

Generic Drugs Policies

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1. Defining Generic Drugs

Generic drugs are interchangeable products with proven bioequivalence with a reference product and standard quality.

There is not an internationally agreed definition of generic drug. Generics might be defined as drugs that are not subject to patents or other forms of exclusive marketing rights, have a proven interchangeability with a reference drug and are sold under an international non-proprietary name (INN). However, the term generics is often legally defined or applied to refer to drugs that are sold under brand names or have not been tested for bioequivalence or another accepted proof of therapeutic equivalence. This makes rigorous comparisons of international data and policies an extremely difficult exercise and can lead to erroneous implications and policies. Box 1 displays a proposed typology of pharmaceutical products that would reduce the coherence of the debate on generics and pharmaceuticals in general.

Because of the importance of drugs in health care, a complex drug regulatory system has been established in order to ensure its efficacy, safety and quality. Before a new drug enters the market the sponsor company must demonstrate the safety, efficacy and quality of the drug to the regulatory authority. This requires expensive laboratory tests and long and expensive clinical trials with animals and humans. Once the original drug is marketed, new versions of the same drug may be introduced by other companies. It would certainly make little sense to require the manufacturers to repeat the same trials that the originator has already performed. This would impose an unnecessary burden on the new companies as well as denying patients in the clinical trial access to an effective treatment. Therefore, in order to allow the new versions are to be used instead of the original product, their sponsor companies are required to demonstrate that their version of the product is interchangeable with the original product. The interchangeability means that the products can be use alternatively without any adjustment in dosage or directions of use.

For two version of the same product been interchangeable they should have the same expected therapeutic effect. The therapeutic effect of other company version of a drug is not demonstrated replicating the clinical trials to measure safety and efficacy. The interchangeability is assumed upon demonstration that the two products:

1. Contain the same active ingredient(s)
2. Are of the same dosage form and route of administration
3. Are identical in strength or concentration
4. Are formulated to meet the same applicable standards (i.e., strength, quality, purity, and identity)
5. Are bioequivalent, that is, they display comparable bioavailability¹ when studied under similar experimental conditions.

¹ Bioavailability means the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action. (FDA). Testing of bioequivalence requires the determination of a "reference product" this product is the one used as a comparator for demonstration of pharmaceutical equivalent and bioequivalence.

The products may differ in characteristics such as shape, scoring configuration, release mechanisms, or packaging.

Products that demonstrated the first 4 requirements are named “pharmaceutical equivalents.” In developing countries, these products, jointly with originator products, are the more commonly available in the private sector. Pharmaceutical equivalence does not necessarily imply that the products can be interchangeable as differences in excipients and manufacturing process can change the bioavailability of the products.

For the products to be interchangeable, the 5 requirements aforementioned must be demonstrated. These products are named “generic drugs.” Generic drugs products may be marketed either under a brand (proprietary) name or under the approved nonproprietary name. The international nonproprietary name, for example, is the shortened scientific name based on the active ingredient. The WHO is responsible for assigning INN to pharmaceutical substances.

Although bioequivalence is usually associated with generic drugs, the concept was initially developed and is still used in order to ease the introduction by the innovator companies of new forms and dosages of the original drug that had been tested with clinical trials.

Box 1: A Proposed Typology of Drugs

ORIGINAL OR REFERENCE DRUG	BRAND	ON PATENT	1 Branded original drug, on patent
		OFF PATENT	2 Branded original drug, off patent
	INN	ON PATENT	3 Generic original drug, on patent
		OFF PATENT	4 Generic original drug, off patent
SECONDARY SOURCE DRUG	BIOEQUIVALENT	BRAND	5 Branded generic drug
		INN	6 Generic drug
	NO BIOEQUIVALENT	BRAND	7 Branded pharmaceutical equivalent
		INN	8 Pharmaceutical equivalent

The 8 categories classification is country-specific, i.e. the same drug might be classified under different headings in different countries.

Classification criteria:

- 1) Type of manufacturer: (innovator vs. secondary source)
- 2) (Product) Patent status in country: on vs. off
- 3) Bioequivalence: Proven therapeutic interchangeability (in the country): yes vs. no
- 4) Commercial name: branded vs. (international) non proprietary name

Indicators derived from the former classification. (TM: Total market)

- A) $1 + 3 / TM$ Proportion of the market value under patent protection. It is an indicator of (potential) monopoly
- B) $1+2+3+4 / TM$ Market share under control of originator
- C) $3+4+6+7 / TM$ Proportion of INN products on total market value. It indicates level of potential price competition
- D) $1+2+5+7 / TM$ Proportion of market value under product differentiation. Indicator of potential for monopolistic competition and brand loyalty
- E) $1+2+3+4+5+6 / TM$ Proportion of originals plus bioequivalent drugs on total market: Indicator of level of (certified) product quality on the market

Originator (of a drug) refer to the patent and brand name holder company

Original drug refers to a product sold by an originator or by a company licensed or authorized by an originator.

Generic original refers to an original drug sold under INN (international nonproprietary name). It is assumed that it will be off patent

Generic drug: Pharmaceutical product that

1. Is off-patent in the country where it is sold (or with patent rights modified in such a way that it can be produced without the patent holder's consent, e.g. due to compulsory licensing)
2. its therapeutic equivalence to a reference drug (usually the innovator) has been certified in the country where it is sold, on the basis of a bioequivalence or a similar test
3. is sold under (international) non-proprietary name. If sold under brand name it will be labeled as a **BRANDED GENERIC**

Pharmaceutical Equivalent: Pharmaceutical product that complies with condition 1, but not with condition 2

II. The Role of Generic Drugs: key issues and options

Generic drugs can improve drug quality and lower drug prices and, consequently, drug expenditure.

Access to quality drugs is a key factor in scaling up most health programs and, certainly, in trying to attain the MDGs. Generic policies is one of the most efficient and sustainable way to improving access to off-patent drugs. Unlike strategies that are still in an exploratory stage – equity pricing, public-private partnerships, etc - generic policies have a relatively long tradition and have been successfully applied in many developed countries, such as the US and the UK. Moreover, generic policies can be implemented by national authorities and do not require the agreement of foreign countries or international organizations.

According to the economic theory, competition between suppliers reduces the price of the products and increases social utility. Generic drugs are the main source of competition in the pharmaceutical market. The development of a competitive generic drug market serves a basic public health objective: the reduction of drug costs that does not compromise quality.

Economic theory predicts that generic policies are likely to reduce drug prices. There is indeed broad evidence that the introduction of generics lowers the prices of a drug. This is not only because generic versions of a drug have a lower price than branded versions, thus lowering the average market price, but also because of the effect that generics have on the price of the brand name versions. The second effect requires, however, not only the availability of low price generics, but also the existence of a set of market conditions and policies that encourage price sensitivity and competition in the market in order to make price reductions benefit the consumer and taxpayer.

Economic analysis provides a clear theoretical justification of the lower prices of generics: In a market of generics, manufacturers have no incentives for spending on advertising, as the effects are likely to benefit all manufacturers. As the product is practically homogeneous, there will be only one price in the market: manufacturers will be price-takers. In the long run the price will be set at the minimum average cost of production. Homogeneity and substitutability is ensured by the therapeutic interchangeability between products that results from drug quality assurance and bioequivalence between the different products intended to be substituted.

In a brand name market, companies have an incentive to advertise their own products and gain brand loyalty. This increases one hand the costs of production. Moreover, faced with a demand with negative slope, each firm will produce at a level of output below the optimum level of output (at the minimum average production cost) and finally at a higher price than in a generic market (see figure 1). This market structure is called monopolistic competition and is a joint result of product differentiation and no entry barriers. If entry

barriers are added to product differentiation the result will be a monopoly or oligopoly with a differentiated product, which will result in still higher prices.

In the theoretical models the product is assumed to be homogeneous and of a standard quality. In practice there have been often concerns with the quality of generics. Competitive bidding with scarce attention on quality has been said to favor cheap substandard drugs and penalize good quality. This problem can be avoided by enforcing adequate quality standards. The World Bank is at present recommending countries that plan to purchase ARV and other HIV-AIDS drugs with Bank loans to restrict bidders to WHO-prequalified manufactures.

The availability of generics drugs alone will not make the generics markets automatically grow. Developing a generics market requires a firm commitment from governments and international organization because, as said before, manufacturers of generics do not have an incentive to advertise. Generic policies include supply side interventions, such as a shorter registration time than other drugs, and demand side interventions, such as education campaigns to physicians and consumers, reference pricing, etc.

In implementing a generics policy the authorities are faced with manifold choices and options, some are specific to generics while others can be applied to generics but do not necessarily require them.

INN vs. Brand names

A policy of branded generics, solely based on the criterion of bioequivalence, is a positive approach as it guarantees quality, but it does not take full advantage of the potential savings that would derive from an INN-generics policy. In Spain, one of the many countries that for a long time allowed new versions of original products to be immediately marketed under brand name, with no requirement of bioequivalence, of original and secondary-source products were often priced at the same level.

Introducing INN is not a simple task. The industry is in many countries used to make business on the basis of brand names and competing on marketing strategies and is likely to oppose a move to INN. They state that brand names are simpler to use, as they are shorter than generic names in terms of both the number of words and the syllable length. Brands are easier to remember, to pronounce and to write in a prescription.² Pharmaceutical brands are important because prescribers use the brand in the prescriptions and influence the product dispensed by the pharmacy. Brand names are extensively use by the pharmaceutical industry in marketing activities, and many times the brand becomes associated with the product itself. Additionally, regulation in many developing countries impedes the substitution of a branded drug by a generic when prescribers write the branded drug name in the prescription.

² For a general discussion of this issue see: Clankie SM. A theory of genericization of brand name change. The Edwin Mellen Press, Ltd: Lewiston, 2002.

If there were no brand name drugs, pharmacies would merely dispense commodities. The pharmacies would be able to source their products from suppliers under normal market conditions. Brand names therefore provide drug manufacturers with a means to influence prescriber and consumer behavior and have a stronger bargaining position when negotiating with pharmacies and other health care providers.³

Requirement of bioequivalence

Nowadays no one would probably recommend a country to implement a generics policy not based on the criterion of bioequivalence. This is not only a public health issue, but also an economic one and a requirement for the long-term success of the strategy. Many health professionals and consumers question the quality of generics, sometimes rightly. A strict and sustained application of quality standard as it is carried out in developed countries with well-established generic policies is a necessary condition to overcome their reluctance. In trying to enforce quality, health authorities might face the opposition of the local industry, which might fear that such a policy would raise its cost and make it less competitive.

Generic policies and IPR

Generics policies can be designed and implemented irrespective of the intellectual property rights policies in the country. As a matter of fact, the majority of drugs on WHO's Essential Medicines list are off-patent. And these drugs are assumed to address the majority of health problems in developing countries. However, a strong patent protection will delay innovations to be produced and join the generics market.

Generics are associated with old off-patent products. However, new products might be developed with the condition of making it available for production to any manufacturer, which should only pay a pre-defined compensation. This alternative approach to the conventional IPR approach would reward the innovator and acknowledge its rights while preserving the competitive forces in the area of manufacturing. Such an approach would be easy to implement in the case of innovations introduced by the public sector and by public private partnerships in the context of initiatives for developing new products for neglected diseases.

Non-specific options

Generic can and should be promoted by means of all the mechanisms at the disposal of the authorities: selective financing (such as reference pricing), information to doctors and consumers, incentives to consumers, doctors and pharmacists (for instance, allowing

³ For a discussion of this issue applied to products in general see: Murphy JM. Brand Strategy. Prentice Hall Inc: Englewood Cliffs, 1990. p. 22.

higher retailer's margins to be applied generic, etc). A more comprehensive list of issues and options is included at the end of the paper (Annex 1)

III. The Generic Pharmaceutical Market: facts and data

The share of the generics in the global pharmaceutical market

Despite large potential savings, use of generic drugs remains low in most countries.

The generic market represents only a small fraction of drug expenditures in the world pharmaceutical market. The world generic pharmaceutical market was estimated to be 46400 US\$ million in 2001, representing 9.2% of the total world pharmaceutical market.⁴ The information currently available for the generic drug market is related mainly with the markets of developed economies. The percentage of the pharmaceutical expenditures varies depending on the country (see Table 1).

Table 1. Generic Drug Expenditures as a Percentage of Total Pharmaceutical Expenditures, Selected Countries, 2001

Singapore	27.3%	Japan	8.0%
UK	22.0%	Australia	8.0%
Germany	19.9%	Colombia	6.9%
South Africa	16.0%	Argentina	3.3%
Netherlands	14.7%	Italy	3.0%
Canada	13.3%	Switzerland	2.6%
Ireland	12.0%	Spain	2.5%
Austria	10.0%	France	2.3%
USA	8.0%	Belgium	2.0%

Source: The World Generic Market Report, 2003. Espicom Business Intelligence. January 2003. page 3.

Several countries have achieved a developed generic market. These countries include large economies such as the U.S., the UK or Canada, but also developing countries such as Singapore or Chile. Other countries, such as France, Italy or Argentina are in a transactional situation towards a developed generic market.

Because of the low price of generic drugs, the generic market share of expenditures is lower than the generic share measured by the number of prescriptions. For example, the UK retail generics market was valued at £713 million in 1997, accounted for more than

⁴ The World Generic Market Report, 2003. Espicom Business Intelligence. January 2003. page 3.

15% of the total UK retail ethical drug market.⁵ Also in Canada in 2001, generic drugs represented 13.8% of the dollar expenditures and 40.2% of all the prescriptions filled.⁶

The number of prescriptions dispensing generically is expanding in developed countries. In UK, for example, the actual number of prescriptions dispensed generically as a percentage of the total number of prescriptions increased from 36% in 1992 to 49% in 1997.⁷ In the US, the number of prescriptions dispensed generically is growing, but the generic share by value has fallen from 11% in 1997 to 9% in 1999 and to 8% in 2001,⁸ largely due the use of new and more expensive patented products.⁹

Many developed economies still have a low generic drug market penetration. In Italy –the fifth largest pharmaceutical market in the world-, for example, generic drugs represented only 1.27% of drug expenditures and 2.12% of units sold in September 2001.¹⁰

Data available for developing countries demonstrates that the development of the generic market can be done through a combination of a generic drug policy and generic promotion in the private health care system. Singapore, for example, achieved a high generic market penetration –27.3% in 2001- that may be explained by the implementations of programs promoting generic drugs by both public and private healthcare service providers.¹¹

The Brazilian generic market represented approximately 6% of the total pharmaceutical market in the year 2002. In a few years this market could reach 40% of total sales.¹²

⁵ www.ims-global.com

⁶ The Canadian Generic Pharmaceutical Association. <http://www.cdma.acfpp.org/en/resourcetrends.html>

⁷ www.ims-global.com

⁸ www.ims-global.com

⁹ www.ims-global.com

¹⁰ Associazione Nazionale Industrie Farmaci Generici, 28 Marzo 2003

¹¹ Meemien Tong. Pharmaceuticals Market. International Market Insight [IMI]. ID: 102585. Country: Singapore. 07/12/2000. U.S. & Foreign Commercial Service and U.S. Department of State.

¹² Jefferson Oliveira. Overview of Pharmaceutical Sector. International Market Insight [IMI]. ID: 106591. 07/26/2002. U.S. & Foreign Commercial Service and U.S. Department of State.

The Generic Drug Industry

Large multinational generic companies and the generic divisions of branded companies control the world's generic market. The domestic industry of most developing countries is very fragmented and produces mostly branded pharmaceutical equivalent products. Domestic companies of developing countries do not have the economies of scale required to compete in the generic market.

The Functions of the Pharmaceutical Industry

The pharmaceutical industry develops a series of functions to bring the product from the laboratories to the pharmacies including: research and development, raw materials manufacturing, finished products manufacturing, packaging and repackaging, and marketing.

The pharmaceutical process starts with the research and development of new drugs. Most pharmaceutical R&D is done in a few developed countries, including the U.S., Japan and selected European countries. The R&D is done through a combination of private and public resources.

Raw material manufacturing aims to produce large volumes of drug ingredients. Most of the raw materials used by the world's generic industry and by the domestic industry of developing countries is imported from China, India, European countries, and the U.S.

Most developing countries, including those with a large domestic pharmaceutical market, produce finished materials from imported raw materials. Brazil, for example, imports approximately 85% of the raw materials used in the production of generic drugs.¹³ The possibility of Brazil becoming a producer of raw materials is low.¹⁴ In another example, 95% of the 1,300 raw materials used to manufacture drugs in Indonesia in the year 2000 were imported.¹⁵

The pharmaceutical industry of the smallest countries package finished drugs produced in other countries, or do the marketing and selling of drugs.

Generic Drug Companies

Generics companies can be independent or a division of an originator company. Several large independent generic companies are becoming multinational generic companies with presence in a large number of countries (see Chart 1). For example, the Israeli company Teva was the largest generic manufacturer in 2001 with sales of 2100 US dollar million.

¹³ Jefferson Oliveira. Overview of Pharmaceutical Sector. International Market Insight [IMI]. ID: 106591. 07/26/2002. U.S. & Foreign Commercial Service and U.S. Department of State.

¹⁴ Jefferson Oliveira - Fernanda Galante. The Dependence on Imports of Raw Materials. International Market Insight [IMI]. ID: 105690. 06/21/2002. U.S. & Foreign Commercial Service and U.S. Department of State.

¹⁵ Pharmaceutical Manufacturers. International Market Insight [IMI] ID: 93291. U.S. & Foreign Commercial Service and U.S. Department of State. 06/05/2000

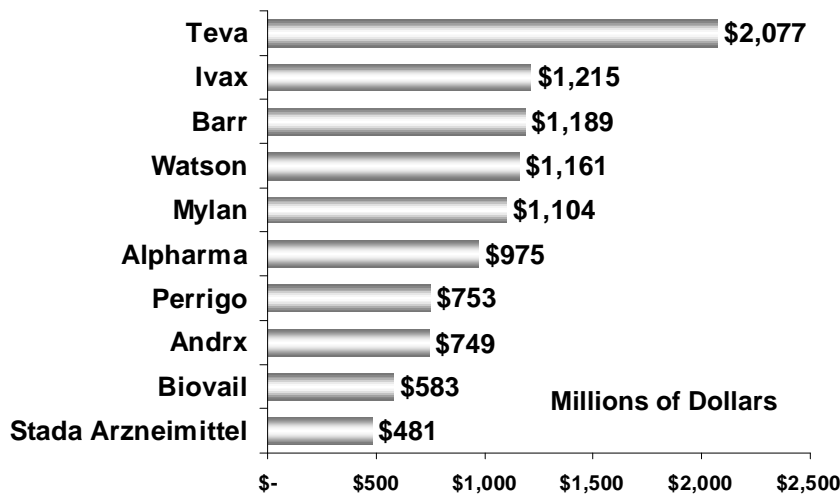
Companies from large developing countries are entering the world generic market, particularly Indian pharmaceutical companies that have presence in the U.S., Germany and Brazil pharmaceutical markets.¹⁶

Independent generic companies have a financial structure very different than the originator companies (See Chart 2). Most of the independent generic expenditures go to the cost of manufacturing the products.

Large multinational originator companies (such as American Home Products, Aventis, Merck, Novartis or Pfizer) established their own generic units or acquired an independent generic company. The generic divisions of originator companies compete in the generic market and allow these companies to achieve economies of scale combining the manufacturing of generics and branded products.

Domestic companies of developing countries are normally of small size and very fragmented, with difficulties to adapt to the economy of scale requirement of the generic market. In Indonesia in the year 2000, for example, there were 193 pharmaceutical manufacturers including 4 state-owned companies and 33 foreign investment companies. Indonesian drug companies are generally small entities, each manufacturing a limited range of products. These companies produce drugs under license from foreign drug firms or, they produce and distribute generic or similar drugs.¹⁷

Chart 1. Top 10 Independent Publicly Trade Generic Pharmaceutical Companies, 2001

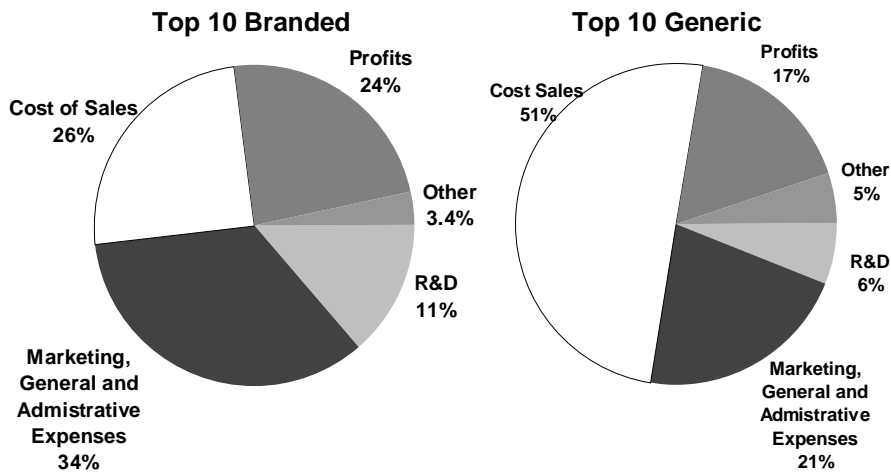


MedAdNews 2002

¹⁶ Script's 2003 Yearbook. 19th Edition. Volume 2. Jan 2003. pag. 213-4.

¹⁷ Pharmaceutical Manufacturers. International Market Insight [IMI] ID: 93291. U.S. & Foreign Commercial Service and U.S. Department of State. 06/05/2000

Chart 2. Financial Information of the World Top 10 Drug Companies Branded and Generic, 2000



Source: Prescription Drug Trends. Kaiser Foundation, November 2001

Generic Drug Regulation and Policy

Availability of generic drugs of standard quality depends on the characteristics of the production and distribution system. Availability requires that generic drugs are developed, registered, produced or imported, and distributed in the market.

The availability of generic drugs does not guarantee drug affordability but generic drugs can reduce the financial resources dedicated to drug expenditures. The role of generic drugs is directly influenced by the characteristics of the financing system, including drug insurance, pricing, acquisition, and payment.

Several functions of the health care system also influence generic drug utilization including: therapy selection, prescription, substitution, and dispensing.

Generic Drug Production and Distribution

Generic drug production and distribution include drug development, registration, production, importation, and distribution in the market.

- Generic Drug Development

Generic companies assume the cost of development of generic drugs needed to the approval and manufacturing of generic products. Brazil drug industrial policy includes partnerships with private companies for development of generic HIV drugs.

In many countries, the general patent system does not allow testing of a product by a competitor company before the expiration of the patent. Therefore, performing the tests needed for drug approval by a company before the patent has expired would constitute "making" and "using" a protected product, leaving a generic company liable for patent infringement. If the generic companies cannot test a drug for approval before the patent that protects this drug has expired, a distortion will occur after the end of the patent term. Generic competitors entry in the market will be delayed for the period of time that companies need to test the product, plus the time the FDA spends in the regulatory process needed to approve the generic drug application. This delay would be two to six years counted from the moment the patent, or patents, protecting the originator product expired.

Recognizing the importance of the delay in generic entry and its effects on drug prices, several countries have approved specific regulations to solve this problem, allowing drug testing by a generic company before the expiration of the patent, thus making it possible for generic manufacturers to market their products as soon as the patents expire. The specific regulation that allows drug testing by generic companies before patent expiration is called "Bolar Provision", This name derives from the Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc., Ruling of the U.S. Court of Appeals for the Federal Circuit of

April 23, 1984, holding that the testing of a patented pharmaceutical compound for possible FDA new drug approval was an infringement of the patented invention when performed by other than the patent owner. Similar exemptions to the U.S. "Bolar Provision" contained in the 1984 U.S. Waxman-Hatch Act have also been approved in other countries, including Argentina (1996), Australia (1997), Israel (1998), Canada (1993), Hungary (1995), and Israel (1998).

Generic drug approval

Developed countries have established an abbreviated drug approval process for approval of generic drugs. Incentives to generic drug production also include free or low cost generic registration.

In developing countries, problems in the speed of generic drugs approval are an important barrier to market entry, especially for imported products. Several developing countries have established new regulation to facilitate generic drug registration.

Brazil is a good example of the importance of expedite approval for development of the generic market. Since the first bioequivalent generics were approved in February 2000, ANVISA (Agencia Nacional de Vigilancia Sanitaria) has given priority to processing generic applications in line with government policy. The monthly rate of approval has increased, reaching 32 new generic registrations in March 2002 compared with 21 in March 2001.¹⁸

Indonesia's drug registration is also favorable to generic drugs, especially for essential generic drugs. These drugs are included in a priority track, Track 1, jointly with the drugs indicated for therapy of serious and human life threatening diseases.¹⁹ The time frame for reaching a decision on the approval of these drugs is 100 working days.

In another example, the Ecuatorian Law 2000-12 promotes the production, importation, and sale of generic medicines for human consumption to provide the low income population with quality medicines at low cost. The Law establishes that imported generics will benefit from mutual recognition of standard requirements (homologation) from countries authorized by the Ministry of Health. The National Hygiene Institute "Leopoldo Izquieta Perez" is in charge of granting the sanitary registration (60 days) as well as the homologation certificates (30 days) prior the corresponding analysis. Accredited laboratories from technical schools and universities may also perform such analysis and both sources will perform random quality control thereafter.²⁰

¹⁸ www.IMS-global.com

¹⁹ Sharon Chandra. Drug Registration Procedures. International Market Insight [IMI]. ID: 91805. 09/30/2000. U.S. & Foreign Commercial Service and U.S. Department of State.

²⁰ Amparo Meneses. 07/23/2000. New Law for Generic Drugs and Pharmaceuticals. International Market Insight [IMI]. ID: 93103 U.S. & Foreign Commercial Service and U.S. Department of State.

Generic Industrial Policy

The goal of a generic industrial policy is the development of the domestic pharmaceutical industry and the investment of multinational companies in the country. The fragmentation of the domestic industry is a barrier to the development of the domestic industry.

An example of the importance of a generic industrial policy, combined with the existence of a large potential public and private market can be analyzed in the case of Brazil. The introduction of generic drugs in the Brazilian market, in 1999, created a dynamic investment process in the pharmaceutical market. Attracted by financial incentives, major international generics companies are setting up local production facilities in Brazil. Canada's Apotex (Canada), Ranbaxy (India), Cadila Healthcare (India), Stada (Germany) and Hexal (Germany) entered the Brazilian generic market. Generic divisions of originator companies -Novartis and Abbott for example- have also presence in this market. Production of these companies will serve the domestic as well as the Mercosur markets.²¹ In 2001, the volume of generic units sold increased 614% compared with 2000. The income from this sector increased from US\$25.4 million in 2000 to US\$126.7 million in 2001. The public health care systems in most Brazilian states are expected to purchase almost the entire production of generic drugs as part of the government's program to distribute medicines to the poorest.²²

Several market anticompetitive barriers are common in developed and developing countries that demand an antitrust regulation and enforcement. These activities include: agreements not to compete, agreements of price-related terms, and horizontal and vertical integrations.

International agreements, particularly WTO, are strengthening the intellectual protection of pharmaceuticals. The basic argument for the existence of intellectual property is the social benefit. Intellectual property promotes scientific progress, encouraging discovery of new products and also facilitating the transfer of technology by requiring public disclosure of inventions. While intellectual property remunerates innovation it also limits competition and consumers end up paying more for a patented drug than they would have paid otherwise for generic substitutes. Intellectual property results in monopolies that lead to standard deadweight losses for society.²³

Generic Drug Imports

²¹ www.IMS-Global.com, 2003

²² Jefferson Oliveira. Overview of Pharmaceutical Sector. International Market Insight [IMI]. ID: 106591. 07/26/2002. U.S. & Foreign Commercial Service and U.S. Department of State.

²³ Varian HR (1998). Markets for Information Goods. University of California, Berkeley (revised: October 16, 1998). Available on the Internet: www.sims.berkeley.edu/~hal/Papers/japan.

Denicolo V (1999). The Optimal Life of a Patent When the Timing of Innovation Is Stochastic. International Journal of Industrial Organization. 17(6):827-46.

Most countries in the world cannot manufacture all drugs required for the domestic needs. Drug imports can be finished products or the raw materials needed for drug production. Imports make drugs available in countries different of the manufacturer country, which increases the drug supply in the country accepting the import. Drug imports may also improve the competition in the pharmaceutical market by increasing the amount of drugs in a certain market.

There are several examples of the use of drug importation. The South Africa government facilitates the import and manufacture of generic HIV drugs.²⁴ In Mozambique, four generic antiretrovirals manufactured by Indian companies are being imported into the country by a public company and will be available through private companies. The price to the public of these antiretrovirals will be regulated with profits margins limited to 15% for pharmacies and 10% for importers.²⁵

Generic Drug Distribution

The drug distribution system in development countries is more favorable for branded than for generic products. Small generic companies cannot use the regular system to distribute their products and assume higher costs for direct distribution to pharmacies and health care providers.

Financing Generic Drugs

The use of generics by the public and private health care systems effectively reduces the financial resources needed for drug expenditures. The use of generic drugs is directly influenced by the characteristics of the financing system, including drug insurance, pricing, acquisition, and payment.

Drug Financing and Insurance

Developed generics markets finance generic drugs when available in the market. The use of generic drugs reduces the financial needs for drug expenditures.

Generic Drug Pricing

²⁴ Script's 2003 Yearbook. 19th Edition. Volume 2. Jan 2003. pag.204-205.

²⁵ Script's 2003 Yearbook. 19th Edition. Volume 2. Jan 2003. pag. 200.

While generic competition can reduce drug prices (See Table 2), several aspects of the market should be taken into account when deciding the drug price regulation of a country.

First, there is no price transparency in the market, and it is difficult to know how pays what and how is being pay for what. Second international drug price comparisons are needed to assess the price level of an individual country. And third, anticompetitive agreement for not to compete are common in the world market.

Table 2. Price Dynamics - Generics (2001)

Country	Average penetration after 4 years	Price differential between brand and generic
USA	60-70%	80%
UK	50-60%	80%
Germany	40-50%	30%
France/Italy/Spain	5-15%	20-30%

Source: IMS, 26 Oct 2001

There are several examples of the importance of generic competition for reducing drug prices in developing countries. In Brazil, for example, competition from generics has contributed to price erosion of original brands, whose average prices have declined in US\$ terms since 1999, when devaluation of the real had a significant impact on prices. Among others, Merck & Co's Renitec© (enalapril) and Bristol-Myers Squibb's Capoten© (captopril), both ACE inhibitors for hypertension, have seen their prices cut by 50% in an attempt to compete with generics.

Although some generics are priced higher than original brands in Brazil, generic prices are on average around 40% below branded products' prices. There are wide variations in the prices of generic versions of the same drug, reflecting differing company approaches to gaining market share. With the decline in drug prices, in the last four years the differential between generics and similar drugs has similarly eroded to reach parity by 2002.²⁶

In Malaysia, a generic tablet costs between US\$0.002 and US\$0.005, as opposed to US\$0.13 for a branded product.²⁷

The use of price discrimination by originator multinational companies has demonstrated the difficulties of established a voluntary system of price discrimination. For example, BMS discontinued supplies of discounted HIV drugs to Kenya because of high demand. Combivir© Glaxo discounted drug also has shortages due to increased demand.²⁸

²⁶ www.ims-global.com, 2003

²⁷ Natila Ahmad. International Market Insight [IMI]. ID: 73733. U.S. & Foreign Commercial Service and U.S. Department of State. 05/17/2001.

²⁸ Script's 2003 Yearbook. 19th Edition. Volume 2. Jan 2003. pag.198-9

Generic Drug Reimbursement

Reimbursement is the most important factor explaining the development of the generic market. Reimbursement measures include: positive and negative drug lists, different levels of co-payment for generic and branded products, and reference or maximum allowed cost. The implementation of these measures help to explain the generic use in countries such as the U.S. Germany or UK.

An adequate level of reimbursement to the industry, distribution and pharmacies is basic for the development of the generic market. The current situation in most developing countries make companies, distributors and pharmacies to prefer the use of more expensive products with higher level of reimbursement instead of using generic drugs. The current proposed systems does not appear to be sufficient to create incentives for the use of generic drugs

In Ecuador for example, Law 2000-12 to promote the production, importation, and sale of generic medicines for human consumption to provide the low income population with quality medicines at low cost. The Law establishes that the Brand pharmaceuticals/drugs and generic medicines are subject to price controls by the National Price Council. The profit margin for the producer or importer will not exceed 20 percent; for distributors 10 percent per product; and for drugstores 20 percent for brand products and 25 percent for generic medicines.²⁹

In Korea, effective November 15, 1999, the Korean Ministry of Health and Welfare (MHW) introduced a new system drugs dispensed for patient treatment are reimbursed at the actual acquisition prices paid by medical institutions under the national health care insurance program. Under the new system, hospitals will be penalized for demanding higher margins from drug suppliers. The new system could benefit branded pharmaceuticals.³⁰

Generic Drug Utilization

Several functions of the health care system influence generic drug utilization including: therapy selection, prescription, substitution, and dispensing.

Therapy Selection

²⁹Amparo Meneses. New Law for Generic Drugs and Pharmaceuticals. International Market Insight [IMI]. ID: 93103 U.S. & Foreign Commercial Service and U.S. Department of State. 07/23/2000.

³⁰Young Kim. New Reimbursement Pricing Sys for Drugs. International Market Insight [IMI]. ID: 90823. U.S. & Foreign Commercial Service and U.S. Department of State. 03/16/2000.

Most developing countries have established an essential drug list as a basic tool to decide the therapies that should be used in the health care system. The majority of the products included in the WHO essential drug list are generically available.

Generic Drug Prescription

Several countries, such as Argentina, require health care professionals to write the prescription with the generic name. In other countries, including the U.S., the prescriber can write indistinctly the generic or the branded name of a product, and the pharmacist dispenses the generic product in the pharmacy.

Generic Drug Substitution

The prescription of a prescribed drug can be substituted for a more efficient and/or affordable alternative. The substitution can be done by replacing the product with a generic product (generic substitution). The substitution can be also done using a product with different pharmaceutical properties and similar therapeutic effects with lower cost or better risk-benefit profile (therapeutic substitution). Generic substitution, in combination with reimbursement measures, explains the high use of generic drugs in the U.S., Germany or UK.

Consumer Education

The importance of the public sector as promoter of the generic market can be seen in most developed countries. In developing countries, the promotion of generics has been assisted by government's public education campaign, complemented by health care providers promotion of generics. In Brazil, for example, consumer awareness is the main driver of generic sales, with 95% of Brazilians familiar with the concept of a generic, according to a national survey by the Ministry of Health in 2002.³¹

³¹ www.IMS-global.com

Annex 1. Policy Options for Improving Drug Access for the Poor Through the Use of Generic Drugs

Barriers to Generic Use

Several reasons could impede the substitution of the brand by the generic product:

- 1) Generic drugs are not available:
 - a. the pharmaceutical industry prefers to market products with a brand name than products under a generic name
 - b. intellectual property rights impede the approval of generic products
 - c. small market size
 - d. lack of incentives for the supply chain (production, distribution, prescription, and dispensing)
 - e. non-bioequivalent pharmaceutical alternatives are available in the market
 - i. bioequivalence is not required for drug approval by the regulatory agency
 - f. regulatory barriers
 - i. an abbreviate approval process is not available
 - ii. high cost of drug approval and registration
 - iii. slow approval process
 - g. problems with market competition in production, importation, distribution, or health care provision
 - h. barriers to drug imports
 - i. public regulation and policy do not support the use of generic drugs
 - j. corruption

- 2) Generic drugs are available but not consumed:
 - a. lack of incentives for the use of generic drug by the supply chain
 - b. economic incentives in the supply chain for use of branded instead of generic products
 - c. the supply chain and the consumers prefer branded drugs because there is not a quality assurance system established in the country
 - i. generic drugs are believed to be lower quality products
 - d. payers pay for branded products when generic products are available
 - e. legal prohibition of generic substitution
 - f. generic drug prices are unaffordable
 - g. negative marketing and public campaigns against the use of generic drugs
 - h. corruption

Generic Drug Regulation and Policy

Written Generic Regulation and Policy

Issue Description

Development of a generic market demands the existence of a written generic drug regulation and policy regulating the different aspects of the pharmaceutical market

Policy Alternatives

1. Approve a written generic drug regulation and policy

Quality Assurance

Issue Description

Lack of drug quality is a problem in most developing countries. Generic drugs are interchangeable with the branded drugs if the quality of the different drug available in the market is assured.

Policy Alternatives

1. Include enough resources in the drug regulatory agency budget for drug quality assurance
2. Establishment of a drug quality assurance system integrating the activities of the public and private sectors. This system should guarantee the quality of all the activities in the pharmaceutical market that could affect patient outcomes, including R&D, registration, international trade, production, distribution, dispensing, prescription, and use
3. Include the requirement of demonstration of bioequivalence for approval and registration of all drugs
4. Incentives to private investment in quality assurance
5. Establishment of multinational regulatory bodies
6. Strengthen the use of the WHO international certification system

Generic Drug Production and Distribution

Generic drug production and distribution includes drug development, registration, production, importation, and distribution in the market.

Generic Drug Development Cost

Issue Description

The cost of generic development is difficult to recover when the size of the market is small. This cost acts as an important barrier to generic market entry.

Policy Alternatives

1. Facilitate private generic drug imports
2. Incentives for drug development (taxes, grants)
3. Private development with public support and licensing
4. Contracts to supply the public sector
5. Public development and licensing to private companies
6. Public/private partnerships
7. Multinational collaborations

Testing of a Generic Product by a Competitor Company for Regulatory Approval Before Expiration of the Patent

Issue Description

In many countries, the general patent system does not allow testing of a product by a competitor company before the expiration of the patent. Performing the tests needed for drug approval by a company before the patent has expired would constitute "making" and "using" a protected product, leaving a generic company liable for patent infringement. If the generic companies cannot test a drug for approval before the patent that protects this drug has expired, a distortion will occur after the end of the patent term. Generic competitors entry into the market will be delayed for the period of time that companies need to test the product, plus the time the regulatory agency spends in the regulatory process needed to approve the generic drug application.

Recognizing the importance of the delay in generic entry and its effects on drug prices, several countries have approved specific regulations to solve this problem, allowing drug testing by a generic company before the expiration of the patent, thus making it possible for generic manufacturers to market their products as soon as the patents expire. The specific regulation that allows drug testing by generic companies before patent expiration in the U.S. is called the "Bolar Provision."

Policy Alternatives

1. Regulation allowing for testing of a generic product by a competitor company for regulatory approval before expiration of the patents

Generic Drug Regulatory Approval Process

Issue Description

In developing countries, problems in the speed of generic drug approval establish an important barrier to market entry, especially for imported products. The cost of registration can also be a barrier for generic drug approval applications. Bioequivalence is not required for approval of a generic drug. The regulation allows for approval of non-bioequivalent pharmaceutical equivalent drugs, including drug combinations not clinically tested.

Policy Alternatives

1. Allocate enough resources for the regulatory agency expedited review and approval of generic drugs, especially essential generic drugs
2. Potentate the collaboration between the regulatory agency and the private sector
3. Education of private sector personnel
4. Regulation establishing an abbreviated approval process for generic drugs.
5. Reduction of the generic approval fees charged by the regulatory agency
6. Include the requirement of demonstration of bioequivalence for all drugs

Generic Drug Production

Issue Description

Large multinational generic companies and the generic divisions of branded companies control the world's generic market. The domestic industry of most developing countries is very fragmented, does not produce pharmaceutical raw materials, and manufactures mostly branded pharmaceutical equivalent products. The fragmentation of the domestic industry is a barrier to the development of the domestic industry.

The goal of a generic industrial policy is the development of the domestic pharmaceutical industry and the investment of multinational companies in the country. Most domestic companies of developing countries do not have the economies of scale and multinational operations required to survive in a competitive generic market. Furthermore, multinational companies concentrate the manufacturing operations in a small number of countries. Additionally, the pharmaceutical market of most countries is not large enough to manufacture generic alternatives for each drug.

Several anticompetitive activities are common in developed and developing countries. These activities include: agreements not to compete, agreements of price-related terms, and horizontal and vertical integration resulting in reduction of competition, higher prices to consumer, and increasing problems with drug affordability.

Policy Alternatives

1. Regional and multinational production
2. Antitrust regulation and enforcement
3. Use of drug imports to increase market competition
4. Incentives for national and regional production of essential drugs
5. Public regional and multinational partnerships
6. Private multi-company agreements
7. Horizontal integration
8. Generic licensing

Intellectual Property

Issue Description

International agreements, in particular the WTO, are strengthening pharmaceutical intellectual property rights. While intellectual property remunerates innovation it also limits competition and consumers end up paying more for a patented drug than they would have paid otherwise for generic substitutes. Intellectual property results in monopolies that lead to standard deadweight losses for society and drugs become unaffordable for a higher number of people.

Policy Alternatives

1. Limit pharmaceutical intellectual property rights to the minimum demanded by international agreements
2. Broad use all the legal possibilities allowed by international agreements
 - a. Parallel importation
 - b. Compulsory licensing
3. International organizations agreement for reduction of pharmaceutical intellectual property rights for developing countries

Generic Drug International Trade

Issue Description

Most countries in the world cannot manufacture all drugs required for domestic needs. Drug imports can be finished products or raw materials needed for drug production. Imports make drugs available in countries different from the manufacturer country, which increases the drug supply in the country accepting the import. Drug imports may also improve the competition in the pharmaceutical market by increasing the number of competitors in the market. There is not assurance of the quality of drugs available in the international market.

Policy Alternatives

1. Reduce taxation of generic drug imports
2. Incentives for generic drug importation
3. International bids for domestic consumption
4. Public importation of drugs
5. Use of WHO international trade certification

Generic Drug Distribution

Issue Description

The drug distribution system in developing countries is more favorable for branded than for generic products. Small generic companies cannot use the regular channels to distribute their products and assume higher costs for direct distribution to pharmacies and health care providers.

Policy Alternatives

1. Antitrust regulation and enforcement
2. Incentives for generic drug distribution
3. Public distribution of generic drugs

Financing Generic Drugs

The use of generic drugs by public and private health care systems effectively reduces the financial resources needed for drug expenditures. The use of generic drugs is directly influenced by the characteristics of the financing system, including drug insurance, pricing, acquisition, and payment.

Drug Financing and Insurance

Issue Description

Out-of-pocket expenditures and co-insurance are important sources of drug financing in developing countries. The poorest sector of the population in developing countries cannot afford to pay any coinsurance or out-of-pocket expenditures in order to access needed drugs.

The use of generic drugs reduces public and private financial needs for drug expenditures. The private health care providers have economic incentives from the pharmaceutical industry to use the most expensive drugs.

Positive financial incentives include reduction of co-payments for generic drugs in comparison with branded products.

Policy Alternatives

1. In public drug procurement, generic drugs should be preferred to non-bioequivalent pharmaceutical equivalents. At similar prices, generic drugs should be preferred to non-generic drugs
2. All incentives for the use of branded, pharmaceutical equivalent or generic pharmaceuticals should be disclosed by regulation.
3. The public sector can establish different levels of co-payment for generic and branded products

Generic Drug Pricing

Issue Description

While generic competition can reduce drug prices, several aspects of the market should be taken into account when deciding the drug price regulation of a country. First, there is not information about drug prices and the distribution of the price among the different market players. Second, international drug price comparisons are needed to assess the price level of an individual country. Thirdly, anticompetitive agreements are common in the pharmaceutical market.

Policy Alternatives

1. The public sector should regulate the pharmaceutical market to make drug prices and actual cost of transactions transparent, including discounts, rebates and any other financial incentive
2. National and international price comparisons should be made publicly available
3. Antitrust regulation and enforcement

Generic Drug Reimbursement

Issue Description

Reimbursement is the most important factor explaining the development of the generic market. Generic products need an adequate level of reimbursement to the industry, distributors and pharmacies. The current situation in most developing countries make companies, distributors and pharmacies prefer the use of more expensive products with higher levels of reimbursement instead of using generic drugs of lower cost. Current systems do not appear to be sufficient to create incentives for the use of generic drugs.

Policy Alternatives

1. Reference or maximum allowed cost to control the cost of reimbursed generic drugs, pharmaceutical equivalent, and originator branded products
2. Reimbursement favorable to generic drugs
 - a. Higher mark-up for generic drugs
 - b. Higher dispensing fees –when available- for using generic drugs
 - c. Establishment of a dispensing fee payment for using generic drugs (when dispensing fees have not been used previously)
3. Establishment of financial incentives for generic drug use by health care providers

Generic Drug Utilization

Several functions of the health care system influence generic drug utilization including: therapy selection, prescription, substitution, and dispensing.

Therapy Selection

Issue Description

Most developing countries have established an essential drug list as a basic tool to decide the therapies that should be used in the health care system. The majority of the products included in the WHO essential drug list could be generically available, but branded therapeutic equivalent drugs, non-bioequivalent drugs and originator drugs are used instead of generic products.

Policy Alternatives

1. Drug selection should prioritize the use of generic drugs included in the essential drug list

2. Drug selection should not include non-bioequivalent drugs
3. Branded products should not be included on the lists or formularies

Generic Drug Prescription

Issue Description

Several countries require health care professionals to write a prescription with the generic name. In other countries the prescriber can write the generic or the branded name and the pharmacy dispenses a generic product.

Policy Alternatives

1. Establish a generic prescribing requirement without giving prescribers the option of using branded names
2. Establish a generic prescribing requirement giving prescribers the option of using branded names and allowing pharmacies to substitute the branded drug with a generic drug
3. Establish a voluntary generic prescribing requirement giving prescribers the option of using only branded names and allowing pharmacy to substitute the branded with a generic product

Drug Substitution

Issue Description

The prescription of a prescribed drug can be substituted for a more efficient and/or affordable alternative. The substitution can be done by replacing a branded product with a generic product (generic substitution), or replacing the branded product with a drug with different pharmaceutical properties and similar therapeutic effects (therapeutic substitution). Generic substitution, in combination with reimbursement measures, explains the high use of generic drugs in developed countries.

Policy Alternatives

1. Allowing voluntary or requiring generic substitution
2. Allowing voluntary or requiring therapeutic substitution
3. Drug substitution should be accompanied by changes in drug selection and reimbursement

Consumer Education

Issue Description

The importance of the public sector as promoter of the generic market can be seen in most developed countries. In developing countries, the promotion of generic drugs has been assisted by government sponsored public education campaign, complemented by health care providers promotion of generic drugs.

Policy Alternatives

1. Public sector programs for educating consumers about the advantages of generic drugs