority Watch List.

Intellectual Property Protection

Brazil issued only 2 non-pipeline pharmaceutical patents in 2002, out of 18,000 regularly filed pending pharmaceutical applications. It has issued only a few dozen pipeline patents since December 1999, when Brazil instituted an improper "fourth criterion" of patentability. The health regulatory agency (ANVISA) has been tasked with approving pharmaceutical patents before they are issued, which appears to be a violation of the WTO TRIPS Agreement (Articles 27 and 62.2). Unauthorized copies of pharmaceutical products have received sanitary registrations relying on undisclosed tests and other confidential data, in violation of TRIPS Article 39.3. Patent applicants were never allowed to claim inventions disclosed in regularly filed applications pending on the date the TRIPS Agreement was implemented. A 20-year patent term was not applied to the patents still enforceable on the same date. Both constitute violations of article 70.2 of the TRIPS Agreement.

On paper, Brazil's industrial property law is quite strong in many respects, providing a 20-year product patent term for products issued after 1997; pipeline protection; basic biotechnology protections; a ban on parallel imports; and early implementation. In recognition of the significance of Brazil's expedited adoption of product patent protection, the research-based pharmaceutical industry invested $ 2.1 billion in Brazil between 1996 and 2000. Unfortunately, in practice, Brazil does not

enforce its patent law consistently. Moreover, part of the Brazilian law directly conflicts with TRIPS Article 27.1, which allows importation as a means of satisfying the requirement that the patent be "worked" in a country. Article 68 of the Brazilian law requires domestic and simultaneous manufacture of every independent claim of a patent. Brazilian health authorities continue to issue sanitary registrations for products whose patents are not due to expire for several years, giving rise to concerns that this is a first step toward compulsory licensing these products and violating the country's specific provision on regulatory review exception.

Another cause for concern is the October 6, 1999 Presidential Decree regulating the implementation of Article 71 of the law, which governs the granting of compulsory licenses in broadly defined situations of national emergency. Beyond any definition-related concerns, this particular decree is troubling because of the broad discretionary powers given to officials below the presidential level, the apparent inconsistency with TRIPS obligations, and the mandatory transfer of technology considered in Article 5, requiring patent owners to transfer any trade secret related to the manufacturing of a product covered by the overruled patent. The Brazilian Government has repeatedly declared its willingness invoke this decree if it cannot coerce lower prices from research-based pharmaceutical producers.

In addition, a 1999 amendment to the patent law included Article 229-C, which gives the National Sanitary Supervision Agency (ANVISA) authority to review all patent applications claiming pharmaceutical products or processes. While our industry has long advocated a formal linkage mechanism between the patent office and ANVISA to ensure that marketing approval is not given to generic copies of patent products (consistent with Brazil's TRIPS obligations), this measure poses numerous problems and has clearly been a major factor in delaying patent approvals even further. Since this change to the patent law was first introduced as a provisional measure in December 1999, only 22 pharmaceutical patents have been issued, and those were for "pipeline" applications. <u>This is one of the most serious problems facing the pharmaceutical industry in Brazil today</u>. We note that Health and Human Services Secretary Thompson formally asked the Brazilian Health Minister to take steps to release dozens of "hostage" patents, i.e., those approved by the patent office but still in limbo with ANVISA. We hope that those patents, and hundreds of others, will be granted as soon as possible. This measure's consistency with the anti-discrimination clause of TRIPS Article 27.1 is questionable, as products from other industries are not subjected to the same review by relevant regulatory authorities. Also, any review of the applications other than for the patentability criteria set forth in TRIPS Article 27.1 would not be consistent with TRIPS, and any review of patentability criteria is beyond the expertise of ANVISA.

In addition to the concerns noted above regarding ANVISA's prior authorization role, we remain concerned about continuing delays in processing patents. Despite collecting several million dollars in application fees each year, the National Institute of

Industrial Property (INPI) has chosen not to invest sufficient resources to process applications in a timely fashion, resulting in a substantial backlog (estimated at 18,000 pending pharmaceutical patent applications, out of approximately 47,000 applications). These delays will seriously hinder our industry's ability to plan effective product launches. To date, INPI has issued only 24 non-pipeline patents out of this 18,000-application backlog. We believe that this is due to deliberate policy and not merely attributable to a lack of resources (although we endorse additional training of INPI staff and a greater allocation of resources for automation and other administrative needs). This delay in examining pharmaceutical patent applications appears to violate Brazil's international obligations, as well as its obligations to applicants who pay considerable application fees and attempt to conduct business in Brazil with the expectation of fair treatment.

Price Controls

Price controls, in effect since July 2000 and slated to remain in place until at least the end of 2002, are one of the most significant barriers to the pharmaceutical industry in Brazil. So-called "voluntary" – in fact, coerced - price controls were imposed in July 2000, and formally extended by presidential decree in December 2000. Those controls were extended again in the fall of 2001 to December 31, 2002. In 2002, the Government allowed pharmaceutical producers to raise prices twice: 4.4% in January and 8.6% in November. These figures were clearly inadequate given Brazil's economic crisis and the devaluation of the *real* and we estimate the increase should have been at least 30%, based on the Government's own price control formula. These arbitrary pricing formulas were imposed without input from industry. The price limitation and freeze takes no account of increases in manufacturers' costs, including Government-mandated salary increases, and the usual increases in the cost of doing business. The decree is completely contrary to the free market principles to which Brazil has committed itself in recent years. It sends an extremely negative message to international investors and bodes ill for other industries as well. This measure violates Brazilian law and will do nothing to improve Brazilian citizens' access to medicines – the Government's purported goal in imposing these controls. Pharmaceutical research is enormously expensive and risky; very few products make it from the laboratory bench to market. Price controls threaten biomedical innovation by undercutting the profits needed to finance research and development.

The research-based pharmaceutical industry's significant investment in Brazil after the passage of the 1996 patent law created jobs, increased tax revenues, boosted exports, and strengthened Brazil's GDP. Unfortunately, some companies have been forced to downsize their operations in Brazil over the last year, in part due to the growing presence of arbitrary Government pricing pressures that minimize return on substantial investments.

Damage Estimate

Brazil is one of the two the largest markets for pharmaceuticals in Latin America. It is not possible at this time to determine the impact on sales of PhRMA member company affiliates in Brazil if the aforementioned provisions were strengthened and renewed pricing concerns resolved. As a result of Brazil's devaluation, compounded by some of the measures described, the Brazilian market declined steeply from an estimated value of $7.2 billion in 1998 to $5.1 billion in 2000– a drop of 25%, reflecting the lingering effects of Brazil's economic crisis and the prize freeze imposed by the Brazilian Government.

CANADA

Although Canada's intellectual property situation was strengthened by its compliance with the ruling of the World trade Organization (WTO) on patent protection, its failure to enforce its protection for data exclusivity remains a cause for serious concern. Price controls, regulatory delays, and restrictions on formulary listing also hamper PhRMA member companies' ability to do business in Canada. In October 2001, the Health Minister approached a generic company about producing infringing copies of a patented medicine effective against anthrax. This failure to follow Patent Act requirements was subsequently reversed and we welcomed subsequent public statements by a number of Ministers about the Government's commitment to respecting Canadian law, specifically the Patent Act. For these reasons, PhRMA requests that Canada be included in the 2003 "Special 301" Priority Watch list, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

After patent protection improved in 1992, several PhRMA member companies made significant investments in Canada. However, Canada's industrial property regime was found lacking in two WTO cases in 2000. Canada agreed to amend its practices and related regulations in the area of allowing generic manufacturers to stockpile pharmaceuticals before patent expiration, and amended its patent law in July 2001 to provide 20-year patent protection to patents filed before October 1, 1989, and which took less than three years to obtain.

Unfortunately, Canada continues in some areas to fall short of the requirements of the Trade Related Intellectual Property Agreement (TRIPS). PhRMA remains seriously concerned by the failure of Canadian regulatory authorities to provide effective enforcement for provisions relating to data exclusivity, as required by TRIPS Article 39.3. Although Canada has statutory data protection, judicial decisions have rendered those protections meaningless. Canadian authorities allow parties other than the right holder to effectively gain marketing approval in direct reliance of protected confidential data. This violates TRIPS Article 39.3 as it eliminates the TRIPS requirement to prevent "unfair commercial use" of protected data. We urge the United States to move data protection to the top of the bilateral commercial agenda with Canada.

Other Obligations

Canada is required under both TRIPS and the North American Free Trade Agreement (NAFTA) to ensure effective enforcement of the standards of patent protection provided for in those Agreements.

Article 28 of TRIPS and Article 1709 of NAFTA require Canada to confer on patent owners the exclusive right to prevent third parties not having the owner's consent from making, using or selling the product or process that is the subject of the patent.

Article 41 and related Articles of TRIPS and Article 1714 and related Articles of NAFTA require Canada to "ensure that enforcement procedures are available under its law so as to permit effective action against any act of infringement of intellectual property rights covered by (these) Agreements, including expeditious remedies to prevent infringements and remedies which constitute a deterrent to further infringements."

Enforcement

In the September 2002 Speech from the Throne, the Canadian Government stated that the knowledge-based economy requires new approaches to regulation. It professed to move forward with a smart regulation strategy to accelerate reforms in key areas to promote health and sustainability, to contribute to innovation and economic growth, and to reduce the administration burden on business.

As part of this strategy, the Government pledged to adapt its intellectual property framework to enable Canada to be a world leader on emerging issues such as new life forms. It undertook to speed up the regulatory process for drug approvals to ensure that Canadians have faster access to the safe drugs they need, creating a better climate for research in pharmaceuticals. It promised to work with provinces to implement a national system for the governance of research involving humans, including national research ethics and standards

Despite these promises, systemic inadequacies in Canada's administrative and judicial procedures call into question whether Canada is meeting its TRIPS and NAFTA obligations with respect to pharmaceutical patents.

These inadequacies allow generic versions of patented medicines to be approved by Health Canada, to be listed for use by doctors and use or even mandatory substitution by pharmacists, and to reach or be ready to reach the market in commercial quantities while valid patents are still in force. This can occur under the *Patented Medicines (Notice of Compliance) Regulations*, the so-called "Linkage Regulations" administered by Health Canada, and as a result of how patent infringement claims are treated in the Canadian Courts. The Linkage Regulations fail to provide for transparent and equitable consideration of the rights of patent owners and prevention of patent infringement.

Under the Linkage Regulations, generic producers can apply at any time for approval by Health Canada of generic medicines. Such generic medicines are

assessed for safety and efficacy against data and clinical trials relating to previously approved patented medicines. These regulations extend significant advantages to generic companies.

The Linkage Regulations indicate that Health Canada must determine whether there are patents registered that could be infringed if approval, i.e., a Notice of Compliance (NOC), were granted for the generic medicine. If a patent is identified, the generic producer is required, in principle, to issue a Notice of Allegation (that there would be no infringement) to the brand name company who, if it believes the allegation is not justified, may challenge that allegation in the Court. Thus, the brand name company has access to a judicial procedure to seek an order of prohibition to prevent the issuance of an NOC.

This arrangement, in principle, could provide the basis for effective protection of pharmaceutical patent owners' rights as required under TRIPS and NAFTA. However, experience suggests that Health Canada is taking steps to avoid the necessary application of the regulations.

Indeed, there is a pattern that reveals clear bias in favor of generic companies. This is seen in a number of ways: The legal burden is on the brand name company to prove that the generic company's allegation of non-infringement is not justified. Access to information on the generic company's product may be restricted, however, because there is no discovery in such proceedings. The brand name company may, therefore, be reliant on whatever information the generic company is prepared to supply or documents from the generic submission, in the event that the brand name company can convince the Court to order such disclosure. This approach is open to abuse to the detriment of the brand name company.

Health Canada has been inconsistent in its policies and practices relating to the listing and delisting of brand name companies' patents and in requiring generic companies to send a Notice of Allegation. In some cases no Notice is provided. This means that the brand name company has no opportunity to present a claim and, in fact, may remain unaware that a generic version of its drug has been submitted for approval until an NOC is issued. This has occurred and could easily occur again in future.

For example, the Federal Court recently held that the Minister of Health erred in failing to require compliance with the Linkage Regulations when an NOC to a generic manufacturer was improperly issued. The evidence before the Court was that the submission filed by the generic company contained a request for approval for the same medicinal ingredient within the wording of the Linkage Regulations. As such, the Court found that the Minister of Health acted improperly in granting marketing approval for the generic product without requiring that the Linkage Regulations be invoked.

The Linkage Regulations do not apply to process patents, notwithstanding the fact that claims to a medicine itself were previously forbidden under Canadian patent law. Furthermore, Health Canada is continually and systematically limiting further the types of patents that can be listed on the Patent Register, even though they clearly relate to the drug product in question. Such examples include drugs sold in dosage forms such as patches or implants which are approved by Health Canada as drugs but which Health Canada then takes a position are medical devices in respect of which patents may not be listed.

Another example is formulation patents that the brand name company may not yet be using itself but which could be copied by a generic competitor. A recent decision of the Federal Court of Appeal determined that Health Canada was incorrect in taking an overly aggressive approach in delisting such formulation patents and that these patents are eligible for listing on the Patent Register.

In a similar fashion, Health Canada has recently taken a position that a number of ongoing innovation patents relating to various drug products may not be eligible for inclusion on the Patent Register. As such, Health Canada started a Reference before the Federal Court to ask the Court's assistance in determining the eligibility of these patents. However, due to inaccuracies in the underlying facts as presented by Health Canada, the proceeding was thrown out. Instead of working to improve the accuracy of the underlying facts, Health Canada then decided to take on the role of the Court itself and hold its own hearing allowing brand name and generic companies to make submissions on the issue. Whether Health Canada removes patents from the Patent Register on the basis of the submissions remains to be seen. However, the process demonstrates that Health Canada continues to take an aggressive stance in removing patents from the Patent Register, thereby limiting the scope of protection available under the Linkage Regulations.

As a result of these inadequacies, there have been dozens of cases since 1993 (when the Linkage Regulations came into effect) in which patentees had an infringement claim but were unable to prevent the issuance of an NOC and the marketing of a generic version of a patented medicine. The Canadian courts fail to provide effective recourse in cases where an NOC is issued for an infringing generic medicine.

If a patentee is unsuccessful in preventing the issuance of an NOC by Health Canada, the next step would be to seek relief through an infringement action. In the first instance, a patentee could apply for an interlocutory injunction to maintain its rights and, in particular, to prevent the marketing of an infringing generic version pending trial. It is virtually impossible, however, to obtain an interlocutory injunction.

The Canadian Courts apply a very high standard of "irreparable harm", the test applied for the granting of an interlocutory injunction. This standard is impossible to

meet in practical terms. A patentee is required to establish that there will be irreparable harm that cannot be compensated by the eventual award of damages. The Courts do not accept that a monetary damage award may not provide full compensation for loss of market share for the product and related products, lost business, lost investment and research opportunities due to the absence of income from sales, or for loss of reputation and goodwill.

It generally takes two to five years before an action for patent infringement goes to trial. After this time, a brand name company's market share has been severely eroded. After this amount of time, a brand name company's market share has been severely eroded. Indeed, in a recent case involving the well know AIDS and HIV drug sold in association with the trademark AZT, the brand name company went through 12 years of litigation to exhaust all appeals while generic competitors continue to sell their products on the market. Even after the 12 years, the brand name company is still required to bring further court proceedings in order to be compensated for its damages. Moreover, these damages cannot constitute triple damages. As a result, the paltry damages that the brand name company could expect to see merely amounts to the cost of doing business to the generic company and is not a realistic deterrent to infringement.

The standards applied by the Canadian Courts are not consistent with the standards provided for in TRIPS and NAFTA.

The fundamental private right under these Agreements is, of course, the exclusive right to prevent the making, use or sale of a patented product or process that is not authorized by the patentee. In terms of the enforcement of that right, Article 50 of TRIPS and Article 1716 of NAFTA call for "prompt and effective" provisional measures, i.e., including interlocutory injunctions, "to prevent an infringement of any intellectual property right, and in particular to prevent the entry into the channels of commerce in their jurisdiction of allegedly infringing goods". The test under TRIPS and NAFTA for provisional measures is that "any delay in the issuance of such measures is likely to cause irreparable harm to the right holder", a clearly lower standard than that applied by the Canadian Courts.

The concerns of pharmaceutical patent owners are serious and have important implications beyond economic losses in Canada. If a major developed country such as Canada is failing and continues to fail to comply with the spirit and letter of TRIPS, this will set a negative example for developing countries. Canadian practices that create a dangerous precedent should be addressed before they are adopted in other jurisdictions.

Although Canada has eliminated its former compulsory licensing system for pharmaceuticals as a result of NAFTA and TRIPS, there continues to be a strong bias favoring the early and often infringing entry of generic versions of patented medicines

into the marketplace. There are systemic inadequacies in administrative and judicial procedures that allow this to occur, resulting in substantial and on-going economic losses to patent owners and calling into question Canada's compliance with its obligations under both NAFTA and TRIPS.

USTR should attach high priority to remedying this situation.

Price Controls

The Patented Medicine Prices Review Board (PMPRB) continues to work toward revising its overall approach to setting price ceilings. Reports emerging from the Federal/ Provincial/Territorial Pharmaceutical Issues Committee suggest the likelihood of increased collaboration among different levels of Government toward more stringent, non-market based interventions.

The use of international price comparisons and the establishment of price ceilings on patented medicines are counterproductive to initiatives to provide high quality health care, and thus improve the health of patients, or to help contain health care spending. The following are among the principal concerns regarding such practices.

- Using international comparisons ignores valid reasons for price differentials across countries. The prices of pharmaceutical products, as well as all other types of goods and services, differ widely across countries, for many legitimate reasons. These include living standards, income levels, consumer preferences, disease and drug consumption patterns, product volume, exchange rates, product liability, regulatory requirements, as well as the degree of competition in the health services and pharmaceutical markets. Superimposed on these factors are Government-mandated reimbursement and price controls, which affect prices throughout the distribution chain. As a result, establishing price ceilings by using prices from other countries ignores prevailing market conditions and impedes biomedical innovation by prohibiting each innovator from establishing prices for its medicines based on market factors.

- There is little evidence that international price benchmarking leading to price controls actually curbs overall pharmaceutical spending. Government-set prices preclude the benefits of price competition. In these circumstances, such Government interventions in the market have little, if any, positive impact on the rate of growth in pharmaceutical expenditures over the long term. Under market conditions, however, price competition has proven to be an effective way to hold overall spending down and to provide high quality health care.

- International price benchmarking threatens patients' health by dampening incentives to improve on today's treatments, thus lowering health care quality. In order to fund critical long-term activities to discover and develop potentially life-saving drugs, pharmaceutical companies must be able to fairly and adequately recoup investment in research and development. Price control practices that prevent innovators from covering their costs will thus impede biomedical innovation and can jeopardize high quality health care for future patients.

In deciding how best to allocate health care resources and resolve the tension between controlling health care spending, improving the health of the population, and ensuring that the research-based pharmaceutical industry can continue to deliver cost-effective innovations for patients, the PMPRB's proposed approach of further restricting pricing flexibility has the potential to negatively impact the latter.

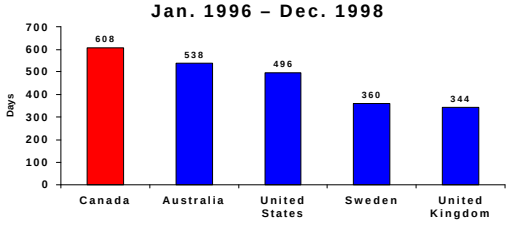
Other Barriers

Additional impediments face innovative products face in Canada, notably a slow drug approval process and inconsistent provincial listing decisions. These impediments, combined with a lack of patent term restoration and stringent price controls, further disadvantage U.S. pharmaceutical companies operating in Canada.

Regulatory Approval of New Medicines

Canada's record on the amount of time it takes to review and approve drug submissions, after showing some improvement in the mid 1990's, has been deteriorating since 1997. By 2001, the average number of days to approval had increased to 717 days. This is nearly seven months longer than the performance of the U.S. Food and Drug Administration (17.6 months), and well beyond Health Canada's own target of 365 days, which was established nearly five years ago. In fact, in a recently published study in the Canadian Medical Association Journal, Canada's regulatory approval time was slower than all the other comparator countries (see Figure 1).

Figure 1: Mean Approval Times in 5 Countries for New Drugs Approved from Jan. 1996 – Dec. 1998



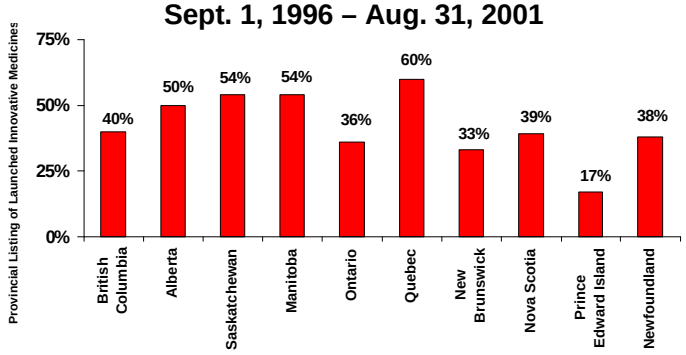
Source: Rawson NSB, Time required for approval of new drugs in Canada, Australia, Sweden, the United Kingdom and the United States in 1996-1998. Canadian Medical Association Journal 2000;162: 501-504.

It is important to note, however, that the Government of Canada did specifically mention the importance of speeding up drug approval times in its September 30th Speech from the Throne (a speech that sets out the Government's direction for the remainder of its mandate). It read as follows, "It will speed up the regulatory process for drug approvals to ensure that Canadians have faster access to the safe drugs they need, creating a better climate for research in pharmaceuticals." We continue to monitor and lobby for the implementation of this Government commitment.

Access of New Medicines to Formularies

There is substantial variability in the decisions to list (with or without restrictions on use) and the time taken to review submissions for adding drugs to provincial formularies. In the five-year period ending August 2001, of the 266 new medicines introduced to the Canadian market, the percentage of these approved for listing on individual provincial formularies ranged from a high of 60% to a low of 17% (see Figure 4).

Figure 4: Launched Innovative Medicines Available on Provincial Formularies Sept. 1, 1996 – Aug. 31, 2001



Note: These statistics are based on the introduction of 266 products.
Source: IMS Health, Provincial Reimbursement Advisor (August 2001).

Access to effective treatments for a disease does not, therefore, depend on what treatments are available, but where one lives. Furthermore, for those drugs that were included in the formularies, the percent that were listed with prescribing restrictions ranged from a low of 25% to a high of 64%.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

DOMINICAN REPUBLIC

The Dominican Republic's seriously flawed industrial property law violates the Trade Related Intellectual Property Agreement (TRIPS) in numerous ways. Implementing regulations set forth in 2001 do not remedy the law's problems. Therefore, PhRMA requests that the Dominican Republic continue to remain on the Priority Watch List in 2003.

Intellectual Property Protection

The Dominican industrial property law's numerous deficiencies make it the worst in the Western Hemisphere. Many of its provisions make it non-compliant with the Trade Related Intellectual Property Agreement (TRIPS), including:

- The law excludes patenting of second uses, does not include patent protection for vegetable obtentions, business or economic plans or non-biological methods and processes connected with living materials.

- Compulsory licensing: The law allows the granting of compulsory licenses on the sole basis of the denial of a contractual license within 210 days after the contractual license is requested. There is no need to prove any fault by the patent holder. The only grounds a patent owner can allege are the impossibility to exploit a patented invention. Additionally, the law allows for issuance of compulsory licenses on patents on raw materials, i.e. the potential licensee would be authorized to finish the product locally, thereby discriminating between imported finished products and those locally produced.

- The above compulsory license is in addition to compulsory licenses granted in cases of lack of exploitation, abuse due to non-competitive practices, public interest and cases of dependent patents.

- Article 39 of the law discriminates between imported finished products and locally manufactured products, by requiring both importation and local manufacture, in a clear violation of Article 27.1 of TRIPS. Furthermore, the law discriminates between foreigners and nationals by requiring foreigners to place a bond in an amount sufficient to cover court costs and legal fees in cases where they appear as plaintiffs in a lawsuit (where the patent or trademark was issued prior to the publication of the new law, that is May 11, 2000). This goes against the national treatment stipulated by Article 3 of TRIPS. (Paradoxically, the new Dominican copyright law adopted in 2000 expressly states that such a bond will not be required in any case.)

- Article 39 of TRIPS contemplates the protection of undisclosed tests or other data filed before sanitary authorities as a precondition of approving the

marketing of pharmaceutical, agricultural, or chemical products. Completely contrary to the spirit of this provision, the Dominican law violates data protection principles by authorizing all uses of a patent that are necessary to obtain health registration or approval for commercialization of a product.

- Additionally, the Department of Health continues its practice of issuing health registrations (equivalent to a permission to commercialize) to products that violate locally registered patents in spite of legal requests to the contrary.

- Article 186 (2) only grants issued patents the term granted pursuant to the old law (fifteen years), thereby denying extension to 20 years in view of Article 70.2 of TRIPS.

Implementing regulations set forth in 2001 do not improve the situation.

Market Access Barriers

Law 173 of 1966 severely limits unilateral termination of distribution agreements. Termination of distribution agreements is only possible by mutual consent or through the award of unreasonable indemnification rights due to the subjective criteria specified by the law. Local distributors have no incentive to pursue aggressive distribution of the goods they represent, since a poor performance on their part does not invalidate the indemnification considered in the law.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

GUATEMALA

The country's Industrial Property Law, which entered into force on November 1, 2000, provided adequate protection – on paper - for patents, trademarks, and confidential test data. However, in practice, confidential data was not protected, and on November 20, 2002, the Guatemalan Congress adopted, for the second time in less than two months, a law (Decree No. 76-2002) that cancels pharmaceutical patent protection until December 2004 and abolishes data exclusivity.[*] This is in clear violation of Guatemala's obligations under the Trade Related Intellectual Property Agreement (TRIPS) s and in our view renders Guatemala ineligible to become a free trade agreement partner with the United States. For this reason, we believe Guatemala should be placed on the 2003"Special 301" Priority Watch List.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

[*] PhRMA will provide a fuller analysis of Decree 76-2002, or a copy of the decree, as needed.

MEXICO

The Mexican Ministry of Health (SSA) has recently instituted new policies with respect to pharmaceutical product approvals that violate its U.S. treaty obligations, particularly NAFTA and World Trade Organization (WTO) Trade Related Intellectual Property Agreement (TRIPS). Furthermore, a lack of linkage between patent and health authorities, combined with TRIPS Article 41 violations, represents potentially devastating commercial losses for PhRMA member companies. The Mexican Government should cancel existing copy-product registrations and cease issuing new registrations. The material subject to patent and data exclusivity protection may also be copyrighted, representing a further violation of intellectual property. The SSA must acknowledge its responsibility, as a part of the Mexican Government, to fulfill international treaty obligations and domestic patent law. The Mexican Government has promised to exclude copy products from Government tenders; we hope this agreement will be implemented fully. Price controls remain in place. Thus, PhRMA believes that Mexico should be designated as a "Priority Watch List" country for 2003.

Intellectual Property Protection

While several PhRMA member companies have seen copies of patented products registered in recent years, there has been an alarming increase in infringing registrations in the last six months of 2002. The SSA continues to grant health registrations to generic products without verifying with the Mexican Institute of Industrial Property (IMPI) whether a patent already exists. Innovator companies are forced to take the patent infringers to court – an expensive and time-consuming process, particularly in the absence of preliminary injunctive relief and other adequate enforcement measures. Such lawsuits also represent a waste of scarce Mexican judicial resources. Several years can elapse before a case is resolved, leading to considerable losses for PhRMA member companies because the infringing products remain on the market during litigation. In total, these deficiencies in Mexico's system represent a violation of TRIPS Article 41 and of Article 70.2 because linkage had been enforced previously on certain products.

In 2002, the Government of Mexico committed at least 31 linkage violations on 16 products of PhRMA member companies. In addition, several copy registration applications remain pending. Many of the linkage violations noted above also constitute data exclusivity violations on products of PhRMA member companies.

Pharmaceutical companies submit to the Mexican SSA undisclosed test and other data in order to obtain sanitary registrations to sell their products in Mexico. The undisclosed test and other data are very valuable, representing a huge investment in research and clinical trials. In return, the SSA is supposed to protect the data from unauthorized or unfair commercial use by providing data exclusivity. Nevertheless, the SSA continues to grant sanitary registrations to generics and branded copies of

innovative products in violation of NAFTA Articles 1711.5 and 1711.6 and TRIPS Articles 39.2 and 39.3. These approvals constitute "unfair commercial use" of PhRMA member companies' data.

The Mexican Government in late 2002 stated that it would not purchase infringing copy products in Government tenders. We welcome this announcement and hope this policy will be implemented fully.

Price Controls

The pharmaceutical industry is still one of the very few in the Mexican economy subject to Government price controls.

Damage Estimate

Mexico is the largest market in Latin America, with at least $6 billion estimated sales for 2002. It is the only major market in Latin America likely to show growth in 2003. If Mexico allows infringing copies to garner market share, it will have a devastating impact on the research-based pharmaceutical industry.

WATCH LIST COUNTRIES

ASIA-PACIFIC

AUSTRALIA

The US research-based pharmaceutical industry views the US-Australian FTA as a win-win opportunity to strengthen protection and enforcement of intellectual property rights, improve access to innovative U.S. medicines, support transparent science-based regulation in Asia Pacific, and improve recognition of the value of biomedical innovation under the for Pharmaceutical Benefit Scheme (PBS).

The successful negotiation of a U.S.-Australia FTA will do much to ensure that Australia remains competitive in the field of global biomedical research and that Australian patients are able to benefit from life-saving advances in treatment for disease and disability. We welcome the launch of U.S.-Australia free trade negotiations and look forward to working with the U.S. and Australian Governments to fashion an FTA agenda that advances policies that promote pharmaceutical and biotechnology and genomic discovery in both the US and Australia. Nonetheless, there are some intellectual property issues that have yet to be addressed. PhRMA therefore requests that Australia be included on the "Special 301" Watch List.

Intellectual Property Protection

Springboarding and Stockpiling

While Australia has strong intellectual property laws, which include patent term extension and data exclusivity consistent with the Trade Related Intellectual Property Agreement (TRIPS) Article 39:3 we are concerned, however, about proposals for expanded export "springboarding" and stockpiling.

Because of lobbying from certain local generic producers, the Australian Government periodically has considered various proposals for extending the existing "springboarding" provisions or "stockpiling" in which infringing medicines could be manufactured for export or stockpiled pending expiration of a patent. Such an approach makes little economic sense, because it would further undermine Australian investment in the innovative life sciences. While Australia's total pharmaceutical exports amount to about A$2.3 billion per year, only 10% of such exports are generics. Thus, for Australia to abandon the innovative patented segment of the pharmaceutical industry, which is characterized by high value-added and advanced scientific discovery, would appear questionable from an industrial policy perspective. In addition, recent springboarding and stockpiling proposals appear to violate TRIPS Article 30, particularly in view of the ruling of the World Trade Organization (WTO) in *Canada – Patent Protection of Pharmaceutical Product*s, WT/DS114/R (2000). Accordingly, the adoption of patent springboarding and/or stockpiling would send an important negative signal about Australia's commitment to the innovative life sciences and the future success of the FTA negotiations.

Market Access Barriers

Due to increasing budgetary pressures, the Australian Government has adopted a series of increasingly restrictive regulatory and budgetary schemes that effectively diminish the intellectual property rights granted to innovative pharmaceutical and biotechnology products. Such practices include:

- Restrictive PBS Listings: The Pharmaceutical Benefits Advisory Committee (PBAC), a body of health and clinical experts appointed by the Australian Health Minister, is responsible for evaluating applications for PBS listings and making recommendations to the Health Minister. The PBAC rejected 40% of major applications for new listings in 1997 and 59% in1998.[6] . Because of its overriding focus on cost-effectiveness, the PBAC devalues quality of life benefits, such as faster recovery times, return to work and function, reductions in patient out-of-pocket costs, etc. Such criteria have the effect of devaluing important benefits, which can have an enormous impact on patients.

- Reference Pricing: Once the PBAC has recommended a PBS listing, the Pharmaceutical Benefits Pricing Authority (PBPA) recommends a price. While the PBPA process is not transparent, it typically involves a comparator pricing methodology in which the price of an innovative drug is evaluated on the basis of (1) any existing chemical analogue of the proposed drug class, or (2) the product most likely to be substituted by the proposed drug on the indication sought. To obtain a premium, the applicant must demonstrate significant clinical advantages over its main comparator and satisfactory cost-effectiveness versus that comparator. The PBPA uses such comparator pricing as leverage in negotiations with the applicant. The reference price is reviewed and maintained throughout the life of the product. If the price of the generic comparator drug decreases for any reason, including patent expiry, the subsidy level of the innovative medicine is also reduced and as Australians expect high levels of subsidy this usually leads to a reduction in price. This practice seriously erodes intellectual property protection, devalues innovation, and discourages investments in new medical discoveries.

- Pharmacoeconomics ("4th hurdle"): The PBAC and PBPA apply mandatory pharmacoeconomic cost-effectiveness criteria. As a result, applicants must justify the listing and price of an innovative drug through economic and therapeutic studies that show a clinical advantage over its main comparator. Data regarding head-to-head comparisons with the PBAC-selected comparator are rarely generated through global Phase III clinical trials for

[6] We are seeking updated data.

regulatory agencies. In addition, the definition of economic benefit is extremely restrictive, and devalues quality of life and patient expense considerations.

Many of these measures lead to a *de facto* reduction in the effective patent life of products, as innovative patented medical discoveries are routinely linked to older, generic products and fail to gain early reimbursement due to the magnitude of the challenge of demonstrating satisfactory cost-effectiveness vs. these older and generic products. This "one size fits all" approach to drug pricing denies any recognition of the improvements which innovative American pharmaceuticals bring to patients, insulates older drugs makers who have failed to innovate, and delays access to important medical breakthroughs.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

INDONESIA

Pharmaceutical Research and Manufacturers of America (PhRMA) and Member companies operating in Indonesia recognize certain efforts of the Indonesia Government to improve the operating environment, specifically with regards to copyright protection. Much work, however, still needs to be done overall to ensure adequate and effective protection for U.S. rights, and to afford fair and equitable market access for U.S. persons that rely on such appropriate protection. In general terms, the current Government appears to be facing serious difficulties in making the long-needed structural adjustments. Therefore, while long-standing issues remain unresolved, Indonesia as a market continues to be of concern to the international research-based Industry. PhRMA requests that Indonesia be included on the 2003 "Special 301" Watch List.

Intellectual Property Protection

Patent Law Amendment

PhRMA is concerned that the Patent Law Amendment has not yet been approved by Parliament. Although there are some positive modifications to the existing law, there are some sections that will remain a non-compliant with minimum international obligations under the World Trade Organization (WTO) Agreement on Trade Related Intellectual Property Rights (TRIPS). Implementation of all IP laws and regulations remains one of the key hurdles for foreign research-based pharmaceutical companies operating in Indonesia.

Counterfeiting

Counterfeiting of medicines is a major concern in many parts of the world including Asia-Pacific and notably, Indonesia. Pirated pharmaceuticals from other countries are currently being imported to Indonesia and this is posing a risk to public health and safety. Perpetrators of these serious crimes are working collaboratively across borders. Audits inside Indonesia have demonstrated that a significant number of local retail outlets carry illegal products in their product portfolios. These are of either local or imported origin (some products are counterfeited but packaged in foreign packaging to appear genuine).

The Badan POM (FDA) has initiated some actions; however, these can still be considered inadequate as violators are subject to only minor penalties that do not act as an effective deterrent to this serious crime.

A comprehensive effort needs to be implemented to reduce the amount and scope of counterfeited medicines in Indonesia. This would include the allocation of adequate resources to combat the problem, the promulgation of effective laws and the

enforcement thereof. Additionally, of key importance would be the metering out of appropriate punishment to perpetrators of counterfeiting crimes - designed to be an effective deterrent.

Trade Secrets Protection

The lack of protection of Trade Secrets remains a key issue for the pharmaceutical industry as it has in past years. These policies deny adequate and effective protection for U.S. intellectual property rights.

Data Protection

PhRMA is also concerned that confidentiality of the files submitted to POM (FDA) is not guaranteed during the process. The Government is encouraged to establish appropriate training for local personnel so as to improve data protection in the broad meaning of the concept.

Damage Estimate

PhRMA Members report that the above issues have had significant commercial impact, not only in economic terms but also in terms of patient health and safety. At this time it is not possible to estimate the extent of the financial impact with precision.

MALAYSIA

There are several main areas of concern for PhRMA member companies operating in Malaysia. These include Government procurement, i.e. preferential treatment of local companies for supply of medicines on Government tender; intellectual property protection, including parallel imports, process patents and pending patents, and compulsory licensing; anticompetitive practices, including applications for Government medicines purchases list; and standards including product registration by the Drug Control Authority. Given these matters, PhRMA recommends that Malaysia be designated as a "Watch List" country for the 2003 "Special 301" review cycle. The following outlines the concerns related to intellectual property rights protection in more detail.

Intellectual Property Protection

Process Patents

Process patents can be registered in Malaysia. However, member companies have experienced difficulty in defending their process patents when products have been copied by local companies. The Ministry of Health (MOH), with knowledge of the Ministry of Trade, allows registration of unauthorized copy products manufactured by the same process. The onus is placed on the owner of the process patent to prove infringement, a process difficult to accomplish. PhRMA recommends instead that proof of non-infringement be placed on the infringing local generic company, as required by the TRIPS Agreement.

Pending Patents

Members advise there have been instances of generics having been registered and brought to market while patents are pending. There appears to be poor understanding or follow through on behalf of the MOH in this area, and members would like to see the general understanding of intellectual property by the MOH personnel improved.

Raised Threats of Compulsory Licensing

The MOH is concerned about the rising cost of medication for HIV/AIDS patients. MOH currently supports patients with single product therapy, but will switch to double product therapy in the future. The AIDS problem is not as significant in Malaysia as it is in other geographies; MOH estimates that there are 45,000 HIV positive patients in a population of 23 million. Considerable pressure has been placed on individual companies to reduce prices over the last 18 months, and companies have responded in a responsible fashion. However, departments in the MOH are moving for compulsory licensing of HIV therapies in order to obtain the lowest possible global

price (in fact, at prices as low as that of generics in neighboring countries such as Thailand). At this stage, the threat of compulsory licensing is believed to be limited to HIV products.

Counterfeiting

Counterfeiting of medicines has become a global problem, specifically in Asia-Pacific. Malaysia has not been spared the impact of this threat to patients and healthcare. The growing presence of counterfeit products on the Malaysia market needs to become a top priority of Government. PhRMA continues to cooperate with the Malaysia Intellectual Property Association (MIPA) to promote education in this area. PhRMA would like to continue to work as a partner with the Malaysia Government to eliminate counterfeit pharmaceuticals and urges that this becomes a high priority issue.

Parallel imports

The discussion on parallel trade issues in Malaysia continues. Non-Government Organizations (NGO) groups have recently raised the profile of this issue. PhRMA remains concerned that Government authorities will be unable to implement and manage a fail-proof process that will protect patients against the dangers of counterfeiting and from wholesalers who refuse to take full responsibility for product management. Studies have shown that the financial gains from parallel importation are not passed on to the patient or healthcare facility, but instead tend to go to the middlemen.

Damage Estimate

PhRMA Members report that the above issues continue to have negative commercial impact. At this time, it is difficult to estimate the extent of the impact with precision. Malaysia needs to ensure that acts, policies and practices that deny adequate and effective protection for U.S. intellectual property rights or fair and equitable access for U.S. persons who rely on intellectual property protection are addressed. It is recommended that Malaysia be placed on the Watch List.

THAILAND

Throughout the year 2002, incremental progress has been made by the Royal Thai Government in meeting its World Trade Organization (WTO) obligations and bilateral commitments, most notably in the field of trade secrets. However, the U.S. research-based pharmaceutical Industry continues to face uncertainty and lost sales due to discriminatory practices and market access barriers. Given the progress Thailand has made in addressing industry's concerns on data exclusivity, PhRMA recommends designating Thailand as a "Watch List" country for purposes of the 2003 "Special 301" review cycle. PhRMA and its member companies are encouraged by direction taken in the new Trade Secrets Law but believe monitoring of developing implementing regulations is critical to ensure that the spirit of the Trade Related Intellectual Property Agreement (TRIPS) defined data exclusivity.

Intellectual Property Protection

Trade Secrets Law

The Royal Thai Government has the opportunity to create the proper environment to encourage further investment in pharmaceutical research and development, and provide for greater access to medicines all the while meeting Thailand's international treaty obligations. In preparation of a new trade secrets law to comply with TRIPS, Thailand can create further positive investment climate by implementing regulations that will ensure the consistency of the Act with the obligations found in the TRIPS Agreement.

Data submitted by PhRMA members as a condition for marketing approval should neither be disclosed to a second applicant nor relied upon by the regulatory authorities in the consideration of another's application during the data exclusivity period. Other applicants seeking drug approval may not make use of the originator's data, but instead must produce their own independent data for regulatory review.

Summary of Industry's Concerns with the New Act

Section 15 of the Act provides that, "in cases where the law requires the applicant for a permit to produce, import, export, or sell Drugs or Agricultural Chemical Products using new chemical substances, to submit information supporting the request for a permit, and if such information, either wholly or partly, is a Trade Secret in the form of test results or other information regarding its preparation, discovery, or development which has involved great effort, and the applicant has requested in writing to the Government entity to preserve such trade Secret, the Government entity therefore has the responsibility to preserve and prevent such Trade Secret from being disclosed, taken away, or unfairly used for commercial purposes, according to the

regulations prescribed by the Minister." The statute further provides that the regulations shall specify

- the time period for the preservation of the Trade Secret;
- the method for the preservation of the Trade Secret, taking into consideration the type of technology and the test results, or information which is a Trade Secret; and
- The duty and responsibility of the state official in relation to Trade Secret preservation.

It is essential that the regulations reflect the intent of the negotiators of the TRIPS Article 39.3 with respect to the time period, method of preservation of the proprietary information and the responsibilities of Government officials in that regard.

Excessive Patent Delays

Though pharmaceutical product patents are available in Thailand, the patent department remains under-resourced. Accordingly, bottlenecks in the Department of Intellectual Property office lead to excessive patent review times, in some cases with patent prosecution delays upwards of five years. PhRMA wishes to work with the Government to improve this situation and is prepared to help support technical and other assistance programs to help improve the situation.

Parallel Imports & Counterfeits

The Thai pharmaceutical market suffers a relatively high level of parallel imports and counterfeits from other parts of Asia. There has been insufficient progress made to rectify the situation. There is recent evidence that the Thai FDA is being more diligent in enforcing restrictions on parallel imports and counterfeits and has offered to work with industry on a guidebook on counterfeit drugs in an effort to prevent proliferation of the problem. The FDA alone, however, cannot end these practices without out other Government agencies and resources. PhRMA encourages the Government of Thailand to drastically increase it involvement in this important public safety issue.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

VIETNAM

While it is acknowledged that some progress has been achieved with improving laws and regulations, most notably with regard to parallel importation, PhRMA member companies continue to face a number of serious barriers to conducting business in Vietnam in several main areas, including those related to Intellectual Property Protection. More specifically, this refers to compulsory licensing, infringement of registered trademarks, inadequate enforcement, insufficient protection for product trade dress, and importantly, counterfeiting - including that of medicines. These fundamental problems need to be addressed. Thus, PhRMA requests that Vietnam be included in the 2003 "Special 301" Watch List.

Intellectual Property Protection

Compulsory Licensing

Under existing law, the National Office of Industrial Property (NOIP) may order a compulsory license. PhRMA believes that patent compulsory licensing systems are seriously counter-productive except in cases of national emergency. Consequently, PhRMA maintains that the current law should be amended to eliminate the existing grounds for granting non-voluntary licenses, and to include conditions provided in the U.S.-Vietnam Bilateral Trade Agreement (BTA) and the World Trade Organization (WTO) Trade Related Intellectual Property Agreement (TRIPS).

To render the Vietnamese law consistent with obligations of Articles 27 and 31 of the TRIPS Agreement (which are incorporated in the U.S.-Vietnam BTA), Vietnam needs to include in its implementation package measures that specify that importation of a patented product will be legally equivalent to manufacturing of the product in Vietnam, and as a consequence, be sufficient to block the grant of a compulsory license based on non-use or inadequate use. In addition, the patent law should be amended to require "compulsory licensees" to pay a level of compensation commensurate with the patent's market value as provided in the TRIPS Agreement and the U.S.-Vietnam trade agreement.

Infringement of Registered Trademarks

Although the new Civil Code and associated implementing legislation provide a clear legal basis for protecting registered industrial property rights in Vietnam, infringement of registered trademarks is systematic and widespread, causing substantial financial losses to members of PhRMA. State-owned pharmaceutical companies under the jurisdiction of the Ministry of Health, and manufacturers and distributors from foreign countries figure prominently in infringement of the registered trademarks of PhRMA member companies.

Inadequate Enforcement

In the absence of a legal basis supporting a formal administrative mechanism for enforcing registered intellectual property rights, a mechanism has evolved in practice to which infringement victims primarily turn when they are unable to settle cases through informal discussions with the infringer. This involves petitioning the National Office of Intellectual Property for a decision of infringement. While the National Office of Intellectual Property has issued decisions of infringement in a responsible and timely manner, victims of infringement have encountered difficulties enforcing NOIP decisions through the *de facto* administrative mechanism for a number of reasons. These include refusal of state-owned manufacturers and importers of pharmaceutical products to comply with the NOIP decisions, confusion over NOIP's authority, and lack of cooperation between NOIP and MOH.

PhRMA believes that Vietnam is obliged under the U.S.-Vietnam trade agreement to change its enforcement environment to remove these deficiencies, particularly with regard to ensuring compliance with National Office of Intellectual Property (NOIP) decisions by manufacturers, distributors, and administrative enforcement bodies.

Insufficient Protection for Product Trade Dress

Vietnam is obligated under the U.S.-Vietnam trade agreement to eliminate loopholes in the current legal framework for protection of trade dress. This phenomenon allows companies to mimic or copy the product packaging of other companies, thereby trading unfairly on the hard-won goodwill associated with such product trade dress. Vietnam needs to amend its legislation to provide protection for both foreign and local companies from this type of unfair competition.

Counterfeiting

Counterfeiting of life-saving and other medicines in Asia-Pacific is of mounting concern, both in terms of 'local' health care and also internationally. There is growing evidence of countries of Indo-China/Mekong River areas being impacted as well as involved in practices and acts related to counterfeiting. Published information in international medical journals and that presented during the Global Conference on Anti-Counterfeiting of Pharmaceuticals held in Geneva in association with the WHO during 2002 suggests that thousands of people are adversely affected by the consumption of counterfeited medicines.

In Vietnam, a very high percentage of branded goods available on the market are acknowledged by the Government to be counterfeited. This concerning reality, if extrapolated to medicines, places the local and international public at risk of consuming

medicines of substandard quality that may for example contain incorrect amounts of active substances/inert ingredients or even toxins. While the percentage of counterfeited pharmaceuticals in distribution in Vietnam has not been clearly established at this point, the subject is of immense and growing concern.

In this connection, it is important that the Vietnam Government takes specific action. This includes ensuring that appropriate laws are in place, and that increasing vigilance and improved enforcement efforts regarding this important aspect of public health are maintained. It is also critical that punishment of criminals involved in counterfeiting of medicines is appropriate to this crime which seriously impacts the health and safety of patients.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, at this time it has not been possible to estimate such impact in financial terms with precision. It is important that Vietnam remains on the Watch List. Where appropriate, P*h*RMA is prepared to continue to support U.S. and Vietnam Government initiatives designed to address the important issues related to counterfeiting. P*h*RMA wishes to work in partnership with all stakeholders to help ensure that intellectual property protection related to medicines is appropriately enforced in Vietnam.

EUROPE

LITHUANIA

PhRMA members continue to suffer from inadequate and ineffective intellectual property protection in Lithuania, including the absence of protection for confidential test data. Given these issues, PhRMA recommends that Lithuania be included on the 2003 "Special 301" Watch List.

Intellectual Property Protection

Lithuania's patent law took effect February 1, 1994, and product patent protection for pharmaceutical products became available. The Agreement between the United States and Lithuania on Trade Relations and Intellectual Property Rights Protection was signed April 26,1994. According to Article VII, paragraph 5, a contracting party shall provide a transitional protection for pharmaceutical products for which product patents were not available prior to February 1, 1994, if the following conditions are satisfied:

- The U.S. patent has been issued for the product based on an application filed 12 months or more before February 1, 1994, but not before February 1, 1984,

- The product has not been marketed in the territory of the Contracting Party providing such transitional protection.

However the Lithuanian Government did not ratify this Agreement because of strong opposition from local pharmaceutical companies. Consequently, the products that could qualify for pipeline protection have now lost this benefit and now must compete against pirate copies. Pipeline protection for marketed pharmaceutical products in Lithuania is needed.

Data Exclusivity

As it takes 10 to 12 years to bring a new medicine to the market, the benefits of the 1994 patent act will not be felt before 2006 because its pipeline provisions are ineffective. Until then, data exclusivity is the only type of protection that may prevent early copying.

However, current Lithuanian law does not include any provisions meeting the requirements of Art. 39.3 of the TRIPS on the use of a previous applicant's documents, and, in particular, does not provide that, in order to refer to documents submitted by a previous applicant, the second applicant has to obtain the consent of the previous applicant.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

ROMANIA

PhRMA members continue to suffer from inadequate and ineffective intellectual property protection in Romania, including the absence of protection for confidential test data. In addition, PhRMA members attempting to do business in Romania continue to suffer from market access barriers, including insufficient transparency in pricing and reimbursement procedures. In light of these issues, PhRMA recommends that Romania be included on the 2003 "Special 301" Watch List.

The Romanian Government has stated that in order to catch up with the economies of other EU accession countries, among which Romania is lagging, a key success factor will be the improvement of the business environment, which in turn will trigger increased foreign direct investment. The Government believes that this can be achieved through economic liberalization, fostering fair competition in a free market, and the rule of law. PhRMA members hope that these principles will be also applied to pharmaceuticals in order to find workable solutions to the many current problems described below, which ultimately are not only barriers to trade but are also barriers to access to high quality medicines for Romanian population.

PhRMA is concerned about several public statements made in late 2001 by high ranking Romanian officials indicating that the local Romanian pharmaceutical industry should be protected and that the Romanian Government is evaluating the possibility of introducing drug import restrictions. These statements have been borne out by several Government ordinances, including the free supply of drugs of Romanian origin only, for low-income retired people.

Intellectual Property Protection

Data Exclusivity and Supplementary Patent Protection

Romania does not protect the costly and confidential test data submitted by pharmaceutical companies to regulatory authorities in order to obtain marketing authorization for innovative products, thus failing to comply with its specific obligations under the U.S.-Romanian Bilateral Trade Relations Treaty, the TRIPS Agreement, and the Association Treaty between EU and Romania. Due to the lack of implementation of data exclusivity provisions, copies are accepted for registration and are granted marketing authorization by the National Medicines Agency based on the safety and efficacy data originated with considerable effort by the innovators. Regulations for the protection of confidential data have been developed by the National Medicines Agency and were supposed to have been implemented on January 1st, 2002. These regulations, however, link data exclusivity to the existence of a valid patent, in violation of the TRIPS Agreement. The scientific council of the National Medicines Agency (NMA), at the request of the industry, has succeeded in separating the existing link

between data exclusivity and GMP. Data exclusivity is not expected by the NMA regulations to be implemented before January 1st, 2004.

Enforcement Issues

The State Office for Inventions and Trademarks (OSIM) is responsible for granting product patents, under the provisions of the 1991 Patent Protection Law and of the 1998 Pipeline Patent Protection Law. However, there is no specific court specialized in intellectual property, thus making the enforcement of existing laws and the efforts of patent holders to protect their rights extremely difficult and final outcomes doubtful. Art. 41 of the Trade Related Intellectual Property Agreement (TRIPS) requires that members of the World Trade Organization (WTO) Members ensure that their enforcement procedures permit "effective action" against intellectual property infringement acts and include "expeditious remedies to prevent infringements and remedies, which constitute a deterrent to further infringements." There are court cases currently pending that were initiated by U.S. companies against copycat companies that infringed valid patents that have lasted for more than 2 years.

Patent Term Restoration

Romanian authorities have committed to pass a law by 2004, which would implement Supplementary Protection Certificates as of 2007 to provide patent term restoration. PhRMA members believe that this timetable should be moved up.

Market Access Barriers

Funding and Debts

The pharmaceutical market suffers from chronic underfunding as the health care sector in general only receives 4.2% of GDP. This results in an allocation for medicines of less than US$ 25 per capita per year, one of the lowest in Central and Eastern Europe.

Debts for drugs and medical services within the health care system have constantly increased. In October 2002 they reached US$ 330 million at end-user prices. This is 70% of total reimbursable consumption (retail and hospital). This makes financial viability a challenge even for large corporations.

The authorities have repeatedly acknowledged the situation but have not yet taken serious corrective measures. In the most recent budget only US$ 30 million were reinvested in the health care system. This debt burden creates uncertainty for pharmaceutical investors.

Government Pricing of Pharmaceuticals

The Government pricing process takes place after the National Medicines Agency issues a marketing authorization for a product and follows a review process at the Price Department at the Ministry of Health and Family (MHF). In December 1999, the Ministry of Health introduced a drug pricing methodology based on cross-border price comparisons.

The new Drug Law 336/2002 (M.O. 418/17.08.2002) transfers authority for price setting from the Competition Office to the MHF. This law has also liberalized prices for over the counter products.

The authorities and the industry are further working together to improve transparency in the Government pricing process, to eliminate discrepancies between domestic and foreign product pricing and to establish clear deadlines for approval. PhRMA members believe that the authorities should appoint an independent body for addressing litigation.

Of the selling price of a drug, the VAT (19%) represents the highest additional cost. Under the 2000-2004 political program, the new Government committed to gradually lower the VAT for medicines making them thus more accessible.

Reimbursement System

In April 2001, the Ministry of Health and MHW decided to align the reimbursement process with the EU Transparency Directive (89/105). Consequently, a Transparency Committee was appointed in June 2001 to set up a transparent reimbursement process. In recent years, industry and the Transparency Committee have tried to develop, improve and apply verifiable and objective criteria for the reimbursement process. The transparency of the reimbursement process would be improved by involving industry and other stakeholders at an earlier stage.

The newly appointed Transparency Committee issued a new and fairly generous reimbursement list (65% of the shelf value) and a gratuity list for chronic diseases (April 2002). Both lists replaced and/or amended the previous heavily dysfunctional lists that had been in force since April 2000. In reality, patient access to the new lists was prohibited by the lack of proper funding, prescription capping (less than US$ 50 USD retail price per prescription), and arbitrary monthly prescribing and dispensing budgets.

In November 2002, in order to contain costs, a new reimbursement list was adopted. It consists of 4 lists: a) 100% reimbursement (for chronic and hospital drugs); b) 50% reimbursement for innovative, branded molecules; c) 65% reimbursement for patent expired molecules and generics; and d) the social list – for low-income retired people that are to receive three Romanian drugs per month for free. The 65% / 50%

reimbursement policy, as is, contradicts EU and WTO policies as it discriminates in favor of locally produced products.

Prescribing and Dispensing Restrictions

Access to medication is further restricted by the monthly-reimbursed drug prescription budgets per physician and per pharmacy that are arbitrarily set by the sick funds. These budgets are different from county to county (for physicians they range between US$ 200 and US$ 600 per month). In the case of primary care physicians who see on average 15 patients per day this amount corresponds to US$ 0.60 to US$1.90 per patient per month.

These cost containment measures generate inequity in access to reimbursed innovative patented products, stimulate informal payments, and oblige general practitioners to refer patients to hospitals for treatment when the patient cannot afford to cover the co-payment. This mechanism may lead to savings in the outpatient care drug bill, but also leads to increased total costs for the health care system, worsens disease outcomes – especially for chronic patients – and increases dissatisfaction in the health care system.

PhRMA members have proposed various solutions for cost-containment that would result in better savings to the system and improved access to all categories of drugs for the population.

Ownership Barriers

The newly passed Drug Law specifically prevents drug producers from owning shares in distribution companies, regardless of the fact that their own products are distributed through various distributors at arms' length and, therefore, without any risk of dominant position in the distribution of drugs. Despite the potential impact of these legal provisions, which will fully apply as of June 30, 2003, officials have thus far failed to issue relevant methodology regarding re-organization of producers, adding to the uncertainty and lack of transparency in the sector.

There are recent reports of attempts to introduce ownership restrictions and other types of restrictions in the pharmacy sector. We are hoping that the process will be carried out with transparency and consultation. PHRMA members also hope that legislative initiatives significant for the pharmaceutical sector will be submitted directly for Parliamentary approval.

Import Policies

- Tariffs for U.S. Products: The regime under which Romania is gradually lowering import tariffs from pharmaceuticals produced in the EU in the context of

EU accession negotiations is becoming a trade barrier. In case of U.S. origin products, the tariff differential versus EU origin products can be as high as 10.5%. Such significant differences in tariffs influence Government decisions on whether or not to reimburse the cost of a medicine, and thus put products of U.S. origin at a great disadvantage. As long as Romania is not a full member of the EU, the Most Favored Nation clause should remain applicable, and tariffs for products should be reduced to EU levels. The Government of Romania should be encouraged to follow the Czech example and sign a zero-for-zero agreement.

- Standards, Testing, Labeling, and Certification: The National Medicines Agency (NMA) (under Ministry of Health and Family) is in charge of issuing marketing authorizations for pharmaceutical products. The time frames established by NMA for the authorization process are often not met as the NMA is understaffed, leading to delayed access to the market.
- Good Manufacturing Practice (GMP) Standards: In order to file for marketing authorization, GMP production standards and data from bio-equivalence tests (that demonstrate that the therapeutic value of the generic product is similar to that of the original) are only required for foreign manufacturers. A number of domestic manufacturers do not produce pharmaceutical products in accordance with these standards. The deadline for GMP implementation set by the Government for domestic producers has been repeatedly delayed. According to the new Drug Law 336/2002, GMP should be fairly implemented starting January 1st, 2004.

Corruption within the Health Care System

The health care sector– similar to other sectors (see also the Strategy Paper and Report of the European Commission on the progress towards accession by each of the candidate countries) -is affected by poor governance and unethical practices, thus making efforts to manage the scarce available resources and to continue the reforms more difficult and less effective (as reported by several trusted organizations like World Bank and Foundation for an Open Society). The International R&D Pharmaceutical Industry Association in Romania, which comprises 19 foremost American and European drug manufacturers, has adopted a business code of conduct for promotional activities and is currently working to build an alliance aimed to promote good governance and ethical business practices in cooperation with the World Bank and the National Medicines Agency.

Damage Estimate

The Romanian pharmaceutical market has had a positive trend in the last few years. A good example for this would be the growth of 10% over 2001, which positioned the industry at an estimated value in 2002 of $555 million (ex-factory prices). PhRMA members cannot at this time provide any reliable estimate of the increase in sales if the aforementioned trade barriers were removed.

RUSSIA

Trade in the Russian pharmaceutical sector is impeded by substantial tariff and non-tariff barriers, non-transparent regulatory procedures and decision-making, preferential treatment of local firms and poor protection of intellectual property. Despite progress achieved by the Russian Government in macroeconomic and taxation reforms, the regulatory and administrative barriers in the pharmaceutical industry remain mostly untouched. Moreover, a significant new trade barrier for medicines was imposed on December 15, 2002 in the form of mandatory certification at market entry despite opposition from industry groups and a number of national Government agencies. For these reasons, PhRMA requests that Russia be included in the 2003 "Special 301" Watch List, and that the U.S. Government continue to seek assurances that the problems described herein are quickly and effectively resolved.

Intellectual Property Protection

The Government has made some progress with regards to amending the IP legislation at the end of 2002. However, IP has not become a priority and weak enforcement presents a major problem. International companies have to postpone or refrain from introduction of their most innovative medicines to this market given the poor intellectual property protection, or in other cases they have had to recall medicines confronted with counterfeits at a significant cost and without an opportunity to receive compensation from perpetrators. Current penalties for intellectual property rights violations are not adequate to compensate for the injury the rights holder has suffered because of an infringement of their intellectual property rights.

Of particular concern is a lack of a unified Government approach to intellectual property protection. At the end of last year, the Russian parliament, at the initiative of Rospatent, made a number of amendments to Russian legislation to improve opportunities for IP protection and enforcement. However, in addition to reviewing these amendments, the Russian parliament was discussing provisions on intellectual property as part of its work on the Civil Code Part IV, which if implemented would preempt current patent and enforcement provisions in Russian patent law and create problems for patent holders.

Counterfeiting

There are insufficient liabilities in the administrative, civil and criminal codes to be imposed on those involved with counterfeit medicines in Russia. Moreover, the Russian Supreme Court has ruled that counterfeiting did not constitute fraud, but only consumer deceit, which calls for lesser penalties. Trademark holders are often left to file suits against shell and short-lived companies while perpetrators can continue their operations freely. There have been no precedent-setting cases involving the prosecution of those involved in producing, importing, storing, and selling counterfeit

medicines. Cases that are being opened against companies suspected of selling counterfeits are often closed for lack of evidence. There is no provision for the visual analysis and testing of counterfeits and the use of these results as evidence for suspending and revoking licenses. Courts in IPR cases do not apply injunction measures. Russian legislation still lacking definition for counterfeit medicine and mechanisms for identification, seizure and destruction of counterfeits (although last year's amendment introduced a definition for a counterfeit product and the Ministry of Health issued its internal rules for destruction of products past expiry date, fakes and illegal copies), and importantly appropriate coordination of Government agencies with legal trademark holders is lacking. The Government should both establish adequate remedies, such as preliminary injunctions and damages and ensure that these remedies are effectively and expeditiously applied by the judiciary in relevant cases. This is something that the Russian Government has failed to do today.

Lack of In-Market Controls

The Ministry of Health and other Government agencies do not use available administrative measures and sanctions such as inspection of wholesale and retail in cooperation with trademark holders and suspension of licenses from suspect perpetrators of IP infringements. Instead, the Ministry of Health introduced mandatory certification for legal trademark holders.

Linkage

The Russian Ministry of Health can register medicines that violate patents or trademarks because there is no formal system of linkage between the regulatory and patent authorities. It is also possible in Russia to register trademarks very similar to the original (according to a current regulation, it is sufficient to show any three minor differences). A majority of such cases have been associated with companies under control of a local parliament member. Despite couple cases won through the Anti-Monopoly Ministry, this practice continues.

Data Exclusivity

Insufficient protection of confidentiality for registration files handed over to the Ministry of Health and a lack of data exclusivity create a problem for registering innovative medicines in Russia. In most industrialized countries, a special legal regime ensures that no person may, without the permission of the person who generated and originally submitted the costly and confidential data, rely on such undisclosed and proprietary test data in support of an application for product approval, not only while the originator's marketing application is pending before the regulatory authorities, but also for a specified period from the marketing approval date of the original product. Russian legislation does not provide for effective protection against unfair commercial use of confidential data submitted by the pharmaceutical companies seeking marketing

authorization. This has left the U.S. research-based pharmaceutical industry vulnerable to copying by domestic or foreign generic companies. While legislative reform is underway, PhRMA members look to the Duma to complete necessary action early in 2003.

Enforcement

Problems remain in the administration and adjudication of patent disputes and violations of registered patents. The only mechanism for challenging patent violators is via lengthy and costly court proceedings. IP proceedings are often delayed. The courts have little experience. Judges need solid training and proper remuneration. The burden of proof on process patents is a problem. Courts have so far not applied the injunction measures which would allow the patent holders temporary relief from detrimental sales by patent violators. The practice of patent rights enforcement is lacking. Often products that violate patents continue to be sold in pharmacies. The institute of bailiffs should be made into an effective body capable of enforcing the court's decisions. High liabilities for non-compliance or untimely compliance with courts' decisions should be introduced.

Market Access Barriers

Mandatory Certification

As of December 15, 2002, the Russian standardization agency, Gosstandard, and the Russian Ministry of Health introduced mandatory certification of medicines at the stage of market entry (mandatory certification existed before in Russia but was applied only for sales within Russia and largely relied on the recognition of certificate of analysis issued by international companies). The introduction of mandatory certification at the market entry was hailed by the Ministry of Health as the only means to counter counterfeit medicines. In practice, it is not possible to properly test all incoming batches of medicines without significant cost and delays. It is also not feasible to imagine that counterfeiters will submit their counterfeit product for such testing. As a result, mandatory certification imposed a substantial barrier for legal manufacturers and trademark holders, thereby making room for more counterfeits in the market. Mandatory certification also increased costs, resulting in significant delays (from one week to three and more weeks) and extra charges in customs clearance, and created opportunities for corruption in the process. The introduction of mandatory certification at market entry has already led to an increase of prices for medicines by an estimated 3%, and a higher price increase is expected in the coming months.

In anticipation of the new certification regulation, international manufacturers had to postpone most of their shipments to Russia for one-to-two months to be able to obtain and study new certification regulations. However, a month following the introduction of the new system, the Ministry of Health and Gosstandard continue to

hastily issue letters, decrees, and instructions regarding application of certification creating a regulatory 'mess' and customs clearance problems.

The requirement of the mandatory certificate is a clear-cut excessive control mechanism that is not justified by safety concerns and is not compliant with international norms for medicines. The main premise of the new mandatory certification is that a certificate of conformity issued by a third party is required at the time of market entry for each batch of medicines, which were already tested and received a registration certificate from the Russian Ministry of Health and which have a certificate of analysis issued by the international manufacturer. To conduct certification, a third party withdraws from shipments samples, some of which could be very expensive and also require special storage conditions, which effectively means losses of these items to the manufacturers.

The Ministry of Health has had to admit that it would not be possible to conduct full testing of all medicines coming to the market. Therefore, at the end of December 2002, the Ministry of Health issued a list of three categories of companies, each with a different assessment procedure: the first category of companies with clean quality record has to undergo certification only on the basis of visual inspection until July 1, 2003; the second category of companies will undergo the same 'reduced' certification but only until April 1, while each fifth batch of their medicines has to be fully tested; and the third category of companies has to undergo full testing of all batches. It is not clear what will happen following April 1 or July 1.

Russian companies are granted about a 33% 'discount' during certification by certification centers. This represents a deviation from the anti-monopoly legislation and unfair treatment of international manufacturers.

The certificate of conformity can be obtained only from a limited number of certification organizations accredited by the Ministry of Health. Companies are effectively forced to sign a contract on non-negotiable terms with the center pre-assigned by some non-transparent procedure. Certification centers indicate they are in a position to 'speed up' the process and 'solve' other problems hinting at a facilitation payment.

Russia still has no procedure for recognition of international GMP certificates of research-based pharmaceutical manufacturers and it could be expected that it will continue to refrain from doing so in order to be able to exert control and introduce new charges for such certification. International GMP-certified medicines have to compete in Russia with local medicines that are widely produced in non-GMP compliant facilities and in substandard conditions. A Russian Government decree requires local producers to upgrade their facilities to GMP standards by 2005. However, the necessary expertise, resources and trained personnel to conduct inspections are lacking.

Lack of Private Medical Insurance

Many of the problems in the sector are due to the lack of financing. Substantial reform of medical insurance is required. Limitations imposed on operations of foreign insurance companies should be lifted. Expenditures on dated and ineffective medicines should be discouraged as they ultimately result in higher patient treatment costs to the budget.

Price Registration

Government price controls were introduced to reduce (or monitor) mark-ups. However, innovative pharmaceutical companies are particularly concerned that pressure is being put on manufacturing prices and margins in an attempt to protect local companies and brands. Discrepancies between federal and regional regulations create contradictions and confusion within the healthcare environment, and also create further pressure on manufacturers to operate multiple pricing schemes for different regions. On top of that, authorities fix prices and mark-ups in rubles which does not take inflation into account. This results in losses for businesses.

Reimbursement and Tenders

Lists of essential and life-saving medicines are drafted without consultation with the industry and are often based on unclear criteria. Reimbursement decisions are not made based on objective and verifiable criteria. Appeal procedures for reimbursement and tender decisions are not clearly set and enforced.

Preferential Treatment

Preferential treatment of local companies is a major concern. Federal and regional authorities often impose preferential treatment for the purchase of goods. Local manufacturers also continue to benefit from preferential treatment in registration procedures and fees. The Ministry of Health requires international pharmaceutical companies that want to conduct multi-center studies in Russia to insure patients only via Russian insurance companies, thus restricting their opportunity to work with those global insurance partners that are known to and approved by their corporate headquarters.

Registration

The Russian Health Ministry has refused to continue recognition of the FDA-approved pharmaceuticals. The U.S.-Russia Memorandum of Understanding on Pharmaceuticals that exempted FDA-approved medicines from local clinical trials has expired and the Ministry of Health declined to renew it on same terms, requesting reciprocity that is not feasible or realistic at this stage.

Opaque Regulations

There are a number of serious issues with regard to opaque regulations and regulatory practices that have been hindering the registration of medicines in Russia. While the Russian Federal Law on Medicines spells out detailed rules governing the registration process, in practice the Ministry of Health's Department on State Quality Control of Medicines and Medical Equipment regularly issues specific regulations which impose arbitrary charges and requirements on manufacturers with little heed to international norms. These rules are typically in the form of 'letters' that have unclear legal status but are in practice obligatory for applicants, effectively creating more and more barriers to market entry for innovative pharmaceutical products.

Lack of Transparency

The registration process administered by the Russian Health Ministry is non-transparent. According to the Federal Law on Medicines, registration should be conducted by the federal body in charge of quality control of medicines. In the absence of such, a subsequent Government decree assigned this function to the Ministry of Health. The Health Ministry in turn uses a 'federal state enterprise' and expert committees with unclear functions and no basis in the Russian Federal Law on Medicines to conduct 'expertise' of medicines submitted for registration as a pre-requisite for their final approval. Without the preliminary approval of these bodies, a medicine can not be registered. Therefore, any applicant is forced to sign a service contract with the body indicated by the Ministry of Health and agree to all its terms. This procedure has no bearing in the Russian Federal Law on Medicines and appears to contradict anti-monopoly legislation.

Questionable and Discriminatory Registration Charge

According to the Law on Medicines, a fee in the form of a state duty is to be paid for state registration. This fee has not been officially set by the Government to date. Instead, an expertise body assigned for obligatory review by the Ministry of Health as a pre-requisite for registration introduced significant charges ($12,000 per each item for foreign producers, while Russian producers pay only half of that amount) for "expertise work".

Unclear Registration Timeline

According to the Law on Medicines, registration should take no longer than six months. However, the process often takes longer than the stipulated period. There is no timetable for different stages of the registration process. Lots of time is wasted with application documents going from one office desk to another, from one federal state organization to the Ministry of Health and back with unclear purpose.

Lack of Communication to the Applicant

The reviewing body assigned by the Ministry of Health and the Ministry of Health's Department for State Quality Control of Medicines and Medical Equipment make no communication on the status of the application documents at any point during the registration process. The applicant company has to go through a great effort to contact various officials, experts of federal state organization and expert committees to identify what happened to their application, what is causing the delay and what other documents may be required.

New Testing Requirement

In December 2002, the Ministry of Health's department in charge of registration issued a letter setting stricter requirements for testing of samples of medicines submitted for registration. This rule is now applied to applications submitted long before that letter was issued causing extra unexpected delays.

Questionable Re-registration Process

The Russian Federal Law on Medicines contains no mention of re-registration concept. However, according to internal rules issued by the Ministry of Health, the registration of medicines is valid only for five years. To have their medicines eligible for marketing, firms have to submit a new application for a lengthy review. Foreign producers of medicines have to pay a $6,000 fee for re-registration, a half of the full registration fee (Russian producers pay less). Instead of the three months stipulated by the internal regulations for the re-registration of medicines, re-registration may take in practice more than a year. At the same time producers are obliged by the Ministry of Health's internal procedure to update their registration file with any new information on an ongoing basis, whenever new data appears, making it available for review. This bureaucratic re-registration procedure creates unnecessary costs and red tape that has nothing to do with the actual analysis of data for safety and quality.

Dated Pharmacopoeia Standards

Russia has no complete pharmacopoeia, but only isolated pharmacopoeia articles. A number of their requirements are dated and contradict international norms. In particular Russian rules require international manufacturers to confirm compliance for certain standards (e.g. microbiological purity, remains, etc.) non-present/non-existent in a given medicine approved by FDA or the EU. Despite that, the international manufacturer has to indicate conformity with these standards otherwise a product registration will be denied.

Import Policies

- Customs Clearance: The import of pharmaceuticals into Russia is subject to cumbersome regulations and includes requirements with regard to licensing, certification, registration, customs duties, VAT and customs controls. While the customs duty on pharmaceuticals is an issue, the administrative and regulatory issues in customs clearance create even higher costs for businesses. This raises prices and reduces access for Russian patients.
- Attempts at Import Restrictions: There are periodical attempts by the Russian Parliament to pass legislation to restrict imports of foreign pharmaceuticals which run contrary to Russia's intentions to join the World Trade Organization (WTO) and promote trade liberalization.
- Application of VAT by Customs: A frequent problem is arbitrary application of federal regulations by the Customs authorities, often compromising the original goal of procedures. This results in the customs authorities demanding higher payments in the form of duties and VAT. Typically, customs officers who are not knowledgeable in the medical goods industry make their own judgments, often questioning the medical purpose of these goods, and ignore accompanying documentation from the Ministry of Health. Specifically, following the elimination of a VAT exemption on medicines and the introduction of a special 10% VAT rate as of January 1, 2002, customs offices particularly in the regions required 20% VAT or they refuse customs clearance. On top of that, the customs officers require payment of 20% VAT for medicines supplied for clinical trials in Russia, claiming that these are not medicines, despite the fact that such shipments have special letters from the Ministry of Health indicating that the product is a medicine. The problems are exacerbated by the frequent unavailability of internal Ministry of Health regulations both to the customs authorities and to firms.
- Interpretation of Procedures by Customs: Another example of arbitrary interpretation of norms by customs is with regard to confirmation of state registration of medicines. Customs officers assert that only a registration certificate is valid for such confirmation, although such requirement is stated in no laws or Government decrees, but only in an internal customs ruling. They refused to accept letters from the Ministry of Health confirming registration, or excerpts from the State Registrar of Medicines, or letters from manufacturers with registration data. This arbitrary requirement has resulted in substantial delays and extra costs for suppliers of pharmaceuticals to Russia in the last two years.
- Limited Competition: There is a lack of transparency in customs clearance and attempts to monopolize the services sector. For example, a joint decree by the Ministry of Health and the State Customs Committee adopted in 2001 called for a fast-track clearance but only through a 'customs broker specialized solely in medical goods'. It was adopted without any consultation with the industry and a without any clear mechanism for implementation. Customs officers are also discussing new rules that would limit the number of customs terminals for medicines.

- Inadequate Customs Clearance/Control Procedure: It is common for a customs post employee to have a question or be in doubt about a certain product and corresponding documents submitted for customs control and clearance. What happens today is a lengthy process of mailing within the customs committee that causes delays and extra costs for businesses. In the meantime, the company loses time and money, and loses yet more time and money trying to appeal the decision through the customs authorities. Mail correspondence sent by the State Customs Committee can take a week to half a month or even more to reach the company while a shipment is being held at the border and fines and charges for storage accumulate.
- Regulatory Process: The State Customs Committee regulations and instructions issued to customs posts become effective immediately. However, there is no publication or notification procedure that would allow businesses to become aware of these instructions, which gives no time to make necessary preparations. While on some issues, where decisions are made based on specific applications by companies, it is indeed vital for a speedy solution to a problem registered at the level of a customs post, in other cases this creates a serious barrier. There should be transition periods for customs directives to avoid practical problems.
- Appeal and Responsibility Mechanisms: There have not been many public cases involving the prosecution of customs officers who have made illegal claims or who have caused delays and extra charges for businesses, while such practices are widespread. Businesses are afraid to directly question or sue the customs authorities because of expected retaliation in the form of problems the customs authorities may easily create for them with any future shipments. It should be proposed that a mechanism be developed for reporting violations, on a confidential basis, to an independent body, which is not responsible for tax collection but rather is accountable to the business community, acting as a forum where such reports could receive a hearing and where investigations could be made.

Currently, import duties on pharmaceuticals range mainly from 5 to 15%, with several groups levied at 0% and some at 20%. Import duties on registered medicines should be eliminated; also no customs duties should be applied to drugs for approved clinical trials, as import duties result in higher prices.

Damage Estimate

The removal of the aforementioned trade barriers would mean elimination of the estimated 50% non-tariff barrier and a 10% tariff, which combined would make the current investments in this market by pharmaceutical manufacturers much more secure and profitable; provide for more reliable business development; and would create an opportunity to introduce their innovative medicines earlier, adding to the increase in their worldwide sales. However, it is difficult to estimate the impact of these trade barriers with precision, and PhRMA does not yet have such an estimate.

SLOVENIA

The Government of Slovenia continues to fall short of providing effective protection for patented pharmaceutical products, processes, and for protected data. In addition, PhRMA members attempting to do business in Slovenia continue to suffer from market access barriers, including a lack of transparency in the Government pricing and reimbursement system for pharmaceuticals. PhRMA therefore recommends that Slovenia be placed on the 2003 "Special 301" Watch List.

Intellectual Property Protection

Data Exclusivity

Slovenia first introduced a six-year data exclusivity provision in early 2000, only to suspend its effect in July 2000. This allowed local industry to copy many products by relying on PhRMA member's proprietary test data to expediently register a great number of copies, half of them leading molecules globally. It was not until January 2002 that the Slovenian Parliament reinstated a six-year period of data exclusivity. Even though a data exclusivity provision is now in place, industry remains concerned that locally-produced copy-cat products may appear on the market. In addition, the provision is still fraught with the original shortcomings: the six year period starts at the earlier of the Slovenian or any EU registration and thus shortens the data exclusivity period as EU registration regularly occur prior to the Slovenia registration. The provision contains a linkage to a valid patent, which is not compatible with the Trade Related Intellectual Property Agreement (TRIPS).

Weak Patent Enforcement

Attempts to enforce existing process patents in the Slovenian courts have been largely unsuccessful. The Slovenian courts have repeatedly denied enforcement measures under TRIPS such as preliminary injunctions and the reversal of the burden of proof. Slovenian courts have held that the burden of proof rests on the plaintiff where the alleged infringing defendant has been granted its own process patent subsequent to the plaintiff's. This interpretation is incompatible with TRIPS and with EU law. Several cases on intellectual property against domestic copy producers have been pending in Slovenian courts for more than four and up to seven years, due the inaction or inappropriate delays of the courts. This results in a de facto denial of fair and equitable enforcement of intellectual property rights as provided for in Article 41 TRIPS.

Effective action, expeditious remedies to prevent infringement and remedies that constitute a deterrent to further infringements are not available. This is evident by the delay of intellectual property proceedings for as much as five years. This is not in compliance with TRIPS Article 41.

In addition, current damages for intellectual property rights violations are not adequate to compensate for the injury the right holder has suffered. It is also rare that the infringer is ordered to pay the right holder's expenses associated with the defense of his intellectual property right, or ordered to recover profits. This is not in compliance with TRIPS Article 45.

Other TRIPS Inconsistencies

The new Slovenian Intellectual Property Act (IPA) has brought a number of improvements and brought Slovenian law considerably closer to EU and TRIPS standards. However, the law still denies injunctions as a remedy rather than merely monetary damages for patents that were reregistered in Slovenia and that had originally been filed in the Yugoslavia. Extremely short appeal periods (as short as 8 days) that may not be extended even after years of litigation to a judgment *de facto* prevent a non-Slovenian speaking plaintiff from effectively analyzing and preparing a proper appeal. This creates an unfair situation against a foreign plaintiff, favors local defendants and obviates a fair trial as mandated under TRIPS Article 41. Moreover, Slovenian law limits the court appointed chemical experts, whose opinion is often decisive for the outcome of the litigation, to Slovenian nationals. Given the limited number of experts available in an environment dominated by the influence of local copy industry, the enforcement system inherently favors local companies and obviates a fair enforcement of intellectual property rights against local infringers.

Contributory Infringement

The Intellectual Property Act (IPA) does not provide for relief against contributory infringements, such as supplying third parties, domestic or foreign, with intermediary products used in the synthesis of a protected substance.

Absence of Provisional Relief

Slovenian law grants relief only against infringements of a patent, but does not specify that this applies also to threatened infringements as required by TRIPS Articles. 41 and 50. Moreover, in deciding whether or not to grant interlocutory injunctions, courts follow only local provisions that require the court to strike a balance between the plaintiff's and the defendant's interests. This, however, increases the burden on the plaintiff and patent holder compared to the more narrow conditions of TRIPS Art. 50 and the Draft EU Regulations for a Community patent. The substance of TRIPS and the Draft Regulations reflect the standard of IP protection in the EU. Under the EU Agreement, Slovenia has promised to achieve the EU level of protection before 2000.

Lack of Pipeline Protection

Product patent protection became available in 1993. However, because there is no pipeline protection, the full effect of this law will not be felt until 2013. Patent applications must be filed very early in the research and development process, and it may take up to 8 – 12 years to develop a patented product to meet safety, efficacy and quality standards before regulatory marketing authorization is granted. Therefore, the majority of currently marketed pharmaceutical products, as well as those that will be launched in the next few years, are protected in Slovenia only by a process patent, and are exposed to easy copying by local firms. Unless appropriate pipeline protection is provided, it will not be until 2013-2018 (20 years from introduction of product protection plus up to five years patent term restoration) that the full product portfolio of R&D companies will enjoy the same level of protection available today in the U.S. and most of the EU. This lack of protection has allowed and continues to allow local and other companies to copy pharmaceuticals patented in the U.S. and EU. Although pipeline protection is not a TRIPS obligation, the absence of it in Slovenia has contributed to a situation where there is little effective protection for patented pharmaceutical products.

Market Access Barriers

Lack of Transparency of Pricing and Reimbursement Procedures

In 2001, Slovenia issued new Pricing and Reimbursement regulations, but they are not followed in a transparent and predictable way. Decisions are not based on objective and verifiable criteria as required by the EU Transparency Directive (89/105). The wholesaler price level can be only 85% of the average price in three reference countries (France, Italy and Germany). The comparison price is the wholesaler price, which has a different structure in Slovenia versus the reference countries. For example, import duties for U.S. products are up to 15% and must be absorbed by the producer in order to match the average in reference countries adjusted by the 0.85. This does not allow new innovative products to be marketed in Slovenia, as long as the calculation of the price is tied to the Anatomical Therapeutic Chemical (ATC) classification. Only the first product registered in Slovenia or EU at ATC level four can be calculated at 96% of the average of the three reference countries, but only for a very short period of time. When a second drug in the same class (even if it is a different molecule) enters the market, both products' prices must be adjusted by 85%. These regulations discriminate against imported pharmaceutical products, to the benefit of local producers and fail to recognize the large investments in research and development that are required to bring new medicines on the market.

However, the implementation of these rules is not used consistently. In the past, the Sick fund has independently tried several times to put arbitrary pressure on companies to lower the prices beyond the level as defined in the regulations.

New Reimbursement regulations include timeframes, and an applicant receives a written decision of the committee, but any appeal has to be referred to the same body that issued the original decision, the reimbursement committee. In addition the actual decision making process is not inline with the EU transparency guidelines requirement (transparent, verifiable….). In particular, the reasons for a negative decision are not provided in a clear and precise way. This makes it almost impossible to prepare an appropriate appeal if deemed necessary.

Import Policies

- Tariffs for U.S. Products: The regime under which Slovenia is gradually lowering import tariffs for pharmaceuticals produced in the EU in the context of EU accession negotiations is becoming a trade barrier. In certain cases, the tariff differential between products of EU origin as opposed to U.S. origin can be as high as 15%. Such significant differences in tariffs influence Government decisions on whether or not to reimburse the cost of a medicine, and thus put products of U.S. origin at a great disadvantage. As long as Slovenia is not a full member of the EU, the Most Favored Nation clause should remain applicable, and tariffs for products should be reduced to EU levels. Slovenia should be encouraged to follow the Czech example and sign a zero-for-zero agreement.

- Standards, Testing, Labeling, and Certification: Every first batch of imported products must be tested, causing further delays in receiving import documentation and additional costs. It takes from six to twelve months to get a date for filing the registration dossier, which delays the whole process for obtaining marketing authorization approval.

Damage Estimate

PhRMA estimates that the industry's losses in Slovenia are in the range of $50 million to $100 million due to the aforementioned trade barriers.

MIDDLE EAST, AFRICA, SOUTH ASIA

EGYPT

PhRMA members continue efforts to work with Egypt cooperatively to achieve compliance with current obligations under the World Trade Organization (WTO) Trade Related Intellectual Property Agreement (TRIPS). We are pleased to note that Egypt has met its January 1, 2000 obligations, including data exclusivity (Article 39.3), exclusive marketing rights (Article 70.9) and enactment of a patent mailbox (Article 70.8) by issuing Law No. 82/2002 for the protection of intellectual property published in June 3rd 2002, and effective since June 4th 2002.

We remain concerned, however, by some ambiguous provisions in law 82/2002. While on a *prima facie* basis law 82/2002 meets TRIPS standard requirements, the executive and implementing regulations ("the pending regulations") enabling the effective application of the law are not yet issued. We await the issuance of these regulations. PhRMA members would strongly support initiation of negotiations for a Free Trade Agreement (FTA) between the U.S. and Egypt, so long as Egypt's pending regulations of law 82/2002 are issued in compliance with all current WTO TRIPS, other national treatment and remaining market access issues, primarily those concerning punitive pricing policies, as described in the section on market access barriers are resolved.

Accordingly, in recognition of a generally compliant new IPR law, and continuing efforts to bring the IP regime to international standards, PhRMA requests that Egypt be designated as a Watch List Country in terms of the "Special 301" cycle for 2003.

Intellectual Property Protection

Current TRIPS Obligations

Egypt's new IPR law demonstrates good progress towards meeting WTO TRIPS obligations. Clarifications are needed to ensure that the law is implemented in a manner in compliance with its obligations. The WTO TRIPS Agreement (TRIPS Article 65.4) requires that Egypt phase in full product patent protection no later than January 1, 2005. Although most WTO TRIPS obligations took effect in Egypt from January 1, 2000, TRIPS Article 65.4 delays the obligation to administer the formal system of patent examination and registration required by TRIPS Articles 27-34 for pharmaceutical and agro-chemical products. Only these TRIPS obligations, and no others, are affected. Egypt must make greater effort in ensuring that the legal rights and implementing and enforcement regulations necessary to enforce those rights are appropriately applied in an expedited manner.

Data Exclusivity

The Prime Ministerial Decree (PM) No. 2211 of 2000 providing for data protection is replaced with Article 56 of the new IPR law. Article 56 of law 82/2002 states that,

> …*The protection accorded by this Law shall extend to the undisclosed information resulting from considerable efforts and submitted to the concerned authorities upon the request of the latter and necessary to authorize marketing of pharmaceutical or agricultural chemical products using new chemical entities. Competent authorities receiving this information are obligated to protect it against disclosure and unfair commercial use from the date submitting the information to these authorities until expiration of the secrecy classification, or for a period not to exceed five years whichever is less. Disclosure of this information by the concerned authorities to protect the public shall not constitute an infringement on the rights of their owner*….

This article obligates the Egyptian Government to respect the undisclosed information of originator firms submitted to the Egyptian Health Authorities for marketing authorization purposes. In implementing this language, it is particularly important that the pending regulations explicitly state that products submitted to the MOH before January 1, 2002 and received its marketing approval after that date must be accorded protection as stipulated by article 56. In addition, the pending regulations must clarify ambiguous provisions of the law both to ensure that the law covers product currently being marketed in the U.S. or elsewhere that have not yet entered the Egyptian market and for a period of protection of at least five years from the date of marketing approvals in Egypt.

Though the new law provides explicit protection against unfair commercial use, it did not include language on both direct and indirect reliance on that information by the Ministry of Health or local competitors. Additionally, PhRMA believes that the pending regulations explicitly clarify that no connection should be made between the status of patent protection and the provision of data exclusivity, consistent with TRIPS requirements.

U.S. and Egyptian Government attention to the implementation of the new law is critical. The Government of Egypt had allowed marketing of at least three important innovative products in spite of the previously controlling data exclusivity language found under the PM Decree 2211.

Exclusive Marketing Rights (EMRs)

The Prime Ministerial Decree No. 547 of 2000 is replaced by Article 44 of the new law. Said article includes provisions ensuring that the Government of Egypt will provide exclusive rights to EMR-holders, and it explicitly states

> *… Taking into consideration, the specified time to commence the examination process of the application related to the products provided in Article 43, the patent applicant shall have the right to request from the concerned Governmental authority the grant of an exclusive marketing right for his or her product provided that: (1) The applicant filed an application for this product at the Egyptian Patent Office with effect from January 1, 1995; (2) The same product was granted a patent in a WTO Member based on an application submitted in that Member with effect from January 1, 1995;(3) The applicant has obtained marketing approval for this product in and the same country from which he obtained the patent with effect from January 1, 1995; and (4) The applicant has obtained marketing approval for this product from the concerned ministry in the Arab Republic of Egypt. The Egyptian Patent Office shall grant an Exclusive Marketing Rights certificate after the approval of the ministerial committee formed for this purpose by a Prime Ministerial decree. Exclusive Marketing Rights certificate shall not be granted if it is explicit from the documents submitted to the Patent Office for the purpose of obtaining a certificate that product was published more than one-year prior to the date of filing the application. The applicant shall enjoy the protection provided by the certificate for his or her products approved by the concerned Governmental authorities until the Egyptian Patent Office agrees to grant a patent or for a period of five years counted from the date of approving such rights or whichever period is shorter. The granted certificate shall be canceled upon the cancellation of the marketing approval issued from the concerned ministry or if the right holder abused his or her rights.*

With adoption of this language, Egypt meets on a statutory basis TRIPS requirements provided in Article 70.8. Though one EMR has been approved under the previous PM Decree language, the system is under challenge by local interests and is being reviewed by the State Counsel Court. The U.S. Government should closely monitor this situation to ensure that the spirit of the WTO obligation is met.

Linkage

In order for data protection and an EMR system to be meaningful, Egypt should consider establishing linkage between the Academy of Scientific Research and Technology (Patent Office) and the Ministry of Health. In basic, there needs to be communication between the Patent Office and the Health Ministry to ensure that the health regulatory authority does not provide marketing authorization for unauthorized

copies of products subject to patent protection. Governments, not patent offices, are bound by the WTO TRIPS Agreement, and it is the responsibility of all relevant Government agencies to ensure that TRIPS obligations on patent protection and data exclusivity are met. Other Governments in the region that have provided such explicit linkage include Jordan, Kuwait, Qatar, and the UAE.

Summary of Concerns with the New IPR (Law 82/2002)

Pending regulations are needed to clarify ambiguities in the following key areas:

- The text of the new law does not clearly prohibit discrimination among fields of technology, as required by the TRIPS Agreement.

- The law is inconsistent with the WTO TRIPS Agreement provisions for use of compulsory licensing in exceptional circumstances. Articles 23-25 of law 82/2002 expand compulsory licensing for public non-commercial use in an unacceptable fashion.

- The regulations need to clarify the provisions as relating to protection for undisclosed information (trade secrets) and for commercially valuable data associated with applications for marketing approval of pharmaceutical products (data exclusivity). Fortunately, the law eliminated the combination of the two distinct types of protection envisioned under Article 39 (i.e. by paragraphs 2 and 3 respectively) by restructuring the provisions as follows.

    - Protection of undisclosed information, or trade secrets, is governed by TRIPS Article 39.2, which requires that protection be extended if the information has a certain character (see TRIPS Article 39.2(a) to (c)) is incorporated into Article 55 of the new IPR law, which, reflects the intent of Article 39.2 (i.e., "Natural and legal persons shall have the possibility of preventing information lawfully within their control from being disclosed to, acquired by, or used by others without their consent in a manner contrary to honest commercial practices").

    - TRIPS Article 39.3 requires the Egyptian Government to protect certain types of information provided to regulatory authorities from unfair commercial use is reflected in Article 56 of the new law. Thus, the law prohibit the Government from granting marketing approval for a specified period of time for a product made by a third party on the basis of a first applicant's approval. The law may allow the third party to generate its own data to support marketing approval; but it prohibits the "free riding" of the third party on the first applicant's work.

On a positive note, PhRMA members note the recent move by the Government of Egypt to join the Patent Cooperation Treaty (PCT). PCT membership will hope to expand opportunities for Egyptian patients to receive new, innovative medicines and improve the environment for expanded investment by PhRMA members.

Market Access Barriers

Egypt maintains an onerous price control system that does not allow for price increases to compensate for inflation. Also, many regulations regarding manufacture and registration are opaque and vague. In fact, the lack of clear accountability, timelines and procedures lead to long delays in new product registration, in some cases as long as two to three years. Delays in new product registration unnecessarily deprive patients of access to new medicines, and constitute a serious trade barrier for foreign manufacturers.

Furthermore, Egypt bans the import of many pharmaceuticals in finished dosage forms, and requires foreign companies to license the manufacture and sale of imported drugs to local companies. All of these requirements appear to violate Egypt's WTO commitments regarding national treatment of foreign investors. Moreover, as the Government has shown considerable progress in divesting and liberalizing large segments of the Egyptian economy, the pharmaceutical sector appears increasingly to be unfairly targeted for control. The sector remains under very tight price controls that distort competition and delay or discourage the introduction of new products. The rate of devaluation of the EGP during a period of 2 years ranged approximately from 40 to 45% without any price adjustment. Meanwhile, other countries in the region showed prompt response to similar cases to ensure the availability of all vital medicines to all sections of the populations and to keep the trend of foreign investments. Egypt is still far from adopting the proper measures to sustain the activities of our members in the Egyptian market, which is considered one of the most important markets for PhRMA members.

Damage Estimate

Egypt has a great deal to gain by coming into compliance with WTO TRIPS obligations, including the possibility of a Free Trade Agreement with the United States, and substantial direct foreign investment opportunities. PhRMA member companies would like to move forward with an estimated $300 million in planned investments in Egypt's pharmaceutical sector. Given its location and large population, if Egypt executive regulations comply with WTO, market-based pricing, and transparent registration procedures, it would become a likely regional center for multinational pharmaceutical production. Even so, Egypt remains one of the largest markets in the Middle East/Africa region.

Not considering delayed or forgone investment in U.S. based company operations in Egypt due to previously poor IPR protection and the current uncertain future, PhRMA estimates current annual losses in Egypt as in excess of $100 million due to non-compliant and or uncertain IPR policies and other existing market access barriers.

SAUDI ARABIA

Saudi Arabia is the only Gulf Cooperation Council (GCC) member state that is not a member of the World Trade Organization (WTO). As a country in the process of WTO accession, Saudi Arabia recently affirmed its longstanding practice of providing patent protection for pharmaceutical products via both domestic and regional GCC law. Unfortunately, the GCC itself has passed legislation taking the lowest common denominator approach and failing to meet minimum international standards. While there is some reason for optimism, we remain concerned that the GCC patent law will weaken compliance with the Trade Related Intellectual Property Agreement (TRIPS) across GCC states, including within Saudi Arabia. PhRMA urges the U.S. to seek changes to the Saudi and GCC patent law to bring it closer to conformity with TRIPS standards for all members.

In addition to intellectual property related concerns, PhRMA members also face other market access barriers in Saudi Arabia, including lack of transparency and threatened unilateral, discriminatory and otherwise unfair decisions adverse to the interests of the industry. We believe that the U.S./GCC consultative mechanism provides a good opportunity to address these concerns, and should be re-instituted as a high-level dialogue. In addition, PhRMA requests that Saudi Arabia be included in the 2002 "Special 301" Watch List.

Intellectual Property Protection

In recent months, Saudi Arabia has reaffirmed its commitment to meet WTO TRIPS disciplines for protection of intellectual property related to pharmaceutical products. PhRMA welcomes this restatement of intent, which reflects more than ten years of practice by the Government of Saudi Arabia.

However, we remain concerned by the overall level of protection provided by the GCC's regional patent law. For example, in the last year the GCC Secretariat approved for sale a number of copycat products produced in the UAE (described above). The GCC is now marketing these pirated products to Ministries of Health throughout the Gulf. GCC Health Ministries appear unaware or unconcerned that these procurement practices violate the TRIPS Agreement. Although the GCC secretariat has declined to release the list of affected products, PhRMA understands that the list includes cutting-edge products from GlaxoWellcome, Johnson & Johnson (doing business as Janssen-Cilag), Merck, Pfizer, and other leading international innovative pharmaceutical companies.

Despite repeated USG and industry communications to the GCC on this subject, the Secretariat has move forward with plans to sell these products throughout the Gulf. The Director General of the GCC Patent Office, Minister of Health Mohammed Al-Rasheed responded to PhRMA's September correspondence via a letter dated

November 19, 2000. In this letter he stated that unless a PhRMA member has sought patent protection through the GCC Patent Office, the GCC secretariat bears no responsibility to protect the intellectual property rights in question. This provides PhRMA members with a condition impossible to meet: because the GCC began issuing patents only within the last year or so, PhRMA members could not have applied for patents with the GCC office at the time that these products were patented in individual GCC member states, or at the time that those members undertook to respect the validity of patents filed in the U.S. or the E.U. In effect, the GCC law acts to nullify patent protection in Saudi Arabia and in other GCC markets. However, we have since that time received confirmation from the GCC Health Council that the GCC will abide by purchasing rules set down by GCC members, so that only drugs registered in Saudi Arabia, Kuwait, or the UAE will be eligible to compete in future GCC tenders.

The GCC's new patent law and regulations were approved by GCC Ministers on November 27, 1999. In theory, they have been implemented by all GCC members. Neither industry nor the USG had the benefit of discussion or review of the proposed patent regime prior to final passage and implementation of the new regime. There are a number of basic problems in the regime, including a lack of data exclusivity, and other WTO-inconsistent provisions. In late November 1999, and again in the fall of 2000, USG representatives raised the issue of the new patent law and regulations with GCC members, but were unable to obtain definitive responses regarding the important issue of legislative preemption. For example, interlocutors were unable to answer whether the GCC laws take precedence over individual state laws that may be more consistent with TRIPS, and the relationship between GCC institutions and national regulatory or judicial bodies. A detailed analysis of the GCC Patent law follows this submission.

Market Access Barriers

PhRMA members are also concerned with unfair market access barriers in Saudi Arabia, which is the largest GCC market. We believe that these issues should be addressed in the context of their ongoing WTO accession negotiation.

For example, the Saudi Government imposes a rigid registration and price control system that lacks transparency and delays product introduction. Saudi Arabia uses a burdensome reference price system. The Government requires PhRMA members operating in Saudi to provide the price of the candidate product in as many as 30 other countries, many of which (e.g. Lebanon or Jordan), are not comparable economically. The authorities will typically choose the lowest of the 30 prices as the Saudi price. Additionally, the Saudi Government is currently proposing a new pricing policy which, again, lacks transparency, is not based on the principle of market-based pricing, and stipulates compulsory price reductions. Introduction of new medicines is also delayed, mainly due to unnecessary laboratory analysis by the Saudi Ministry of Health, a requirement even for products approved by the FDA & European Medicine

Evaluation Agency (EMEA). In early 2002, the Saudi Arabia Ministry of Health (MOH) floated a price reduction proposal for a large percentage of products marketed by PhRMA members there. This policy is now under further review, and PhRMA supports a holistic approach to cost-containment in the entire health care sector. Moreover, PhRMA members are experiencing new problems in gaining marketing approval for certain package sizes[7] and we fear that the MOH may try to target certain products to reduce their public price regardless of the merits of the situation. We hope that we can initiate a dialogue between industry and the MOH in the coming weeks to resolve these important issues.

Because Saudi Arabia does not allow foreign direct investment, foreign investors are required to partner with local distributors who are the actual legal representatives of the company in the Kingdom. Accordingly, foreign companies have no legal status in the Kingdom. Saudi nationals must control or own 51% of enterprises. These requirements are explicitly prohibited under the WTO and must be resolved prior to WTO accession. In addition, the system discriminates in favor of local or regional (GCC) companies, providing both faster registration and preferential pricing (a 10% advantage in tenders as compared to multinational companies).

Finally, since the Gulf War, the Kingdom has experienced varying degrees of cash-flow problems. As a result, the Department of Health has stopped remitting payments on pharmaceuticals sold to Government-run institutions. A recent industry estimate indicates that more than $200 million in overdue receivables are held by international pharmaceutical companies. The combination of arbitrary price reductions, Government mandates, such as local hiring, that drive up the cost of business, and lack of payment for sales made to the Government, are creating a rapidly deteriorating commercial environment in Saudi Arabia.

Damage Estimate

The Saudi pharmaceutical market is estimated at more than $1 billion. If the GCC Secretariat continues to undermine the ability of its member states to provide TRIPS-consistent patent and data protection, the damage to the U.S. research-based pharmaceutical industry will be substantial, amounting to tens of millions of dollars per year on a conservative basis. PhRMA asks that the U.S. reinvigorate the U.S./GCC dialogue at a higher political level in order to seek clarification and improved protection for intellectual property, as required by TRIPS, and to remove other market access barriers that discriminate against the pharmaceutical industry. Further, PhRMA asks that the U.S. Government, prior to Saudi WTO accession, receive assurances from Saudi Arabia that it will follow GCC practices only insofar as they do not weaken the minimum protections contained in the WTO TRIPS Agreement.

[7] There is a recent occasion where the MOH has canceled the registration of a big size of existing products.

WESTERN HEMISPHERE

CHILE

Chile remains the last country in South America that has not passed Trade Related Intellectual Property Agreement (TRIPS)-compliant legislation – more than three years past the World Trade Organization WTO-imposed deadline. The copying situation in Chile is very troubling, with almost half of patented products having an average of three infringing copies registered by Chilean health authorities. However, it appears that the U.S.-Chile Free Trade Agreement will prospectively institute strong intellectual property protections going forward.

PhRMA requests that Chile be included in the 2003 "Special 301" Watch List, and that the U.S. Government urge Chile to cancel existing copy registrations and adopt a strong intellectual property law.

Intellectual Property Protection

We welcome the significant improvements that will flow from the U.S.-Chile Free Trade Agreement's intellectual property chapter. However, Chile currently falls short of its international obligations. Of the 30 patented pharmaceutical products currently on the market, 14 have been copied, leading to millions of dollars of lost sales for the innovator. Unable to rely on the Chilean Government's honoring of its commitments, the patent holder must take costly and lengthy legal action to defend his/her patents, while the unauthorized copy garners market share that in practice can never be regained. Copy registrations accelerated during 2002. This clearly violates Article 39.3 of TRIPS, which obligates Chile to safeguard confidential data from unfair commercial use, and has the effect of appropriating PhRMA members' property without due process or compensation. However, it is our understanding that Chilean authorities have undertaken to halt inappropriate copy registrations, and the terms of the U.S.-Chile Free Trade Agreement, if implemented, will eliminate this problem going forward. Chile should cancel existing copy registrations.

Chile's current patent law, implemented in 1991, offers an inadequate patent term (15 years from approval) and no transition (i.e. pipeline) protection for pharmaceuticals. Draft legislation designed to bring Chile into compliance with TRIPS obligations has not yet been adopted, more than three years past the WTO-imposed January 1, 2000 deadline. Chile should take prompt steps to bring its legislation into conformity with its international legal obligations.

Although the draft legislation pending in Congress represents an improvement over the existing law, several aspects are problematic. The 1991 law contained no mention of parallel imports; the new law does, which we regard as a step backward. The language of Article 51, which discusses compulsory licenses, should be modified to avoid ambiguity about when such licenses might be issued. The research-based pharmaceutical industry also advocates greater linkage between health authorities and

patent officials, particularly in a country like Chile, where copying is a serious problem. To that end, the new law should require so-called "second applicants" (i.e. applicants seeking to copy existing products) to demonstrate that the product for which they seek approval from health authorities is not the subject of a valid patent or a pending application. Amendments recently made to this legislation include allowing copiers to use confidential data during the period between its submission as part of the regulatory approval process and the date that innovative product is registered.

We welcome Chile's acceptance of provisions in the U.S.-Chile FTA to implement and enforce provisions guarding against the unauthorized commercial use of company proprietary data, as per the principles outlined in TRIPS Article 39.3. As is described in several other country sections in this submission, allowing the registration of "generic" products that use, or incorporate by reference, the company proprietary data of the innovator is an unfair trade practice that severely if not completely undercuts intellectual property protection for pharmaceuticals. This past practice in Chile has caused significant commercial damage to PhRMA members and we look forward to having five years of meaningful data protection when the FTA is adopted.

Market Access Barriers

The Chilean health registration system (e.g. Sanitary Code/Decree 1876) sets a higher standard for innovative products than for copy products seeking registration in Chile. This process discriminates against the research-based pharmaceutical industry when introducing original products into Chile, whereas it allows the swift introduction of copies in the Chilean market.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

CENTRAL AMERICA

(COSTA RICA, EL SALVADOR, HONDURAS AND NICARAGUA – PLEASE SEE PRIORITY WATCH LIST FOR GUATEMALA)

None of the five beneficiaries of the proposed U.S.-Central America Free Trade Agreement adequately protect confidential test data and there are numerous copy products on the market. El Salvador has not yet updated its intellectual property law to comply with the Trade Related Intellectual Property Agreement (TRIPS). Guatemala's Congress has passed and proposed legislation that clearly discriminates against research-based pharmaceutical products. A November 2002 decree could affect more than 750 patent applications; more than half of which were filed by American companies. Costa Rica's data protection and patent regimes are flawed. A regulatory proposal in the Central American Customs Union would discriminate against imported products. Some countries also apply discriminatory taxes; inappropriate tariffs on medical samples with no commercial value; and measures that unfairly privilege local distributors of PhRMA members' products. Honduras, Nicaragua and Panama have imposed price controls on innovative pharmaceutical products.

Intellectual Property Protection

The proposed U.S-Central America Free Trade Agreement (CAFTA) represents an important opportunity to improve standards in the region. While PhRMA strongly supports the expansion of free trade, ongoing TRIPS violations in Central America, particularly the failure to protect confidential test data, threaten efforts toward trade progress. Unfortunately, none of the five proposed beneficiaries of the CAFTA adequately protect confidential test data. Health authorities allow copiers to rely on innovators' data in violation of TRIPS Article 39.3. We are also concerned that El Salvador has not yet updated its intellectual property legislation to comply with the TRIPS agreement and that Guatemala's Congress passed and proposed legislation that clearly discriminates against research-based pharmaceutical products. PhRMA respectfully suggests that the CAFTA, which will set a precedent for the Free Trade Area of the Americas (FTAA), include strong protections for intellectual property, including a term of at least five years of data exclusivity for pharmaceuticals. In the interim, CAFTA candidate countries must abide by their existing TRIPS obligations before becoming eligible for expanded trade benefits.

National treatment must be confirmed and extended in any free trade agreement. While PhRMA recognizes the importance of regional integration and harmonization of standards, proposals arising from the ongoing Central American Customs Union negotiations appear to limit market access, such as discriminatory provisions against imported medicines. From the perspective of PhRMA members, Governments have decided to discriminate against foreign producers of pharmaceutical products by

granting locally manufactured products automatic health registration and imposing additional regulatory requirements on foreign manufacturers. Some countries also apply higher taxes on foreign producers seeking health registration, another clearly discriminatory practice. Other non-tariff barriers include duplicative or otherwise onerous import registration requirements and licenses; improperly applied tariffs on medical samples with no commercial value; discrimination in Government procurement.

In several countries, most notably Honduras, PhRMA companies must contend with a market access barrier imposed by laws unduly privileging local distributors, making the termination of a distribution agreement extremely onerous and costly. In effect, this practice means that even if a distributor performs poorly, the companies cannot terminate a distribution agreement, enabling those distributors to hold our products "hostage." It is hoped that the CAFTA will eliminate this and other market access barriers.

The situation facing the pharmaceutical industry is as follows:

COSTA RICA

Costa Rica enacted a specific law for undisclosed information (Law number 7975). However, it sets no specific term of protection. Article 8 of the law, which refers to data submitted for marketing approval, includes other exemptions that are not allowed under Article 39.3 of TRIPS. Information may be disclosed in order to protect the public but can also be used by the Government itself. Authorities are entitled to use test data (without disclosing it) when necessary to prevent practices that could mislead the consumer; to protect human health , animals, plants, or the environment; or in order to prevent the abuse of IP rights or practices that limit trade with no justification. The exemption is difficult to interpret, and could be open to varied interpretations; the use of the undisclosed information under the exemptions provided may include unfair commercial use. Costa Rica's law includes exemptions not allowed in TRIPS.

Costa Rica is about to issue a new data protection regulation. PhRMA hopes that it will improve upon the flawed protection provided by the law. Only a revision of the law will fully protect pharmaceutical intellectual property rights. The draft regulation, as of late June 2002, contained language that should be deleted in order to provide adequate data protection: paragraph 4 of article 11 and amending letter b, paragraph 2 of article 13.

Law No. 6867 is the patent law in Costa Rica, amended by Law 7979 in December 1999. Originally, Law 6867 provided a 1-year term for patent protection, counted from the day of grant. With the amendments, the law will provide with a 20-year term protection only if the original filing takes place in Costa Rica, a burdensome and unnecessary requirement. TRIPS establishes that those countries which do not

have a system of original grant may provide that the term of protection shall be computed from the filing date in the system of original grant. However, Costa Rica does not rely on other countries or regional patent offices for filing and examination. The only way to obtain 20 years of patent protection in Costa Rica is filing in Costa Rica as first country and then proceed to file in third countries. This provision may also violate article 4*bis* (1) and (2) of the Paris Convention.

Costa Rica's current legislation establishes that failure to work the patent in its territory may lead to compulsory license or to exhaustion of the patent. This may occur four years after the filing date in Costa Rica or three years from grant, whichever occurs first. According to article 18.5, after the terms that have been referred (3 and 4 years) expire, exhaustion of the patent occurs. Such provision establishes at the same time both the possibility of obtaining a compulsory license and the exhaustion of the patent. This expressly infringes Paris Convention article 5 (A.3) and (A.4).

EL SALVADOR

El Salvador is one of only two countries in Latin America whose patent law has not been updated to conform to TRIPS, although their current law (dating from 1993) was an improvement over former legislation. The industry's current priority is to amend Article 177 of the law, which governs data protection, by a decree that reflects TRIPS Article 39.3 including a minimum term of at least five years of protection. The Salvadoran Government is currently working on the decree; PhRMA hopes the U.S. Government will encourage the establishment of a strong standard. In addition, the following provisions of the current IP law should be amended:

1. Articles 106: definition of invention and exceptions to patentability. The definition of invention should be expanded.

2. Article 110: 15-year term for patent protection, thus short of the 20-year term required by TRIPS. El Salvador has argued that since its Constitution provides for self-execution of international agreements, the 20-year term applies in its territory. However, the law should be amended to make this commitment explicit.

3. Articles 133, 134 and 135 regulate compulsory licenses and need to be amended to comply with TRIPS provisions. The law currently fails to require, among other TRIPS provisions that the proposed user proves that s/he has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions. It also fails to regulate authorization of so-called second use patents.

HONDURAS

The Honduran Industrial Property Law, Decreto No. 12-99E, protects patents and trademarks. The law essentially echoes TRIPS. However, a provision that may limit patent rights refers to previous "good faith" uses of a patented product or process. This same provision appears both in Costa Rica's and Nicaragua's patent laws. The Honduran patent office, due to resource constraints, has a limited ability to appropriately address patent filings. A regional mechanism would solve this problem.

Articles 77 and 78 of the law make reference to undisclosed data that has to be submitted to regulatory authorities in order to obtain market approval. Those provisions echo TRIPS article 39.3 but fail to provide adequate and clear protection against unfair commercial use. Provisions have to be improved to make clear that market approval for second applications cannot be granted until a certain minimum period of time has expired, or if the second applicant proves to hold a license from the innovator.

NICARAGUA

Patent protection is regulated by Law No. 354, in force since Nov. 25, 2000. It essentially echoes TRIPS. A provision that may limit patent rights refers to previous "good faith" uses of a patented product or procedure. The Nicaraguan patent office, due to resource constraints, has a limited ability to appropriately address patent filings. A regional mechanism would solve this problem.

Article 125 of the Law makes reference to undisclosed data that has to be submitted to regulatory authorities in order to obtain market approval. The provisions fail to provide adequate and clear protection against unfair commercial use. Provisions have to be improved making it clear that market approval for second applications cannot be granted unless a certain minimum period is over, or if the second applicant proves to have a license from the innovator.

Market Access/Discriminatory Measures

While we recognize the importance of regional integration and harmonization of standards, we are concerned by proposals arising from the ongoing Central American Customs Union negotiations, such as discriminatory provisions against imported medicines. It is our understanding that Central American Governments have decided to discriminate against foreign producers of pharmaceutical products by granting locally manufactured products automatic health registration and imposing additional regulatory requirements on foreign manufacturers. Some countries also apply higher taxes on foreign producers seeking health registration, another clearly discriminatory practice. Other practices that need to be addressed in the FTA negotiations include duplicative

or otherwise onerous import registration requirements and licenses; improperly applied tariffs on medical samples with no commercial value; and discrimination in Government procurement. In several countries, most notably Honduras, our companies must contend with unfair conditions of competition imposed by laws unduly privileging local distributors, making the termination of a distribution agreement extremely onerous and costly. In effect, this practice means that even if a distributor performs poorly, our companies cannot terminate a distribution agreement, enabling those distributors to hold our products "hostage."

Price Controls

Honduras, Nicaragua and Panama have imposed price controls on innovative pharmaceutical products. Such price controls are often *de facto* discriminatory. In the absence of a viable local industry, Governments impose a disproportionate share of cost containment burdens on innovative U.S. pharmaceutical firms. Such price controls threaten U.S. global leadership in biomedical innovation.

Damage Estimate

PhRMA members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

COLOMBIA

Intellectual Property Protection

Colombia continues to be a serious violator of intellectual property in Latin America. However in 2002, Colombia took an important step by passing Decree 2085 to remedy a major TRIPS deficiency, lack of enforcement of the Article 39.3 of the Trade Related Intellectual Property Agreement (TRIPS). We welcome Decree 2085 as a step toward Colombia's commitment to implement its TRIPS obligations but Decree 2085 also needs to be implemented properly before Colombia's intellectual property regime can be considered to be improved.

For this reason, PhRMA requests that Colombia be placed on the 2003 Watch List. Please note that we advocate placing the other Andean Community countries on the Priority Watch List (see separate section).

Data Exclusivity Protection

The Colombian Government's issuance of Decree 2085 provides the domestic legal basis for proper implementation of an overdue obligation under TRIPS Article 39.3, which requires Governments to protect confidential test data from "unfair commercial use".

Decree 2085 establishes a data exclusivity period during which no third party may obtain a health registration for a pharmaceutical product relying on safety and efficacy studies filed by the innovator. Although Decree 2085 provides a good legal basis for enforcement of TRIPS Article 39.3, serious implementation questions remain.

For example, the local health registration authority (INVIMA) recently issued a letter stating that the data exclusivity period was not applicable if the applicant filed bioequivalence studies. Not only does this position defy a literal reading of Decree 2085, it undermines the very purpose of data exclusivity protection and of important bilateral commitments to the USG.

Mention should also be made of ongoing Andean Community negotiations seeking a harmonized community-wide pharmaceutical regime. Specifically, the Colombian Government should support legislation in the Andean pharmaceutical regime which is consistent with Decree 2085. We note with concern that a regime without the inclusion of such protection would effectively nullify Decree 2085 and other sanitary regulations such as Good Manufacturing Practice (GMP), and bioavailability and bioequivalence studies.

Patents for Second Uses

The Andean Court of Justice has issued several sweeping legal opinions forcing Andean Community member's to not recognize patents for second uses, in violation of TRIPS Art. 27.1 and contrary to long standing precedent in numerous jurisdictions. Andean member countries have either been compelled by the ACJ or chosen to honor Andean treaty obligations while ignoring their Uruguay Round Treaty obligations with the United States. The failure to provide patents for second uses particularly affects the pharmaceutical industry, which dedicates many of its research dollars to evaluating additional therapeutic benefits of known molecules (second uses) in order to provide effective solutions for unsatisfied medical needs.

Patents for Improvements of Known Molecules (e.g.: polymorphs, isomers, processes)

Some recent decisions suggest that the Colombian Patent Office is applying more reasonable standards of novelty and inventive level. However, there are still decisions applying prohibitive standards making it extremely difficult to obtain patents for improvements, which are otherwise patentable in the rest of the world. The most troublesome aspect of this situation is that these standards discriminate against the chemical arts, which evidently singles out the pharmaceutical R&D industry. These standards also constitute a technical sector-specific protectionist barrier, as they clearly benefit the local copy industry, which can gratuitously exploit the improvement in Colombia by not having a patent.

Patents for Biotechnology

Article 15 of Andean Community Decision 486 excludes a great part of all biotech innovation, by considering that "all or part of living beings as they are found in nature ... existing biological material or that which can be isolated" are not considered an invention. This exclusion is in clear violation of TRIPS Art. 27 as it is not one of the acceptable patentability exceptions. Indeed, it is worth noting that, in an apparent effort to circumvent TRIPS obligations, Andean Community negotiators shifted this exclusion from a patentability exception in prior Andean Decision 344, to an article that establishes what is not an "invention" in Decision 486.

Damage Estimate

PhRMA member companies have lost market share to dozens of infringing copies of their most important innovative products on the market in Colombia, representing millions of dollars in losses.

PARAGUAY

Paraguay's patent law is not fully compliant with the Trade Related Intellectual Property Agreement (TRIPS). Moreover, in late 2002 Paraguay adopted legislation to cancel patent protection until 2005, in clear violation of its TRIPS obligations. Counterfeiting is also a serious problem in Paraguay. Given these circumstances, PhRMA requests that Paraguay be designated as a Watch List country for the 2003 "Special 301".

Intellectual Property Protection

Paraguay updated its patent law in 2001 by passing Law 1630, the Law of Patents of Invention. It does not comply with TRIPS in several respects. Compulsory licensing is very broadly established and equitable remuneration is not envisaged for patent owners whose rights are exploited by third parties producing or preparing to produce the product before the patent was processed. The transition period for pharmaceutical products provides protection only from the date of granting the patent, rather than from the date of application. Exclusive Marketing Rights are jeopardized by language allowing unauthorized third parties to block those rights via the local health regulatory authorities. In addition, appeals are to be resolved by the same official (Director of the Patent Office) making the original decision regarding the granting of a patent.

On December 29, 2002, Paraguay adopted Law 2047, which modified article 90 of the patent law (Law 1630), postponing from January 1, 2003 to January 1, 2005 the date upon which pharmaceutical patents would be granted. Thus, no pharmaceutical patents are available in Paraguay, in contravention of its TRIPS obligations.

Due to weak Government enforcement, counterfeiting is a significant problem in Paraguay.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

URUGUAY

Uruguay's patent law is not fully compliant with the World Trade Organization (WTO) Agreement on Trade Related Intellectual Property Rights (TRIPS). Thus, PhRMA recommends that Uruguay be included on the 2003 "Special 301" Watch List.

Intellectual Property Protection

Uruguay updated its 1941 patent law on August 19, 1999 by passing Law 17.164, the Law of Patents of Invention, Utility Models and Industrial Designs. It does not comply with TRIPS in several respects.

- Compulsory licensing is very broadly established;
- Data exclusivity is omitted, contrary to Article 39.3;
- Exclusive marketing rights are not considered;
- Pipeline patent protection is not considered;
- Parallel importation is allowed.

Moreover, Uruguay appears to be an entry point into the Southern Cone region for copy products originating in India and elsewhere.

Damage Estimate

PhRMA Members report that the above barriers have had significant commercial impact. However, it is difficult to estimate such impact with precision, and PhRMA does not yet have such an estimate.

APPENDICES

APPENDIX A

ENFORCING DATA EXCLUSIVITY

What is Data Exclusivity?

Data exclusivity safeguards the commercially valuable and confidential data in the clinical dossier submitted by innovative firms to the health regulatory agencies. Data exclusivity ensures that information provided by an innovator to regulatory authorities will not be disclosed to the public or to other manufacturers, or relied upon either directly or indirectly, for a fixed period of time. This protection is provided in recognition of the investment of hundreds of millions of dollars made in expensive and time-consuming pre-clinical and clinical trials that constitute the majority of the $800 million dollar investment needed, on average, to bring one successful product to market (see box below). (I imagine you may have discussed this, but some may ask that if most of the $800 m is data, then aren't we double counting to say that patent protection is necessary to recoup that amount?)

The considerable effort that research-based pharmaceutical companies undertake to gain marketing registration of their innovative pharmaceutical products is recognized by the WTO TRIPs Agreement, which requires its Member countries to provide data exclusivity. TRIPS Article 39.3 obligates WTO members to provide a period of data exclusivity during which all proprietary information submitted to a regulatory body is to be protected from unfair commercial use. All WTO Members, with the exception of its least developed country Members, have been obligated since January 1, 2000 to implement the TRIPs provisions on data exclusivity.

The TRIPs Agreement recognizes data exclusivity as an intellectual property right that is independent from patent protection. They are two separate and distinct forms of intellectual property and under WTO rules require separate legal protections. This independence is reflected in the fact that the two obligations are contained in separate and parallel sections in Part II of the TRIPs Agreement.

Many WTO Members, including some developing countries, have enacted TRIPs-compatible data exclusivity. Other WTO members representing significant markets to the research-based pharmaceutical industry, however, have failed to do so and are challenging the accepted interpretation of the obligation contained in TRIPs Article 39.3. Notwithstanding the progress that the US Government has made in confirming the obligation through the use of bilateral and regional instruments, the time may have come for the US Government to launch a WTO multilateral dispute settlement case to define the obligation contained in TRIPs Article 39.3.

Rationale for Data Exclusivity

There are two steps in bringing an innovative drug to market: (1) the discovery of the new pharmaceutical compound and (2) the demonstration to regulatory authorities of the safety, quality and efficacy of the drug. Patents provide the incentive for the first step—the discovery and development of the innovative drug (molecule). They represent a "social contract" between the innovator and society in which the government provides a period of exclusivity to the innovator in exchange for the disclosure of the invention. Effective data exclusivity ensures that the second step is completed. It is, however, not a social contract but a limitation on the government's ability to use an individual's proprietary data, which is derived from the "considerable effort" needed to demonstrate safety, quality and efficacy of the innovative drug to regulatory authorities.

If it were not for the obligation to provide test data to governments to gain marketing approval, data generated at considerable cost, time and risk would be considered a trade secret. As such, it would be protected by TRIPs Article 39.2 against unauthorized acquisition or use "in a manner contrary to honest commercial practices" so long as the information were kept secret; had commercial value because of its secrecy; and was subject to the taking of reasonable steps to keep information secret. Under TRIPs Article 39.2, such protection is open-ended. However, in the case of pharmaceuticals, governments require the submission of test data to gain marketing approval. As a result, the data is no longer in the originator's control, although the information continues to have considerable value.

Were it not for the obligation to provide data to the government, the data would have remained completely under the control of the originator. TRIPs Article 39.3 imposes an obligation on governments to respect the confidentiality of the information that it receives and not to rely on the data for a fixed period of time.

Data Exclusivity, that is, the adoption of a period during which the governmental health authorities respect confidentiality of the data ("non-reliance"), provides a balance between innovation and repetitive tests and trials. The fixed period recognizes proprietary nature of data and, once the time expires, reference is permitted to the data on file with the health authorities. And, generics need only show bioequivalence of their product to the originator's drug, which results in a lower cost to bring a generic product to market, while respecting the proprietary nature of originator's data.

Both forms of protection are necessary.

Data Exclusivity Benefits the Host Country

Host countries will also benefit from the implementation of an effective data exclusivity regime.

In the first instance, patients will benefit by gaining immediate access to new medicines and expanding clinical research. A system of data exclusivity facilitates the originator's decision in favor of launching new and innovative products in the local market. Under such a system, the originator is able to launch his product with the understanding that, during the period of non-reliance, generic copies can only get on the market if the copiers undertake their own pre-clinical and clinical trials. As a result, the originator will be willing to undertake the necessary up-front pre-launch expenses associated with promoting the product and educating the local medical community on its use.

Local pharmaceutical and biotechnological companies and research bodies will also stand to gain from partnerships with foreign research organizations and investors that are only possible when the appropriate incentives for innovation, such as data exclusivity, are in place. Data exclusivity provides an administrative mechanism to protect clinical data, which, in turn, encourages the growth of pharmaceutical research and development in the country.

Implementation of TRIPs Article 39.3

WTO Members have adopted anywhere from five to ten years as the period of exclusivity. The United States defines the period of confidentiality or protection from use or reliance as five years for new chemical entities.[8] The periods of data exclusivity are enforced through the refusal of the US Food & Drug Administration (FDA) to even accept a generic manufacturer's application during the first five years after the originator's drug has received marketing approval, regardless of the patent status of the originator's drug.

Under EC Directive 2001/83, Article 10(1) (a) (iii), European Union member states currently either grant six or ten year exclusivity periods. The EU is currently in the process of convergence for a standard ten-year period of data protection.

China, as part of its obligations undertaken in association with its recent accession to the WTO, agreed to implement data exclusivity with a term of protection of

[8] "New chemical entity" is a regulatory concept and should not be confused with the "novelty" requirement of a patent. Drug regulatory agencies, such as the U.S. FDA and the national agencies in Europe, define a "new chemical entity" as a new compound with no prior approval as a drug, that has undergone full development and testing, and is proven to be safe and effective. "New chemical entity" status does not relate to the time when the active ingredient was first discovered or synthesized.

six years. This protection of data will be available to all pharmaceutical and agricultural products that utilize new chemical entities, irrespective of whether they are patent-protected or not. China has recently published its final regulation which appears to provide effective protection for six years from the date of marketing approval.

In addition, the four free trade agreements that the United States has negotiated since the advent of the TRIPs obligations (NAFTA, Jordan, Singapore and Chile) have confirmed five year periods of non-reliance for pharmaceutical products.

Nevertheless, some have asserted that TRIPs Article 39.3 does not require the implementation of the type of data exclusivity that the United States, EU and other countries provide for pharmaceutical products.[9] Both the US Government and the European Commission, however, have declared that Article 39.3 requires periods of non-reliance, which is the cornerstone of a data exclusivity regime.

In 1995, the Office of the USTR General Counsel declared

> "With regard to the second requirement … TRIPs Agreement negotiators understood it [the term "unfair commercial use"] to mean that the data will not be used to support, clear or otherwise review other applications for marketing approval for a set amount of time unless authorized by the original submitter of the data. Any other definition of this term would be inconsistent with logic and the negotiating history of the provision."[10]

In a written communication to the WTO, the European Commission supported this view when it pointed out

> "…Both the logic and the negotiating history of Article 39.3 of TRIPs leave no doubt that providing data exclusivity for a certain period of time was the envisaged way to protect data against unfair use as prescribed by Article 39.3… Whether any system other than data exclusivity over a reasonable period of time would meet the requirements of Article 39.3 of the TRIPs Agreement is to be assessed on a case-by-case basis, but examples of actual application by WTO Members of alternative--and TRIPs compliant—systems to non-reliance over a reasonable period do not appear to exist."[11]

<u>Consideration Should be Given to the Launch of a WTO Dispute Settlement Case on Data Exclusivity</u>

[9] See, for example, "EGA Position paper: TRIPs Article 39.3 Does Not Require Data Exclusivity Provisions," European Generic Medicines Association (Brussels), July 2000.
[10] "The Protection of Undisclosed Test Data in Accordance with TRIPs Article 39.3," USTR Office of the General Counsel, May 1995.
[11] "Questions on TRIPs and Data Exclusivity: An EU Contribution," Spring 2001.

Not all WTO members have implemented the obligations contained in TRIPs Article 39.3. Some, like India, Israel, Taiwan and Turkey, do not provide for any data exclusivity in their national laws. Other countries have adopted data exclusivity but across the spectrum of TRIPs-compatibility.

- Some, like Argentina, assert that their trade secret protection—akin to the obligation found in TRIPs Article 39.3—covers their TRIPs Article 39.3 obligation on data exclusivity.

- Others, such as Brazil, have introduced patent-like restrictions in their data exclusivity protection that seriously negates the value of such protection.

- Other countries—especially in Central Europe, improperly link data exclusivity to the life of the underlying patent.

- Finally, some countries, like Canada and Mexico, fail to properly enforce the data exclusivity that they do provide in their legislation and regulations.[12]

Given the negotiating history of TRIPs Article 39.3 and the growing consensus that the Article 39.3 obligation requires non-reliance for a minimum five year period, it is not necessary to engage in any debates with WTO members that either do not provide any data exclusivity or provide TRIPs-incompatible data exclusivity. While we appreciate the on-going bilateral pressure that the US Government continues to exert on these countries to provide TRIPs-compatible data exclusivity, unfortunately, from a multilateral point of view, the debate will not be resolved until a WTO panel rules in a WTO dispute settlement case. In addition, the pursuit of TRIPs-compatible data exclusivity via bilateral and regional instruments is a relatively slow approach that is resource-intensive and time consuming. While we may achieve positive results in the target countries, our data in other countries representing significant markets to the industry, remain unprotected against reliance.

We believe that the time has come for the US Government to consider the launch of a WTO dispute settlement case on data exclusivity. While we believe that the US and EU definition of the TRIPs Article 39.3 obligation would be upheld in a dispute settlement case against any of the counties cited above, the simplest and most straight-

[12] For a recent compendium of data exclusivity legislation, see "A Review of Existing Data Exclusivity Legislation in Selected Countries" (revised version), International Federation of Pharmaceutical Manufacturers Associations (IFPMA), Geneva, July 2002.

forward case might be against a WTO member that does not provide any data exclusivity at all.

APPENDIX B

THE IMPORTANCE OF PHARMACEUTICAL TRADEMARKS FOR PATIENTS

Introduction

Improved protection of trademarks relating to pharmaceutical products provides good news for patients, but this important feature of intellectual property has gotten lost in the current debate over access to medicines. This brief paper will explain why strong and enforceable trademark standards should be as important to patients in the developing world as it is to PhRMA members. The short answer: because stronger protections for trademarked pharmaceutical products provide an initial form of consumer protection for anyone who needs to rely on the integrity of a trademarked product.

Speaking generally, trademarks serve both to identify a product and its manufacturer and to avoid consumer confusion. When the product is a medicine, and a potentially life-saving medicine is inside the bottle, everyone—and especially the patient-- has an interest in maintaining the qualitative integrity of the product. Trademarks help to do just that. While in the U.S. this is just the first level of consumer protection, in least developed countries the trademark may be the patients' most reliable or only recourse to avoid spurious or unsafe products. In recognition of the importance of trademark protection, the World Trade Organization's (WTO) Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) provides protection for trademarks.[13] While many WTO members have now incorporated trademark protections into their national IP laws, developing country members and particularly least developed countries (LDCs), may lack the domestic resources to fully implement and enforce trademark protections. In addition, it is in these LDCs where patients most need the consumer protection afforded by trademarks. Sadly, these countries face severe pressure to adopt policies like international exhaustion that directly undercut trademark benefits to patients. Accordingly, PhRMA members ask the U.S. Government to devote more resources to trademark advocacy, capacity building and enforcement training over the next year.

What Makes Trademarks Unique?

Trademarks are different from any other form of intellectual property. Copyrights provide protection for authors of creative works;[14] patents recognize the economic importance of inventions to society;[15] and protection is provided for trade secrets and

[13] WTO TRIPS Articles 15 – 21, and enforcement provisions found in Article 41 et seq. Additionally, one benefit of recent U.S. Free Trade Agreements (FTAs) with Chile and Singapore has been the inclusion of provisions to enhance the trademark protections found in the WTO TRIPS Agreement with respect to labeling requirements for trademarked goods.

[14] Examples include books, music or sound recordings, software, games, and movies.

[15] In order for an invention to qualify for patent protection, it must be novel, include an inventive step (non-obviousness), and be capable of commercial application. An individual inventor creates a

other forms of undisclosed information in recognition of the investment made in generating the data needed to prove the safety and efficacy of the underlying product.[16] The common element in the foregoing is that these protections all are provided in recognition of the economic and cultural value of the content contained in the copyrighted works, patented products and related trade secrets/undisclosed information.

Unlike copyrighted works, patented inventions, or clinical dossiers, trademarks contain no content beyond the mark itself.[17] And unlike other forms of intellectual property that from their inception were intended to protect IP owners, trademarks have a different origin and purpose. Trademarks provide consumer protection both by providing product identification and avoiding consumer confusion.[18] It is that simple.

A trademark is a pledge or promise by the manufacturer to stand by the product, which, in turn, provides a measure of confidence to consumers that the product is safe and effective and that in case of any problem the manufacturer or his agent will stand by the product.[19] Trademarks become valuable because of their importance as a standard of quality and that is why they are of increasing significance to PhRMA members.

Trademarks Protect Patients in the Developing World

For pharmaceutical products, trademarks and house-marks, whether on a package or an individual pill, provide an assurance to medical personnel, pharmacists and patients that the product is what it is represented to be. In the U.S. and Europe, improved trademark protection for medicines provides heightened, independent protection for patients beyond that put in place by health regulatory authorities.

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potentially valuable product and society provides a limited period of exclusive rights to the invention in return for disclosure to the public of information concerning the invention.

[16] The secret formula for Coca Cola ™ remains perhaps the archetypal example of a trade secret; which unlike data exclusivity periods for pharmaceutical clinical data has no expiration date.

[17] But trademarks may now include a variety of media, including colormarks and other sophisticated marks. "A trademark can be a letter, number, word, phrase, sound, smell, shape, logo, picture, aspect of packaging or any combination . . . used to distinguish goods and services of one trade from those of another." "Protecting Medicines & Pharmaceuticals: A Manual of Anti-Counterfeiting Solutions," 2002, p. 60.

[18] WTO TRIPS Article 16.1 states that "The owner of a registered trademark shall have the exclusive right to prevent all third parties not having the owner's consent from using in the course of trade identical or similar signs for goods or services which are identical or similar to those in respect of which this the trademark is registered where such use would result in a likelihood of confusion." In the case of well-known marks, no registration is required. TRIPS Article 16.2.

[19] "[C]onsumers, directly or indirectly, must be able to obtain accurate information and to distinguish producers. The latter goal is served by trademarks." Thomas G. Field, Jr., "Pharmaceuticals and Intellectual Property: Meeting Needs Throughout the World," 31 IDEA: The Journal of Law and Technology 3 (1990).

It is important to maintain this independent measure of protection, particularly overseas. Trademarks should not be held hostage to the imposition of improper and unfair conditions by foreign regulatory authorities that undermine the protection and value of trademarks. Wherever restrictions are imposed,[20] they may weaken the clarity of the mark, and lead to patient confusion and potential health risks. In LDCs and in developing countries, where regulatory authorities are weaker than in the U.S. and Europe and medicines are taken with little medical supervision,[21] consumers are sometimes left with no marker of quality and safety beyond the trademark, which is intended to provide the assurance of the company that the product is reliable. So while IP owners may seek patents and copyrights more aggressively in OECD-level markets than in LDCs,[22] trademarks are actually much more important to consumers in less developed markets where they have fewer viable options for safety and quality assurance.[23]

In all developing countries, therefore, strong trademark protection may provide the most effective protection available against both counterfeit and substandard or spurious medicines.[24] This is particularly true in some Asian and Sub-Saharan African countries where there is extensive documentation of the frequently low quality of medicines for sale in registered pharmacies.[25] In this regard, research in Southeast

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[20] Trademarks are too important to patients to be left to tender mercies of health regulatory officials in developing countries that have already failed to provide any other forms of protection for their citizens. To this end, PhRMA members appreciate the inclusion of language in recent FTA Agreements with Singapore and Chile that guards against arbitrary or capricious labeling requirements that reduce the value of the mark to patients. In addition, such restrictions should preclude health regulatory authorities from conditioning the initial registration of a trademark or its renewal, or the recordation of trademark licenses on proof of "satisfactory" license terms and conditions (e.g., royalty amounts or product prices).

[21] Michale Kremer, "Pharmaceuticals and the Developing World," 16 Journal of Economic Perspectives 4, Fall 2002, p. 81.

[22] Amir Attaran and Lee Gillespie-White, "Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?" Journal of the American Medical Association, October 17, 2001, pp. 1886-1892.

[23] "Particularly in countries without extensive consumer safety regulation, a trademark owner's investment in goodwill may provide the most reliable assurance of safe product design and assurance of quality in manufacturing and distribution." Thomas G. Field, Jr., "Pharmaceuticals and Intellectual Property: Meeting Needs Throughout the World," 31 IDEA: The Journal of Law and Technology 3 (1990).

[24] Two problems have been identified through these investigations have surfaced two different problems: counterfeit drugs are products that involve a material misrepresentation of the manufacturer and/or origin of the product, whereas a substandard or spurious drug is more often a locally manufactured product that was not produced in accordance with Good Manufacturing Practices (GMP) and so either lacks bioequivalence (does not have the right ingredients) or is not bio-available (does not metabolize appropriately when ingested).

[25] R.B. Taylor et al, "pharmacopoeial quality of drugs supplied by Nigerian pharmacies," 357 The Lancet 1933 – 1936, June 16, 2001 (finding that nearly 50% of drugs sampled failed to provide appropriate levels of active ingredients due in large part to poor quality control and quality assurance during manufacture, but also raising concerns about imported counterfeit products); Paul Newton, et al "Fake artesunate in southeast Asia," 357 Lancet 1948 - 1950, June 16, 2001 (finding that up to 38% of a common anti-malaria treatment purchased in South East Asian countries failed to contain any active ingredient due to illicit trade on counterfeit products).

Asia indicates that physical examination of medicines for trademarks is important to avoid counterfeit products.[26] Overall estimates of the current level of counterfeits or substandard pharmaceutical products in developing countries range from 50 – 70%.[27] The prevalence of counterfeits/spurious drugs in developing countries,[28] underscore the "breakdown of drug-regulatory control in those countries."[29]

Absence of Enforcement Mechanisms Undermine Trademark Protections

Although WTO members have adopted trademark provisions as part of the overall WTO TRIPS legislation, PhRMA members encounter varied levels of awareness and understanding of the protections provided under the TRIPS Agreement. That is, while the majority of developed and developing country WTO members have conforming regimes on paper, much work remains to provide technical assistance and training to developing country WTO members both in terms of the benefits of trademark protection to their own consumers and the steps needed to effectively enforce TRIPS protections. PhRMA supports expanded USG advocacy to promote better trademark protections across the board, including of course for pharmaceutical products.

Other Policies Erode Trademarks, Harm Patients

In addition to the general lack of effective enforcement for trademarks, we encounter a more troubling development that has taken root over the last year, where LDCs and some developing countries have been lobbied hard to adopt policies that would weaken trademark protection for pharmaceutical products. These include efforts to protect local industries (labeling requirements to favor copies of PhRMA member trademarked products), and pressure to adopt parallel trade for pharmaceutical products. Despite evidence that patents are scarce and trademarks are valuable to patients in the poorest countries, anti-TRIPS activists call for policies that would undermine the consumer protection provided by trademarks.

It has become an article of faith that parallel trade will help developing countries, despite evidence to the contrary. By introducing avenues for the introduction of trademarked pharmaceutical products from unauthorized importers, parallel trade separates the product from the manufacturer's chain of custody and accordingly

[26] Newton, et al.
[27] Opening Statement of Congressman Fred Upton, Chairman, Subcommittee on Oversight and Investigations Hearing on Counterfeit Bulk Drugs, June 3, 2000.
[28] "More Substandard Medicines Spread in Worldwide Traffic," Agence France Presse, May 19, 2000, see also, "Dozens Dead In Cambodia From Counterfeit Drugs," United Nations Foundation, UNWire, May 30, 2000. These counterfeit medicines pose grave risks to patients in developing countries: "Every day people die because of counterfeit drugs," Dr. Isdrissou Abdoulaye, Ministry of Health, Benin, World Health Assembly, Geneva, 17 May 2000.
[29] Alain Li Wan Po, Commentary, 357 The Lancet, June 16, 2001.

undermines PhRMA members' ability to ensure its quality.[30] And in recent months, PhRMA members have seen low-cost medicines intended for Sub-Saharan Africa diverted to rich European markets by unscrupulous parallel traders.[31]

Widespread parallel importation would actually hurt and not help poor countries gain access to medicines, by creating market forces that would shift supplies of lower priced products from less developed to more developed economies. Parallel importation would also eliminate important consumer protection provided by trademarks, and weakening current levels of protection would increase the public health threat of counterfeit medicines. [32] Lowering the bar for trademark standards in particular may create deadly risks for patients in the developing world. Instead, we should all be thankful for trade negotiators who recognize the importance of the consumer protection provided by trademarks and continue to improve international standards for protection. We should work for the benefit of all patients, in the poorest countries, and continue to strengthen the trademarks that patients rely upon to protect their health in the absence of viable health regulatory systems.

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[30] "Protecting Medicines & Pharmaceuticals: A Manual of AntiCounterfeiting Solutions," 2002, p. 17 – 19 (pointing to parallel trade as a major cause of counterfeit or other substandard products.)

[31] See THE JAKARTA POST, March 2, 2002, ("The Indonesian Health Consumer Empowerment Foundation said in a report that up to half of all subsidized medicines, including donations from foreign Governments intended for the poor, had found their way onto the black market, earning hefty profits, needless to say.") http://globalarchive.ft.com/globalarchive/article.html?id=020302004418. See also, "HIV Drugs for Africa Diverted to Europe," The Washington Post, October 3, 2002, at http://www.washingtonpost.com/wp-dyn/articles/A35216-2002Oct2.html, and "Pharmaceutical Counterfeiting: Fears into Facts," Authentication News, October 2002, Vol. 8, No. 7.

[32] Statement by Secretary of Health and Human Services Tommy G. Thompson that reduced intellectual property protection in the form of reimportation "would increase the likelihood that the shelves of pharmacies in towns and communities across the nation would include counterfeit drugs, cheap foreign copies of FDA-approved drugs, expired drugs, contaminated drugs, and drugs stored under inappropriate and unsafe conditions." HHS News, July 10, 2001, available at www.hhs.gov/news/press/2001pres/20010710.html.

Adoption of international exhaustion as promoted by activists under the guise of improving access to pharmaceutical products thus harms most the most vulnerable patients in least developing countries.

Conclusion

In the context of PhRMA member overall IP goals for the coming year, we ask that the U.S. Government provide heightened emphasis on the importance of enforcing minimum international standards for trademarks. This includes both expanded technical assistance and training for enforcement officials and advocacy to counter undue pressure to adopt policies which undermine the protective value of trademarks to patients in the developing world.

APPENDIX C

THE COSTS TO RESEARCH-BASED PHARMACEUTICAL COMPANIES OF INADEQUATE DATA EXCLUSIVITY IN ARGENTINA[33]

Charles River Associates Inc.
Washington, D.C.

August 2001

I. Introduction and Overview

This study estimates the annual costs of inadequate pharmaceutical data exclusivity protection in Argentina, to research-based pharmaceutical companies. The costs are measured by foregone sales and foregone returns to investment. Using a conservative methodology, we found these yearly costs to be over $260 million.

Data exclusivity protection confers on developers of new pharmaceutical products a period during which the innovator will be the sole entity marketing the approved product. According to PhRMA, data exclusivity alone is sufficient to confer market exclusivity because it prevents market entry by parties wishing to sell the same product. It is not necessary to use data exclusivity in conjunction with other IP protections for it to be effective.

Data exclusivity systems rely on the market access procedures for pharmaceutical products. In particular, they rely on the new and generic (off-patent) drug approval processes administered by the health agency of each country. To gain approval for a generic drug, the producers must provide their own data supporting its safety and efficacy to the administering health agency. They cannot rely on the data supplied by the innovator. It is in this sense that the data generated by the innovator is exclusive. Market exclusivity is achieved by denying marketing approvals to other companies wishing to market unlicensed generic versions (i.e., biologically equivalent versions of the same chemical formulation) of the pioneer drug product unless they provide the appropriate data. By denying third parties the right to market generic versions of the product, the pioneer pharmaceutical developer enjoys de facto market exclusivity with respect to the product that has been approved.

Data exclusivity protection is linked to each specific approved product. Data exclusivity protection systems do not preclude other parties from obtaining marketing

[33] Charles River Associates Inc. (CRA) prepared this study at the request of PhRMA. Contact Richard D. Boltuck, Seth T. Kaplan, David A. Riker or Spencer R. Graf.

approval for the same product on the basis of their own test data establishing that the product is safe and effective.

In most countries that provide data exclusivity protection, the protection is conferred for *at least* five years for the pioneer pharmaceutical producer.[34] Further, both the research based industry and its critics concur that data protection effectively provides marketing exclusivity for the innovator, in that third parties are unable or unwilling to independently generate the data necessary to demonstrate the efficacy and safety of the new drug comprising a new chemical entity.[35] Consequently, five years is a conservative estimate of the protection data exclusivity normally confers. In keeping with these conservative assumptions, we analyzed drugs that were introduced to the Argentine market within the last five years.

The study relies on market data obtained from IMS HEALTH (IMS) together with a CRA-designed simulation model that estimates costs associated with the competing sales of infringing products in each of the markets for products containing individual specified molecules in Argentina.

A random sampling process was applied to select the molecules that were analyzed. The representative sample consists of 15 percent of the universe of molecules that are sold in Argentina identified as eligible for data exclusivity protection. The estimates of losses based on this sample was then projected or extrapolated to the universe of pharmaceutical sales in Argentina according to standard sampling theory. The result is an estimate of lost sales revenue and lost investment returns for the entire national pharmaceutical market.

The two pillars of this analysis are:

- Market data – that is, sales value by producer and pharmaceutical molecule – obtained from IMS HEALTH, the only entity that collects this information in the required detail.

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[34]TRIPS does not specify a minimum time period for data exclusivity. However, according to PhRMA, data exclusivity protections should last a minimum of five years from the time that the product is approved for sale. In the United States, exclusivity lasts five years for new products and an additional three years for new indications. In the EU, six to ten years of data exclusivity protection is granted. In the course of its WTO accession discussions, China has indicated that it will provide six years of protection for this commercially valuable, protected data. Many other developing countries have chosen a period of five years of protection. Under the U.S./Jordan FTA, Jordan will provide five years with an additional three-year period of protection for new uses.

[35] See Letter from James Love, Director of CP Tech and Robert Weissman, Co-Director of Essential Action, to USTR, concerning the US-Chile Free Trade Agreement, January 29, 2001, stating: "In many instances, if a generic company cannot use the already-generated registration data, it will not introduce a generic version of the patented product; the price of generating the data may be too high, or, just as important, take several years to replicate."

- An economic simulation model that appropriately estimates the returns on investment foregone by PhRMA member companies consequent to competition with infringing "copy" products.

The results of this analysis are summarized in Section II.

The economic model we have constructed compares the initial, observed market equilibrium – which generally includes both legitimate and imitator products – to a hypothetical equilibrium that would exist if the imitator products were not sold in the market. The model applies standard microeconomic techniques and assumptions, the mathematical details of which are set out in Section III.[36] Models that are structurally similar, for instance, are common in a variety of Government applications, including the analysis of the effects of dumping and countervailable subsidies in injury investigations before the United States International Trade Commission (USITC). The USITC also typically relies on such models in preparing competitiveness studies and other Section 332 reports for Congress and the United States Trade Representative (USTR).

Section IV discusses the elasticity estimates used in the model. Section V discusses the market data used in the model. Section VI discusses the sampling and estimation techniques, and Section VII offers concluding remarks.

II. Summary of Estimated Costs

Table 1 summarizes the estimated losses to research-based pharmaceutical companies measured by the cost of lost revenue and the cost of foregone returns to investment on sales in Argentina due to inadequate data exclusivity regulations. This table also reports a calculated standard deviation for the estimate, derived from the dispersion of estimates within the sample, and the size of the sample in relation to the size of the universe.

- Lost sales revenue of research-based pharmaceutical companies in Argentina due to inadequate data exclusivity regulations amount to an estimated US $262,224,000 per year.

- Foregone investment returns to research-based pharmaceutical companies in Argentina due to inadequate data exclusivity regulations amount to an estimated US $134,266,000 per year.

III. Description of the Model

The comparative static model requires a minimal set of parameters. The first set of inputs to the model are the annual expenditure values on both legitimate products

[36] Technically, the model is a comparative static non-linear (exact functional form, exact solution) partial equilibrium model, where the products are imperfectly substitutable for each other.

(embodying intellectual property used by the owner or licensee) and imitator products (where no compensation is paid for the use of the intellectual property that should be entitled to the protection afforded by data exclusivity). Legitimate product expenditures are denoted by R in the equations that follow. Expenditures on imitator products are denoted by R*.

The second set of inputs to the model are elasticity parameters that describe consumer demand, that is, consumer responsiveness to price changes: a composite demand elasticity for products made with each pharmaceutical molecule, namely η (a negative number) that applies in the initial, observed equilibrium, and an elasticity of substitution between legitimate and imitator products, namely σ. The selection of elasticity values is discussed further in Section III.

The structure of the model, and its solution, can be set out in a few equations corresponding to a conventional imperfect-substitutes framework. Assuming both legitimate and imitator products are sold within a market, the demand for the composite product, Q, is a linear function of the price of the composite product, P:

$$[1] \qquad Q = a - bP$$

where a and b are constants that are selected to correspond to the initial equilibrium.

Note that total expenditure in the full market, PQ, equals R + R*. Based on this relationship, it will prove convenient in solving the model to select P=1 (in the initial equilibrium) and Q=R + R*. Moreover, the demand elasticity, η, may be derived from equation 1 as,

$$[2] \qquad h = \frac{-bP}{a - bP} = \frac{-b}{a - b}$$

It is thus simple to solve for *a* and *b*:

$$[3] \qquad \begin{aligned} a &= (R + R^*)(1 - h) \\ b &= -h(R + R^*) \end{aligned}$$

The composite product represented by a conventional constant-elasticity-of-substitution (CES) aggregation function, which in turn implies that the composite price (unit cost) also has a CES functional form:

$$[4] \qquad P = (p^{1-s} + p^{*1-s})^{\frac{1}{1-s}}$$

where p is the price of the legitimate product and p* is the price of the imitator product.

Equation 5 represents the demand for the legitimate product: [5]

$$q = (a - bP)(\frac{p}{P})^{-s}$$

Equation 5 (and the symmetric equation for q*) implies that the ratio of prices, p/p*, equals $(\frac{R}{R*})^{\frac{1}{1-s}}$, noting that pq=R and p*q*=R*. From these relationships, it follows that in the initial equilibrium (where P=1), $p = (\frac{R*}{R} + 1)^{\frac{-1}{1-s}}$.

We assume that the legitimate drugs may be manufactured at constant marginal cost, c. Equation 6 defines the returns on investment from producing the pharmaceutical products:

[6] $$p = (a - bP)(\frac{p}{P})^{-s}\ (p - c)$$

Conventional microeconomic theory indicates that the legitimate producer sets a price (and corresponding volume) such that the first order condition, $\frac{dp}{dp} = 0$, is satisfied.

Finally, in the hypothetical or counterfactual equilibrium in which an adequate data exclusivity regime is in place, we assume that the imitator product disappears from the market.

Once we have found P_L, it is straightforward to calculate the hypothetical prices and revenues if data exclusivity protection were in place. The volume of sales is determined by equation 1, evaluated at P_L, and revenue is the product of volume and price.

IV. Elasticity Assumptions

The economic model described in the previous section requires two demand parameters in each market, namely an elasticity of demand for the composite product

and an elasticity of substitution between the legitimate and imitator product. The existing research literature on demand for drugs is sparse and not of obvious applicability to our markets outside of the United States. We have based our judgments on the estimation method applied in trade dispute analyses performed at the USITC, in which product markets that are generally defined in similarly narrow fashion are often evaluated. We believe our approach is reasonably consistent with that used at the USITC.

Drug purchases are typically prescribed or advised by a physician, and sometimes the costs incurred are covered by health insurance. They are regarded as important or critical parts of treatment programs to alleviate symptoms or cure diseases. The drugs in our data set, in particular, are most often for severe conditions, such as viral infections, disorders of the central nervous system, and other similar ailments. These circumstances indicate that consumers are somewhat insensitive to price in making purchase decisions from within a pharmaceutical-molecule market, i.e. demand for the composite product is moderately inelastic in the initial, observed equilibrium. Accordingly, we have assumed a base case demand elasticity of –0.75.

In each particular market, the demand elasticity is influenced by a variety of product-specific factors. The existence of significant therapeutic substitutes based on other active ingredients is one such factor. We lacked sufficient information to adjust for such differences.

However, we did account for factors that we could evaluate based on information about the molecule class in the 2000 edition of the Physician's Desk Reference. For instance, it is likely that demand would be more elastic for drugs used to treat chronic rather than acute conditions, since patients are better able to learn about therapeutic substitutes and other treatment alternatives over greater periods of time. Similarly, it is likely that demand would be more elastic for drugs intended to treat less severe or non-life threatening diseases. We adjusted our base line assumption about the demand elasticity to account for such product attributes listed in Table 3.

In our base line case, we assumed a moderate elasticity of substitution of 4.5. This value balances a variety of characteristics that weigh in favor of greater or lesser substitutability. In many instances, the imitator drug is indistinguishable chemically or therapeutically from the legitimate drug, imparting a high degree of fungibility. But in some instances, quality-control, and the consumer perception of quality control for production on non-branded imitator drugs, instills concern among purchasers about whether the imitators really provide the same functionality as the legitimate product. Table 2 identifies the adjustments that we made to the base line elasticity of substitution value based on the product attributes. For instance, consumers are likely to be more concerned about perceived quality differences if the disease to be treated is more severe, or if comparatively small deviations in the amount of the active ingredient could cause serious or life-threatening conditions.

V. Market Data

The IMS data set is unique and the best available for the type of analysis that we have undertaken. Nonetheless, it presents several significant challenges. The data generally describe whether a product is branded or not, the date of entry into the Argentine market, the manufacturer of the product, the location of its headquarters, and the value of sales by product.

IMS collects data through in-country offices that conduct a survey of drug sales by wholesale distributors and sometimes retail pharmacies. The sample is generally quite large, and is projected on the universe. IMS attempts to validate some of its market data each year through direct contacts with pharmaceutical manufacturers. The data are regarded as reliable, although subject to some undercounting, which would tend to result in estimates that understate the full losses to PhRMA member companies.

We encountered a variety of specific challenges in using this data set, which we generally resolved by adopting classification rules that we regarded as the most reasonable available.

VI. Sampling Procedure and Estimation Methodology

The CRA analysis consisted of three major steps:

1) Identify appropriate samples of molecules sold in Argentina that are likely to be entitled to data exclusivity.
2) Perform a simulation analysis with respect to the market for each such sampled molecule. This analysis requires several sub-steps:
    (a) Estimate market shares of legitimate and infringing imitator products based on a set of classification rules;
    (b) Estimate the elasticities of composite demand for products containing each molecule, and estimate the elasticities of substitution among differing products containing the same molecule, in both cases by adjusting base-line elasticity assumptions for variations associated with ascertainable product attributes;
    (c) Apply the simulation model to estimate lost sales revenue and lost investment return costs for each molecule.
3) Project the estimated lost-sales revenue and lost investment-return costs on to the universe of all markets for molecules that are entitled to data exclusivity.

Table 2 lists all of the molecules sold in Argentina that were identified through FDA lists of molecules patented in the United States as containing protectable IP,

which in turn is a subset of a master list of molecules sold in each country as provided by IMS.[37]

From the list in Table 2, a random sample consisting of 15 percent of the molecules was selected. Table 3 presents a list of all of the molecules in the sample for which relevant attributes could be ascertained through the *Physicians Desk Reference*, together with the attributes thus obtained.

Table 4 sets out a comprehensive list of the molecules included in the 15 percent samples, together with the adjustments to base-line demand and substitution elasticities based on the molecule-specific attributes reported in Table 3.

The standard deviation of the estimate as reported in Table 1 is based on the following estimator:

$$std.dev.(\hat{Y}) = \left\{ \frac{N^2(1-\frac{n}{N})}{n(n-1)} \left[\sum_{i=1}^{n} (y_i - Rx_i)^2 \right] \right\}^{1/2}$$

where $\hat{Y}$ is the estimated loss, N is the number of molecules in the universe, n is the number in the sample, y_i is an individual sample molecule i's estimated annual loss, and x_i is total annual sales of sample molecule i.

VII. Conclusion

PhRMA member research-based pharmaceutical companies, when rewarded with adequate returns in the marketplace, have demonstrated a distinctive ability to discover and develop significant new pharmaceutical products affording increasingly effective therapies across a wide variety of afflictions. The integrity of market-based incentives in global markets, however, has been undermined by weak and inadequate IP regimes in many countries. The lack of data exclusivity in Argentina is a prime example. The losses to research-based firms are sizeable. The model-based estimates indicate that lost revenues in Argentina sum to approximately US $262 million per year while lost returns on investment sum to approximately US $134 million per year.

This study estimates losses to research-based pharmaceutical companies that are attributable to inadequate data exclusivity protection in Argentina. It does not, however, quantify the social costs, in the form of fewer or later pharmaceutical

[37] IMS provided specific data for sales of products containing each molecule in each country, including the total sales value, and whether each individual product containing the molecule is branded or generic, the sales value for the individual product, the nationality of the product's manufacturer, the name of the manufacturer, and the name of the product. For FDA patented-molecule lists, *see* www.fda.gov.

discoveries, imposed by the failure to fully incentivize the very firms that have proven themselves to be the world's engines of pharmaceutical innovation.

Table 1: Estimated Annual Lost Sales Revenue and Returns to Investment in Argentina

Lost Sales Revenue		Lost Return on Investment	
Estimate	**Standard Deviation**	**Estimate**	**Standard Deviation**
$262,224,000	**$48,685,000**	**$134,266,000**	**$30,649,000**

Table 2: Molecules In Argentina Identified as Containing Protectable IP.

ABACAVIR
ADAPALENE
ADENOSINE
ADENOSINE PHOSPHATE
ALBENDAZOLE
ALLOPURINOL
ALPRAZOLAM
ALPROSTADIL
AMIFOSTINE
AMIODARONE
AMLODIPINE
AMPHOTERICIN B
AMPRENAVIR
ANASTROZOLE
APRACLONIDINE
ASTEMIZOLE
ATORVASTATIN
ATROPINE
AVOBENZONE
AZELAIC ACID
AZELASTINE
BECLOMETASONE
BENAZEPRIL
BERACTANT
BETAMETHASONE
BETAXOLOL
BICALUTAMIDE
BISOPROLOL
BLEOMYCIN
BRIMONIDINE
BRINZOLAMIDE
BROMPHENIRAMINE
BUDESONIDE
BUSPIRONE
BUSULFAN
CABERGOLINE
CALCITRIOL
CANDESARTAN CILEXETIL
CARBIDOPA
CARBOPLATIN
CARMUSTINE
CARTEOLOL
CARVEDILOL
CELECOXIB
CERIVASTATIN
CETIRIZINE
CHLORHEXIDINE
CHLORTALIDONE
CICLOPIROX
CILOSTAZOL
CIMETIDINE
CIPROFLOXACIN
CISAPRIDE
CISATRACURIUM BESYLATE
CISPLATIN
CITALOPRAM
CLADRIBINE
CLOBETASOL
CLONAZEPAM
CLOPIDOGREL
CLOTRIMAZOLE
CYANOCOBALAMIN
CYCLOPHOSPHAMIDE
DAUNORUBICIN
DESMOPRESSIN
DESOGESTREL
DEXRAZOXANE
DIAZEPAM
DOXEPIN
DOXORUBICIN
EFAVIRENZ
ENALAPRIL
ENOXACIN
ENOXAPARIN SODIUM
ENTACAPONE
EPTIFIBATIDE
ESMOLOL
ESTRADIOL
ETHINYLESTRADIOL
ETOPOSIDE
EXEMESTANE
FAMCICLOVIR
FAMOTIDINE
FELODIPINE
FENOFIBRATE
FENTANYL
FERUMOXIDES
FEXOFENADINE
FINASTERIDE
FLECAINIDE
FLUCONAZOLE
FLUDARABINE
FLUMAZENIL
FLUNISOLIDE
FLUOCINOLONE ACETONIDE
FLUOROURACIL
FLUOXETINE
FLUTAMIDE
FLUTICASONE
FLUVASTATIN
FLUVOXAMINE
FOSCARNET SODIUM
GABAPENTIN
GANCICLOVIR
GATIFLOXACIN
GEMCITABINE
GLATIRAMER ACETATE
GLIMEPIRIDE
GLIPIZIDE
GOSERELIN
GRANISETRON
HYDROCHLOROTHIAZIDE
HYDROCODONE
IBUPROFEN
IFOSFAMIDE
IMIQUIMOD
INDINAVIR
INSULIN LISPRO
IOPROMIDE
IOVERSOL
IPRATROPIUM BROMIDE
IRBESARTAN
IRINOTECAN
ISONIAZID
ISOTRETINOIN
ISRADIPINE
ITRACONAZOLE
KETOCONAZOLE
KETOROLAC
KETOTIFEN
LAMIVUDINE
LAMOTRIGINE
LANSOPRAZOLE
LATANOPROST
LEFLUNOMIDE
LETROZOLE
LORAZEPAM
LOSARTAN
LOTEPREDNOL
LOVASTATIN
MEFLOQUINE
MEGESTROL
MELOXICAM
MELPHALAN
MESALAZINE
MESNA
METFORMIN
METHOXSALEN
METHYLDOPA
METHYLPHENIDATE
METOCLOPRAMIDE
METOPROLOL
METRONIDAZOLE
MICONAZOLE
MIDAZOLAM
MILRINONE
MINOXIDIL
MIRTAZAPINE
MISOPROSTOL
MITOXANTRONE
MIVACURIUM CHLORIDE
MODAFINIL
MOMETASONE
MONTELUKAST
NABUMETONE
NAFARELIN
NAPROXEN
NARATRIPTAN
NEDOCROMIL
NEFAZODONE
NELFINAVIR
NEVIRAPINE
NICARDIPINE
NICOTINE
NIFEDIPINE
NILUTAMIDE
NIMODIPINE
NISOLDIPINE
NITROFURANTOIN
NITROGLYCERIN
NONOXINOL 9
NORFLOXACIN
OCTREOTIDE
OFLOXACIN
OLANZAPINE
OLOPATADINE
OLSALAZINE
OMEPRAZOLE
ONDANSETRON
ORLISTAT
OSELTAMIVIR
OXAZEPAM
OXCARBAZEPINE
OXICONAZOLE
OXYBUTYNIN
OXYCODONE
PACLITAXEL
PANTOPRAZOLE
PAROXETINE
PENTOSAN POLYSULFATE SODIUM
PERGOLIDE
PERINDOPRIL
PILOCARPINE
PIOGLITAZONE
PSEUDOEPHEDRINE
QUETIAPINE
QUINAPRIL
RABEPRAZOLE
RALOXIFENE
RAMIPRIL
RANITIDINE
RANITIDINE BISMUTH CITRATE
REMIFENTANIL
REPAGLINIDE
RIBAVIRIN
RILUZOLE
RISEDRONATE
RISPERIDONE
RITONAVIR
RIZATRIPTAN
ROFECOXIB
ROPINIROLE
ROPIVACAINE
ROSIGLITAZONE
SALMETEROL
SAQUINAVIR
SERTRALINE
SEVOFLURANE
SIBUTRAMINE
SILDENAFIL
SIMVASTATIN
SOTALOL
STAVUDINE
SULFADIAZINE
SULFASALAZINE
SUMATRIPTAN
TACRINE
TALC
TAMOXIFEN
TAMSULOSIN
TAZAROTENE
TELMISARTAN
TEMOZOLOMIDE
TERAZOSIN
TERBINAFINE
TESTOSTERONE
THEOPHYLLINE
TICLOPIDINE
TIMOLOL
TIOCONAZOLE
TIROFIBAN
TIZANIDINE
TOBRAMYCIN
TOLCAPONE
TOLTERODINE
TOPIRAMATE
TOPOTECAN
TOREMIFENE
TRAMADOL
TRANDOLAPRIL
TRETINOIN
TRIAMCINOLONE
TRIAMCINOLONE ACETONIDE
TRIMETHOPRIM
TRIMETREXATE
TRIPTORELIN
TROGLITAZONE
TROVAFLOXACIN
VALACICLOVIR
VALSARTAN
VENLAFAXINE
VERAPAMIL

Table 3: Characteristics of Drugs in the Sample*

Molecule Group	Overdose Fatalities	Severe Adverse Effects	Treats Chronic Condition	Might be taken for more than one year	Treats life-threat. condition
Abacavir	Yes	Yes	Yes	No	No
Allopurinol	No	Yes	No	Yes	No
Alprostadil	No	No	Yes	No	No
Amphotericin B	No	No	No	No	No
Beclometasone	No	No	Yes	No	No
Candesartan	No	No	Yes	No	No
Carboplatin	No	Yes	Yes	No	No
Cimetidine	No	No	No	Yes	No
Cisplatin	Yes	Yes	No	Yes	No
Cladribine	No	Yes	No	Yes	No
Digoxin	Yes	No	Yes	No	No
Diltiazem	No	No	Yes	No	No
Eptifibatide	No	No	No	No	Yes
Flunisolide	No	No	Yes	No	No
Ganciclovir	No	Yes	Yes	No	No
Glimepiride	No	No	Yes	Yes	No
Ibuprofen	No	No	No	No	No
Itraconazole	No	No	No	No	No

Source: *Physician's Desk Reference*.

Molecule Group	Overdose Fatalities	Severe Adverse Effects	Treats Chronic Condition	Might be taken for more than one year	Treats life-threat. condition
Lomefloxacin	No	No	No	No	No
Loratadine	No	No	No	Yes	No
Losartan	No	No	Yes	No	No
Mefloquine	No	No	No	Yes	No
Metformin	No	No	Yes	Yes	No
Mitoxantrone	Yes	Yes	No	Yes	No
Modafinil	No	No	Yes	No	No
Olsalazine	No	Yes	No	Yes	No
Oxcarbazepine	No	Yes	Yes	No	No
Quetiapine	No	No	Yes	No	No
Ramipril	No	No	Yes	No	No
Ranitidine Bismuth Citrate	No	No	Yes	No	No
Risperidone	No	Yes	Yes	No	No
Ropinirole	No	Yes	Yes	No	No
Tacrine	No	Yes	Yes	No	No
Tamsulosin	No	No	Yes	No	No
Terbinafine	No	No	No	No	No
Topotecan	No	Yes	No	Yes	No
Venlafaxine	No	No	Yes	Yes	No
Vincristine	Yes	Yes	No	Yes	No

Source: Physician's Desk Reference.

* - A very few molecules were not indexed in the Physician's Desk Reference, and those are excluded from this list, but included with default assumptions regarding elasticity values in Table 4.

Table 4: Estimated Demand Elasticities

Molecules	Elasticity of Subsitution	Elasticity of Demand for the Composite Product
ABACAVIR	4	-0.95
ALLOPURINOL	4.25	-0.85
ALPROSTADIL	4.5	-0.95
AMPHOTERICIN B	4.5	-0.75
BECLOMETASONE	4.5	-0.75
BLEOMYCIN	4.25	-0.85
BUSPIRONE	4.5	-0.75
CANDESARTAN CILEXETIL	4.5	-0.95
CARBOPLATIN	4.25	-0.95
CIMETIDINE	4.5	-0.85
CISPLATIN	4	-0.85
CLADRIBINE	4.25	-0.85
DIGOXIN	4	-0.95
DILTIAZEM	4.5	-0.95
EPTIFIBATIDE	4	-0.75
FLUNISOLIDE	4.5	-0.95
GANCICLOVIR	4.25	-0.95
GLIMEPIRIDE	4.5	-0.95
IBUPROFEN	4.5	-0.75
IOPROMIDE	4.5	-0.75
ITRACONAZOLE	4.5	-0.75
LOMEFLOXACIN	4.5	-0.75
LORATADINE	4.5	-0.85
LOSARTAN	4.5	-0.95
LOTEPREDNOL	4.5	-0.75
MEFLOQUINE	4.5	-0.85
METFORMIN	4.5	-0.95
MICONAZOLE	4.5	-0.75
MITOXANTRONE	4	-0.85
MODAFINIL	4.5	-0.95
OLSALAZINE	4.25	-0.95
OXCARBAZEPINE	4.25	-0.95
PRAMIPEXOLE	4.25	-0.95
QUETIAPINE	4.5	-0.95
RAMIPRIL	4.5	-0.95
RANITIDINE BISMUTH CITRATE	4.5	-0.95
RISPERIDONE	4.25	-0.95
ROPINIROLE	4.25	-0.95
SEVOFLURANE	4.5	-0.75
SULFADIAZINE	4.5	-0.75
TACRINE	4.25	-0.95
TAMSULOSIN	4.5	-0.95
TERBINAFINE	4.5	-0.75
TOPOTECAN	4.25	-0.95
TROGLITAZONE	4.5	-0.75
VENLAFAXINE	4.5	-0.95
VINCRISTINE	4	-0.85

APPENDIX D

THE COSTS TO RESEARCH-BASED PHARMACEUTICAL COMPANIES OF INADEQUATE INTELLECTUAL PROPERTY PROTECTION IN ARGENTINA, BRAZIL, INDIA, AND ISRAEL

By Richard D. Boltuck, David A. Riker, and Spencer R. Graf

Charles River Associates Inc.
Washington, D.C.

May 2001

Introduction and Overview

Charles River Associates Inc. (CRA) prepared this study at the request of PhRMA. It reflects CRA's continuing applied economic research directed at developing and implementing methods appropriate for use in estimating the cost to research-based pharmaceutical companies of lax intellectual property (IP) regimes in selected countries that are TRIPS non-compliant. CRA's initial study was presented in February 2000 as part of PhRMA's annual "Special 301" Submission to USTR (henceforth cited as "CRA 2000").[38] The present study focuses on the annual costs, as measured by foregone sales and foregone returns to investment, imposed on research-based pharmaceutical countries by lax IP regimes in Argentina, Brazil, India, and Israel.

Like CRA 2000, the present study relies on market data obtained from IMS HEALTH (IMS) together with a CRA-designed simulation model that estimates costs associated with the competing sales of infringing products in each of the markets for products containing individual specified molecules in each of the priority countries.[39]

This year's study, however, represents a significant methodological advance over last year's effort. Last year's study was restricted to estimating costs associated with the markets for a common set of 20 specific molecules in each of the examined countries. Necessarily, these estimates represented an

[38] *Estimating the Cost to PhRMA Member Companies of Inadequate Intellectual Property Protection: A Study of Five Priority Countries and 20 Drug Markets*, by Richard D. Boltuck and David A. Riker, Charles River Associates Inc., in PhRMA "Special 301" Submission to USTR, February 2001, Appendix B at 133-158.

[39] The simulation model applied in the present study is identical to last year's model. For mathematical details of the CRA simulation model, see CRA 2000 at 138-141. This model estimates the present relationship between prices and marginal production cost based on market shares and demand-side elasticity assumptions. It then estimates the extent to which the legitimate producer/IP owner could increase sales and investment return in the hypothetical, or counterfactual, absence of infringing imitator products.

unknown but small fraction of the full costs attributable to lax IP protection in each of the countries studied.

By contrast, in the present study, a random sampling process was applied to select the molecules that were analyzed. A separate representative sample was constructed for each priority country consisting of 15 percent of the universe of molecules identified as containing protectable IP. The estimates of losses based on the four national samples were then projected or extrapolated to the universe for each country based on standard sampling theory, thus generating an estimate of lost sales revenue and lost investment returns associated with each entire national pharmaceutical market.

Summary of Estimated Costs

Table 1 summarizes the estimated losses to research-based pharmaceutical companies measured by the cost of lost revenue and the cost of foregone returns to investment on sales within each priority country. This table also reports a calculated standard deviation for each estimate, derived from the dispersion of estimates within each sample, and the size of the sample in relation to the size of the universe.

Thus, for instance, foregone investment returns to research-based pharmaceutical companies in Brazil attributable to lax IP protection amount to an estimated US$324,459,000 per year. With 95 percent confidence, the true value of lost investment returns falls within roughly plus or minus 1.7 standard deviations of this estimate – that is, between US$225,326,970 and US$423,591,030.[40]

Total lost sales revenue in the four countries examined amount to an estimated US$2,031,656,000 per year, whereas total foregone investment returns amount to an estimated US$1,386,906,000 per year. Additional uncertainty arising from the underlying simulation estimates is not reflected in these confidence intervals.

Sampling Procedure and Estimation Methodology

The CRA analysis consisted of three major steps:

1) Identify appropriate samples of molecules sold in each priority country that are believed to embody protectable IP.
2) Perform a simulation analysis with respect to the market for each such sampled molecule in each priority country. This analysis requires several sub-steps:

[40] The reported confidence interval assumes that the estimator is normally distributed about the true value for each country.

(a) Estimate the elasticities of composite demand for products containing each molecule, and estimate the elasticities of substitution among differing products containing the same molecule, in both cases by adjusting base-line elasticity assumptions for variations associated with ascertainable product attributes;[41]
(b) Estimate market shares of legitimate and infringing imitator products based on a set of classification rules;[42]
(c) Apply the CRA simulation model developed and presented as part of CRA 2000.

3) Project the estimated lost-sales revenue and lost investment-return costs for each national sample on to the universe of all markets for molecules that are believed to contain protectable IP, based on the IMS list of molecules sold in the country and the FDA lists of patented molecules.

Table 2 lists separately for each priority country all of the molecules sold in each country that were identified through FDA lists of molecules patented in the United States as containing protectable IP, which in turn is a subset of a master list of molecules sold in each country as provided by IMS.[43]

From each list in Table 2, a random sample consisting of 15 percent of the molecules was selected. Table 3 presents a pooled list of all of the molecules in the four national samples for which relevant attributes could be ascertained through the Physicians Desk Reference, together with the attributes thus obtained.

Table 4 sets out a comprehensive list of the molecules included in each of the 15 percent samples, together with the adjustments to base-line demand and substitution elasticities based on the molecule-specific attributes reported in Table 3.

Finally, Table 5 presents the estimated lost sales revenue and lost

[41] *See* CRA 2000, section IV at 142-144 for a discussion of how attributes are determined through reliance on the Physicians Desk Reference, and how adjustments are made to base-line elasticity assumptions for each molecule.
[42] *See* id., section V at 144-145 for a discussion of the classification rules, and the 10-year "old-technology" rule for determining whether specific products are entitled to the presumption that they contain protectable IP.
[43] IMS provided specific data for sales of products containing each molecule in each country, including the total sales value, and whether each individual product containing the molecule is branded or generic, the sales value for the individual product, the nationality of the product's manufacturer, the name of the manufacturer, and the name of the product. For FDA patented-molecule lists, *see* www.fda.gov.

investment returns per year for each national sample.[44] These losses are projected to the universe by dividing by the ratio of total sample sales to total universe sales also reported in this table, and the resulting estimated losses for the universe are reported in Table 1.[45]

The standard deviation of the estimate as reported in Table 1 is based on the following estimator[46]:

$$std.dev.(\hat{Y}) = \left\{ \frac{N^2(1-\frac{n}{N})}{n(n-1)} \left[\sum_{i=1}^{n} (y_i - Rx_i)^2 \right] \right\}^{1/2}$$

where $\hat{Y}$ is the estimated loss, N is the number of molecules in the universe, *n* is the number in the sample, y_1 is an individual sample molecule i's estimated annual loss, and x_1 is total annual sales of sample molecule i.

Conclusion

PhRMA member research-based pharmaceutical companies, when rewarded with adequate returns in the marketplace, have demonstrated a distinctive ability to discover and develop significant new pharmaceutical products affording increasingly effective therapies across a wide variety of afflictions. The integrity of market-based incentives in global markets, however, has been undermined by weak and inadequate IP regimes in many countries. In just the four countries examined in this study – Argentina, Brazil, India, and Israel – foregone investment returns to research-based firms amount to an estimated US$1,386,906,000 per year.

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[44] The reported estimates do not attempt to distinguish between investment returns attributable specifically to IP or to other sources, although it is generally understood that IP accounts for the bulk of investment. The estimates also do not account for the potential operation of any Trade Related Intellectual Property Agreement (TRIPS)-compliant policies that might tend to limit pharmaceutical prices below the optimum prices selected by legitimate producers in the simulation analysis.
In applying a simulation model in which the composite product in each molecule-level market combines specific products through use of a constant-elasticity of substitution (CES) function, it is well known that extreme market shares can lead to results that are sometimes difficult to interpret. This arises because the CES specification assumes that consumers value variation or diversity in the marketplace, whereas in this study, it is assumed that absent the infringing product, the legitimate producer would not continue manufacturing the imitator. In the few cases where anomalies related to this feature of the specification were apparent, the lost investment returns were bounded between zero and the value of lost sales revenue.

[45] For a technical discussion of the use of ratio estimators, *see* Sampling Techniques, 3rd ed., by William G. Cochran, John Wiley & Sons: New York, 1977, section 6.3 at 153ff. Although 15 percent of the molecules within the universe might account for either more or less than 15 percent of the total sales value, the true value of this ratio as reported in Table 5 is derived for each national sample through use of the sales value data supplied by IMS for each national market associated with each molecule.

[46] Id., eq. 6.9 at 155.

This study estimates losses to research-based pharmaceutical companies that are attributable to inadequate IP protection. It does not, however, quantify the social costs, in the form of fewer or later pharmaceutical discoveries, imposed by the failure to fully incentivize the very firms that have proven themselves to be the world's engines of pharmaceutical innovation. Generating such estimates offers an important direction for future analysis.

Table 1: Estimated Annual Lost Sales Revenue and Returns to Investment for the Molecules in Universe

Country	Lost Sales Revenue (000s)		Lost Returns to Investment (000s)	
	Est. Lost Sales Revenue	*Standard Deviation in Est.**	*Est. Lost Returns to Investment*	*Standard Deviation in Est.**
ARGENTINA	491,394	80,193	261,613	57,823
BRAZIL	459,159	78,202	324,459	58,937
INDIA	976,726	22,177	729,012	36,239
ISRAEL	104,378	11,986	71,823	9,453
Total	**2,031,656**	**114,812**	**1,386,906**	**90,662**

Note: *It is assumed that lost sales revenue and returns to investment by country are independent of one another so that the cross-national covariances of lost sales revenue and returns to investment are zero.

Table 2a: Molecules In Argentina Identified as Containing Protectable IP.

ABACAVIR
ADAPALENE
ADENOSINE
ADENOSINE PHOSPHATE
ALBENDAZOLE
ALLOPURINOL
ALPRAZOLAM
ALPROSTADIL
AMIFOSTINE
AMIODARONE
AMLODIPINE
AMPHOTERICIN B
AMPRENAVIR
ANASTROZOLE
APRACLONIDINE
ASTEMIZOLE
ATORVASTATIN
ATROPINE
AVOBENZONE
AZELAIC ACID
AZELASTINE
BECLOMETASONE
BENAZEPRIL
BERACTANT
BETAMETHASONE
BETAXOLOL
BICALUTAMIDE
BISOPROLOL
BLEOMYCIN
BRIMONIDINE
BRINZOLAMIDE
BROMPHENIRAMINE
BUDESONIDE
BUSPIRONE
BUSULFAN
CABERGOLINE
CALCITRIOL
CANDESARTAN CILEXETIL
CARBIDOPA
CARBOPLATIN
CARMUSTINE
CARTEOLOL
CARVEDILOL
CELECOXIB
CERIVASTATIN
CETIRIZINE
CHLORHEXIDINE
CHLORTALIDONE
CICLOPIROX
CILOSTAZOL
CIMETIDINE
CIPROFLOXACIN
CISAPRIDE
CISATRACURIUM BESYLATE
CISPLATIN
CITALOPRAM
CLADRIBINE
CLOBETASOL
CLONAZEPAM
CLOPIDOGREL
CLOTRIMAZOLE
CYANOCOBALAMIN
CYCLOPHOSPHAMIDE
DAUNORUBICIN
DESMOPRESSIN
DESOGESTREL
DEXRAZOXANE
DIAZEPAM
DOXEPIN
DOXORUBICIN
EFAVIRENZ
ENALAPRIL
ENOXACIN
ENOXAPARIN SODIUM
ENTACAPONE
EPTIFIBATIDE
ESMOLOL
ESTRADIOL
ETHINYLESTRADIOL
ETOPOSIDE
EXEMESTANE
FAMCICLOVIR
FAMOTIDINE
FELODIPINE
FENOFIBRATE
FENTANYL
FERUMOXIDES
FEXOFENADINE
FINASTERIDE
FLECAINIDE
FLUCONAZOLE
FLUDARABINE
FLUMAZENIL
FLUNISOLIDE
FLUOCINOLONE ACETONIDE
FLUOROURACIL
FLUOXETINE
FLUTAMIDE
FLUTICASONE
FLUVASTATIN
FLUVOXAMINE
FOSCARNET SODIUM
GABAPENTIN
GANCICLOVIR
GATIFLOXACIN
GEMCITABINE
GLATIRAMER ACETATE
GLIMEPIRIDE
GLIPIZIDE
GOSERELIN
GRANISETRON
HYDROCHLOROTHIAZIDE
HYDROCODONE
IBUPROFEN
IFOSFAMIDE
IMIQUIMOD
INDINAVIR
INSULIN LISPRO
IOPROMIDE
IOVERSOL
IPRATROPIUM BROMIDE
IRBESARTAN
IRINOTECAN
ISONIAZID
ISOTRETINOIN
ISRADIPINE
ITRACONAZOLE
KETOCONAZOLE
KETOROLAC
KETOTIFEN
LAMIVUDINE
LAMOTRIGINE
LANSOPRAZOLE
LATANOPROST
LEFLUNOMIDE
LETROZOLE
LORAZEPAM
LOSARTAN
LOTEPREDNOL
LOVASTATIN
MEFLOQUINE
MEGESTROL
MELOXICAM
MELPHALAN
MESALAZINE
MESNA
METFORMIN
METHOXSALEN
METHYLDOPA
METHYLPHENIDATE
METOCLOPRAMIDE
METOPROLOL
METRONIDAZOLE
MICONAZOLE
MIDAZOLAM
MILRINONE
MINOXIDIL
MIRTAZAPINE
MISOPROSTOL
MITOXANTRONE
MIVACURIUM CHLORIDE
MODAFINIL
MOMETASONE
MONTELUKAST
NABUMETONE
NAFARELIN
NAPROXEN
NARATRIPTAN
NEDOCROMIL
NEFAZODONE
NELFINAVIR
NEVIRAPINE
NICARDIPINE
NICOTINE
NIFEDIPINE
NILUTAMIDE
NIMODIPINE
NISOLDIPINE
NITROFURANTOIN
NITROGLYCERIN
NONOXINOL 9
NORFLOXACIN
OCTREOTIDE
OFLOXACIN
OLANZAPINE
OLOPATADINE
OLSALAZINE
OMEPRAZOLE
ONDANSETRON
ORLISTAT
OSELTAMIVIR
OXAZEPAM
OXCARBAZEPINE
OXICONAZOLE
OXYBUTYNIN
OXYCODONE
PACLITAXEL
PANTOPRAZOLE
PAROXETINE
PENTOSAN POLYSULFATE SODIUM
PERGOLIDE
PERINDOPRIL
PILOCARPINE
PIOGLITAZONE
PSEUDOEPHEDRINE
QUETIAPINE
QUINAPRIL
RABEPRAZOLE
RALOXIFENE
RAMIPRIL
RANITIDINE
RANITIDINE BISMUTH CITRATE
REMIFENTANIL
REPAGLINIDE
RIBAVIRIN
RILUZOLE
RISEDRONATE
RISPERIDONE
RITONAVIR
RIZATRIPTAN
ROFECOXIB
ROPINIROLE
ROPIVACAINE
ROSIGLITAZONE
SALMETEROL
SAQUINAVIR
SERTRALINE
SEVOFLURANE
SIBUTRAMINE
SILDENAFIL
SIMVASTATIN
SOTALOL
STAVUDINE
SULFADIAZINE
SULFASALAZINE
SUMATRIPTAN
TACRINE
TALC
TAMOXIFEN
TAMSULOSIN
TAZAROTENE
TELMISARTAN
TEMOZOLOMIDE
TERAZOSIN
TERBINAFINE
TESTOSTERONE
THEOPHYLLINE
TICLOPIDINE
TIMOLOL
TIOCONAZOLE
TIROFIBAN
TIZANIDINE
TOBRAMYCIN
TOLCAPONE
TOLTERODINE
TOPIRAMATE
TOPOTECAN
TOREMIFENE
TRAMADOL
TRANDOLAPRIL
TRETINOIN
TRIAMCINOLONE
TRIAMCINOLONE ACETONIDE
TRIMETHOPRIM
TRIMETREXATE
TRIPTORELIN
TROGLITAZONE
TROVAFLOXACIN
VALACICLOVIR
VALSARTAN
VENLAFAXINE
VERAPAMIL

Table 2b: Molecules In Brazil Identified as Containing Protectable IP.

ABACAVIR
ADAPALENE
ADENOSINE
ALBENDAZOLE
ALLOPURINOL
ALPRAZOLAM
ALPROSTADIL
AMIFOSTINE
AMIODARONE
AMLODIPINE
AMPHOTERICIN B
AMPRENAVIR
ANASTROZOLE
APRACLONIDINE
ASTEMIZOLE
ATORVASTATIN
ATROPINE
AVOBENZONE
AZELAIC ACID
AZELASTINE
BECLOMETASONE
BENAZEPRIL
BETAMETHASONE
BETAXOLOL
BICALUTAMIDE
BISOPROLOL
BLEOMYCIN
BRIMONIDINE
BRINZOLAMIDE
BROMPHENIRAMINE
BUDESONIDE
BUSPIRONE
BUSULFAN
CABERGOLINE
CALCITRIOL
CANDESARTAN CILEXETIL
CAPECITABINE
CAPTOPRIL
CARBIDOPA
CARBOPLATIN
CARMUSTINE
CARVEDILOL
CELECOXIB
CERIVASTATIN
CETIRIZINE
CHLORHEXIDINE
CHLORTALIDONE
CICLOPIROX
CIMETIDINE
CIPROFLOXACIN
CISAPRIDE
CISPLATIN
CITALOPRAM
CLADRIBINE
CLOBETASOL
CLONAZEPAM
CLOPIDOGREL
CLOTRIMAZOLE
CYANOCOBALAMIN
CYCLOPHOSPHAMIDE
DALTEPARIN SODIUM
DAUNORUBICIN
DESMOPRESSIN
DESOGESTREL
DIAZEPAM
DICLOFENAC
DIGOXIN
DIHYDROERGOTAMINE
DORZOLAMIDE
DOXAZOSIN
DOXORUBICIN
EMEDASTINE
ENALAPRIL
ENALAPRILAT
ENOXAPARIN SODIUM
ENTACAPONE
ESTRADIOL
ETHINYLESTRADIOL
ETOPOSIDE
EXEMESTANE
FAMCICLOVIR
FAMOTIDINE
FELODIPINE
FENOFIBRATE
FENTANYL
FEXOFENADINE
FINASTERIDE
FLUCONAZOLE
FLUDARABINE
FLUMAZENIL
FLUNISOLIDE
FLUOCINOLONE ACETONIDE
FLUOROURACIL
FLUOXETINE
FLUTAMIDE
FLUTICASONE
FLUVASTATIN
FLUVOXAMINE
FOSCARNET SODIUM
FOSINOPRIL
GABAPENTIN
GANCICLOVIR
GATIFLOXACIN
GEMCITABINE
GLIMEPIRIDE
GLIPIZIDE
GOSERELIN
GRANISETRON
HYDROCHLOROTHIAZIDE
IBUPROFEN
IFOSFAMIDE
INSULIN LISPRO
INSULIN LISPRO PROTAMINE
IPRATROPIUM BROMIDE
IRBESARTAN
IRINOTECAN
ISONIAZID
ISOTRETINOIN
ISRADIPINE
ITRACONAZOLE
KETOCONAZOLE
KETOROLAC
KETOTIFEN
LAMIVUDINE
LAMOTRIGINE
LANSOPRAZOLE
LATANOPROST
LEFLUNOMIDE
LETROZOLE
LEVOCABASTINE
LEVOCARNITINE
LEVOFLOXACIN
LEVONORGESTREL
LIDOCAINE
LISINOPRIL
LODOXAMIDE
LORATADINE
LORAZEPAM
LOSARTAN
LOVASTATIN
MAFENIDE
MEGESTROL
MELOXICAM
MELPHALAN
MEQUINOL
MESALAZINE
MESNA
METFORMIN
METHYLDOPA
METHYLPHENIDATE
METOCLOPRAMIDE
METOPROLOL
METRONIDAZOLE
MIBEFRADIL
MICONAZOLE
MIDAZOLAM
MILRINONE
MINOXIDIL
MIRTAZAPINE
MITOXANTRONE
MOMETASONE
MONTELUKAST
NABUMETONE
NAFARELIN
NAPROXEN
NARATRIPTAN
NEDOCROMIL
NEFAZODONE
NICOTINE
NIFEDIPINE
NILUTAMIDE
NIMODIPINE
NISOLDIPINE
NITROFURANTOIN
NITROGLYCERIN
NIZATIDINE
NONOXINOL 9
NORFLOXACIN
OFLOXACIN
OLANZAPINE
OLOPATADINE
OMEPRAZOLE
ONDANSETRON
ORLISTAT
OSELTAMIVIR
OXAZEPAM
OXCARBAZEPINE
OXICONAZOLE
OXYBUTYNIN
OXYCODONE
PACLITAXEL
PANTOPRAZOLE
PAROXETINE
PENCICLOVIR
PENTOSAN POLYSULFATE SODIUM
PERGOLIDE
PERINDOPRIL
PILOCARPINE
PIOGLITAZONE
POTASSIUM
PRAMIPEXOLE
PRAVASTATIN
PRAZOSIN
PREDNICARBATE
PROGESTERONE
PROPAFENONE
PROPOFOL
PROPRANOLOL
PSEUDOEPHEDRINE
QUETIAPINE
QUINAPRIL
RABEPRAZOLE
RALOXIFENE
RAMIPRIL
RANITIDINE
RANITIDINE BISMUTH CITRATE
REPAGLINIDE
RIBAVIRIN
RILUZOLE
RIMEXOLONE
RISEDRONATE
RISPERIDONE
RIZATRIPTAN
ROFECOXIB
ROPIVACAINE
ROSIGLITAZONE
SALMETEROL
SAQUINAVIR
SERTRALINE
SIBUTRAMINE
SILDENAFIL
SIMVASTATIN
SOTALOL
SULFADIAZINE
SULFASALAZINE
SUMATRIPTAN
SUPROFEN
TACRINE
TALC
TAMOXIFEN
TAMSULOSIN
TELMISARTAN
TERAZOSIN
TERBINAFINE
TERCONAZOLE
TESTOSTERONE
THEOPHYLLINE
TICLOPIDINE
TIMOLOL
TIOCONAZOLE
TIROFIBAN
TIZANIDINE
TOBRAMYCIN
TOLCAPONE
TOLTERODINE
TOPIRAMATE
TOPOTECAN
TOREMIFENE
TRAMADOL
TRANDOLAPRIL
TRETINOIN
TRIAMCINOLONE ACETONIDE
TRIMETHOPRIM
TRIPTORELIN
VALACICLOVIR
VALSARTAN
VENLAFAXINE
VERAPAMIL
VINCRISTINE
VINORELBINE
ZAFIRLUKAST
ZALCITABINE

Table 2c: Molecules In India Identified as Containing Protectable IP.

ADENOSINE
ALBENDAZOLE
ALLOPURINOL
ALPRAZOLAM
ALPROSTADIL
AMIFOSTINE
AMINOSALICYLIC ACID
AMIODARONE
AMLODIPINE
AMPHOTERICIN B
ASTEMIZOLE
ATORVASTATIN
ATROPINE
AVOBENZONE
AZELAIC ACID
AZELASTINE
BECLOMETASONE
BENAZEPRIL
BETAMETHASONE
BETAXOLOL
BISOPROLOL
BLEOMYCIN
BRIMONIDINE
BUDESONIDE
BUSPIRONE
BUSULFAN
CALCITRIOL
CANDESARTAN
CAPTOPRIL
CARBIDOPA
CARBOPLATIN
CARVEDILOL
CELECOXIB
CERIVASTATIN
CETIRIZINE
CHLORHEXIDINE
CHLORTALIDONE
CICLOPIROX
CIPROFLOXACIN
CISAPRIDE
CISPLATIN
CLOBETASOL
CLONAZEPAM
CLOTRIMAZOLE
CYANOCOBALAMIN
CYCLOPHOSPHAMIDE
DALTEPARIN SODIUM
DAUNORUBICIN
DESMOPRESSIN
DESOGESTREL
DIAZEPAM
DICLOFENAC
DIGOXIN
DIHYDROERGOTAMINE
DILTIAZEM
DINOPROSTONE
DOCETAXEL
DOXAZOSIN
DOXEPIN
DOXORUBICIN
ENALAPRIL
ENALAPRILAT
ENOXAPARIN SODIUM
EPTIFIBATIDE
ESMOLOL
ESTRADIOL
ETHINYLESTRADIOL
ETOPOSIDE
FAMOTIDINE
FELODIPINE
FENOFIBRATE
FENTANYL
FEXOFENADINE
FINASTERIDE
FLUCONAZOLE
FLUNISOLIDE
FLUOCINOLONE ACETONIDE
FLUOROURACIL
FLUOXETINE
FLUTAMIDE
FLUTICASONE
FLUVOXAMINE
GABAPENTIN
GEMCITABINE
GLIMEPIRIDE
GLIPIZIDE
GOSERELIN
GRANISETRON
HYDROCHLOROTHIAZIDE
IBUPROFEN
IFOSFAMIDE
INSULIN LISPRO
IOPROMIDE
IPRATROPIUM BROMIDE
IRBESARTAN
IRON DEXTRAN
ISONIAZID
ITRACONAZOLE
KETOCONAZOLE
KETOROLAC
KETOTIFEN
LAMIVUDINE
LAMOTRIGINE
LANSOPRAZOLE
LATANOPROST
LEVOCARNITINE
LEVOFLOXACIN
LEVONORGESTREL
LIDOCAINE
LISINOPRIL
LOMEFLOXACIN
LOPERAMIDE
LORATADINE
LORAZEPAM
LOSARTAN
LOVASTATIN
MEFLOQUINE
MELOXICAM
MELPHALAN
MESALAZINE
MESNA
METFORMIN
METHOXSALEN
METHYLDOPA
METOCLOPRAMIDE
METOPROLOL
METRONIDAZOLE
MICONAZOLE
MIDAZOLAM
MILRINONE
MINOXIDIL
MITOXANTRONE
MOMETASONE
NABUMETONE
NAFARELIN
NAPROXEN
NEVIRAPINE
NICOTINE
NIFEDIPINE
NIMODIPINE
NITROFURANTOIN
NITROGLYCERIN
NORFLOXACIN
OCTREOTIDE
OFLOXACIN
OLANZAPINE
OMEPRAZOLE
ONDANSETRON
OXAZEPAM
OXICONAZOLE
OXYBUTYNIN
PACLITAXEL
PANTOPRAZOLE
PERINDOPRIL
PILOCARPINE
PIOGLITAZONE
POTASSIUM
PRAZOSIN
PREDNICARBATE
PREDNISOLONE
PROGESTERONE
PROPAFENONE
PROPOFOL
PROPRANOLOL
PSEUDOEPHEDRINE
RAMIPRIL
RANITIDINE
REPAGLINIDE
RIBAVIRIN
RISPERIDONE
ROCURONIUM BROMIDE
ROFECOXIB
ROSIGLITAZONE
SALMETEROL
SERTRALINE
SIMVASTATIN
SPARFLOXACIN
STAVUDINE
SULFADIAZINE
SULFASALAZINE
SUMATRIPTAN
TALC
TAMOXIFEN
TERAZOSIN
TERBINAFINE
TERCONAZOLE
TESTOSTERONE
THEOPHYLLINE
TICLOPIDINE
TIMOLOL
TIZANIDINE
TOBRAMYCIN
TOPIRAMATE
TRAMADOL
TRETINOIN
TRIAMCINOLONE
TRIAMCINOLONE ACETONIDE
TRIMETHOPRIM
VENLAFAXINE
VERAPAMIL
VINCRISTINE
ZALCITABINE
ZIDOVUDINE
ZINC
ZOLPIDEM

Table 2d: Molecules In Israel Identified as Containing Protectable IP.

ADAPALENE
ALLOPURINOL
ALPRAZOLAM
ALPROSTADIL
AMIODARONE
AMLODIPINE
AMPHOTERICIN B
ANASTROZOLE
APRACLONIDINE
ASTEMIZOLE
ATORVASTATIN
ATROPINE
AZELAIC ACID
BECLOMETASONE
BENAZEPRIL
BETAMETHASONE
BETAXOLOL
BICALUTAMIDE
BISOPROLOL
BRIMONIDINE
BRINZOLAMIDE
BUDESONIDE
BUSPIRONE
BUSULFAN
BUTENAFINE
CABERGOLINE
CANDESARTAN CILEXETIL
CAPTOPRIL
CARBIDOPA
CARVEDILOL
CELECOXIB
CERIVASTATIN
CETIRIZINE
CETRORELIX
CHLORHEXIDINE
CHLORTALIDONE
CICLOPIROX
CIMETIDINE
CIPROFLOXACIN
CISAPRIDE
CITALOPRAM
CLOBETASOL
CLONAZEPAM
CLOPIDOGREL
CLOTRIMAZOLE
CYANOCOBALAMIN
CYCLOPHOSPHAMIDE
DALTEPARIN SODIUM
DAPIPRAZOLE
DESMOPRESSIN
DESOGESTREL
DIAZEPAM
DICLOFENAC
DIDANOSINE
DIGOXIN
DIHYDROERGOTAMINE
DILTIAZEM
DONEPEZIL
DORZOLAMIDE
DOXAZOSIN
DOXEPIN
DOXORUBICIN
EFAVIRENZ
EMEDASTINE
ENALAPRIL
ENOXAPARIN SODIUM
ENTACAPONE
ESTRADIOL
ETHINYLESTRADIOL
ETOPOSIDE
FAMCICLOVIR
FAMOTIDINE
FELODIPINE
FENTANYL
FEXOFENADINE
FINASTERIDE
FLECAINIDE
FLUCONAZOLE
FLUMAZENIL
FLUNISOLIDE
FLUOCINOLONE ACETONIDE
FLUOROURACIL
FLUOXETINE
FLUTICASONE
FLUVASTATIN
FLUVOXAMINE
FOSINOPRIL
GABAPENTIN
GLIPIZIDE
GOSERELIN
GRANISETRON
HYDROCHLOROTHIAZIDE
IBUPROFEN
IMIQUIMOD
INSULIN LISPRO
INSULIN LISPRO PROTAMINE
IPRATROPIUM BROMIDE
IRBESARTAN
ISONIAZID
ISOTRETINOIN
ITRACONAZOLE
KETOCONAZOLE
KETOROLAC
KETOTIFEN
LAMIVUDINE
LAMOTRIGINE
LANSOPRAZOLE
LATANOPROST
LETROZOLE
LEVOCABASTINE
LEVOCARNITINE
LEVOFLOXACIN
LEVONORGESTREL
LIDOCAINE
LISINOPRIL
LODOXAMIDE
LOMEFLOXACIN
LOPERAMIDE
LORATADINE
LORAZEPAM
LOSARTAN
LOVASTATIN
MEFLOQUINE
MEGESTROL
MELPHALAN
MESALAZINE
METFORMIN
METHOXSALEN
METHYLDOPA
METHYLPHENIDATE
METOCLOPRAMIDE
METOLAZONE
METOPROLOL
METRONIDAZOLE
MICONAZOLE
MIDAZOLAM
MIDODRINE
MINOXIDIL
MIRTAZAPINE
MISOPROSTOL
MOMETASONE
MONTELUKAST
MORPHINE
NABUMETONE
NAFARELIN
NAPROXEN
NARATRIPTAN
NEDOCROMIL
NEFAZODONE
NELFINAVIR
NICOTINE
NIFEDIPINE
NIMODIPINE
NITROFURANTOIN
NITROGLYCERIN
NONOXINOL 9
NORFLOXACIN
OCTREOTIDE
OFLOXACIN
OLANZAPINE
OLSALAZINE
OMEPRAZOLE
ONDANSETRON
ORLISTAT
OSELTAMIVIR
OXAZEPAM
OXCARBAZEPINE
OXYBUTYNIN
OXYCODONE
PANTOPRAZOLE
PAROXETINE
PENCICLOVIR
PERGOLIDE
PILOCARPINE
POLYETHYLENE GLYCOL P.ISOOCTYLPHENYL
POTASSIUM
PRAVASTATIN
PRAZOSIN
PREDNISOLONE
PROCAINAMIDE
PROGESTERONE
PROPAFENONE
PROPRANOLOL
PSEUDOEPHEDRINE
RALOXIFENE
RAMIPRIL
RANITIDINE
REPAGLINIDE
RISPERIDONE
RIZATRIPTAN
ROFECOXIB
ROPINIROLE
ROSIGLITAZONE
SALMETEROL
SAQUINAVIR
SERTRALINE
SEVELAMER
SIBUTRAMINE
SILDENAFIL
SIMVASTATIN
SOTALOL
STAVUDINE
SULFADIAZINE
SULFASALAZINE
SUMATRIPTAN
TACRINE
TALC
TAMOXIFEN
TAMSULOSIN
TERAZOSIN
TERBINAFINE
TERCONAZOLE
TESTOSTERONE
THEOPHYLLINE
TICLOPIDINE
TIMOLOL
TOBRAMYCIN
TOLCAPONE
TOLTERODINE
TOPIRAMATE
TRAMADOL
TRETINOIN
TRIAMCINOLONE
TRIAMCINOLONE ACETONIDE
TRIMETHOPRIM
TRIPTORELIN
VALACICLOVIR
VALSARTAN
VENLAFAXINE
VERAPAMIL
VINORELBINE
ZAFIRLUKAST

Table 3: Characteristics of Drugs in the Four Samples*

Molecule Group	Overdose Fatalities	Severe Adverse Effects	Treats Chronic Condition	Might be taken for more than one year	Treats life-threat. condition
Abacavir	Yes	Yes	Yes	No	No
Allopurinol	No	Yes	No	Yes	No
Alprostadil	No	No	Yes	No	No
Amphotericin B	No	No	No	No	No
Azelaic Acid	No	No	Yes	No	No
Beclometasone	No	No	Yes	No	No
Benazepril	No	No	Yes	No	No
Betametha-sone	No	No	No	No	No
Bleomycin	No	Yes	No	Yes	No
Brimonidine	No	No	No	Yes	No
Cabergoline	No	No	No	Yes	No
Candesartan	No	No	Yes	No	No
Captopril	No	Yes	Yes	No	No
Carboplatin	No	Yes	Yes	No	No
Celecoxib	No	No	Yes	No	No
Cerivastatin	No	No	Yes	No	No
Cetirizine	No	No	No	Yes	No
Ciclopirox	No	No	No	No	No
Cimetidine	No	No	No	Yes	No
Cisplatin	Yes	Yes	No	Yes	No
Cladribine	No	Yes	No	Yes	No
Dalteparin Sodium	No	No	No	No	No
Daunorubicin	No	Yes	No	Yes	No
Desmopressin	No	No	No	No	No
Desogestrel	No	No	No	Yes	No
Diclofenac	No	No	Yes	No	No
Didanosine	No	Yes	Yes	No	No
Digoxin	Yes	No	Yes	No	No

Source : *Physician's Desk Reference*.

Molecule Group	Overdose Fatalities	Severe Adverse Effects	Treats Chronic Condition	Might be taken for more than one year	Treats life-threat. condition
Dihydroergo-tamine	No	No	No	Yes	No
Diltiazem	No	No	Yes	No	No
Doxazosin	No	No	Yes	No	No
Doxepin	No	No	No	No	No
Doxorubicin	Yes	Yes	No	Yes	No
Enalapril	No	No	Yes	No	No
Eptifibatide	No	No	No	No	Yes
Esmolol	Yes	No	No	No	Yes
Fentanyl	Yes	No	Yes	Yes	No
Finasteride	No	No	Yes	No	No
Fludarabine	Yes	Yes	No	Yes	No
Flumazenil	Yes	Yes	No	No	No
Flunisolide	No	No	Yes	No	No
Fluocinolone Acetonide	No	No	No	No	No
Fluvoxamine	No	No	Yes	No	No
Ganciclovir	No	Yes	Yes	No	No
Gemcitabine	No	Yes	No	Yes	No
Glimepiride	No	No	Yes	Yes	No
Hydrochloro-thiazide	No	Yes	Yes	No	No
Ibuprofen	No	No	No	No	No
Insulin Lispro	No	No	Yes	No	No
Ipratropium Bromide	No	No	Yes	Yes	No
Irbesartan	No	No	Yes	No	No
Itraconazole	No	No	No	No	No
Lansoprazole	No	No	No	No	No
Leflunomide	No	No	Yes	No	No
Levocarnitine	No	No	Yes	No	No
Levofloxacin	No	No	No	No	No
Levonorgestrel	No	No	No	Yes	No

Molecule Group	Overdose Fatalities	Severe Adverse Effects	Treats Chronic Condition	Might be taken for more than one year	Treats life-threat. condition
Lomefloxacin	No	No	No	No	No
Loperamide	No	No	No	No	No
Loratadine	No	No	No	Yes	No
Losartan	No	No	Yes	No	No
Lovastatin	No	No	Yes	No	No
Mefloquine	No	No	No	Yes	No
Megestrol	No	Yes	No	Yes	No
Meloxicam	No	No	Yes	No	No
Metformin	No	No	Yes	Yes	No
Methoxsalen	No	Yes	No	Yes	No
Metoprolol	No	No	Yes	No	No
Midazolam	No	Yes	No	No	No
Mitoxantrone	Yes	Yes	No	Yes	No
Modafinil	No	No	Yes	No	No
Mometasone	No	No	No	No	No
Naproxen	No	No	Yes	No	No
Nicotine	No	No	No	No	No
Nifedipine	No	No	Yes	No	No
Nitroglycerin	No	No	No	No	Yes
Ofloxacin	No	No	No	No	No
Olsalazine	No	Yes	No	Yes	No
Omeprazole	No	No	No	No	No
Oxcarbazepine	No	Yes	Yes	No	No
Oxybutynin	No	No	Yes	No	No
Oxycodone	Yes	Yes	No	No	No
Pilocarpine	Yes	No	Yes	No	No
Pioglitazone	No	No	No	Yes	No
Pravastatin	No	No	Yes	No	No
Prednicarbate	No	No	No	No	No

Molecule Group	Overdose Fatalities	Severe Adverse Effects	Treats Chronic Condition	Might be taken for more than one year	Treats life-threat. condition
Prednisolone	No	Yes	No	Yes	No
Propranolol	No	No	Yes	No	No
Quetiapine	No	No	Yes	No	No
Ramipril	No	No	Yes	No	No
Ranitidine Bismuth Citrate	No	No	Yes	No	No
Ribavirin	No	Yes	No	Yes	No
Rimexolone	No	No	No	No	No
Risperidone	No	Yes	Yes	No	No
Ropinirole	No	Yes	Yes	No	No
Rosiglitazone	No	No	Yes	No	No
Salmeterol	No	No	Yes	No	No
Saquinavir	No	No	Yes	No	No
Simvastatin	No	No	No	Yes	No
Tacrine	No	Yes	Yes	No	No
Tamoxifen	No	No	No	Yes	No
Tamsulosin	No	No	Yes	No	No
Terbinafine	No	No	No	No	No
Testosterone	No	No	No	Yes	No
Ticlopidine	No	Yes	Yes	No	No
Timolol	No	No	Yes	No	No
Tizanidine	No	Yes	Yes	No	No
Topotecan	No	Yes	No	Yes	No
Tretinoin	No	No	Yes	No	No
Triamcinolone Acetonide	No	No	Yes	No	No
Trimethoprim	No	No	No	No	No
Valsartan	No	No	Yes	No	No
Venlafaxine	No	No	Yes	Yes	No
Vincristine	Yes	Yes	No	Yes	No

Source : Physician's Desk Reference.

*** - List of all molecules includes all four samples pooled and listed**

alphabetically. A very few molecules were not indexed in the Physician's Desk Reference, and those are excluded from this list, but included with default assumptions regarding elasticity values in Table 4.

Table 4: Estimated Demand Elasticities

Molecules	Elasticity of Substitution	Elasticity of Demand for the Composite Product*	Individual Country Samples: Included Molecules			
			Argentina	Brazil	India	Israel
ABACAVIR	4	-0.95	x			
ALLOPURINOL	4.25	-0.85	x			
ALPROSTADIL	4.5	-0.95	x			
AMPHOTERICIN B	4.5	-0.75	x			
AZELAIC ACID	4.5	-0.95				x
BECLOMETASONE	4.5	-0.75	x			
BENAZEPRIL	4.5	-0.95				
BETAMETHASONE	4.5	-0.75				x
BETAMETHASONE	4.5	-0.75			x	
BLEOMYCIN	4.25	-0.85	x			
BLEOMYCIN	4.25	-0.85			x	
BRIMONIDINE	4.5	-0.85		x		
BUSPIRONE	4.5	-0.75	x			
CABERGOLINE	4.5	-0.85		x		
CANDESARTAN	4.5	-0.95			x	
CANDESARTAN CILEXETIL	4.5	-0.95	x			
CAPTOPRIL	4.25	-0.75		x		
CARBOPLATIN	4.25	-0.95	x			
CELECOXIB	4.5	-0.95			x	x
CERIVASTATIN	4.5	-0.95		x		
CETIRIZINE	4.5	-0.85			x	
CICLOPIROX	4.5	-0.75				x
CIMETIDINE	4.5	-0.85	x	x		
CISPLATIN	4	-0.85	x		x	
CLADRIBINE	4.25	-0.85	x			
DALTEPARIN SODIUM	4.5	-0.75		x		x
DAUNORUBICIN	4	-0.95		x		
DESMOPRESSIN	4.5	-0.75		x	x	
DESOGESTREL	4.5	-0.85		x		x
DICLOFENAC	4.5	-0.95			x	
DIDANOSINE	4.25	-0.95				x
DIGOXIN	4	-0.95	x			
DIHYDROERGOTAMINE	4.5	-0.85				x
DILTIAZEM	4.5	-0.95	x		x	
DOXAZOSIN	4.5	-0.95		x		
DOXEPIN	4.5	-0.75				x
DOXORUBICIN	4	-0.85				x
ENALAPRIL	4.5	-0.95			x	
EPTIFIBATIDE	4	-0.75	x			
ESMOLOL	4	-0.75			x	
FENTANYL	4	-0.95			x	
FINASTERIDE	4.5	-0.95			x	
FLUDARABINE	4	-0.85		x		
FLUMAZENIL	4	-0.75				x
FLUNISOLIDE	4.5	-0.95	x		x	
FLUOCINOLONE ACETONIDE	4.5	-0.75		x		
FLUVOXAMINE	4.5	-0.95		x		
GANCICLOVIR	4.25	-0.95	x	x		
GEMCITABINE	4.25	-0.85			x	
GLIMEPIRIDE	4.5	-0.95	x			
HYDROCHLOROTHIAZIDE	4.25	-0.95				x
IBUPROFEN	4.5	-0.75	x			
INSULIN LISPRO	4.5	-0.95				x
INSULIN LISPRO PROTAMINE	4.5	-0.95				x
IOPROMIDE	4.5	-0.75	x			
IPRATROPIUM BROMIDE	4.5	-0.95		x		
IRBESARTAN	4.5	-0.95		x		
ITRACONAZOLE	4.5	-0.75	x			
KETOTIFEN	4.5	-0.75			x	
LANSOPRAZOLE	4.5	-0.75			x	
LEFLUNOMIDE	4.5	-0.95		x		
LEVOCARNITINE	4.5	-0.95				x

Table 5: Estimated Annual Lost Sales Revenue and Returns to Investment in Each National Sample

Country	Lost Sales Revenue (000s)	Lost Returns to Investment (000s)	Total Sales of Sample as a Percentage of Universe
ARGENTINA	38,309	20,395	12.63%
BRAZIL	31,019	21,919	14.52%
INDIA	165,645	123,634	16.96%
ISRAEL	3,568	2,455	10.26%
Total	**238,541**	**168,404**	