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Post-Trips Options for Access to Patented Medicines in Developing Countries

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Post-Trips Options for Access to Patented Medicines in Developing Countries*

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1. INTRODUCTION

In April 1994, with the conclusion of the seven-year long Uruguay Round of multilateral trade negotiations, a wide-ranging international agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) was finalized. The agreement entered into force with the formation of the World Trade Organization (WTO) in January 1995.[1] The minimum obligatory standards for the protection of intellectual property rights (IPRs) under TRIPS with respect to the patenting of medicines are generally closer to the pre-Uruguay Round norms that existed in the United States and the European Union than those that existed in some major developing countries. This has given rise to controversy on the possible impediments to patented medicine access by the poor in some developing countries. TRIPS, it is feared, could lead to higher prices for patented medicines. Since developing countries spend a much larger percentage of their private household health expenditures on drugs, [2] the affordability of patented medicines is particularly important. The HIV/AIDS pandemic has focused acute awareness on access and affordability questions.

This paper surveys the available evidence on patents and prices and explores the implications and limitations of policy instruments permitted under TRIPS, including compulsory patent licenses, parallel imports and price controls, for affordable access to

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[1] The text of TRIPS is available at www.wto.org.

[2] A survey in selected developing countries found that expenditures on modern drugs constitute 80 – 90 percent of private household health expenditures in Africa and South Asia, while being in the range of 35 percent in Latin America (WHO, 1997, 33 – 34). In contrast, on an average, public expenditure represented more than 60 percent of total pharmaceutical expenditure in the majority of the OECD countries (OECD, 2000, 30).

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patented medicines considered essential in developing countries. It also examines the opportunities for expanding drug donations to poor countries by research-based pharmaceutical companies and the role of aid through intergovernmental and non-governmental organizations. It does not deal with other TRIPS provisions relevant to pricing in the pharmaceutical sector, such as trademark protection for brand names, copyright protection for labels, or the protection of test data and trade secrets.

2. IMPLEMENTATION OF TRIPS PHARMACEUTICAL PATENT OBLIGATIONS IN DEVELOPING COUNTRIES

TRIPS obliges all WTO members to make available twenty-year patent protection for novel, non-obvious and useful[3] inventions, whether products or processes, in all fields of technology, including pharmaceuticals, with very few exclusions and limitations.[4] Interestingly, as of January 1995, fewer than 20 of the current WTO developing country and least developed country members excluded pharmaceutical products *per se* from the grant of patents.[5] Others already allowed such product patents in their law by this time, either because they had not changed older laws instituted by their colonial masters or because they had recently amended their laws. Some erstwhile colonies of the United Kingdom (UK) adopted, at least for some period after independence, an automatic registration system validating in their jurisdictions patents filed in the UK. Others, like the present members of the African Intellectual Property Organization (better known by the French acronym OAPI) have long made available product patent protection for pharmaceutical inventions. Still others, such as the Republic of Korea, Mexico, Chile, Thailand, Indonesia and the Andean Group countries (Bolivia, Colombia, Ecuador, Peru

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[3] Footnote 5 of TRIPS clarifies that "non-obvious" is synonymous with "inventive step" and "useful" with "capable of industrial application". However, none of these terms are defined under TRIPS and there is no obligation to follow the characteristically low thresholds set for the patentability criteria in the United States.

[4] The provisions of TRIPS relevant to patent rights are Articles 27, 28, 30, 31, 32, 33, 34, 40, 65 and 70.

[5] The nations excluding pharmaceutical products from patentability were Angola, Argentina, Bangladesh, Brazil, Cuba, Egypt, Guatemala, India, Kuwait, Madagascar, Morocco, Pakistan, Paraguay, Qatar, Tunisia, Turkey, United Arab Emirates and Uruguay. See p. 8 of the Background Note prepared by Jayashree Watal for the WHO-WTO Workshop on Differential Pricing and Financing of Essential Drugs available at www.wto.org.

and Venezuela)[6] had responded to US pressures and amended their patent laws during the late 1980s or early 1990s to allow the patenting of pharmaceutical products.[7] Argentina, Brazil, Guatemala, Morocco and Turkey introduced pharmaceutical product patents since 1995. Developing country members who acceded to the WTO after 1995 but excluded product patents for pharmaceuticals, notably Jordan and Mongolia, had to comply fully with TRIPS in order to gain entry.

For WTO members that require national patent law amendments to introduce product patents for pharmaceuticals, such action can be delayed up to January 2005 in developing countries and economies-in-transition (i.e. Central and Eastern Europe). All TRIPS obligations can be delayed up to January 2006 in the least developed countries.[8] However, product patent applications for pharmaceutical inventions have to be accepted for filing in all WTO member countries from 1995 onwards. With the priority grace period of one year recognized in pre-existing international accords and incorporated into TRIPS, this means that at the minimum all pharmaceutical inventions for which patent applications were sought in any WTO member nation from 1994 onwards are covered by TRIPS obligations. WTO members which defer formal patent grants for pharmaceuticals up to 2005/6, exclusive marketing rights (EMRs) providing protection similar to that given by product patents must be granted to the patent applicant for five years from the date of marketing approval in these countries, or until the patent is granted or rejected, whichever period is shorter. Since the year 2000, such EMRs are being applied for and granted in relevant WTO member countries. Violations of TRIPS obligations, if determined to be so by WTO dispute settlement bodies and if not remedied in the reasonable period of time fixed, can lead to trade retaliation by or compensation to

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[6] Decision 486 of the Andean Community, which took effect from 1 December 2000, changes the earlier Decision 344 to establish a common regime on intellectual property, no longer excluding essential drugs from patentability.

[7] Some of these countries, such as Republic of Korea, Mexico, Thailand and Brazil agreed to protect pharmaceutical products patented elsewhere retrospectively, even though they were no longer "novel" under patent law.

[8] The WTO recognizes the classification of the United Nations to designate countries as least-developed countries (LDCs). There are currently 48 least developed countries on the UN list, 29 of which, to date, have become WTO members. See www.wto.org for the list of LDC members of the WTO.

affected WTO members.[9] In sum, all developing country WTO members that did not previously do so have to make available patent-like protection for pharmaceutical inventions from 1995 onwards, the economic effects of which can be expected to begin at the earliest from 2000 onwards (when new drugs begin to get exclusivity under TRIPS provisions) and plateau by 2015 (when newly patented products may be offset by older products losing their patent protection).

It should be noted that many of today's developed countries also excluded pharmaceutical products from patent protection until quite recently: Germany until 1968, Switzerland until 1977, Italy until 1978, Spain until 1992, Portugal until 1992, Norway until 1992, Finland until 1995 and Iceland until 1997.[10] In addition, special and more liberal compulsory licenses were provided for drugs in Canada, France and the United Kingdom, to name just a few countries. Even in the United States, a debate weighing the benefits of patents to induce technological innovations against the resulting high drug prices arose from time to time, beginning with the Kefauver Committee hearings in 1959 and continuing in a recent debate during the year 2000 over re-importation of prescription drugs.

Patents are especially important to pharmaceutical inventors in capturing the potential profits from new products, which otherwise could be copied more easily than products whose production processes can be kept secret, or for which the time and relative expense needed to copy the invention are much higher (Levin et al, 1987). Because they normally cover well-defined chemical molecules, substitution around which could require expensive new clinical trials, pharmaceutical product patents are particularly effective in limiting competitive entry into the production of specific new drugs and, hence, in permitting the producer to hold prices well above production costs. The public policy question, as a consequence, is how to balance the desire to make new drugs affordable to all those who need them, and yet retain strong incentives for

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[9] Violations of other WTO agreements can also lead to withdrawal of concessions under TRIPS. Subramanian and Watal (2000).

[10] See http://clea.wipo.int/lpbin/ for the text of patent laws of these countries.

inventing and developing new and better treatments. Most developed countries attempt to achieve this balance through various types of insurance schemes. For poorer countries with little or no research and development (R&D) capability and with small markets, whose demand adds only marginally to profits of multinational pharmaceutical companies and, hence, with at most a small impact on their R&D decisions, the question is how to keep patented medicine prices at the lowest possible level consistent with international obligations. It is the latter question, which is of immediate importance for the developing world, that is addressed in this paper.

3. EVIDENCE ON PATENTS AND PRICES

There is a widespread belief that the introduction of pharmaceutical product patents in less-developed nations will lead to higher prices. This assertion has been questioned by the research-based pharmaceutical industry.[11] Clearly, there can be no grounds to believe that the prices of existing or non-patentable medicines will change appreciably on account of the introduction of product patents. The question addressed by this section is whether there is a relationship between the absence or presence of patents and the prices of medicines.

One study conducted in 1995[12] claims to show that nations strengthening intellectual property protection for pharmaceuticals did not experience higher prices after such changes were effected. However, the study only demonstrates that the relevant countries did not have greater price *increases* with respect to existing products, or to an unspecified mix of existing and new products, 18 months after instituting protection. This does not answer the essential question on the relationship between patents and price levels. To capture any difference in prices attributable to patent protection, a price index of a basket of new drugs not previously patented under the old regime has to be compared with the basket of new and patented drugs. Such a comparison requires careful statistical

[11] See, for example, International Federation of Pharmaceutical Manufacturers' Association (2000).

[12] See Rozek and Berkowitz (1998).

controls for the relative quality of the new as compared to earlier drugs and their therapeutic substitutes, which has not been done.

There is extensive evidence from nations with product patent protection that average pharmaceutical product prices fall sharply when generic entry occurs following the expiration of the patents, as predicted by economic theory (Scherer, 2000, pp.1322–1324). Caves et al. (1991) estimated that in the United States, the average generic substitute's wholesale price was 60 percent of the branded drug's price with just one generic entrant, 29 percent with 10 entrants, and 17 percent with 20 entrants. Some, but far from all, of this price reduction at the wholesale level tended to be offset by the higher absolute retail margins charged by pharmacists on the generics (Masson and Steiner, 1985, p. 36 and Grabowski and Vernon, 1996, p.117). With higher retail margins on generics, Masson and Steiner found for a 1980 sample of 37 US drugs that the average saving at wholesale of 45 percent was reduced at retail to 24 percent. There is also evidence that when generic competition emerges, the price of the patent-expired but still branded product may be raised in an attempt to exploit brand differentiation and market segmentation (Grabowski and Vernon, 1992 and Frank and Salkever, 1997).

Even though the front-end investments incurred to introduce a generic substitute are typically much lower than those associated with new drug discovery and development, generic entry is more likely to be undertaken when the prospective market is relatively large, and hence when sufficient sales can be anticipated to defray initial investments. This is shown *inter alia* by a comparison of generic substitution experiences for 25 – 63 high-volume drugs in the United Kingdom, the United States, Germany and Japan.[13] The proportion of sampled products with generic competition ranged from 70 percent in the large US market down to 37 percent in the United Kingdom (where price controls on original but off-patent products reduced the potential profitability of generic products). The attractiveness of generic production can be increased not only by increasing the size of the potential market, but also by avoiding unnecessary front-end investment outlays. In the

[13] John Hudson, (2000).

United States, for example, the Waxman-Hatch Act of 1984 significantly reduced the costs of demonstrating therapeutic equivalence and the time required to enter the market after patents expired, raising generic drugs' quantity share of all prescriptions dispensed from 19 percent in 1984 to 47 percent in 1999. The extent to which generic products capture market share from patented precursors can be enhanced appreciably when public and private health insurance systems create positive incentives for physicians, patients and pharmacists to favour generic substitution. (see McRae and Tapon (1985), Masson and Steiner (1985), and Scherer (2000).)

Even where no generic substitutes exist, the monopoly power of patented drugs is, in most instances, constrained by competition from other medicines that treat the same disease condition.[14] Lu and Comanor (1998) found that of the 148 new drugs introduced into the United States market between 1978 and 1987, only 13 had no close substitute in their therapeutic class. This, they discovered, affected pricing strategies. Drugs classified by the Federal Drug Administration (FDA) in category 'A', providing significant therapeutic gain, were launched at prices averaging 3.1 times the average price of existing substitute products, and those offering moderate gains, or 'B' drugs at 2.2 times, and those providing little or no therapeutic gain, the 'C' drugs, at about the same level. However, eight years after product launch, the inflation-adjusted prices of 'A' drugs averaged only 7 percent higher than their launch prices, 'B' drugs 32 percent higher, and 'C' drugs 62 percent higher than their price at launch. Therefore, how much more expensive a new patented medicine is depends not only upon how much of an improvement it offers over existing medicines but on the marketing strategies pursued and patterns of substitute product entry over time. Recognizing these patterns, concern over the prices of patented medicines needs to be focused primarily on relatively new breakthrough drugs that face little therapeutic competition in treating critical and widespread disease conditions.

[14] See Ellison et al (1997) on estimates of demand elasticities for generic and therapeutic substitutes among the cephalosporins. Their basic conclusion is that there is relatively high demand elasticity between generic substitutes and smaller, but nonetheless significant, demand elasticity between therapeutic substitutes in this group of drugs.

Given the difficulties in estimating the effects of national policy changes introducing pharmaceutical product patents, economists have attempted to simulate the likely price and welfare effects.[15] The numbers generated by these models are sensitive to the assumptions on which they are based. Nevertheless, it is striking that with different methodologies, three studies using detailed market data on new pharmaceutical products predict upper-bound mean price increases of well over 200 percent with the introduction of product patents: Challu (1991), Fink (2000) and Watal (2000). These studies also shed light on the impact of competition in developing countries that do not allow product patents and have generic drug manufacturing capability.

4. ANALYSIS OF PRE-PATENT COMPETITION IN DEVELOPING COUNTRIES

In developing nations that denied product patent protection, were new medicines typically priced competitively? Competitive pricing might not emerge if there are other (non-patent) factors that restrict entry and competition, the most important being inadequate local manufacturing capabilities. Most least-developed and developing countries do not have such capabilities locally, and so imports dominate domestic consumption of pharmaceuticals. According to calculations by UNIDO,[16] 46 of the 133 non-OECD countries, or about one-third, imported 100 percent of their requirement of medicines in 1989. This count goes up to about two-thirds when we include all nations importing more than 50 percent of consumed medicines by value. Only 31 developing countries (or less than one-quarter) supplied three-fourths or more of their consumption domestically.[17] Even amongst this minority, the share of locally-owned companies was more than one-half of total domestic production in only a few: Argentina, Bangladesh, China, Egypt, India, the Republic of Korea, Thailand and Turkey. Indeed, developing nations originated only about 28 percent of total world pharmaceutical production in

[15] See Maskus (2000), pp. 159 – 165 for a survey of this literature.

[16] UNIDO (1992).

[17] These were Angola, Argentina, Bangladesh, Brazil, Colombia, Chile, China, Ghana, India, Indonesia, Iran, Malawi, Mexico, Morocco, Pakistan, Papua New Guinea, Paraguay, Peru, the Philippines, Republic of Korea, Sierra Leone, Solomon Islands, South Africa, Syria, Taiwan, Thailand, Turkey, Uruguay, Venezuela and Yugoslavia.

1990,[18] and even fewer countries, that is, seven, contributed about half of the total. These were Argentina, Brazil, China, India, Iran, Mexico and the Republic of Korea (Ballance et al, 1992). India and China were the only developing countries amongst the 20 largest exporters of pharmaceutical preparations in the world during 1990 (UNIDO, 1992).[19]

Among the countries with generic drug manufacturing capability, there are only two—Argentina and India—for which the effects of pre-patent competition in new drug markets have been studied in some detail. Challu (1991, 107–109) shows that in Argentina, across the 12 new drug product markets studied, the number of competitors played an important role in bringing down prices, on an average by about 50 percent. For 18 pharmaceutical products marketed in Argentina in mid-1991, in 17 cases the prices of foreign suppliers were higher compared to those of independent domestic companies. Watal (2000) examines the impact of seller concentration in 22 new drug product markets in India for 1994. The number of competitors ranged from only one to over fifty. Yet the share of the top four sellers ranged from 100 percent in nine markets to a low of 55–60 percent only in two markets. Econometric analysis of 15 new product markets over seven years, 1987–1993, shows that in the absence of product patents, market shares of firms were higher for large-sized sellers and those that introduced products first into the market, even when the "first-mover" advantage was only a few months. In related analyses, prices were found to be higher in new drug product markets when the number of competitors was smaller, the relative importance of the drug in its broader therapeutic category higher,[20] the market share of multinational companies was higher, or alternatively, when larger-sized firms dominated the market (Watal, 1995).

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[18] Developing countries contributed to roughly the same proportion, viz. 30 percent of world consumption of pharmaceuticals.

[19] Much of these exports are destined for the United States and Europe, putting into question arguments implying poor quality of pharmaceutical products produced in developing countries. In 1994–95, China, India, Singapore, Mexico, the Republic of Korea, the Bahamas, Cuba and Brazil were among the top ten developing country exporters of medicinal and pharmaceutical products, with the first three accounting for more than half of total exports from the developing world (UNCTAD, 1996/1997, p. 194).

[20] This is denoted by the sales of the drug to the sales of the therapeutic group or sub-group.

On a cognate question, we investigated whether countries that did not provide patent protection for pharmaceuticals suffered from either non-availability or delayed availability of patented medicines. We found that of the 33 products categorized by the United States Federal Drug Administration between 1980 and 1990[21] as 'A' category or "priority" drugs, 21 or about two-thirds, were marketed in India by October 2000.[22] It is possible that others were not introduced because of limited demand,[23] because the production technology was particularly difficult to master,[24] or perhaps due to decisions by some large Indian companies in the early 1990s to join hands with large multinationals and not to copy patented drugs.[25] Where production technologies are hard to replicate, cooperation of the patent owner might be needed to make new products available. This may be why only five of the 14 HIV/AIDS anti-retroviral were produced by local companies in India as of June 2000.[26] New analysis of data on 17 new drugs marketed up to 1994, as reported in Watal (2000),[27] shows that as Indian industry became adept at reverse-engineering new products, patients have been getting new products with increasingly short time lags from the date of introduction in the United States. Among these 17 products, seven products introduced in the United States before 1985 took an average of over five years to be introduced in India; whereas for the 10 products

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[21] It is possible that after 1990, knowledge of an impending TRIPS played a role in marketing strategies of multinational and local pharmaceutical companies.

[22] Twelve products were introduced by end of 1994 and another nine by October 2000.

[23] Even in the US only two 'A' category drugs appear in the 1994 list of the top 200 prescription drugs by sales volume in the United States (calculated by the authors from *Pharmacy Times*, April 1995).

[24] This was the case, for example, with cefaclor. See Lanjouw (1998).

[25] Eli Lilly set up a joint venture to do R&D with Ranbaxy Laboratories, a leading Indian drug supplier. The no-copying strategy may have changed again in recent years, since in October 2000 Ranbaxy, along with three other companies, announced plans to launch competitive versions of Pfizer's Viagra. See www.ranbaxy.com

[26] Taken from the 1995–2000 IMS-Health data on HIV/AIDS drugs in 23 developing countries made available to us by the Center for International Development at Harvard University.

[27] This analysis excludes five molecules, three of which were not supplied in the United States market. Outliers like albendazole, which was introduced in the United States 10 years later than in India, and cefaclor, whose availability in India lagged the US by 11 years, are also excluded.

introduced in the United States after 1985, the time lag to Indian availability averaged two years. [28]

5. PATENTS, MARKET EXCLUSIVITY AND RESEARCH AND DEVELOPMENT

Although policy incentives for increasing R&D in pharmaceuticals lie outside the scope of this paper, it is relevant to ask whether the market exclusivity provided by patents will encourage R&D investments in developing countries and for relevant products. The answer may have important implications for the policy options that developing countries adopt in order to improve affordable access to patented medicines.

The limited evidence currently available leaves it unclear whether introducing product patents for pharmaceuticals in the developing world will, by itself, induce significantly increased pharmaceutical R&D expenditures in or for these countries. The experience in Italy in the 12 years after the introduction of product patents for pharmaceuticals reveals that neither R&D expenditure growth nor new product introductions, measured by quantity and quality, accelerated after the patent regime changed in 1978, although Italian firms' propensity to seek patents in the United States increased (Scherer and Weisburst, 1995). The growth of R&D expenditures in Canada after patent law amendments in 1993 can be attributed, at least in part, to a commitment by the research-based pharmaceutical industry to raise such expenditures to 10 percent of annual pharmaceutical sales in Canada by 1996.[29] Survey evidence from India reveals that a few private pharmaceutical companies are increasing R&D expenditures in anticipation of the TRIPS regime. Not surprisingly, these companies are also focusing on diseases, such as diabetes or cancer with large global markets and perhaps also higher effective demand locally. As of 1999, only 16 percent of research or development expenditures in India was targeted at tropical diseases or developing country markets,

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[28] To our knowledge there were no dramatic changes in marketing approval procedures during this period.

[29] Letter of the President of PMAC, the Hon. J. Erola, to the Hon. Michael Wilson, Minister of Industry, Science & Technology, June 10, 1993, cited in http://www.cbhr.ca/patent-a/c91-web.htm. The developing countries missed an opportunity to negotiate such an agreement with the net technology-exporting countries at the time of finalizing TRIPS in the Uruguay Round.

about half of the 16 percent was focused on developing more suitable products for diseases of global incidence (Lanjouw and Cockburn, 2000). It is precisely because there is little purchasing power amongst those inflicted with such diseases that market incentives, such as increased patent protection, work poorly. Additional incentives appear to be needed to induce future cures for these diseases (Sachs, 1999; Kremer, 2000).

A related question is: how innovative would be the products that might result from increased R&D expenditures in developing countries? Judging from the experience in the United States, a country with strong patent protection and no ostensible price controls, it is clear that only a minority of the new chemical entities entering the marketplace will open up new therapeutic possibilities. Of the 255 new prescription drugs introduced in the United States between 1980 and 1992, only 47 were accorded an 'A' rating by the Federal Drug Administration, indicating a significant therapeutic gain.[30] And these drugs were not necessarily the best sellers. Only two of the 35 'A' category drugs approved between 1980 and 1993 appeared on a list of the top 200 prescription drugs, ranked by 1994 sales volumes. R&D costs are recovered mainly from the relatively few commercially successful products. Recognizing this, it seems clear that a rather substantial increase in R&D expenditures directed toward tropical disease would be required to generate a portfolio of new products including several new drugs that open up quantitatively significant therapeutic advances. In sum, developing countries, whose companies are increasing R&D expenditures in anticipation of TRIPS, should expect to see much of these expenditures devoted to process innovations concerning existing drugs or "me-too" drugs that have large global or local markets.

6. IMPLICATIONS OF TRIPS-COMPATIBLE POLICY OPTIONS FOR DEVELOPING COUNTRIES ON ACCESS TO PATENTED MEDICINES

How the introduction of product patents will change developing nations' access to low-price medicines will vary with these nations' pre-TRIPS patent regimes and drug

[30] In 1992 the USFDA changed its classification system for new drug approval priority candidates from A=significant therapeutic improvement; B=moderate therapeutic improvement; C=little or no therapeutic improvement to P=priority and S=standard for internal use on time limits for the approval process. We are grateful to Joseph DiMasi for providing us these data.

procurement strategies. In the pre-TRIPS period, products still protected by patents in the most industrialized nations were available in lower-cost generic versions from at least some suppliers. Those sources could dry up for post-1994 patented pharmaceutical inventions. The nations most significantly affected by the new TRIPS environment will be those that harboured a vibrant domestic generic drug producing industry and those that, lacking domestic production, actively encouraged the importation and use of generic substitutes from nations with export-oriented generic suppliers for example, Italian firms in the 1960s and 1970s, Chinese, Indian, Canadian, Korean and Israeli enterprises more recently. Nations that relied mainly on the research-oriented multinational pharmaceutical enterprises for their drug supplies, either through production by local branch plants or importation, tended to pay relatively high (and often unnecessarily high) prices for state-of-the-art medicines before TRIPS was negotiated and, absent policy changes, will continue to do so in the new environment.

The key question is: what measures might less-developed nations adopt in the new TRIPS environment to enhance low-cost access to the newest drugs, retaining benefits they enjoyed pre-TRIPS if they pursued aggressive generic substitution policies previously, or capturing some of those benefits if they recognise belatedly the advantages of pro-substitution policies? Several policy options—notably, compulsory licensing, utilizing parallel trade, enforcing price controls, encouraging the donation of vital medicines and cooperating in international drug procurement efforts—might be adopted without running afoul of the obligations imposed by TRIPS. We analyse those options here.

6.1 Compulsory Licensing

To achieve economical access to patented drugs once TRIPS has been fully implemented, one option available to developing nations is the issuance of compulsory licenses, which are authorizations permitting a third party to make, use or sell a patented invention without the patent owner's consent. TRIPS does not define or limit the circumstances under which patented inventions can be subjected to compulsory licensing. However, TRIPS makes a distinction concerning conditions under which compulsory

licenses are to be granted on the basis of whether they have been granted to correct anti-competitive practices or otherwise.

An important condition listed under Article 31 of TRIPS is that a prospective licensee should have been unsuccessful within a reasonable period of time in negotiating to obtain from the patent holder authorization to use the patented invention "on reasonable commercial terms and conditions." The failed negotiations clause can be waived in the case of national emergency or extreme urgency or for non-commercial public use. Although no examples are given, non-commercial public use might occur when national health authorities distribute drugs at a zero price or at cost through public health care networks. Any use of compulsory licenses must be "predominantly for the supply of the domestic market" of the authorizing nation, and the user must pay to the patent holder "adequate remuneration," taking into account "the economic value of the authorization." Each compulsory licensing case must be considered on its individual merits and subject to judicial or other independent review. Other conditions, for example, limiting the scope and duration to the purpose for which it was authorized or allowing the compulsory license to be terminated upon request if the circumstances that led to it cease to exist, are not particularly restrictive when WTO members are free to decide the circumstances.

Article 40 permits WTO member nations to take appropriate measures, including authorizing the compulsory licensing of specific patented inventions, under conditions that constitute "an abuse of intellectual property rights having an adverse effect on competition in the relevant market." Such abuse has to be determined to be anti-competitive after due judicial or administrative process. Nations invoking this article are also required to participate in consultations with the patent-holder's home nation upon request when anti-competitive patent practices are alleged. The article offers a non-exhaustive list of cases under which compulsory licensing might be authorized, including insertion of exclusive grantback conditions into patent licenses, conditions preventing challenges to a licensed patent's validity, and coercing a licensee to pay for packages including unwanted patents. The article's language appears to track in a general way the "abuse" doctrine of US patent antitrust law, although the article as a whole can be reconciled with European legal

traditions holding that failure to supply or license a patented product at all, or supplying the product at unreasonably high prices, might be deemed abusive. Article 31(k) states that the need to correct anti-competitive practices may be taken into account in determining the amount of remuneration paid to the patent holder in Article 40 cases, that is, that payments might be less than in other compulsory licensing cases. Similarly, such compulsory licenses, unlike others, could be granted predominantly or even solely for export.

Both articles embody language sufficiently vague, no doubt as a result of compromises made during the Uruguay Round negotiations, that several key provisions will be clarified only when disputes are processed through the WTO panel process or through future amendments in the treaty text. The following discussion offers historical background for understanding the implementation of compulsory licensing and an analysis of issues likely to be controversial in subsequent test cases.

6.1.1 Actual Compulsory Licensing Regimes

Many nations, industrialized and developing, have included in their patent laws provisions permitting compulsory licensing of patents under specified conditions.[31] The most common statutory ground for compulsory licensing has been non-working of the patented invention within the patent-granting nation, that is, supply of the relevant product through importation rather than domestic production. Since Article 27 of TRIPS requires that "patents shall be available and patent rights enjoyable without discrimination as to ... whether products are imported or locally produced," this historical basis for compulsory licensing is ignored in this paper. The available evidence suggests that it has been invoked infrequently even when it was available statutorily.

Under US law, the federal government may utilize technology patented in the United States when such utilization serves the national interest and reasonable compensation is paid.[32] In effect, the government issues itself or its designated private sector agent a

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31. See e.g. Neumeyer (1959).

32. 28 U.S. Code 1498.

compulsory license. During the 1950s and early 1960s, the US Department of Defense exercised its right to procure patented pharmaceutical products at substantially reduced prices from sources other than the patent holder—in most cases, from producers in nations, such as Italy that provided no patent protection for pharmaceutical products.[33] The practice was ended after a clause prohibiting importation of patented pharmaceutical products was attached as a rider to a foreign economic assistance bill in August 1961.[34] In 1999, the US Supreme Court ruled that individual states could emulate the federal government in infringing without fear of injunction valid US patents for governmental purposes if they followed appropriate legal procedures, including the determination of reasonable compensation.[35]

The United States has led the world in issuing compulsory licenses to restore competition when violations of the antitrust laws have been found, or in the negotiated settlement of antitrust cases before full adjudication has occurred.[36] By the end of the 1950s, compulsory licenses had been issued in roughly 100 antitrust cases covering an estimated 40–50 thousand patents, including AT&T's basic transistor concept patents, IBM's computer and tabulating card machine patents, General Electric's fluorescent and incandescent lamp patents, Du Pont's nylon patents and Eastman Kodak's colour film processing patents. Additional cases since then have led to the licensing of Xerox's plain paper copying machine patents, the tranquilizer Meprobamate, synthetic steroids, the antibiotic Griseofulvin, Cytokine biopharmaceutical patents owned by Novartis and Chiron, and the 9-AC cancer drug patent rights assembled under the merger of Pharmacia AB with

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33. See "Pentagon Discloses Policy on Drug Buying Abroad; Announces 3 Purchases," *Wall Street Journal*, January 20, 1961, p. 3. Savings on the order of 65 percent were claimed. In one case, however, antibiotics procured abroad may have been produced using cultures and processes stolen from the Lederle Laboratories Division of American Cyanamid Corp. See US v. Bottone, Salb, and Sharff, 365 F. 2d 389 (1966).

34. Public Law 87–195, sec. 606(c). The amendment was offered on the floor of the House of Representatives by Rep. Richard Roudebush of Indianapolis, Indiana, and, after a brief debate, accepted for inclusion by a vote of 87 to 65. *Congressional Record*, August 18, 1961, pp. 16283–16285. The amendment's language was amended insignificantly in conference committee. U.S. House of Representatives, Report No. 1088, Foreign Assistance Act of 1961 (Washington: USGPO: 1961).

35. Florida Prepaid Postsecondary Education Expense Board v. College Savings Bank, 119 S. Ct. 2199 (1999).

36. See Hollabaugh and Wright (1960); and Scherer (1977).

Upjohn. Some of the US antitrust decrees, such as those covering General Electric's incandescent lamp patents and the 8,600 patents in AT&T's portfolio, required licensing at zero royalty rates. Most provided for "reasonable" royalties, whose more precise meaning will be investigated subsequently.

The kind of circumstances under which compulsory licensing has been ordered in fully litigated US antitrust cases include the use of patents as a basis for price-fixing or entry-restricting cartels, the consummation of market-concentrating mergers in which patents played an important role, and practices that extended the scope of patent restrictions beyond the bounds of the patented subject matter. Charging high prices has not in its own right been deemed actionable under US precedents. Nor has the accumulation of monopoly power through pyramided patents gained through internal inventive efforts been found in litigated cases to warrant compulsory licensing. However, General Electric and other incandescent lamp patent holders restrictively cross-licensing each other were ordered to license their patents royalty-free when they were found to be "mounted upon an arsenal of a huge body of patents that can easily overwhelm and defeat competition."[37]

The competition policy precedents of leading European nations and the European Community are in this respect more expansive than those of the United States. A company that controlled patented processes used to produce a key chemical intermediate for a drug effective against tuberculosis was found under Article 86 of the European Community treaty to be abusing its monopoly power when, after entering into production of the drug through its subsidiary, it subsequently refused to sell or license the intermediate to an independent pharmaceutical manufacturer.[38] The manufacturer was ordered to resume third-party intermediate sales. European Community competition authorities are more inclined to issue such "conduct" orders than the US authorities, who under similar circumstances would

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37. U.S. v. General Electric Co. et al., 115 F. Supp. 835, 844 (1953).

38. ICI and Commercial Solvents Corporation v. Commission of the European Communities, 1974 E.C.R. 223, 250 (1974). The European Court's decision is abstracted in "Refusal by a Dominant Firm To Sell Raw Materials," *Antitrust Bulletin*, vol. 19 (Fall 1974), pp. 605–618.

probably have ordered a "structural" remedy, for example, divestiture of the integrated firm's pharmaceutical operations and/or compulsory patent licensing.[39]

Reacting to the "stagflation" tendencies of the 1970s, the German Federal Cartel Office instituted a series of actions asserting that enterprises with dominant market positions, based in some cases on patent rights, had abused their monopoly power by effecting unjustified price increases.[40] The most thoroughly litigated case focused on the tranquilizers Valium (at the time, the most-prescribed drug in Germany) and Librium. In the end, Hoffmann-LaRoche (HLR), the products' manufacturer, was not required to adjust its prices downward because no adequate basis for comparing HLR's prices against those of an "as if effectively competitive" supplier could be found. It seems clear from the various higher German court decisions, however, that high monopolistic prices would have been ruled abusive if competitive benchmarks could be established despite the existence of substantial research, development and marketing costs. The "as if" problem could be surmounted if in some parts of the world generic substitutes are supplied by competitive firms paying "reasonable" royalties to the patent holder and not subjected to governmental price controls—the obstacles found to be decisive in the Valium-Librium case by the German courts.

The United Kingdom and Canada provide the leading examples of compulsory licensing of drug patents without a finding that the anti-monopoly laws have been violated. In the United Kingdom, Section 41 of the Patents Act of 1949 distinguished foods, medicines and surgical devices from other patent-protected products by articulating a rebuttable presumption in favour of compulsory licensing to ensure that the products are "available to the public at the lowest prices consistent with the patentees' deriving a reasonable advantage from their patent rights." Between 1953 and 1971, a total of 20 compulsory licenses were granted in response to 54 applications, covering *inter alia* such important products as Chloromycetin, Librium and Valium. A 1967 US government study

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39. See e.g Fox (1986).

40. See Kaufer (1980); and Schmidt (1983).

speculated that the UK compulsory licensing provisions may have been used infrequently "because of the cumbersome and time-consuming procedures involved," which among other things permitted compulsory licensing only after a patent had been in force for at least three years.[41]

With the United Kingdom's ratification of the Uruguay Round treaty and accession to the World Trade Organization, the UK laws on compulsory licensing were amended.[42] For UK patents held by residents of WTO signatory nations, provisions authorizing compulsory licensing of inventions not worked within the UK were eliminated. Also removed were the provisions singling out food, drug and surgical device patents as subject to especially strong presumptions in favour of compulsory licensing. However, compulsory licensing of WTO-member nationals' patents can be ordered under Section 48 of the Patents Act when the UK demand for a patented invention is not being met "on reasonable terms," or when the patent owner has refused to grant a license "on reasonable terms," or (under Section 51) when a monopoly found by the UK competition policy authorities to be operating against the public interest has refused to make patent licenses available "on reasonable terms."

Canada's experience has been more far-reaching. Since 1923 Canada had a law providing for compulsory licensing of the right to manufacture within Canada drugs (and also food products) protected by patents (usually process patents, since product patents were not available at the time). The law saw little use, at first because few important drugs were covered by patents up to the time of World War II, and later because the Canadian market was considered too small to realize all economies of scale in the production of bulk therapeutic ingredients and because long delays in the granting of licenses left little or no profit to be realized by small-scale domestic generic producers.[43] Recognizing that importation of bulk ingredients was virtually essential if Canadian consumers were to

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41. U.S. Department of Health, Education, and Welfare, (1968), p. 177.

42. The amended provisions can be found at the United Kingdom Patent Office's website, http://www.patent.gov.uk.

receive the intended benefit of medicines "available ... at the lowest possible price consistent with giving to the patentee due reward for the research leading to the invention," the Canadian Parliament amended the law in 1969 to permit compulsory licenses for importation. The new law also required the responsible Commissioner of Patents to approve or disapprove a license application within 18 months of its receipt.

Between 1969 and 1977, 227 licenses were issued, only eleven of them calling for domestic production alone without the right of importation.[44] The most typical approach has been for the active ingredients to be imported in bulk, with encapsulation and packaging occurring in Canada. Among 47 drugs for which licenses were issued between 1970 and 1978, the average number of licensees for the same drug was three, with a range from one to eleven. Although some license recipients did not follow through by actually supplying the drug in Canada, in many cases, and especially for the drugs with substantial sales volume, competition was secured in the generic provision of drugs that would otherwise have been monopolized by the patent owner. On an average, generic drugs supplied under compulsory license captured roughly 19 percent of the total sales of the product lines in which they competed, with penetration rates varying widely across Canadian provinces, depending upon the extent to which provincial drug reimbursement rules encouraged or discouraged generic substitution.[45] In Ontario, where the rules were most conducive to substitution, penetration rates were as high as 55 – 64 percent at the retail level.[46] Gorecki estimates that for drugs on which competition through compulsory licensing occurred, prices during the late 1970s would have been 20 percent higher in the absence of such competition.[47] A later study of 29 drugs subjected to compulsory licensing in Canada but patented in the United States revealed that the Canadian prices were on an average 47 percent lower than their US

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43. See Gorecki, (1981), pp. 28 – 34.

44. Gorecki (1981), p. 46. Some companies received multiple licenses to import and/or produce a given drug, so the total number of non-duplicating licenses out of 227 approvals was 152.

45. Gorecki (1981), p. 86.

46. Gorecki (1981), p. 89. See also McRae and Tapon, (1985), pp. 43-61.

47. Gorecki (1981), p. 149.

counterparts in 1982.[48] For Valium, one of the world's best-selling drugs during the 1970s and the licensed drug sales leader in Canada, the price to hospitals fell from $42 per 1,000 units before licensing to $4.10 by the end of the 1970s.

Despite opposition from consumer advocates and Canadian generic drug providers, the Canadian compulsory licensing law was weakened in 1987, with the imposition of a seven year to ten year exclusivity period for drug patent holders, and eliminated altogether in 1992. The principal impetus was lobbying by US and European pharmaceutical manufacturers anticipating the debate over the proposed free trade treaties between Canada, the United States and (later) Mexico. As a *quid pro quo*, the multinational drug manufacturers agreed to locate in Canada drug research and development activities roughly proportional to Canada's share of their world sales and to accept a new regime of "reasonable price" controls by the Canadian Patented Medicines Review Board.

6.1.2 Determining License Compensation Rates: The Theory

Third-party use of patents under compulsory licenses or infringement for government purposes is usually accompanied by a condition that the user pay "adequate remuneration" or "reasonable compensation" for its use of the patented technology. The extent to which price-reducing competition can arise through compulsory licensing depends critically upon the criteria imposed to determine the magnitude of the compensation paid.

In recent years, the US federal judicial system has been at the forefront among world patent jurisdictions in compensating patent holders generously for infringements of their patents. This does not appear to have been the case throughout all time. In 1983 the US Congress created a new Appellate Court for the Federal Circuit, with responsibility for hearing all appeals from district court decisions on private sector patent matters. Previously, appeals had been scattered over 11 regional circuits, resulting in standards that varied widely

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48. On this and other price comparison studies, see the submission of Lawson A. W. Hunter, Director of Investigation and Research under the Combines Investigation Act, to the Commission of Inquiry on the Pharmaceutical Industry, August 14, 1984, p. 6. The study cited in the text was by Tom Brogan, Mario Deschamps, and Guy Roberge, "Drug Cost Differential Between Canada and U.S.A." (Ottawa: Consumer and Corporate Affairs: 1983).

from one circuit to another, but that took a characteristically skeptical stance towards patent claims. There is no evidence that the Congress intended to change the substance of patent law through this procedural shift, but the new court was staffed with judges who had previously practised intellectual property law in the private sector. Bringing a relatively pro-patent stance to its decisions, the court articulated among other things new guidelines giving the benefit of doubt to patent owners in disputes over liability and the size of awards for patent infringement. As a result, there were record-breaking awards in a number of important cases, for example, $900 million for Kodak's infringement of Polaroid patents, $550 million to the Lemelson trust for bar coding, $212 million from Steelcase to Haworth for movable office panels, and $171 million from Mobil to Exxon for a plastic catalyst.

The US Patent Code, 35 US Code 284, provides that in cases of patent infringement, the damages awarded shall be:

> ... *adequate to compensate* for the infringement but in no event less than a *reasonable royalty* for the use made of the invention by the infringer, together with interest and costs [emphasis added].

One implication, confirmed by court decisions, is that there are two potentially different standards, with the "reasonable royalty" standard tending to be less generous and/or second-best.

Figure 1 shows how the new Appellate Court for the Federal Circuit has interpreted the "adequate to compensate" provisions of the US statutory law. Suppose the demand curve for a drug product is as marked in the figure[49] and marginal production costs are $20 per standard prescription package. In the absence of competition, the patent holder is in

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[49] It has the equation $P = 100 - 0.1\ Q + .00003\ Q^2$, where P is price and Q is the quantity sold (in thousands of packages).

effect a monopolist in the sale of its product.[50] It derives its marginal revenue function (dashed line marked MR), equates marginal revenue with marginal cost, and sets a price of $55 per package, producing 530,000 packages to satisfy the demand. Its contribution to profits and the repayment of research and development costs is 530,000 x (55-20) = $ 18.55 million per year. If another firm enters and supplies VW packages (= 175,000), inducing the patent holder to reduce its output to 355,000 packages, the infringer deprives the patent holder of profits measured by the area rectangle STWV, or 175,000 x (55-20) = $6.125 million per year, and under the "adequate to compensate" law as interpreted, that is the initial measure on the basis of which damages are computed. If assessed on an ad valorem basis, the royalty would approximate 64 percent of the infringer's sales.

Suppose, however, that because it lacks a well-known brand name or other first-mover advantages, the infringer can only obtain a price of $40 per package for its version of the drug. Then the highest royalty it could agree to in arms-length negotiations would be $20 per package. If the courts accepted those facts as a basis for awarding royalty, the royalty rate would be reduced to 50 percent ad valorem on the infringer's lower-priced sales (which is 36 percent relative to the patent holder's price). If the infringer's lower price forced the patent holder to reduce its price (which is unlikely, given evidence that branded drug sellers tend not to reduce their prices in the face of generic competition), the court under a "profits lost" standard would count as additional damages to be paid by the infringer the profit loss per package still sold by the patent holder due to price suppression times the number of packages sold by the patent holder. Given a downward-sloping demand curve, however, the lower price will lead to higher unit sales by the patent holder, complicating the damages assessment problem in ways beyond the value of further exploration here.[51]

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50. This does not mean that there are no other chemically different products with similar therapeutic effects; it only means that the products are sufficiently differentiated that the drug's patent holder faces a downward-sloping demand curve which takes into account the availability of imperfect substitutes.

51. For an analysis showing that price suppression and loss of output by a dominant patent holder tend not to coincide, see the declaration of F. M. Scherer submitted in the matter of Mahurkar Double Lumen Hemodialysis Catheter Patent Litigation, MDL-853, U.S. Federal District Court for the Northern District of Illinois, September 1992.

Two things are evident from this elementary exposition. First, if "adequate remuneration" were to be construed under the simplest of the "profits lost" tests analyzed here, compulsory licensing would impose such high royalty payments on the licensed producer that there could be no price reduction and hence no expansion of drug availability at all. Since the purpose of virtually all known compulsory licensing schemes is to increase competitive supply and reduce prices, the "profits lost" test cannot logically be the standard to be met in determining compensation for compulsory licensing. Second, it is evident from a large number of cases that the royalties awarded in actual compulsory licensing cases have been much lower than the 50–64 percent ad valorem rates derived in our simple "profits lost" example. On this second point, we now examine relevant evidence, dealing first with patent infringements by the US government, then with compulsory licensing orders used as antitrust remedies, and finally with compulsory licensing directed specifically towards pharmaceuticals. The following section draws heavily from the US experience only because this is where the most extensive jurisprudence, albeit confined to antitrust and government use cases, exists on this subject.

6.1.3 Actual Compensation Determination Experience

For US government use of Enrico Fermi's patent governing plutonium production, a payment of $300,000 was made—less than one percent of the government World War II investment in the Hanford plutonium extraction facilities. The heirs of Robert S. Goddard were paid $1 million for the government's use of Goddard's rocket engine patents—about 0.01 percent of the value of the liquid-propelled rockets produced by the US government during the life of the patents.

In what was initially described as the largest patent compensation case in history, Hughes Aircraft claimed a 15 percent royalty, or $3.3 billion in total, on the value of 81 government satellites using Hughes' geostationary orbit technology. The US government argued for one percent royalty.[52] The government's one percent proposal was accepted by

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52. See "Patent Case May Cost U.S. Billions," *New York Times*, April 22, 1989, p. D1

the US Court of Claims and sustained on appeal.[53] According to a 1991 survey, the highest royalty rate paid by the US government in compensation for the use of a portfolio of pioneering private patents was 10 percent.[54] Rates of 6 percent were said to be applied "as a general rule" in the absence of contrary evidence. In one such case, a relatively small firm, Tektronix, asked for recovery of its profits, said to be in the range of 24–28 percent on commercial sales, when the government authorized another company to use the Tektronix patent portfolio in delivering at substantially lower quoted prices special-design oscilloscopes.[55] The court of appeals observed that had Tektronix earned such high profits on sales to the government, they might have been reduced under the profit renegotiation procedures applicable at the time. It went on to observe that under precedents interpreting claims against the US government under 28 US Code 1498:[56]

> [The] goal of "complete justice" implies that only a reasonable, not an excessive, royalty should be allowed where the United States is the user—even though the patentee, as a monopolist, might be able to extract excessive gains from private users. Much of the content of the constitutional requirement of just compensation derives from the equitable principles of fairness as between the Government and its citizens.

In another case that led to a compensation award of 10 percent on the patent-infringing government contractor's sales, the appellate court noted that in dollar magnitude, the approved compensation was roughly half of what the government saved by purchasing from a designated infringer rather than from the patent holder.[57]

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53. Hughes Aircraft Co. v. United States, 86 F. 3rd 1566 (June 1996), affirming 31 Fed. Cl. 481 (1994).

54. McGrath, (1991).

55. Tektronix Inc. v. United States, 552 F. 2nd 343 (1977).

56. 552 F. 2d 343, 351 (1977).

57. Leesona Corporation v. United States, 599 F. 2nd 958 (1969).

Some important US antitrust judgments, as noted earlier, have required that patent portfolios be licensed at zero royalty rates. In the more typical cases, royalty rates have been modest. For example, licensees were required to pay 0.5 percent ad valorem for the first Xerox plain paper copying machine patent they used, an additional 0.5 percent for the second patent, and then an additional 0.5 percent (implying a maximum royalty of 1.5 percent) for the remainder of Xerox's vast patent portfolio.[58] At the time, Xerox was devoting 5.6 percent of its sales revenue to research and development. In a decision later overturned on procedural grounds unrelated to the compensation question, the Federal Trade Commission ordered that the patent covering the antibiotic tetracycline be licensed at an ad valorem royalty rate of 2.5 percent. Before generic competition began, tetracycline was sold at wholesale for a price of $30.60 per 100 capsules. Production costs were of the order of $3.00, so a "profits lost" royalty rate would have been of the order of 90 percent.[59] In most compulsory licensing cases, royalties were left to be settled through negotiations by the parties, so no public record exists. But in the minority of cases requiring the courts to step in and settle disputes, royalties of from 0.2–3.0 percent have been reported.[60] The merger of Ciba-Geigy with Sandoz was approved in 1997 by the US Federal Trade Commission under an order requiring *inter alia* that Cytokine patents be licensed at royalty rates not exceeding 3.0 percent and gene therapy patents at a flat payment of $10,000 plus a royalty rate exceeding by not more than 1.0 percent the royalty the merged firm was required to pay to the US National Institutes of Health, which had made important contributions to the technology.[61]

The United Kingdom Comptroller of Patents pursued an essentially cost- and profit-based approach to setting royalties for compulsory licenses to drugs under section 41 of the UK Patents Act. To research, development and testing costs averaged over the licensing

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58. In the matter of Xerox Corporation, 86 F.T.C. 364 (1975).

59. Scherer, (1980), pp. 517-518.

60. Scherer, (1977), pp. 49-50.

61. In re Ciba-Geigy Ltd. and Sandoz Ltd., decision and order, Federal Trade Commission docket C-3725 (March 1997).

firm's pharmaceutical operations, a fairly generous profit margin was added to arrive at the royalty per kilogramme. In an early case, this led to an ad valorem royalty rate of 18 percent.[62] A similar approach led to a fixed royalty per kilogramme of the tranquilizer Librium that approximated 18 percent of the average price received by Hoffmann LaRoche on its UK sales, but a higher percentage rate on the lower sales price attainable by generic producers. On Librium's more potent sister drug Valium, the per kilogramme royalty was set at roughly 22 percent of the selling price received by Hoffmann-LaRoche.[63] These royalties, although much less than the marginal profit rates realized by the patent-holding drug manufacturers, were sufficiently high to have impaired significantly the market inroads of compulsory-licensed substitute drugs.

During the 1970s and much of the 1980s, Canada had the world's most far-reaching compulsory drug licensing programme, at least in part because of the royalty determination approach adopted. The enabling statute declared that:[64]

> ... in ... fixing the amount of royalty or other consideration available, the Commissioner shall have regard to the desirability of making the medicine available to the public at the lowest possible price consistent with giving to the patentee due reward for the research leading to the invention.

In an early test case, the Commissioner of Patents rejected a fixed per-kilogram royalty proposal by Valium patent holder Hoffmann- LaRoche, which would have amounted to 30 percent of HLR's selling price and a substantially higher percentage of a generic substitute's price. Instead, an ad valorem rate (against the licensee's price, not the licensor's) of 4.0 percent was set. On appeal, the Exchequer Court affirmed the Commissioner's 4.0 percent rate, among other things rejecting the suggestion that royalties on licensed sales should reimburse a pro-rated share of the patent holder's research and development programme

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62. In the matter of J. R. Geigy S.A.'s Patent, 1964 R.P.C. 391, discussed in Scherer (1977), p. 45.

63. See again Scherer (1977), pp. 44–45.

64. Section 41(4) of the Canadian Patent Act, as amended in 1969.

outlays.[65] The 4.0 percent royalty rate was applied almost uniformly in subsequent compulsory licensing orders, among other things avoiding a detailed inquiry into unique cost factors by the Commissioner of Patents and the reviewing courts and hence facilitating procedures that expedited the entry of generic substitute drugs into the Canadian market.

To sum up, there is wide variation in the way responsible government agencies and courts have set the amount of compensation awarded to patent holders when patents have been subjected to compulsory licensing. The United Kingdom has provided the most generous compensation in its drug patent licensing decisions; the United States the least generous compensation in key antitrust case orders. None of the royalty determinations on which information is available have established rates approaching those that would emerge under a "lost profits" criterion.

There are important lessons here for nations that seek to apply the compulsory licensing provisions available under the TRIPS agreement. High royalty rates, as in the British drug licensing experience, could undermine the objective of making drugs widely available to low-income consumers on competitive terms; low royalty rates, as in the Canadian experience, could provide the basis, assuming that other conditions are satisfied, for competitive drug supplies while compensating patent holders to at least some extent for their research and development contributions. The choices made in industrialized nations provide ample precedent for royalty-setting on the modest side of the range of possibilities.

6.1.4 Other Obstacles

The longer the issuance of compulsory licenses is delayed after patented drugs enter the marketplace, the less time licensees have to recover their start-up costs and the more difficult it is to achieve effective competition among multiple generic substitute suppliers. Thus, if compulsory licensing is to be successful, expeditious licensing procedures are a necessity. TRIPS Article 31 requires judicial or other independent review of the decisions

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65. Hoffmann-LaRoche Ltd. v. Frank W. Horner Ltd., 61 C.P.R. 243 (1969), 64 C.P.R. 93 (1970). In 1985 the so-called Eastman Commission recommended that the royalty rate be increased to 14 percent, compensating estimated R&D costs amounting to 10 percent of sales and promotional outlays of 4 percent..

taken by the licensing authority. Here, the experience in Canada is relevant. The licensing authority there was required to reach its decisions within 18 months of a license application. In fact, the median time to reach a decision was 10 months for applications filed between 1969 and 1977.[66] It will also be essential for the designated authorities to establish clear and transparent precedents in early cases, as was done in Canada, so that they can perform subsequent reviews efficiently. In developing countries where the courts are overburdened with cases of all kinds and time taken for disposal is very long, it may be advisable to designate independent administrative authorities to hear appeals on compulsory licensing cases.

The requirement under TRIPS that any compulsory drug patent license be authorized predominantly for the supply of the domestic market is most likely to pose serious problems to less-developed nations that lack the infrastructure and technical capabilities to build a domestic industry reliably able to supply modern pharmaceutical products. Even Canada, with high income per capita, excellent universities, and a population during the 1970s of roughly 22 million, found it necessary to import most of the bulk pharmaceuticals ultimately supplied under compulsory licenses. Thus, smaller less-developed nations will have to issue their compulsory licenses mainly for importation rather than domestic production. This, in turn, requires that competitive world market supply sources exist. The "predominantly" term in Article 31(f) clearly implies that some exportation under compulsory license in the exporting nation will be allowed. A crucial determination will have to be made by a future WTO panel as to what the term means in terms of proportion of volume or value of domestic sales. A restrictive interpretation will severely limit the ability to achieve effective world market competition. Under such circumstances, the principal suppliers are likely to be large nations, such as India, China or Brazil. It will also be important that such would-be exporters recognize their comparative advantage in being the world's principal suppliers under compulsory license and are not discouraged from assuming that responsibility. Clarifying language in subsequent

66. Gorecki (1981), p. 41.

amendments of the TRIPS Agreement or from WTO panel adjudications is much to be desired.

Compulsory licenses should not, however, be seen as a "magic wand" for obtaining affordable access to patented medicines in developing countries, as there are some basic limitations:

First, compulsory licensees must have the capability to "reverse-engineer" or import the product without the cooperation of the patent owner.[67] Increasingly, larger domestic companies in developing countries are raising their R&D investments and are collaborating with multinational companies to achieve advanced capabilities and reach more markets. Such cooperation may be accompanied by tacit agreement to restrict competition in some markets.

Second, exports of compulsorily licensed products from large markets destined for small, least-developed countries can only work where the disease patterns are common to both markets.

Third, compulsory licensees will be only attracted to large and profitable drug markets, and so essential medicines with small potential volumes or mostly poor patients will not attract many applicants, however important it is from the perspective of public health. Manufacture in government-owned facilities may be a solution in such cases, although an element of public subsidy may be necessary.

6.2 Parallel Trade

Parallel trade occurs when a product covered by intellectual property rights sold by or with the right holder's consent in Nation A is re-sold in another nation B without the rights holder's authorization. The incentive for its occurrence is a sufficient difference in

[67] Transfer of technology, often recommended as a solution, requires the active cooperation of the patent owner or, in the context of South-South cooperation, of his competitors.

prices between the price paid by the first purchaser and prices charged in Nation B to cover shipping and other transaction costs and still offer gains to both the shipper and the Nation B buyer. It is therefore a form of arbitrage, tending to reduce differences in prices across diverse markets. For the incentive to engage in parallel trade to materialize, there must be underlying market imperfections, for example, stemming from monopoly power attributable to unique product patents, strong brand image differentiation, or lack of price transparency, which are exploited by the original seller through a strategy of price discrimination.

Patents on drug products offering unique therapeutic features often give the sellers of the drugs sufficient pricing discretion to engage in the cross-national price discrimination that creates incentives for parallel trade. So also may trademarks signaling the reputation a well-known multinational drug producer enjoys *vis à vis* legitimate generic imitators. However, even when it is permitted under relevant laws, parallel importation may be thwarted by differences in product approval and labeling standards enforced by national regulatory authorities, or by differences in physical product characteristics (such as pill shape or colour) or trademark names in diverse markets.

Since price discrimination is widely practised by multinational pharmaceutical firms and because the costs of shipping drugs from one nation to another are modest in relation to product prices, incentives for parallel trade emerge. For reasons that will become clear, parallel trade reduces the profitability of original drug manufacturers and has therefore been opposed vigorously by them. The conflict of interest between drug sellers and ultimate buyers has led to considerable controversy over national and international policies governing parallel trade.

National and International Policies

Parallel trade in patented articles is legally permissible under what is called the exhaustion of rights doctrine. This doctrine states that once the producer of a patented product or its agent has sold its product in good faith to an independent party, the patent holder's right to determine the conditions under which the product is resold is exhausted. If

there are price differences among customers of the original manufacturer, any customer can engage in arbitrage transactions that exploit those differences.

Where controversy emerges is over the rights of a patent holder to limit parallel trade in its products across national borders. Jurisdictions that allow only national exhaustion as distinguished from international exhaustion maintain that, while the first sale on a market exhausts rights within that market, the rights holder can still exclude unauthorized transactions from another national market to the one allowing only national exhaustion. Neither the Paris Convention on industrial property nor the TRIPS Agreement established rules determining when cross-border parallel trade could occur or be restrained. The intersection of patent rights with parallel trade was vigorously debated at the negotiations leading to the TRIPS Agreement. The participants essentially agreed to disagree, establishing in Article 6 of TRIPS language excluding the patent rights exhaustion question from the World Trade Organization's dispute resolution jurisdiction, and hence leaving the matter to be decided at the individual nation level. Member nations are only required to apply most-favored nation and national treatment systematically.[68] As a result, widely varying national policies exist across countries and between different intellectual property regimes within countries. For instance, the provisions on exhaustion differ *inter alia* for goods protected by trademarks (with parallel imports allowed by most nations) as compared to patents (with parallel imports discouraged by most developed and now many developing nations).

Seeking to create a true "common market," one feature of which is a tendency for differences in product prices to be arbitraged away, the European Community has sharply discouraged impediments to parallel trade within the Community's jurisdiction. In pharma-ceuticals, upon which (along with automobiles) EC authorities have focused with

[68] Under this resolution, a nation such as the United States might seek to influence other nations' rules by declaring them to be unfair trade practices under Section 301 of the U.S. trade code or its equivalent. But given the U.S. Congress' recent efforts to authorize parallel drug imports, as explained further on in the text, this variant of "aggressive unilateralism" (Cf. Bhagwati and Patrick, eds., 1990) seems an improbable future strategy.

special vigor,[69] Bayer AG was fined 3 million ECUs in 1996 for attempting to restrict reshipment of the cardiovascular drug Adalat by wholesalers in Spain and France, where the wholesale price was relatively low, to the United Kingdom, where prices were 53–94 percent higher.[70] However, Community rules prevent unauthorized parties from importing drugs enjoying patent protection within the Community from nations outside the Community.

Although many nations share the European Community's ban on parallel imports of patented products from outside their borders, some less-developed nations, including Argentina, Thailand and South Africa, have enacted laws permitting parallel imports -- in the case of drugs for South Africa, at the discretion of the Minister of Health. The South African law was challenged in a national court by multinational pharmaceutical companies, but the suit was abandoned in April 2001. Concerned over the likelihood that governmental drug reimbursement programmes would be extended to cover senior citizens and the high cost of pharmaceutical products, the US Congress also swerved from its long-standing antipathy toward parallel imports in September 2000, passing bills that would permit the re-importation of patented drugs from sources such as Canada and Mexico, where prices charged by the patent-holding manufacturers have tended to be lower than in the United States. However, in December 2000 the law was declared by the Clinton Administration to be unworkable because of difficulties in establishing quality control and labeling standards.[71]

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[69] See Sir Leon Brittain, "Making a Reality of the Single Market: Pharmaceutical Pricing and the EEC," address before the IEA Health and Welfare Unit, December 1, 1992, anticipating future EC actions against barriers to parallel trade. In 1990, parallel pharmaceutical imports amounted to an estimated 8 percent of domestic consumption in the United Kingdom, 5 to 10 percent in the Netherlands, and 1 percent in Germany -- nations with relatively high drug prices. See Gernot Klepper, "Pharmaceuticals," in Pierre Buigues, Alexis Jacquemin, and Andre Sapir, editors, European Policies on Competition, Trade and Industry (Aldershot, UK: Edward Elgar, 1995), p. 335. In Sweden, parallel imports amounted to six percent of total 1998 pharmaceutical sales. Matthias Ganslandt and Keith E. Maskus, "Parallel Imports of Pharmaceutical Products in the European Union," working paper, January 2001.

[70] Commission decision in re Adalat, Case IV/34.279/F3, decided January 10, 1996.

[71] See "In a Turnaround, White House Kills Drug-Import Plan," New York Times, December 27, 2000, p. 1.

The Underlying Theory

To understand why parallel trade is such an important and controversial issue, one must know why prices are set at widely varying levels in different national markets and what the consequences of such price discrimination are. Figures 2(a) and 2(b) tell the basic theoretical story.

They assume two nations, A and B, with roughly equal numbers of cases in which use of a particular drug product might be indicated. At a zero price then, equal quantities of the drug -- one million prescriptions (Rx) per month -- would be demanded. However, Nation A is assumed to have high average income per capita, while Nation B has low income per capita. This "income effect" leads to different demand curves, assumed for illustrative purposes to be straight lines, for the two different nations, with the demand curve for Nation A being higher and (at any given positive price) less price-elastic than the demand curve for Nation B.[72] We assume also that the drug can be produced and distributed at a constant marginal cost of $18 per Rx, shown by the horizontal lines marked MC.[73] Patent protection permits the drug's producer to maximize its profits, given demand and cost, in each market separately or in both markets together. In wealthy Nation A, the firm will derive its marginal revenue curve MR_A, equate marginal cost with marginal revenue at an output of 410(000) Rx, and set the corresponding price at $59 per Rx, earning a contribution to the repayment of its research and development outlays and to its profits measured by the rectangular area (59-18)(410,000) = $16.8 million per month.

If it must charge a uniform price in every national market, the drug's producer recognizes that at the price maximizing profits in Nation A, it can sell nothing in low-income Nation B, since the $59 price is higher than the maximum $35 price any consumer

[72] Where Q is quantity consumed per month and P is the price, the inverse demand curve for Nation A is assumed to be $P_A = 100 - 0.1\ Q_A$; and the curve for Nation B $P_B = 35 - 0.035\ Q_B$.

[73] Economies of scale or cost savings through learning by doing might invalidate this assumption, strengthening incentives for parallel trade and in some cases leading to price reductions in the nations paying high prices. For vaccine production, there is evidence of substantial cost savings with high-volume production. See case study 14-98-1450.1, "Vaccines for the Developing World: The Challenge To Justify Tiered Pricing (Sequel)", John F. Kennedy School of Government, Harvard University," (1998).

in Nation B is able and willing to pay. To sell anything at all in Nation B under a uniform price policy, the firm must reduce its price in Nation A to less than $35, entailing a profit and R&D cost recovery sacrifice in Nation A of at least (59-35)(410,000) less (35-18) (240,000) (i.e., the surplus of a $35 price less marginal cost on additional sales of 240,000 Rx) = $5.76 million. This sacrifice is larger than the zero profit the firm could make at a $35 price in Nation B. For prices lower than $35, it can be shown, the sacrifice in Nation A also exceeds the gain in Nation B, given the assumed demand functions.[74] Thus, if forced to charge a uniform price, the firm will not sell in Nation B.

If, however, it can engage in price discrimination, the firm will find it profitable to sell in both markets. It will derive its marginal revenue curve MR_B in national market B, equate marginal cost with marginal revenue at an output of approximately 243,000 Rx, and set a much lower $26.50 price, which maximizes profits in Nation B. Relative to selling only in Nation A, this is clearly profitable for the drug's producer. It contributes incrementally to the firm's profits and R&D cost recoupment by (26.50-18)(243,000) = $2.07 million. Relative to the no-sales-in-B case, it is also beneficial to the citizens of Nation B, adding consumers' surplus measured by the dot-shaded triangular area, or approximately $1.04 million per month. Ignoring any fixed costs that might be incurred setting up a sales outlet in Nation B, the drug producer will find it worthwhile to sell at a relatively low price in Nation B as long as at least part of Nation B's demand curve lies above the marginal cost line -- a condition, to be sure, that may not be satisfied in the very poorest nations.

Thus, under the not implausible conditions assumed here, both LDC consumers and the drug producer are better off with price discrimination than under uniform pricing. Although not valid under all plausible conditions, this case is typical of a broader range of economic situations conducive to what is called Ramsey-Baumol-Bradford pricing, or more

[74] If demand for the drug at relatively low prices in Nation B were many times higher than demand at the same prices in Nation A, an exception to this uniform price case could arise, and profits would be maximized by selling in both markets at a price much lower than the price that maximizes profits in Nation A.

simply, Ramsey pricing.[75] In the classic formulation, it is necessary to recover a substantial block of fixed costs (e.g., for research and development) by setting prices in a diversity of markets with differing demand elasticities. It can be shown that the most efficient solution is one in which prices are elevated above the marginal costs of production more, the less elastic demand is in any given market. "Most efficient" in this sense means that the fixed costs are recovered and the sum of producer's surplus (e.g., contributions to fixed costs and profits) plus consumers' surplus (i.e., the amount consumers are able and willing to pay, less what they actually pay) is maximized.[76] Discriminatory pricing along Ramsey lines approaches as closely as one can reasonably hope to an ideal price-setting method in an intrinsically imperfect world.

Parallel trade is relevant to this analysis because it takes advantage of the fact that prices are set lower in some markets than in others, reallocating output from the low-price markets to the higher-price markets. Its consequences are analyzed in Figure 3, which reproduces Figure 2(a) with additional assumptions. It is assumed that 15,000 units of output (Rx) are diverted monthly from low-price Nation B to high-price Nation A. This shifts the demand curve remaining to be satisfied locally in Nation A to the left by 15,000 units, yielding the new, more elastic demand curve D*. The drug producer confronted with this change in demand conditions will reconsider its pricing decision, deriving marginal revenue MR* and maximizing profits by equating revised marginal revenue with marginal cost at an output of 335,000 Rx, leading to the reduced price of $51.50 -- which is still high enough to attract parallel imports from Nation B. The drug producer's contribution to profits and R&D cost reimbursement in national Market A is reduced by the dot-shaded L-shaped

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[75] The relevant theory, attributable to Frank P. Ramsey (1903-1930), was brought back to the forefront of interest after long neglect by Baumol and Bradford, (1970), pp. 265-283. The simpler version analyzed here was actually proposed in 1839 by a railroad engineer, Charles Ellet Jr., in An Essay on the Laws of Trade (New York: Kelley reprint, 1966). In transportation circles it has been called "value of service" pricing. Its application to the parallel trade aspects of drug pricing has been proposed *inter alia* by Yarrow, (1995) in Towse, ed., (1995), pp. 1-11; and Danzon, (1997), Chapter 7.

[76] Under the form of Ramsey pricing proposed for regulated utility price-setting by Baumol and Bradford, the regulator can squeeze the producer's profits down to the point at which only normal returns on investment are realized. When profits are subjected to such a squeeze, the so-called Ramsey number has a value less than unity. When firms are allowed to engage in price discrimination of the type illustrated here with no profit constraint, the Ramsey number has a value of unity, in which case it conforms to the model originally proposed by Ellet in 1839.

area in Figure 3, whose magnitude is (59-51.50) (410,000) + (51.50-18)(75,000) = $5.59 million. Recognizing that parallel exports from Market B are significantly eroding its surplus in Market A, a rational drug producer will reduce the quantity it offers for sale in Nation B. This will lead to some combination of decreased supply to and reduced parallel exports from Nation B, the first effect implying (absent ceiling price regulation) a price increase in Nation B. Consumers in Nation B are made worse off by this reaction, at least by the reduction in quantities available domestically and also (absent price controls) by an increase in domestic prices. If the drug producer recognizes that it cannot control the quantities obtained by Nation B's parallel exporters and that the parallel export process will progress to such an extent that perfect arbitrage occurs, the situation reverts to the uniform price case discussed previously. And under the demand conditions postulated, forced to accept a uniform price, the drug producer will maximize its profits by ceasing to supply low-income Nation B altogether.

It follows that, absent complications ignored thus far, low-income nations are likely to receive patented pharmaceuticals at lower prices when drug producers engage in cross-national price discrimination than when parallel trade arbitrages price differences and forces prices toward uniformity. For those who are concerned, as we are, about achieving the largest feasible supply of life-saving, debility-reducing drugs to less-developed nations, parallel trade can plausibly be seen as doing more harm than good. Its encouragement within the European Common Market must be interpreted as a consequence of the desire to make pricing within the market more uniform for its own sake, sacrificing the welfare of some consumers in lower-income member nations.[77]

Evidence on the Pricing of AIDS Drugs

It is useful to pause at this point and ask whether multinational pharmaceutical firms have in fact engaged in Ramsey pricing strategies across the various nations, rich vs. poor,

[77] See e.g. Darba and Rovira, "Parallel Imports of Pharmaceuticals in the European Union," (1998), pp. 129–136.

of the world.[78] That they have done so in the pricing of vaccines is well documented.[79] To shed new light on this question we have obtained from IMS, the leading collector of data on pharmaceutical product sales, detailed information on sales revenues and quantities sold for 15 AIDS anti-retroviral drugs in 18 nations or national groups, all with low or intermediate per capita incomes, over the years 1995 through 1999. The nations or national groupings comprise Argentina, Brazil, Central America, Chile, Colombia, the Dominican Republic, Ecuador, French West Africa, India, Indonesia, Malaysia, Mexico, Peru, the Philippines, South Africa, Thailand, Uruguay and Venezuela. The data cover wholesale transactions, usually on sales to retail outlets, although for four nations (Indonesia, the Philippines, Thailand and South Africa), sales to hospitals are also included. The reported wholesale sales revenue of each product sold in each national market in any given year was divided by quantity sold to obtain average price realizations for standardized dosage forms—expressed here as the price paid for a standard daily dose. For the analysis that follows, these standardized prices were expressed as a ratio of Red Book wholesale list prices for the same products in the United States. These will be called US price relatives. The published Red Book prices, it must be emphasized, do not necessarily reflect the prices at which actual transactions occurred. During the past decade there has been extensive discounting off wholesale list prices on drug sales to U.S. hospitals and health maintenance organizations as well as on transactions reimbursed under the government's Medicaid programme and by pharmaceutical benefit management intermediaries.[80] Discounts in the range of 15–25 percent are not unusual. Thus, a US price relative of 0.80 should be interpreted as implying rough parity with actual transaction prices prevailing in the United States.

Data were available for a total of 586 nation-product-year triplets. Of these, 461 were supplied by clearly identifiable multinational pharmaceutical companies. Some of the remaining 125 US price relatives may have come from companies that were acting as agents to multinational enterprises; others were known to be locally-owned companies. Our

[78] Research assistance for this section from Joan-Ramon Borrel, post-doctoral fellow at Harvard University, is gratefully acknowledged.

[79] See the John F. Kennedy School of Government case study, "Vaccines for the Developing World" (1998).

[80] See Scherer, (1997), pp. 239–256; U.S. General Accounting Office, (1997); and Doonan, (2001).

analysis here focuses on the pricing policies of the known multinationals. However, a preliminary analysis was conducted to determine whether there were discernible differences between known multinational and other company prices. In a regression equation, the price relatives (again, the ratio of a sample company's price to the comparable US list price) were found to be about 20 percent higher for multinational enterprises than those of companies not identified as MNEs, controlling also for the general molecule type and whether hospital sales were included in the transaction data. The relatively new protease inhibitors were, as expected, significantly more expensive, with a price relative premium of 0.25 above reverse transcriptase inhibitor (RTI) drugs. This difference was 31 percent of the overall sample mean price relative. Non-nucleoside RTIs were insignificantly more expensive than nucleoside analogue RTIs—the latter group including AZT, the first effective anti-AIDs drug.

Our basic question is: do the prices of multinational pharmaceutical companies exhibit patterns suggesting Ramsey pricing? If they do, we should expect to find systematically lower prices or price relatives, the lower GNP per capita is in a sample nation. Since even the most affluent nation in our sample had GNP per capita less than one-third the GNP per capita in our benchmark price nation, the United States, and since the average across all sample nations was roughly one-eighth US GNP per capita, we should expect the price relatives in our sample to be less than the 0.80 value that would (taking into account off-list discounts) imply parity with US pricing.

Figure 4 provides preliminary insight. It arrays all 461 price relative data points for the multinational companies, distinguished by year, against the sample nations' GNP per capita, expressed in contemporary purchasing power parity terms.[81] There is only a faint indication of a systematic income-correlated pattern. The average price relative is 0.847, indicating that prices in our sample of nations were approximately equal on average to presumed U.S. transaction prices. However, in 98 out of the 465 cases, they were higher than the U.S. list price parity value of 1.0, sometimes very substantially. The simple

[81] The source is the World Bank's *World Development Indicators Database*, available on the worldwide web.

correlation between the price relatives and GNP per capita was +0.212, which is significantly different from zero at the 99 percent confidence level. Pricing did conform in a crude way to the Ramsey predictions, but with a great deal of variation about central tendencies. Squaring the correlation coefficient, we find that the GNP variable "explains" only about 4.5 percent of the variance in price relatives.

Figure 5 provides a more aggregated view of the same data. It correlates against GNP per capita the average price relatives experienced by the various nations during 1999. The price relatives are weighted averages of individual product price relatives, with the weights being the number of daily doses sold for each product. Here the tendency for prices to rise with GNP per capita is more visible, although the simple correlation is only +0.285 -- not much higher than the correlation obtained with disaggregated data. Relatively wealthy Uruguay is found to have paid the highest average prices; middle-income Brazil the lowest prices.[82]

To gain further insight into pricing patterns, we use multiple regression analysis. But first we must confront a methodological problem. Any statistical analysis can be distorted by observations known as "outliers" that is, data points whose values depart by an unusually great amount from the mass of observations. The most extreme of these, we see in Figure 4, imply overseas prices four to five times as high as counterpart US prices -- prices that, absent restrictions on parallel trade, would create strong incentives for parallel imports from the United States or a fortiori lower-price nations. These high values could be the consequence of some special market circumstances, or they may have resulted from the data reading or coding errors that invariably invade complex real-world data sets. The best way to deal with such "outliers" is to exclude values beyond some plausible threshold value, but to check the sensitivity of the results to the exclusions. In the analysis that follows, we exclude the 13 relative price observations exceeding 2.0. Sensitivity tests including all observations and, alternatively, deleting the 23 relative price observations with values exceeding 1.5, yielded qualitatively identical results.

[82] For a probable explanation of the low Brazilian price relatives, see Tina Rosenberg, "Patent Laws Are Malleable: Look at Brazil," New York Times Magazine, January 28, 2001, pp. 28–31.

Multiple regression analysis was used to determine how price relatives PRICE were influenced by national GNP per capita, taking into account other plausible variables that might have been expected to influence local pricing. In addition to a variable YEAR (last two digits only) distinguishing the year for which price relatives were recorded, the following explanatory variables were used:

PROT — Dummy variable with value of 1 if the molecule sold was a protease inhibitor; otherwise zero. (Mean value = 0.23)

NONNUC — Dummy variable with a value of 1 if the molecule sold was a non-nucleoside RTI; otherwise zero. (Mean value = 0.043)

INCOME — National GNP per capita at purchasing power parity exchange rates (in thousands of US dollars). (Mean value = 3.635)

MAGHIV — Conservatively estimated number of persons infected with HIV in the nation in a given year (measured in logarithms to the base 10 of the number of cases, in thousands). (Mean antilog value = 187,000)

HOSP — Dummy variable with value of 1 if hospital sales are included in a nation's transaction data. (Mean value = 0.286)

PATENT — Dummy variable with value of 1 if the relevant nation granted patent protection on drug products at the time the relevant molecule was patented in the United States; otherwise zero. (Mean value = 0.395)

The regression equation utilizing 448 observations on these variables, with t-ratios presented in subscripted brackets, is as follows:

(1) PRICE = 8.04 + 0.142 PROT + 0.159 NONNUC + 0.018 INCOME

[7.68] [4.59] [2.51] [2.77]

-0.044 log MAGHIV - 0.074 YEAR - 0.072 HOSP - 0.077 PATENT;
[2.01] [6.93] [2.21] [2.46]

$R^2 = 0.224$; N = 448.

Consistent with the Ramsey pricing hypothesis, price relatives increase with GNP per capita. The relationship is statistically significant at the 99 percent confidence level, although it cannot be said to be strong. An extra $1000 in income per capita adds 0.018 to the price relatives (whose average value, again, was 0.847). The newer protease inhibitor and non-nucleoside RTI molecules are sold at higher price relatives than older drugs such as AZT. The coefficient on the MAGHIV variable is significantly negative, revealing lower prices in nations with large numbers of HIV cases. This could be due to economies of scale in providing drugs to those markets, the tendency for generic competition to be more vigorous in larger markets, or to drug companies' compassion in providing economical therapy for severely impacted nations. The effect is of modest magnitude; a tenfold increase in HIV incidence leads to a decline of 0.044 in the price relative. Prices are lower on average when sales to hospitals are included along with sales to retail outlets. The explanatory variable with the highest t-value is YEAR, indicating that with each passing year from 1995 to 1999, HIV drug price relatives fell by about 0.074, or by about 8.7 percent relative to their mean value. We return to this finding momentarily.

We expected a positive sign on the PATENT variable, but it is significantly negative. The variable is poorly measured; it tells only whether product patent protection was available in the subject nation, not whether it was actually sought for any given molecule (on which we have no information). The negative sign may also reflect complex interrelationships with other variables, e.g., the relatively high-priced molecules that entered the market late were more apt to emerge after drug patent rights were authorized under changing national laws. But for the present this persistent result must be considered anomalous.

The YEAR variable is particularly interesting. Holding all the other variables at their means and taking into account their effects, given the estimated regression coefficients, we arrive at the following price relative predictions for various covered years:

1995	0.974
1996	0.901
1997	0.827
1998	0.753
1999	0.679

Thus, to the extent that the multinational companies were consciously charging less in the relatively low-income nations covered by our sample, as implied under a crude Ramsey pricing strategy, it would appear that the phenomenon is a new one. They priced above parity to presumed United States transaction prices on average in 1995 (assuming an average discount of 20 percent from Red Book prices) but reduced average prices to below those of US counterparts by 1998 and 1999.

Additional light is shed on the relationships by reconfiguring the regression equation to introduce YEAR only as an influence interacting multiplicatively with the GNP per capita variable INCOME, i.e., as INCOME x YEAR. The resulting regression equation is as follows:

(2) PRICE = 0.819 + 0.122 PROT + 0.140 NONNUC - 0.039 log MAGHIV
[14.63] [3.90] [2.17] [1.73]

- 0.100 PATENT - 0.067 HOSP + 1.273 INCOME - 0.0128 INCOME x YEAR;
[3.24] [2.01] [5.00] [4.91]

R^2 = 0.190, N = 448.

The coefficients for most of the variables are similar to those of regression (1) above. But now we find a strong positive income effect, offset by a negative interaction of income with time. These relationships are most easily interpreted with the help of a graph, Figure 6, which plots the predicted values of the price relatives for diverse values of the GNP per capita variable by year. What we find is that in 1995, consistent with the Ramsey pricing theory, relative prices rose with GNP per capita. But as time passed the systematic relationship became increasingly weak, so that by 1999, there is virtually no evidence of a rise in prices with increasing national affluence. The statistical "fit" of equation (2) is inferior to that of equation (1), revealing that the general relative price decline story is more compelling than the abatement of Ramsey pricing story, although both analyses add insight.

The evidence available from our sample of HIV anti-retroviral is at best weakly consistent with the proposition that multinational drug companies were pursuing a Ramsey pricing strategy between 1995 and 1999. The preponderant impression is one of much randomness among prices charged in low- and moderate-income nations relative to those quoted in the United States. To the extent that there were systematic patterns, a weak correlation between national price relatives and GNP per capita eroded during the late 1990s, implying a departure from sophisticated Ramsey pricing, while there was a stronger movement over time permitting the nations in our sample to benefit across-the-board from price concessions relative to prices prevailing in the United States.

In the years 2000 and 2001, which are not covered by our statistical sample, multinational pharmaceutical companies began offering very substantial AIDS drug price discounts to some low-income nations.[83] Whether these recent developments will lead to a world price structure more closely resembling what would emerge under Ramsey pricing remains to be seen.

[83] See "Africa's AIDS War," New York Times, March 10, 2001, p. 1; "South Africa May Cite Crisis To Lower Cost of AIDS Drugs," New York Times, March 12, 2001, p. A3; "Maker Yielding Patent in Africa for AIDS Drug," New York Times, March 15, 2001, p. 1; "6 Companies in New AIDS Pact," New York Times, April 6, 2001, p. C12; and "Lifting the Curtain on the Real Costs of Making AIDS Drugs," New York Times, April 24, 2001, pp. C1 and C10.

Complications

We return now to our theoretical analysis, addressing some complications ignored in the basic analysis. They may help explain the diversity of results obtained in our examination of real-world HIV drug data.

One is suggested by a possible mismatch between the theory and some salient facts. If systematic price discrimination works to the benefit of lower-income nations, but generates incentives for the products sold at low prices in those low-income nations to be re-exported to high-income, high-price nations, why does a relatively poor nation such as South Africa adopt policies encouraging parallel imports? An answer could be that for some drugs (although not, from the evidence in Figure 5, the principal HIV anti-retroviral), the multinational drug companies do not set their wholesale prices on the unambiguous assumption that South Africa is a low-income nation. Income in South Africa is unusually unequally distributed; a small minority enjoys industrialized nation income levels while most of the population is poor. The affluent minority tends also to have comprehensive health insurance that covers *inter alia* prescription drug purchases. Under these circumstances, demand conditions in South Africa are best portrayed in Figure 7 by the kinked demand curve D_1D_2, the upper segment representing the demands of well-off citizens and the lower segment those of the poorer majority. The corresponding marginal revenue function begins as MR_1 and then jumps at point F to MR_2. There is a uniform-price local profit-maximizing equilibrium that entails selling to both consumer groups at a price of $24 per Rx, at which price 240,000 Rx are filled monthly. However, the drug supplier finds it more profitable to sell only to the more affluent minority.[84] Thus, a price of $59 is set, leading to the sale (only in Market 1) of 102,500 Rx per month.[85] Profits under this high-price strategy are (59-18)(102,500) = $4.2 million per month, compared to (24-18)(240,000)

[84] The situation here is quite similar to what happens after patents expire in a wealthy nation, such as the United States and the original drug producer, with a brand image that commands sales from loyal and risk-averse prescribing physicians, finds the market for its chemical entity bifurcating into low- and high-elasticity segments. See Scherer, (1996), p. 377.

[85] The price here is identical to that charged for Nation A in Figure 1 because the demand function is linear and pivoted inward from a vertical intercept value of 100. With constant marginal costs, such demand curve shifts yield unchanged prices.

= $1.44 million with the low-price strategy. Market segmentation of this sort apparently engendered incentives for parallel imports of some drugs by South Africa from middle-income nations, such as Spain and Portugal.[86] In such cases, parallel trade confers upon low-income nations benefits in the form of reduced prices to affluent consumers and perhaps, but with less certainty, the possibility that some less affluent citizens will be able to afford the drug.

Second, the demand functions confronting pharmaceutical makers may not be simple straight lines, as assumed thus far. Economic theory textbooks often assume for reasons of mathematical tractability demand functions to be of a curvilinear form known as Cobb-Douglas. Figure 8(a) shows the demand relationships that would exist with the simplest Cobb-Douglas demand curves, assuming a consistent income elasticity of unity (i.e., a 100 percent increase in per capita income leads to a 100 percent increase in consumption, all else equal) and constant price elasticities of -1.3. In such cases, since the demand curves have the same price elasticity at all relevant points, the same profit-maximizing price prevails regardless of the assumed income elasticity for example, with marginal costs of $10 per unit, the same $43.15 price will be set in every market. In this special case, no price discrimination will be observed. It is not necessary, however, to have invariant price elasticities with demand curves of the general shape shown. Figure 8(b) illustrates an alternative case in which the price elasticity (the exponent of the P variable, in parentheses) becomes lower in absolute value with higher per capita income. In this case, profits will be maximized by setting lower prices in the markets with lower incomes. Real world demand curves probably have shapes somewhere between the extremes of Figure 2 and Figure 8. The Figure 8 demand curves are unrealistic in implying that prices can be raised to nearly infinite levels without choking off all demand and in assuming a huge expansion of quantity demanded as prices are reduced within the lowest range of possible values.

[86] See "South Africa's Bitter Pill for World's Drug Makers," New York Times, March 29, 1998, sec. 3, p. 1. We have also benefited from conversations with a South African government official.

Third, parallel trade may occur not because prices are kept low to satisfy demand in low-income, high-elasticity nations, but because some nations, however affluent they may be, impose more stringent government controls on prices than do others. The possibilities here are quite complex, but Figure 9(a) and Figure 9(b) capture their core tendencies. We assume two nations, A and B, of equal size and with equal per capita incomes and the same straight-line free-market demand curves as those assumed for Nation A in Figure 2. Absent price controls and parallel imports from less-affluent nations, a rational firm enjoying patent protection in both nations on some more or less unique drug would set prices at the identical $59 level in the two markets. Now suppose the government of Nation A sets a $40 ceiling price in its home market. Readers with only a faint exposure to economic theory may be surprised to learn that, because the price ceiling nullifies a monopolist's ability to gain by restricting output, the drug producer has an incentive to expand its supply in the price-controlled market so that the full demand of 600,000 Rx per month at the $40 price is satisfied.[87] The immediate implication of such controls is to reduce market A's contribution to the drug producer's fixed R&D costs and profits by the amount of the rectangle (59-40)(410,000) less the (necessarily smaller) rectangle (40-18)(190,000), or by a total of $3.61 million. Thus, consumers in the price-controlled market pay less than their Ramsey-efficient contribution to the coverage of R&D costs.[88] If such controls are expected to be applied on future (i.e., new) products, R&D investments are likely to be cut back.[89] If on the other hand the controls are believed to be "one off" and not imposed on future products, the reduction in profits represents pure expropriation with few direct R&D investment implications.

The difference in prices between national markets may lead to parallel exports from Nation A to Nation B. If (paralleling the analysis of Figure 3) 15,000 units are transferred to Nation B, the demand curve in Nation B (Figure 9(b)) will be shifted to the left and, after

[87] An early proof of this proposition is found in Robinson, (1934), Chapter 13.

[88] The negative contribution impact might be reduced if, under the Dorfman-Steiner theorem, lower profit margins lead to lower expenditures on advertising and other forms of product promotion, such as direct company-to-physician "detailing."

[89] For the analytic apparatus needed to demonstrate this point, see Scherer, (1996) pp. 364–366.

new marginal revenue calculations are completed, the price in Nation B will be reduced from $59 to e.g. $51. Consumers in Nation B benefit, but there is a further reduction (dot-shaded area) in the contribution to the producing firm's profits and R&D reimbursement. From our analysis of Figure 3, we know that this reduction amounts to $5.59 million per month. What happens then in Nation A depends upon how the drug producer reacts to the product diversions of its middlemen. If it increases output by 15,000 units monthly to keep Nation A's market fully satisfied, there are no further ramifications, although the additional profit contribution RUVS in Nation A ((40-18)(15,000) = $330,000) partly (but less than fully) compensates the loss of profits (dot-shaded area) from the impact of parallel imports on prices and quantities in Nation B. If (more plausibly) it restricts its supply to less than 600,000 Rx (needed to satisfy demand in Nation A) plus 15,000, and if 15,000 units continue to be diverted to the higher-price market B, there will be "shortages" in Market A that is, supply in Market A will be less than the 600,000 units demanded. The welfare consequences of those shortages depend upon the mechanism used to ration scarce drug supplies among consumers willing and able to purchase them. It is not implausible that some consumers to whom the drug has very high value for example, the consumer located at point J on Nation A's demand curve -- will be deprived.[90] If so, substantial losses of consumers' surplus in the price-controlling nation can occur.[91]

The correlation of prices with per capita income may also deteriorate when nations use a method of price controls known as external reference pricing, setting local price ceilings on the basis of prices observed in other (notably, low-price) nations. In this case, drug producers rationally fear that charging lower prices in low-income nations could rebound to hurt them by influencing prices in more affluent nations imposing such price controls. This could happen even if the external reference pricing is not linked to a formal price control system, for example, when drug procurement officers or politicians in the high-price jurisdiction insist, "You're setting much lower prices in low-income nations; you

[90] Unless black markets materialize, in which case matters become even more complex.

[91] This inference depends upon the assumption that ability and willingness to pay measure the social value of a drug's provision -- a debatable proposition. However, absent a rationing system that reliably allocates scarce supplies to those most "in need," it remains true that appreciable welfare losses ensue.

should do the same for us or we will make your life unpleasant here." In either situation, willingness to offer lower prices in less affluent nations will be curbed.

Implications

To sum up, there is much to be said for price discrimination in multinational drug markets. Setting prices lower in low-income nations than in high-income, low price elasticity markets achieves two desirable ends -- it helps low-income nations' consumers obtain vital drug supplies, and it enhances drug producers' net revenues, which, if accurately foreseen, stimulates investment in research and the development of new drugs. To the extent that parallel trade interferes with the attainment of these results, there is reason to discourage it. A nuanced policy that makes the best of an inherently imperfect situation is likely to have the following characteristics:

1) To encourage the low-price provision of drugs to low-income nations, low-income nations should be allowed to bar parallel exports of drugs received at preferential prices. Pharmaceutical manufacturers should be given the legal means to discourage parallel importation into high-income markets of the patented drugs they have sold at lower prices in nations identified as less-developed under United Nations criteria.

2) To reduce the adverse consequences from multinational drug providers' niche-pricing strategies, parallel imports into low-income nations should be allowed.

3) To reduce the product misallocations and impairment of research and development capacity caused by price controls in affluent nations, parallel exports would not be permitted from price-controlled jurisdictions. High-income nations should also agree not to base the prices they allow under their price control regimes on the prices observed in low-income nations, that is, to limit the geographic scope of any external reference price-based controls. Since foregoing external reference pricing may not be in the interest of high-income nations, an international covenant may be required to achieve this desirable result.

6.3 Price Controls

Many countries, developed and developing, regulate the prices of pharmaceutical products. The primary objective of price control programmes is to make drugs affordable to the local population and control public expenditures on drugs. However, some nations also use price control programmes to achieve secondary industrial policy objectives, such as encouraging local investment, employment or R&D conduct within their jurisdictions (Danzon, 1997). Controls on producer prices of pharmaceuticals have been conveniently classified into three categories (WHO, 1997):

1. *Cost-plus pricing*: Prices are fixed product-by-product based on the costs of production and distribution, with "reasonable" profit margins added.
2. *Reference pricing*: Product-by-product maximum price reimbursements or price ceilings are based on prices of comparable products, either in other similarly-placed countries (external reference pricing) or in the same therapeutic class within the national market (internal reference pricing).
3. *Profit-based price controls*: Ceilings are placed on profits or returns on capital invested for each pharmaceutical company, taking account of the company's R&D expenditures.

In most developed countries, with the notable exception of the United States, pharmaceutical expenditures are covered extensively by public health insurance. Even in the United States, out-of-pocket expenses fell from 54 percent of the total national outpatient drug expenditures in 1987 to 29 percent in 1997 (US General Accounting Office, 1999). In OECD countries as a group, almost 75 percent of pharmaceutical expenditures are reimbursed in some way (OECD, 2000, 4). With the power to include or exclude new drugs in formularies for authorized or reimbursed drugs, national authorities can negotiate lower initial prices, or extract assurances that prices will not be raised above the introductory levels. Some, like the United Kingdom, also impose profit controls. Canada has a Patented Medicines Price Review Board that closely monitors the prices of patented medicines through external reference pricing and takes steps to check "excessive" pricing. Australia, New Zealand and since 1989 Germany set reference

prices for reimbursement of the cost of medicines, using the prices of similar medicines within the therapeutic group to do so. Maximum reimbursement limits are set, and if a choice is made for a higher-priced drug, the difference has to be borne by the patient. [92]

In contrast, few developing countries have universal public health insurance schemes or public drug reimbursement systems. Government hospitals and dispensaries are chronically under-financed and suffer from drug shortages. Private health insurance, where available, benefits only a small proportion of the population. In addition, governments have weak infrastructure to monitor costs of production or prices. Despite these problems, some developing country governments have attempted to regulate prices, typically using cost-plus methods. We draw from two country experiences: Colombia and India.

Colombia attempted comprehensive control of drug prices beginning in 1968. After many changes, Colombia focused in 1992 on "critical drugs", defined as those with fewer than five suppliers. These comprised about 20 percent of total pharmaceutical supply. The manufacturers of these drugs had to inform the government in advance of price changes. Government price monitors could require cost data and impose the price they deemed appropriate. However, because it lacked the capacity to follow price changes, Colombia returned in 1994 to cost-plus pricing, setting a ceiling price of 3.4 times the production cost (WHO, 1997, 58). It is not clear whether this generous limit of 240 percent over production cost would reduce prices from profit-maximizing prices otherwise set by producers.

India has one of the most extensive pharmaceutical price control regimes among developing countries. Until changes were implemented in 1995, over 70 percent of the total pharmaceutical market was under price control (Redwood, 1994, 4). Even after the new Drugs Prices Control Order (DPCO) of 1995, 50 percent of the market remained under price control (Lanjouw, 1998). Prices are fixed for each dosage form and pack size

[92] A study of the change in Germany from a flat fee per prescription to this reference pricing system showed that producers reacted by lowering prices by 10 – 30 percent. See Pavcnik (2000), NBER.

for the bulk drugs selected for price control by the government.[93] Under Section 7 of the DPCO 1995, the maximum retail price calculation for a pharmaceutical formulation under the cost-plus method is as follows:

Retail Price = (MC +CC + PM + PC) * (1+ MAPE/100) + ED, where

MC = Material cost, including bulk pharmaceuticals used and allowance for wastage,

CC = Conversion cost: labor, energy, R&D, etc.

PM and PC = Packing materials and packing charges

MAPE = Maximum allowable post-manufacturing expenses, including distribution and retail margins (100% at present) [94]

ED = Excise duty

Under the new drug policy announced at the end of 1994, a drug is subject to price control if its annual turnover in the audited retail market is more than Rs. 40 million (approximately $900,000 at current exchange rates). Drugs with turnover above this minimum revenue level may be exempted if there are at least five bulk producers and at least 10 formulators, none with more than 40 percent of the audited retail market. Any bulk drug with a turnover above Rs. 10 million (or $200,000), with one formulator supplying 90 percent or more of the market, is also subject to price control. Given this last criterion, *all* patented pharmaceuticals would be subject to price control unless they are widely licensed -- an unlikely scenario.[95]

Lanjouw (1998) surveys the on-going disputes between the government in India and the industry over DPCO criteria, data provision, definition of wastage, etc. and

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[93] In addition to price ceilings, maximum returns are also fixed at 18 percent on net worth (defined as paid-up share capital plus free reserves readily deployable surpluses) or 26 percent on capital employed, where production is from the basic bulk drug manufacturing stage. This part of the DPCO has not come into operation, as no firm's profitability comes close to these limits (Lanjouw, 1998).

[94] The previous 1986 drug policy allowed only 75 percent margins for essential drugs required under national health programmes.

[95] There is a possibility that patent owners may defeat the purpose of the DPCO by licensing several small formulating units, selling the bulk drug to them, thus effectively controlling the final sale price.

identifies a general lack of cooperation by industry in the price control exercises. Under these circumstances, further reduction of the profit margins under MAPE is not a realistic option. In addition, in the case of an imported formulation,[96] a maximum MAPE of only 50 percent of the landed cost (c.i.f. price plus customs duty and clearing charges) is allowed. This, however, is probably not an effective way to counter the manipulation of sale prices between the parent multinational company and its local subsidiary, since the landed transfer price can usually be raised to offset price regulators' actions.

Developing countries must strike a fine balance between lower prices and availability of patented medicines. A strictly enforced price control regime may scare away potential manufacture of patented pharmaceuticals within the country, or even lead to a decision not to supply the market through imports. On the other hand, if the price controls are typically lax, the administrative costs of establishing and maintaining an effective price control regime over *all* patented pharmaceuticals may outweigh the benefits. Even assuming that costs can be correctly ascertained and prices fixed on a cost-plus basis, the experience of India and Colombia in monitoring costs and enforcing prices has been poor. The alternative external or internal reference pricing method may be ineffective for a developing country that does not have extensive public health insurance coverage or public expenditures on drugs. However, simulating price controls by applying the Indian formula to 1994 price data shows that such controls, where effective, do leave consumers better off while leaving patent owners only negligibly worse off. Price decreases for widely used patented pharmaceuticals that have few substitutes increases consumers' surplus significantly (Watal, 2000). Thus, selective cost-plus price controls on a few patented medicines in developing countries, with relatively strict limits on distribution and profit mark-ups (i.e. with Indian, not Colombian, mark-ups), may work towards maintaining a satisfactory balance between benefits and costs. In addition, as seen in the previous section, parallel imports from price-controlled jurisdictions in the developed world may allow countries to benefit from whatever monopsony power they might possess. The threat of compulsory licensing can also enhance nations' bargaining

[96] A more likely scenario, as TRIPS now obliges non-discrimination on patent rights between imported and locally produced products.

power. With the increasing introduction of private and public health insurance schemes in the developing world, some nations may be able to use reference-pricing systems.

6.4 Drug donations and international assistance for drug procurement

When the potential recipients of drug therapy have too little income to purchase a needed drug even at discriminatory prices close to the marginal cost of production, pharmaceutical companies sometimes provide their products through outright donations. In 1998, four drug companies led the list of leading corporate philanthropists in the United States.[97] Many of their contributions were for purposes other than providing medicines in kind, and most went to domestic rather than international causes. However, more detailed data reveal an impressive history of in-kind medicine donations to less affluent nations. Merck of the United States set an example in 1987 by announcing that it would donate, rather than sell, its Ivermectin drug, effective against the worms that cause river blindness, for use in needy nations. Between then and 1998, nearly 25 million individuals were treated with the donated drug.[98] Over the years 1970 to 1999, Merck reported total product donations (including other drugs) valued at more than $235 million.[99] Other important drug donation programmes include the provision of the anti-malaria drug Malarone by Glaxo Wellcome, the antibiotic Zithromax by Pfizer, and the anti-elephantisis drug Albendazole by SmithKline Beecham.[100]

Under the tax laws of the United States, which is the only nation for which we have detailed information, donations sometimes permit sufficient tax savings to entail little or no out-of-pocket cost to the drug manufacturers. For charitable donations in general, corporations can take the accounting cost of the good donated as a deduction against net income on which the corporate income tax is levied. Suppose, for example, a company

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[97] "The List: Corporate Giving," Business Week, January 24, 2000, p. 8.

[98] See Peter Wehrwein, "Pharmacophilanthropy," www.hsph.harvard.edu/review/summer_pharmaco.shtml.

[99] From the Taft Group, "Top 10 Givers in the Top 9 Categories - 1999," www.taftgroup.com/taft/topnews, October 27, 2000.

[100] Wehrwein, op. cit.

donates to an appropriately accredited charitable organization drugs whose accounting cost is $100,000. Taxable income is reduced by the amount of that cost. Since the marginal corporate income tax rate for a large and profitable corporation is 34 percent, the deduction entails a tax saving of 0.34 x $100,000 = $34,000, which only partly offsets the cost of the products donated. Although, as we shall see, this may be too pessimistic a view of the company's net sacrifice, it would appear that the donor must expend more on production than its tax saving in making the donation.

There is an alternative tax provision, however, with more interesting implications. Under Section 170(e)(3) of the US Internal Revenue Code, special deductions apply for donations to qualified charitable organizations when the donated property is used by the donee "solely for the care of the ill, the needy, or infants." To qualify under Section 170(e)(3), drug products must also satisfy applicable regulations issued by the Food and Drug Administration, which means *inter alia* that their remaining shelf life must not be too short.[101] For drugs subject to these special provisions, the donor can take a deduction against taxable income equal to the accounting cost of the product donated plus one-half of the so-called "step-up," that is, the difference between the fair market value of the product and its accounting cost, provided that the deduction cannot be more than twice the accounting cost of the product.[102] The total of such deductions is limited to 10 percent of total taxable corporate income.

To illustrate, suppose a pharmaceutical manufacturer donates drugs whose accounting cost is $1000 and which are normally sold in the US market at a net wholesale price of $4000. The amount deductible from pre-tax corporate income is $1000 + 0.5 ($4000 - $1000) = $2500. Ignoring the two-times cost cap, the tax saving would be 0.34 x

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[101] Reich et al. (1999) report that pharmaceutical companies sometimes use their donation programmes as a method of inventory management, and that roughly 30 percent of the donated drugs surveyed by a Harvard University team had expiration dates less than one year from the time of shipment.

[102] The "one-half" fraction will be called a step-up factor in our subsequent analysis. For fairly understandable explanations of a complex subject, see Merten's Law of Federal Income Taxation (Deerfield, IL: Clark Boardman Callaghan: 2000), p. 31-194; and CCH Federal Income Tax Code and Regulations, 1998/1999 loose-leaf version, para. 11,675.0204.

$2500 = $850. However, the cap applies here, so the deduction can only be $2000, and hence the tax saving is 0.34 x $2000 = $680. With tax savings of $680 and a product cost of $1000, it would appear that the company incurs net out-of-pocket costs of $320 in making its donation.

However, this mildly pessimistic conclusion ignores that fact that costs as computed by tax accountants are not the same as marginal or incremental costs as computed by economists. In producing the extra units of product needed for its donation, the company incurs only the marginal costs of production, which are almost surely lower than the costs company accounts record in valuing the product for inventory record-keeping purposes. The "inventoriable" costs normally include in-factory costs that are more or less fixed, regardless of the production volume, and perhaps also allocations of corporate overhead costs which are invariant over appreciable changes in production volume. In the specific example at hand, the company actually increases its net after-tax profits if true marginal costs are less than 68 percent (i.e., twice the corporate income tax rate) of inventoriable accounting costs. In other words, if true marginal cost in the above example were only 67 percent of the $1000 accounting cost, the company would expend $670 out-of-pocket to produce the donated drugs and obtain a tax saving of $680.

To glean insight into the structure of drug production costs, aggregated data published by the US Census Bureau for 1992 on SIC industry 2834, "Pharmaceutical Preparations," were analysed.[103] Assuming all materials and production worker labour costs to be marginal and other reported in-plant costs to be fixed, the breakdown is as follows, in millions of dollars:

Materials costs	13,545
Production worker wages	1,867
Production worker fringe benefits	299
Subtotal: incremental costs	15,709

[103] U.S. Bureau of the Census, 1992 Census of Manufactures, Industry Series report MC92-I-28C, "Drugs" (June 1995).

Salaried employee compensation	3,083
Salaried employee fringe benefits	493
Depreciation	934
Rentals	186
Total reported costs	20,405

By these tabulations, incremental costs are roughly 77 percent of total in-plant costs -- nine percentage points too high for tax deductions to reach the level of marginal production costs. However, if companies' inventoriable costs include additional corporate overhead loadings, and especially if the drug makers produce intermediate materials in other plants and transfer them to the reporting plants at values exceeding marginal costs, which must happen frequently, true marginal costs could very easily be less than 68 percent of the costs reported for tax purposes. In such cases, pharmaceutical companies can do well, that is, increase their after-tax profits, by doing good.

The relationships among prices, inventoriable costs, and true marginal cost leading to a zero net out-of-pocket cost in making drug donations entail moderately complex nonlinearities. Figure 10 plots break-even lines under existing US tax policies and plausible changes in the tax parameters. When inventoriable costs are one-third or less of the product's normal market price, the company gains in the net whenever its marginal costs are less than 68 percent of costs used in valuing inventories for tax purposes. When inventoriable cost is higher than one-third of the normal market price, lower ratios of marginal to inventoriable costs are required to break even. All price-cost combinations southwest of the lines marked "Existing Policy" and "Step-up Factor = 0.5" yield tax savings in excess of marginal production costs. If the law were changed to allow deductions up to three times inventoriable cost, the break-even line shifts upwards so that, at high product price/cost values, donors gain in the net if their marginal costs are even slightly below book cost values. Raising the step-up factor, that is, the fraction applied to the difference between price and inventoriable cost, to 0.67 instead of the currently applicable 0.5 expands further the set of donation possibilities profitable in the net. To encourage substantially increased donation programmes, the tax laws would also have to be revised to allow corporations to

deduct more than 10 percent of their taxable income. Thus, by modifying the parameters of the tax deduction provisions, the government can increase the profitability of donations by drug companies.

To be sure, strengthening incentives for product donations by revising tax rules in more generous directions implies a sacrifice of tax revenue by the US Treasury. Why should the US government be willing to forego tax revenues when politicians are clamoring to channel existing budget surpluses into tax relief and increased "pork barrel" spending? Ignoring moral justifications as a domain into which it is hazardous for us to intrude, we can cite three other reasons. Reducing the spread of infectious diseases such as AIDS and tuberculosis on other continents has spillover benefits in reducing disease risks at home (e.g., as fewer overseas air travellers ingest resistant tuberculosis bacilli); healthier citizens in developing nations provide better markets for US high-technology exports; and better health in the Third World may lead to a lower incidence of civil strife requiring costly intervention by First World military forces.

Certainly, there are precedents for using the tax code to promote economic development abroad -- notably, the decision of the US government in 1950 to treat crude oil severance payments to the governments of crude oil-producing nations (initially, those located in the Middle East) as income taxes rather than royalties, allowing the multinational petroleum companies to take tax credits for them rather than treating them as deductible costs.[104] This permitted the oil companies to negotiate more generous revenue-sharing formulas with the oil-exporting nations, enhancing those nations' prosperity, encouraging their affiliation with the United States rather than the Soviet Union, and delaying expropriation initiatives until the 1970s. As a result of the tax credit treatment for severance payments, US-based multinational oil companies paid little or no US corporate income tax

[104] See US Senate, Committee on Foreign Relations, (1975), especially Chapter IV. At p. 81, the report cites a U.S. Department of State policy paper observing that the tax strategy could "help protect and preserve overall U.S. interests in the [Persian Gulf] area, e.g., removal of the sources of Communism and attainment of overall U.S. policy objectives such as economic and political stability, increased standards of living, and the development of Western orientation and democratic processes."

on their multi-billion-dollar profits from overseas crude oil operations during the 1950s and 1960s.

Tax incentives for drug donation can be combined with the drug procurement efforts underway in intergovernmental organizations like the WHO or UNICEF or by non-governmental organizations, like the International Dispensary Organization in the Netherlands or Action Medeor in Germany, in order that expensive patented medicines, considered essential for treatment of diseases in developing countries, be efficiently procured and distributed. These procurement efforts are largely financed by bilateral donations (i.e. donation from one country to another specified country) or from the budgets of inter-governmental organizations. The United Nations has recently estimated that $7 – 10 billion may be required annually in low-and middle-income countries to implement effective prevention and care strategies for HIV/AIDS alone.[105] In a pre-TRIPS world, the equivalents of patented medicines could be procured cheaper from countries where the patents were not effective. For example, praziquantel was procured from Korea and Egypt (Reich et al, 1995). This option can only be exercised in the post-TRIPS world under compulsory licenses, which have limitations discussed previously, or by voluntary price reductions or outright donations by the patent owner.

The lesson that we can draw is that in a post-TRIPS world, multilateral procurement of patented medicines based on aid may not fully satisfy demand unless financial commitments from developed country governments and patent owners increase dramatically. This, however, requires a radical change in the willingness on the part of developed countries to increase aid unconditionally – a willingness not seen thus far.

7. CONCLUSION

The TRIPS agreement is important. How it is interpreted and implemented may have life or death consequences for the citizens of less-developed nations. Some nations -- especially those that in the past have actively encouraged generic substitution for drugs

[105] See Declaration of Commitment on HIV/AIDS adopted at the Twenty-sixth special session of the UN General Assembly on 27 June 2001 (Document number A/S-26/L.2).

protected elsewhere by patents -- will experience a larger economic shock, compensated to some unknown degree by an increase in pharmaceutical innovation, than nations that have not pursued active generic substitution policies. But consequences will resound throughout the world health system. The intent of this paper has been to explore policies consistent with the TRIPS agreement that minimize the adverse consequences for the world's least affluent inhabitants.

In any set of future policies, generic drugs must play a crucial role. Thousands of effective medicines are available without the protection of recently or long-expired patents. Vigorously competitive supply of such drugs can do much to extend the benefits of modern pharmaceutical technology to a wider array of consumers. This is not merely an admonition, in the spirit of Marie Antoinette, to "Let them take generics." Even in the United States, whose consumers' ability to pay is great and whose respect for intellectual property is exceeded by few other nations, generics fill nearly half of all prescriptions. Many less developed nations have hurt themselves by not taking full advantage of the opportunities for encouraging generic substitution. Some labour at a disadvantage in this respect because their markets are too small and their technological resources too limited to support broad-based indigenous generic drug suppliers. For them, vigorous international trade in generic drugs must provide a solution -- inhibited, to be sure, by limited purchasing power and binding foreign exchange constraints. Policy makers responsible for setting the rules governing international trade should make every effort to ensure that trade in generic drugs is not restricted and that vigorously competitive world markets emerge.

The TRIPS agreement affects the evolution of generic drug supplies by delaying until patents have expired the opportunities for producing generic versions of the newest, most technologically advanced drugs. This is a real constraint, but it is not absolute. TRIPS allows compulsory licensing of drug (and other) patents under a specified array of conditions. To make life-saving new drugs available at affordable prices and to strengthen the development of internationally competitive generic drug industries, the compulsory licensing opportunities opened up by TRIPS should be seized selectively and imaginatively. This will require *inter alia* the creation of national regulatory and judicial institutions

ensuring expeditiously that the TRIPS rules are respected. Two issues are likely to be particularly important in determining the scope and effectiveness of compulsory licensing programmes.

For one, WTO member nations cannot simply free-ride on the research and development efforts of multinational pharmaceutical enterprises; they must pay appropriate compensation for the patents subjected to licensing. The question is, how much compensation is appropriate? It seems clear from precedents established in industrialized nations that a "reasonable" royalty is one that is higher than zero, but much less than the royalty that would compensate a patent holder fully for the loss of whatever monopoly position it might enjoy by virtue of the patent. Within that range, considerable discretion exists for national decision-makers to do what is right.

Second, as we have argued above, vigorous international trade respecting the principles of comparative advantage is essential if the smallest, least-affluent nations are to be supplied with generic drugs, among other things, under compulsory licenses. This necessity may conflict with the TRIPS requirement that compulsory licenses be issued "predominantly for the supply of the domestic market" of the authorizing nation. What "predominantly" means in this context could best be settled by multilateral negotiations, but failing that, by dispute resolution bodies of the WTO. The less-developed nations should be aggressive in pressing for expansive interpretations, and all WTO members should be sensitive to the important welfare consequences that will follow from such decisions. To ensure that full advantage is taken, multilateral mechanisms should be created to ensure that compulsory licensing orders issued by importing nations are coordinated with parallel orders issued by nations host to generic drug exporters.

WTO dispute resolution panels will also have to define more precisely when abuses of intellectual property rights have an adverse effect on competition and hence warrant compulsory licensing of drug patents. Here too, relatively expansive precedents can be drawn from the competition policy experiences of the most highly developed nations.

Parallel trade and patent rights intersect in important ways. In an ideal world, pharmaceutical manufacturers would engage in Ramsey-Baumol-Bradford discrimination, setting relatively high prices for their patented products to recover drug discovery and development investments in the most affluent nations and selling drugs at only a modest mark-up above marginal production and distribution cost in nations with the least ability to pay. For a variety of reasons, the world is far less than ideal. Parallel exportation of drugs sold at low prices in less developed nations could undermine the willingness of the pharmaceutical manufacturers to sell at those low prices or even to supply low-income markets at all. To avoid these ill effects, there should be an international agreement or understanding to bar parallel imports into high income countries from low-income or price-controlled jurisdictions while allowing parallel exports to low-income countries, including exports from price-controlled jurisdictions. This agreement would allow low-income countries to permit parallel imports and prohibit parallel exports, whenever it is in their interest to do so.

The logic of parallel trade also conflicts with the propensity of nations, rich and poor, to solve domestic health budget problems by imposing price controls on drug products. If the controls were coordinated to ensure that the most affluent nations pay the highest mark-ups of wholesale prices over costs, severe inequities could be avoided. But coordination is politically infeasible. Therefore, some of the world's most affluent nations impose stringent controls and attempt to cheap-ride on the contributions of others, rich and poor. In a highly imperfect world, each nation is likely to advance its own narrow interests, imposing controls (unless high weight is placed on avoiding the other market-distorting tendencies of controls). For less developed nations, this means that price controls can be an additional instrument for moderating health care costs, assuming that the controls are not implemented so clumsily that they drive supplies of critical drugs from the local market altogether. Feasible improvements over the status quo might be achieved through multilateral accords: (a) allowing low-income nations to import price-controlled medicines from higher income countries; and (b) barring national price control systems in high-income countries from using the uncontrolled prices set by multinational drug producers in low-income nations as external reference prices.

At the end of the day, it must be recognized that the poorer residents of the world's least affluent nations cannot even pay the marginal cost of drugs that might save their lives or permit them to become productive workers. Here, the only alternative to death or debility is charity. Charity, like high-technology drugs, is often in short supply. We have shown that it could be facilitated if corporate income tax laws, at least in the United States, are interpreted so that outright donations of essential drugs confer tax advantages sufficiently large as to impose no net cost on the donor, with the burden falling upon the tax collector. Charity through non-transparent tax expenditures is often more feasible politically than outright governmental gifts and grants. It should be aggressively exploited as a means of increasing the supply of life-saving drugs to the world's poor.

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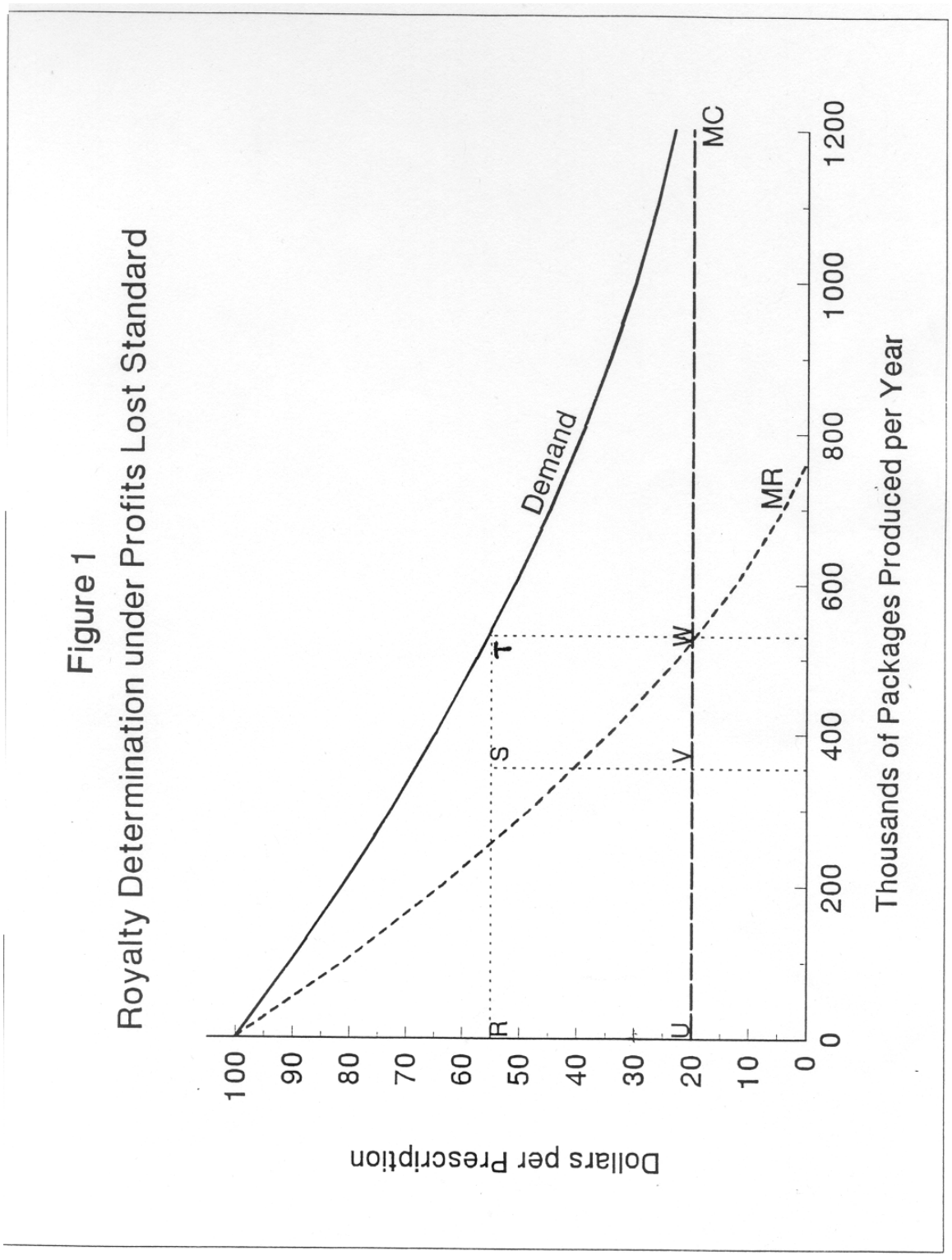


Figure 1
Royalty Determination under Profits Lost Standard
Dollars per Prescription
100
90
80
70
60
50
40
30
20
10
0
0
200
400
600
800
1000
1200
Thousands of Packages Produced per Year
Demand
MR
MC
R
S
T
U
V
W

Figure 2. Price Discrimination between Markets of Differing Wealth

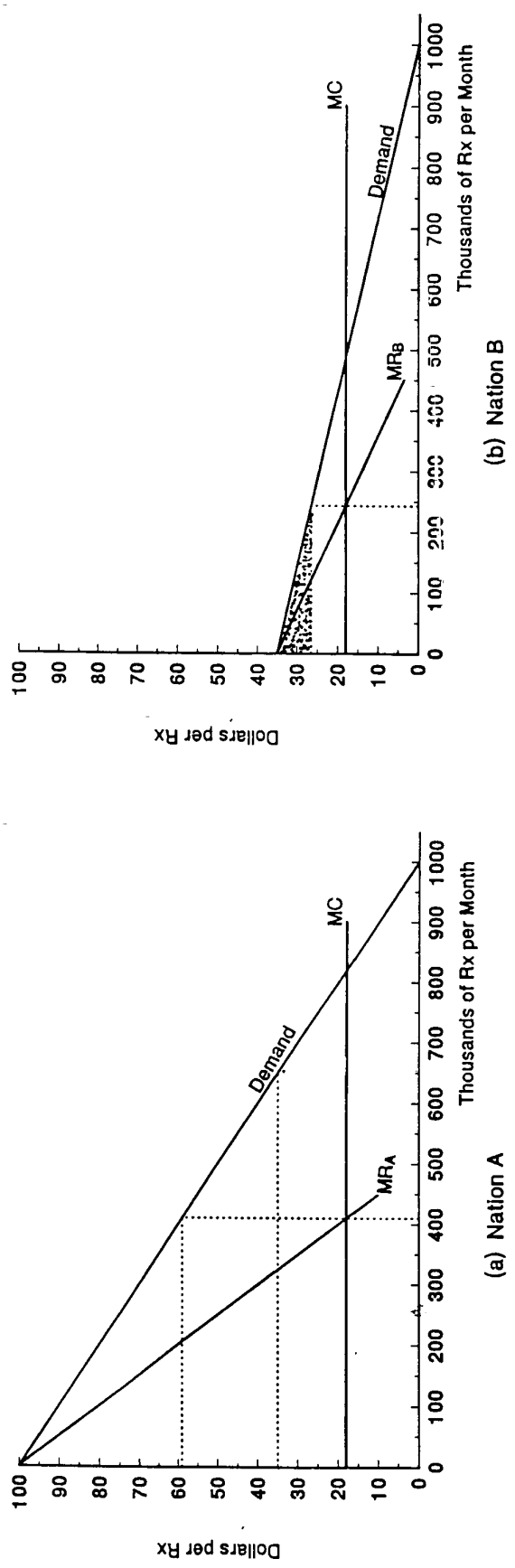


Figure 3 How Parallel Imports Affect Prices in Market A

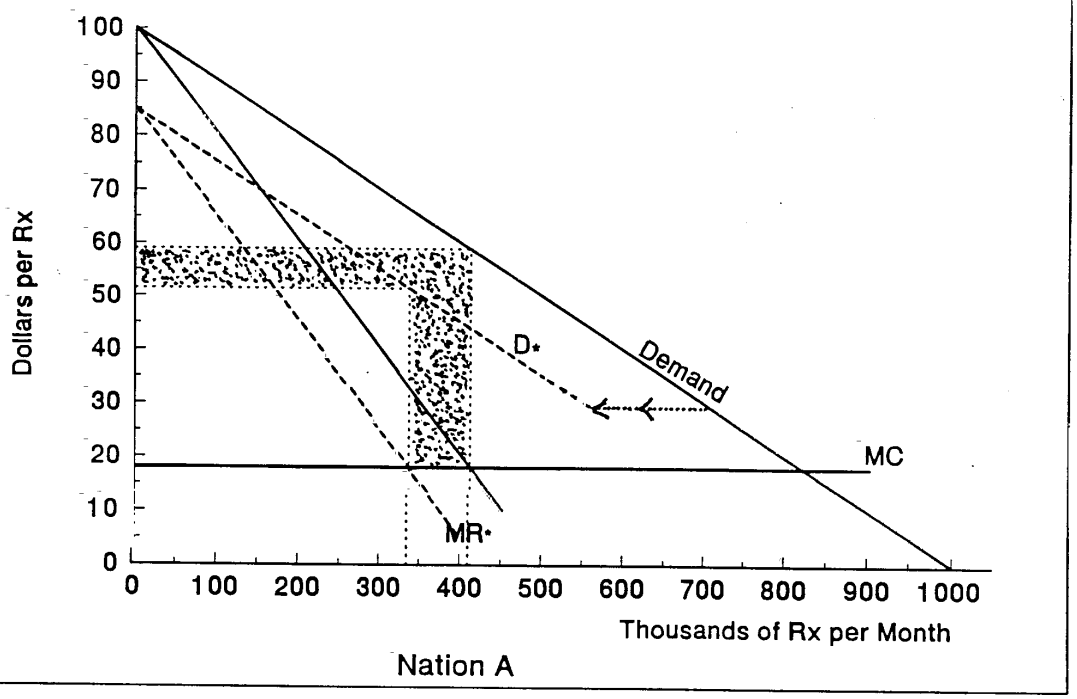


Figure 4
Scatter Diagram Relating MNEs' AIDS Drug Prices Divided by Comparable U S Prices to National GDP per capita

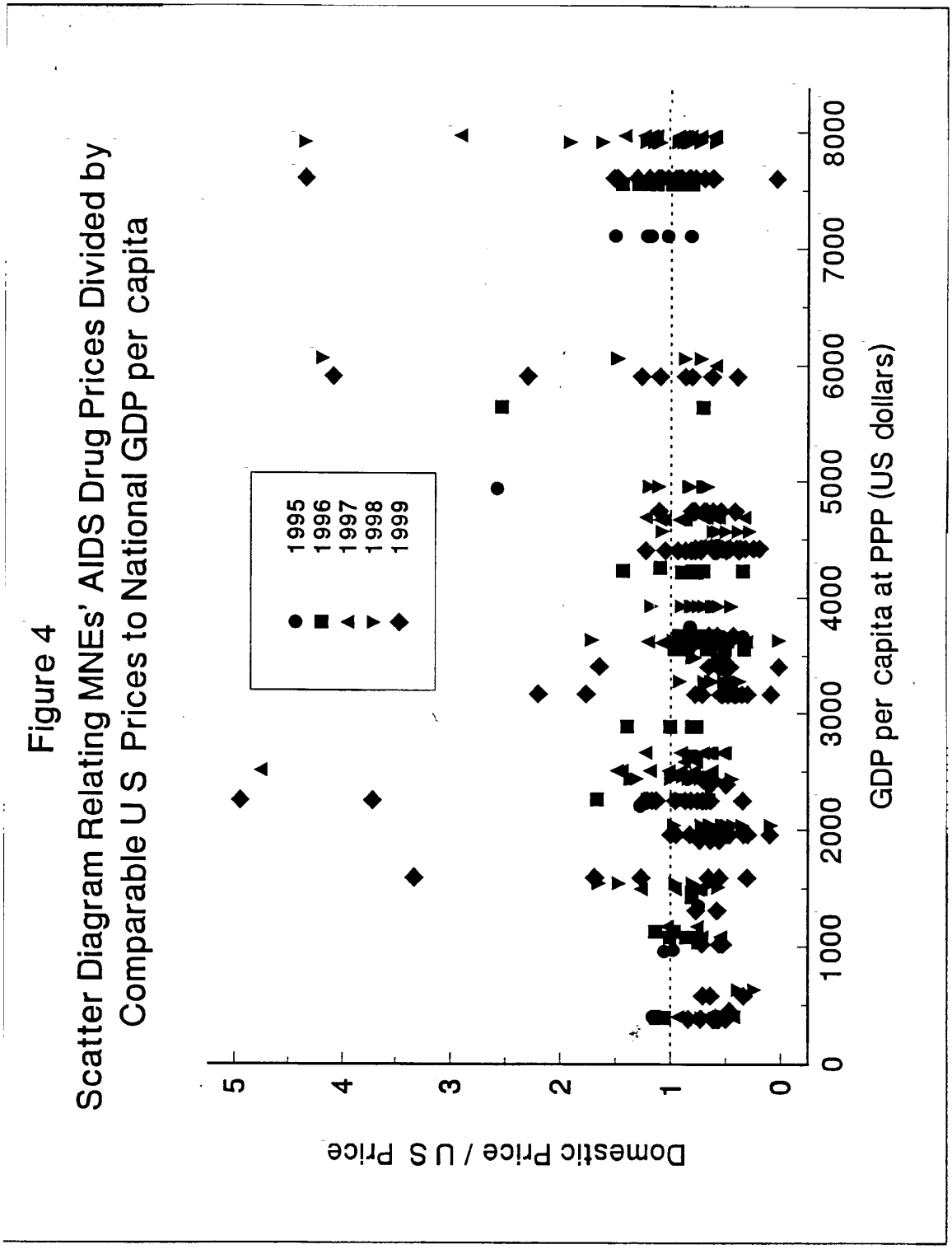
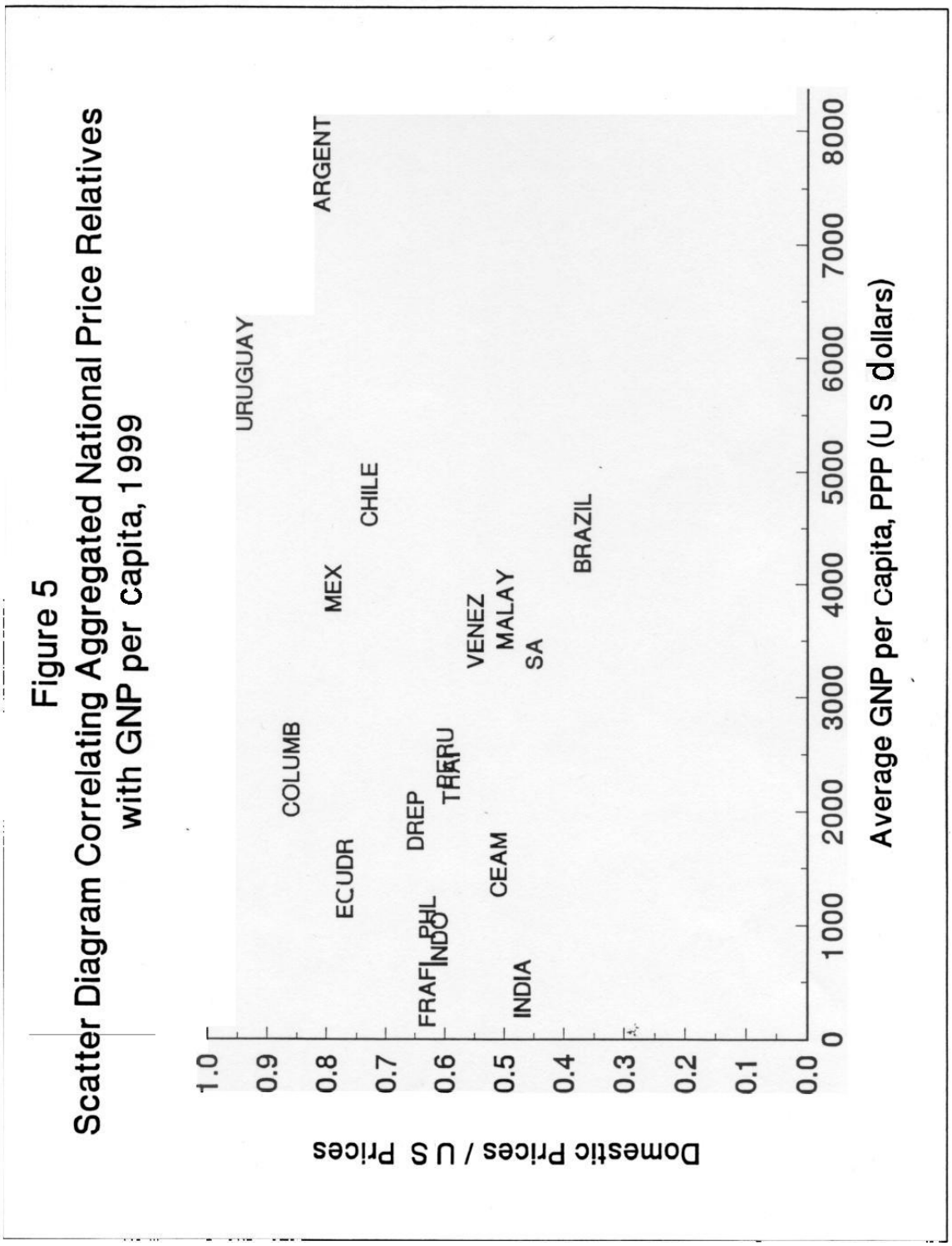


Figure 5
Scatter Diagram Correlating Aggregated National Price Relatives with GNP per capita, 1999



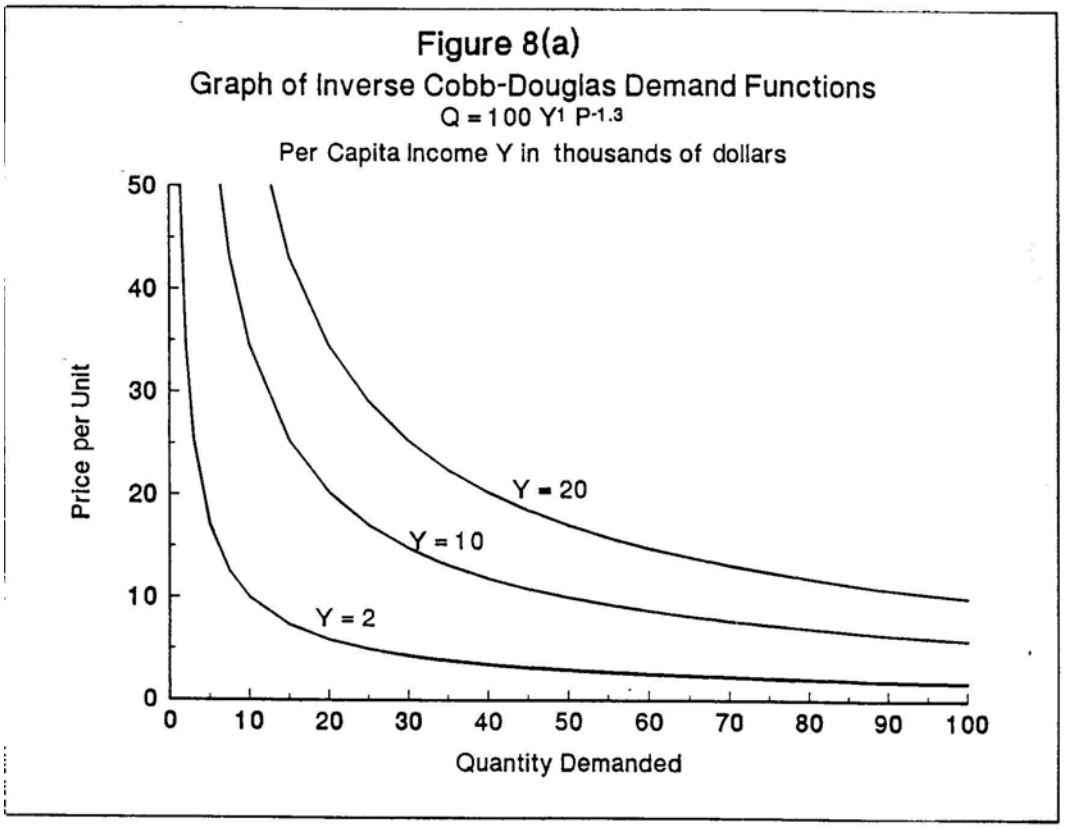


Figure 8(a)
Graph of Inverse Cobb-Douglas Demand Functions
Q = 100 Y1 P-1.3
Per Capita Income Y in thousands of dollars
Price per Unit
Quantity Demanded
Y = 20
Y = 10
Y = 2
0
10
20
30
40
50
60
70
80
90
100

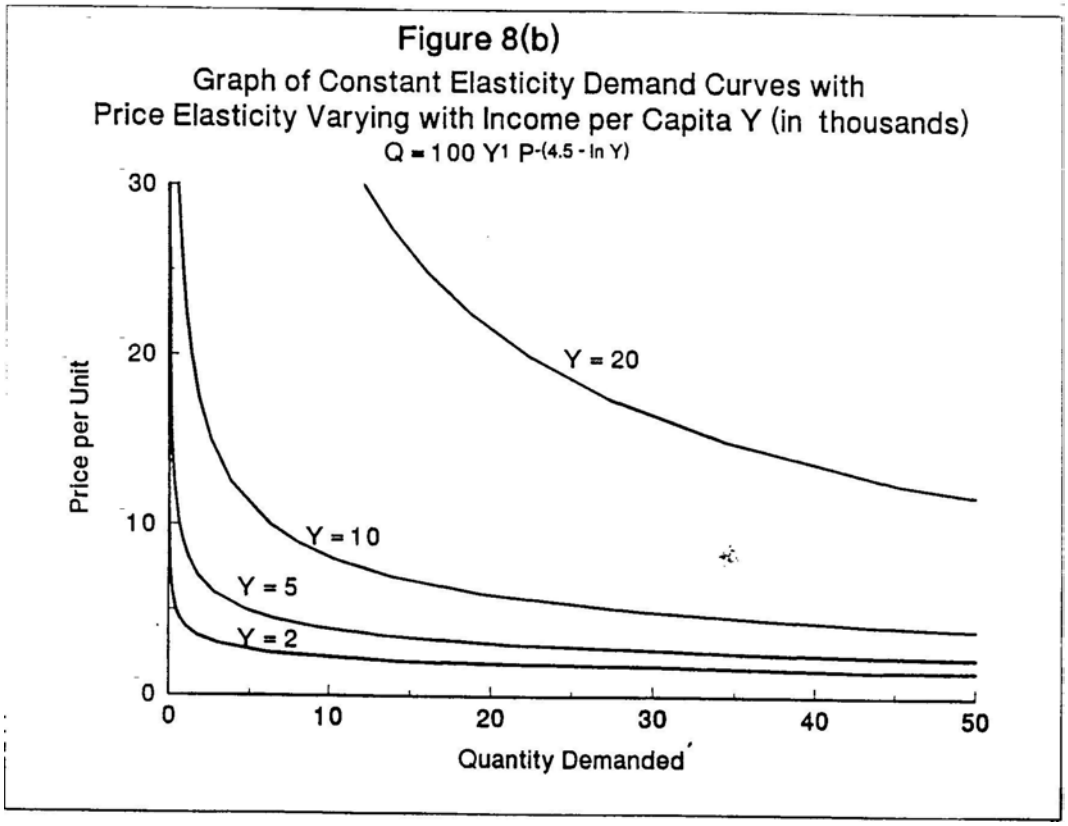


Figure 8(b)
Graph of Constant Elasticity Demand Curves with
Price Elasticity Varying with Income per Capita Y (in thousands)
Q = 100 Y1 P-(4.5 - ln Y)
Price per Unit
Quantity Demanded
Y = 20
Y = 10
Y = 5
Y = 2
0
10
20
30
40
50

Figure 9. How Price Controls Induce Parallel Imports

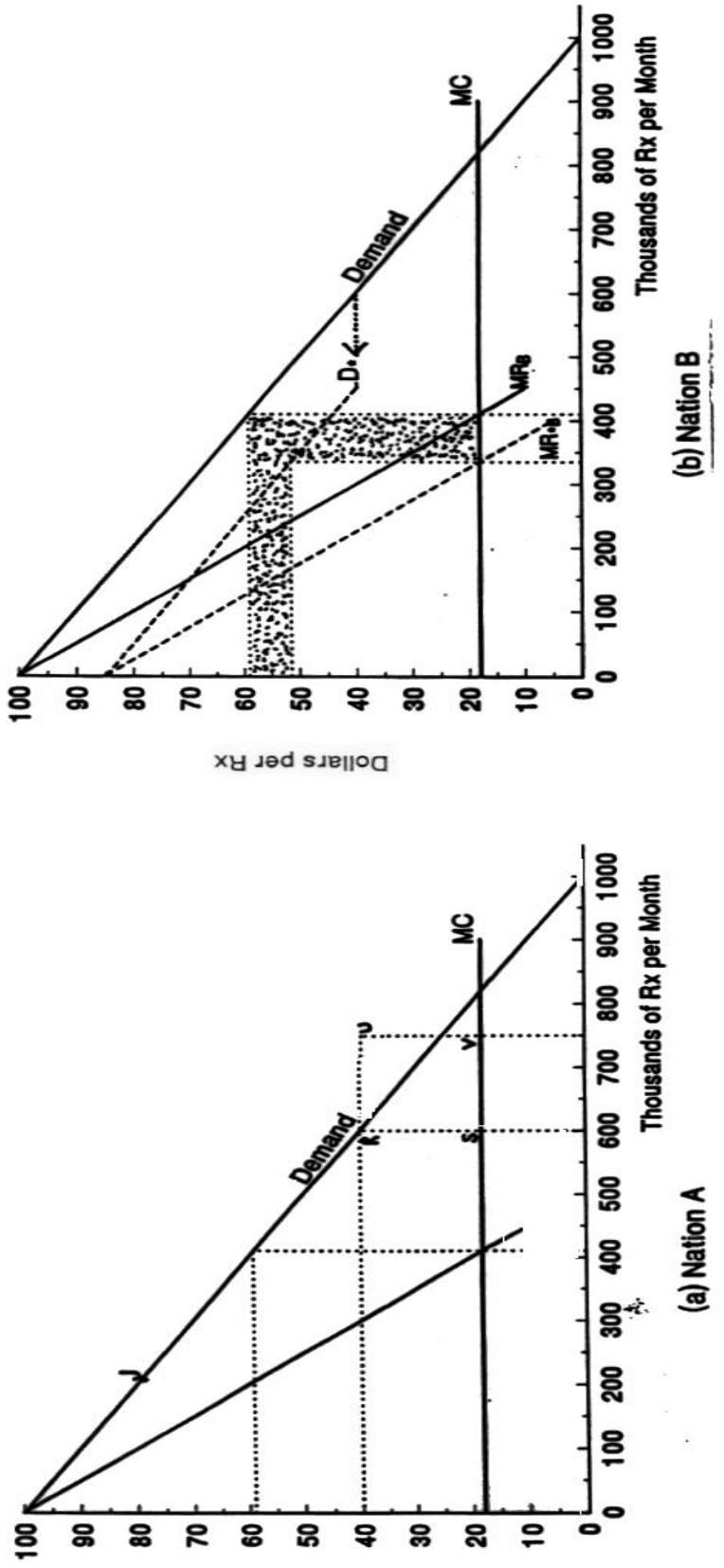


Figure 10

Breakeven Lines for Alternative Deduction Policies