

Pharmaceutical Market and Regulatory Contents for Export of Pharmaceutical Products to Latin American Countries

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Abstract: Indian Pharmaceutical industry is one of the world's largest and most developed, ranking fourth in terms of volume and thirteenth in terms of value. The country accounts for an estimated 10% of global production and 2% of world markets in pharmaceuticals. The regulatory process to obtain marketing authorizations (MAs) for drugs in Latin American (LATAM) countries, despite regional harmonization efforts, is highly country-specific. Complex and evolving ad-hoc requests from reviewers must be proactively addressed to avoid costly delays or show-stoppers to pharmaceutical products import from India. The comforts and confronts faced by pharmacy companies in India. It is of case study approach and presented the Indian pharmacy export advantages, the Government initiatives toward the export market, problems, the recent US trademark legislation issues, and the opportunities in a nutshell. Indian companies have focused on export prospects in both formal and informal markets globally. Keeping the high credibility of serving quality products in the complex market, India has gained a strong reputation among the global place.

Keywords: Latin American (LATAM) Countries, Marketing Authorization (MA), Pharmaceutical Market.

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I. Introduction

Indian Pharmaceutical Market

The Indian Pharmaceutical Industry has acquired a noteworthy position in the global pharmacy sector and has been achieving significant growth in the recent years. Indian pharmaceutical industry is one of the high performing knowledge based segments of the manufacturing sector.

Phase-I (Before 1970) Early stage:

The history of Indian pharmaceutical companies goes back in the early stages of the twentieth century. The nationalism movement also had impact on the scientific sector, which motivated many entrepreneurs, academicians and leaders, to establish scientific oriented companies. It also led to initiate the establishment of modern pharmaceutical companies in India. In 1901, Acharya Prafulla Chandra Roy, a renowned scientist and academician, established Bengal Chemical and Pharmaceutical Works Limited (BCPW) in Kolkata and in 1907, Alembic Chemical Works Co. Ltd., was established in Vadodara by TK Grajjar, Rajmitra and BD Amin. Both the companies had scientific and modern approaches to the pharmaceutical sector. After independence, Hindustan Antibiotics Ltd (HAL) established in 1954. It was wholly owned Government Company established with assistance of with WHO / UNICEF and engaged in the Manufacturing & Marketing of Life Saving Drugs. In the year 1961, Indian Drugs & Pharmaceuticals Limited (IDPL) was incorporated as a public limited company under the Companies Act, 1956. Private players such as Cipla in 1935 also entered in the market during this phase

Phase-II (1970-1980) Government control:

During the period 1970-1990, many local companies were started operating in the pharmaceutical sector. The public sector undertakings such as, Karnataka Antibiotic & Pharmaceuticals Limited (KAPL) in 1981 at Bangalore, Karnataka and Rajasthan Drugs & Pharmaceuticals Limited (RDPL) in 1978, at Jaipur, Rajasthan, were established during this period.

Phase-III (1980-1990) Development phase:

The private companies like Sun Pharma, established in 1983 and Dr.Reddy's Lab, established in 1984, started showing the impact in the market. This period also marked by some government control over pharmaceutical sector, through passing of Indian patent act 1970 and capping the drugs price. The government also took initiative to export the pharmaceutical products during this period.

Phase- IV (1990-2000) Growth phase:

The pharmaceutical sector saw many developments during this period. The Major development was the liberalization of market, which led many multinational pharmaceutical companies to enter into the Indian market. Competition started to increase and many Indian pharmaceutical companies started operating in foreign countries. During this period, Patent (Amendment) Act 2005 was passed, which led to the adoption of product patent in India. VAT has been introduced on medicine and was kept at 4 percent, Pharmaceutical Research and Development Support Fund (PRDSF) was established during this period. During this Growth Phase, the patents filed by pharmaceutical companies increased, and also, spending on R&D by leading pharmaceutical companies increased. The pharmaceutical companies started an aggressive marketing by adopting new sales modules such as Channel Management, Key Accounts Management (KAM), and Contract Sales Organization (CSO).

Phase-V (2000-2011) Acceleration phase (innovation & research)

This period was witnessed by many changes in the pharmaceutical sector. The major policy changes adopted during this period were The National Pharmaceutical Pricing policy 2012 (NPPP-2012) and adoption of New Drug price control order 2013, issued by director of food and drugs, intended to reduce the prices of the drugs. Other policy changes during this period were, allowing of 100% FDI in the medical device industry, National Health policy draft 2015 to increase expenditure in health care sector and Patent Act Amendment 2015, which includes amendments in Patent Act 2002. The period also accounts with second largest number of Abbreviated New Drug Applications (ANDAs) and India is the world's leader in Drug Master Files (DMFs) applications with the US. Leading pharmaceutical companies raised funds for acquisitions and increase their product portfolio during this period.

Latin America Pharmaceutical market

The LATAM pharmaceuticals market has grown steadily in the past 15 years. It has also been dominated by multinational companies based in Europe and the US. The rapid introduction of high-technology medicines into import, export and distribution networks makes Latin Americans increasingly visit their pharmacy.

Since 2008, the region is by far the fastest growing pharmaceutical market in the world. By 2017, Brazil will become the fourth largest pharmacy market, behind the U.S., China and Japan. But, this impressive growth story is not a victory for multinationals. The real winners are Latin American generic drug makers and locally owned retailers.

Latin American generics have evolved from a nuisance to the international laboratories into the dominant force in most medication categories. The most accommodating market in the region is Argentina. Patents were only first legally recognized starting in 2000.

Latin America's \$100 billion pharmaceutical industry is today dominated by Latin American firms. Brazilian, Argentine and Cuban generics producers already export their goods to other emerging markets in Asia, Africa and the mid-East. It may not be long before Latin American pharmacy giants do the same. Perhaps then, the multinational players will finally act upon the opportunities south of the Rio Grande.

II. Aim

- To understand pharmaceutical market in India and Latin America countries (Argentina, Mexico, Brazil, Colombia, Venezuela, Chile)
- To understand regulatory approval process for pharmaceutical products exportation to Latin America.
- List out the administrative requirements of documents for export of drug products to Latin America countries.

III. Objective

The primary objective of this guidance documents are to provide transparent and clear guidelines and procedures for the exportation of pharmaceutical products to Latin America countries.

IV. Discussion

India is among the top six global pharmaceutical producers in the world. Indian vaccines are exported to 150 countries. India produces 40-70 per cent of the WHO demand for DPT & BCG and 90 per cent of measles vaccine. Approximately 70 per cent of the patients in developing countries receive Indian medicines through NGOs like The Clinton Foundation, Bill & Melinda Gates Foundation, Doctors without Borders, the UNCTAD etc.

Presently there are 10,500 manufacturing units and over 3,000 pharmacy companies in India, growing at an exceptional rate. India has about 1,400 WHO GMP approved manufacturing units. India has been

accredited with approximately 1,105 CEPs, more than 950 TGA approvals and 584 sites approved by the USFDA. Globally more than 90 per cent of formulations approvals for Anti-Retroviral (ARVs), Anti-tubercular & Anti-malarial (WHO pre-qualified) have been granted to India. Manufacturing costs in India are approximately 35-40 per cent of those in the US due to low installation and manufacturing costs. India ranks amongst the top global generic formulation exporters in volume terms. India's exports of pharmacy and drugs stood at US\$ 16.8 bn. India exports all forms of pharmaceuticals from APIs to formulations, both in modern medicine and traditional Indian medicines. The country's pharmaceutical industry accounts for about 1.4 per cent of the global pharmaceutical industry in value terms and 10 per cent in volume terms.

Structure of Indian Pharmaceutical Sector

The Indian pharmaceutical sector can be divided into two major segments, namely, Active Pharmaceutical Ingredients (API) or bulk drugs and Formulations. The API can be branded or Generic and these ingredients will be part of Formulations, which will be used to treat Acute or chronic diseases.

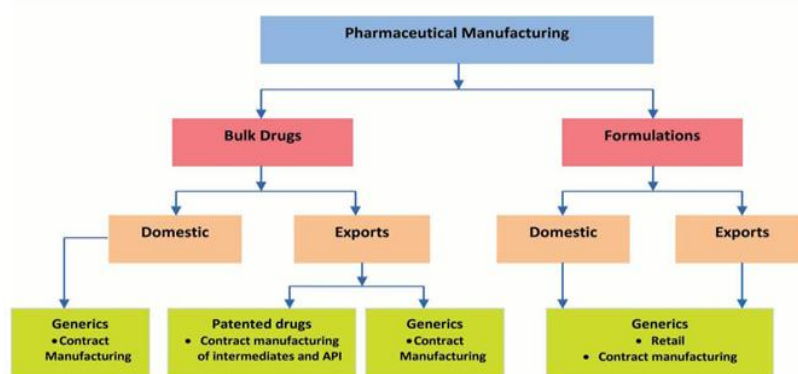


Figure 1: Manufacturing by Indian Pharmaceutical Players

India gained a foothold in the global arena, with reverse-engineered generic drugs and active pharmaceutical ingredients (API). India now seeks to become a major player in outsourced clinical research and the contract research and manufacturing services (CRAMS) segments. India has the highest number of manufacturing facilities (332 sites) approved by the US Food and Drug Administration (US FDA). Further, in 2011, one third of all Abbreviated New Drug Applications (ANDA) approved by the US FDA, belonged to Indian companies.

Trends in Indian Pharmaceutical sector

Focus on Research & Development

Globally, investments in Research & Development (R&D) is about 15 percent of sales turnover and the Indian pharmaceutical companies invested about less than two percent of sales turnover until beginning of the new millennium. The investment was a peak in 2005-06 and showed slower rate in further years. Presently, R&D investment in India is about 8-11 percent of total turnover, which is less than a global investment in R&D and it is expected to increase further because of competition.

Export

Indian Pharmaceutical export market is thriving due to the strong presence in the generic market, which supplies about 20 percent of the global market in terms of volume. Pharmaceuticals Exports Promotion Council is estimated that, export will reach about USD 18.02 billion in 2016.

Joint venture

The focus on joint venture in pharmaceutical sector is increasing. Many foreign companies are joining hands with Indian companies to develop new drugs. The advantages seen in the R&D is contributed by cost effectiveness, availability of skilled employees and government incentives and so on. Cipla signed exclusive partnership with serum institute of India to sell the vaccines in south Africa. "LAZOR" an alliance of six leading pharmaceutical companies formed to share best practices and improve their efficiency and reduce operating costs.

Less time for approval

In order to compete with global market, the drug approval process has been simplified and approval time for new plant has been reduced. In the draft Patent (Amendment) Rules 2015, the time period of patent grant has been reduced from 12 months to 4 months.

Market Size

The Indian pharmacy industry, which is expected to grow over 15 per cent per annum between 2015 and 2020, will outperform the global pharmacy industry, which is set to grow at an annual rate of 5 per cent between the same periods. The market is expected to grow to US\$ 55 billion by 2020, thereby emerging as the sixth largest pharmaceutical market globally by absolute size, as stated by Mr Arun Singh, Indian Ambassador to the US. Branded generics dominate the pharmaceuticals market, constituting nearly 80 per cent of the market share (in terms of revenues). India has also maintained its lead over China in pharmaceutical exports with a year-on-year growth of 11.44 per cent to US\$ 12.91 billion in FY 2015-16, according to data from the Ministry of Commerce and Industry. In addition, Indian pharmaceutical exports are poised to grow between 8-10 per cent in FY 2016-17. Imports of pharmaceutical products rose marginally by 0.80 per cent year-on-year to US\$ 1,641.15 million.

V. Administrative Requirements Of Documents And Procedure For Export Of Drugs From India

Explains export process of Pharmaceutical Products, government rules to export Pharmaceutical Products, export documentation to export Pharmaceutical Products.

A. Introduction

A manufacturer holding valid license copy in Form -25 and from- 28 can obtain No Objection Certificate from Zonal/Sub Zonal offices of Central Drugs Standard Control Organisation (CDSCO) for export purpose only for approved / unapproved new drug / banned drug in India.

B. Purpose

Requirement for the common submission format for issuance of No Objection Certificate for export of unapproved/approved new drugs/Banned drugs from India. This document made as per guidelines issued by Ministry of Health and Family Welfare for Export purpose and Rule 94 of the Drugs and Cosmetic Act, 1940.

C. Scope

This document is applicable for the manufacturer to obtain No Objection certificate Zonal/Sub Zonal offices of Central Drugs Standard Control Organisation (CDSCO) for export purpose.

D. Procedure

Requirement for Common submission Format for issuance of No Objection Certificate for export of unapproved / approved new drugs / Banned drugs from India

The Following documents are required to be submitted in the following manner and order for issue of the No Objection Certificate for export of drugs from India: -

- 1. Covering Letter:** The covering letter is an important part of the application and should clearly specify the intent of the application. The list of documents that are being submitted (Index with page no's) as well as any other important and relevant information may be provided in the covering letter. The covering letter mentioning list of products to be exported clearly indicating name of the drug, dosage form, composition and strength pack size along with quantity and country to be exported duly signed and stamped by the authorized signatory, indicating the name & designation of the authorized signatory along with the name and address of the firm. Each application should be made by the manufacturer only.
- 2. Purchase Order:**
 - a.** Order from the foreign buyer either in the name of manufacturer or in the name of trader mentioning list of products to be exported clearly indicating name of the drug, dosage form, composition and strength pack size duly signed by the competent authority with specific destination point of the importing country. In case of purchase order in the name of trader further a letter from the trader in the name of manufacturer is required to be submitted along with the application
 - b.** It should be signed by the competent authority/person with a valid purchase order no. and recent date not more than 6 month prior to the application made by the firm.
- 3. Manufacturing License:** - License issued by the State Licensing Authority should be enclosed along with each application for the required location to manufacture the drug for export purpose.

4. Performa Invoice:

- a. A copy of Performa invoice from the importing country should accompany with application for import of unapproved Active Pharmaceutical Ingredients, used in the drug formulation.
- b. A copy of Performa invoice duly signed by the competent authority should be addressed to the manufacturer mentioning the required quantity of the bulk drug.

5. Registration Certificate:

- a. For the export of drugs which are banned in India by Central government, which coming under list of drugs prohibited for manufacture and sale through gazette notifications under section 26a of drugs & cosmetics act 1940 by the ministry of health and family welfare.
- b. A copy of registration certificate from the specific importing country along with composition and strength of the drug should accompany with the application
- c. Registration certificate should be provided in the name of manufacturer.

VI. Rules Related To Export Of Drugs From India

Rule 94: Labelling and Packing Of Drugs Other Than Homoeopathic Medicines

- (1) Labels on packages or containers of drugs for export shall be adapted to meet the specific requirements of the law of the country to which the drug is to be exported but the following particulars shall appear in a conspicuous position on the innermost container in which the drug is packed and every other covering in which that container is packed:
 - (a) Name of the drug;
 - (b) The name, address of the manufacturer and the number of the license under which the drug has been manufactured;
 - (c) Batch or lot number;
 - (d) Date of expiry, if any:

[Provided that where a drug, not classified under Schedule F, Schedule F(1) and Schedule X, blood products, Narcotic and Psychotropic Substances is required by the consignee to be not labelled with the name and address of the manufacturer, the labels on packages or containers shall bear a code number as approved by the Licensing Authority mentioned in Rule 21.]

- [(2) The provisions of Rules 96 to 101 inclusive, shall not apply to a medicine made up ready for treatment, whether after or without dilution, which is supplied on the prescription of a registered practitioner provided that:
 - (i) The medicine is labelled with the following particulars: –
 - (a) The name and address of the supplier;
 - (b) The name of the patient and the quantity of the medicine;
 - (c) The number representing serial number of the entry in the prescription register;
 - (d) The dose, if the medicine is for internal use;
 - [(e) The words For External Use Only shall be printed on the label if the medicine is for external application].
 - (ii) Condition (3) of the conditions in Rule 65 is satisfied.]

Rule 95. Prohibition of sale or distribution unless labelled. Subject to the other provisions of these Rules, no person shall sell or distribute any drug (including a patent or proprietary medicine) unless it is labelled in accordance with these Rules.

Rule 96. Manner of Labelling .— (1) Subject to the other provisions of these Rules, the following particulars shall be either printed or written in indelible ink and shall appear in a conspicuous manner on the label of the innermost container of any drug and on every other covering in which the container is packed, namely :—

- (i) the name of the drug
For this purpose,[the proper name of the drug shall be printed or written in a more conspicuous manner than the trade name, if any, which shall be shown immediately after or under the proper name and shall be]
- (a) For drugs included in the Schedule F or Schedule F (1), the name given therein;
- (b) for drugs included in the Indian Pharmacopoeia or the official pharmacopoeias and official compendia of drug standards prescribed in Rule124, the name or synonym specified in the respective official pharmacopoeias and official compendia of drug standards followed by the letters I.P., or, as the case may

be, by the recognized abbreviations of the respective official pharmacopoeias and official compendia of drug standards;

- (c) For drugs included in the National Formulary of India, the name or synonym specified therein followed by the letters _N.F.I.
- (d) for other drugs, the international non-proprietary name, if any, published by the World Health Organization or where an international non-proprietary name is not published, the name descriptive of the true nature or origin of the substance;^[6]

Guidelines For The Export Of Drug Issued By Ministry Of Health And Family Welfare Subject: - Clarification about issuing NOCs for manufacture of new Unapproved drug solely for export.

With reference to the above subject, the undersigned is directed to inform you that following consultation with the Ministry of Law and in consonance with their advice, you may resume the earlier practice of issuing NOC's to applications received for the above purpose .

While processing such applications the following conditions shall be taken into consideration:

1. The application shall provide copy of valid export order and NOC will be issued on a case by case basis against each such order.
2. The applicant shall identify the premises where the drug will be manufactured for export.
3. The applicant should mention whether the batch to be exported has undergone Quality control testing or shall be tested at the destined site.
4. The applicant shall ensure that the drug(s) manufactured on the basis of NOC given as per (1) above its exported and that no part of it is diverted for domestic sale in India.
5. The applicant shall make available for inspection of the appropriate authorities, on completion of the export orders, information regarding each consignment dispatched, remaining stock of drug and related raw materials and intermediates in hand.
6. The applicant shall ensure physical destruction of all unexported quantity of drugs. This should be included as a condition of manufacturing license issued to the applicant by the State licensing authority.
7. The applicant shall ensure that the drug for which NOC has been given shall cease to be manufactured or exported if the drug is prohibited in future in the country or in the importing country.

It is requested that immediate action may be taken to operationalise the process and a report on action taken in this regard to clear the pending applications may be sent to this office by 22.3.99. A monthly agreement may hereafter be sent of the NOCs issued by DCG (I) in an appropriate format.^[7]

Regulatory Approval Process in Latin America

The regulatory process to obtain marketing authorizations (MAs) for drugs in Latin American (LATAM) countries, despite regional harmonization efforts, is highly country-specific. Complex and evolving ad-hoc requests from reviewers must be proactively addressed to avoid costly delays or show-stoppers to local product launches. This article offers a practical overview of product registration processes in LATAM, resulting from more than a decade of experience in a biotech company, to ensure successful global regulatory strategy.

Registration Of Pharmaceuticals Products In Brazil

a) PART 1 – Scope and Definitions

1. The provisions of this document shall apply to manufacturers and importers of medical products.
2. For the purposes of registration, the classification, the procedures and the specifications described in this document shall apply to medical products and their accessories.
3. The definitions shall be adopted for the purposes of this document.
4. This document shall not be applicable to used or reconditioned medical products.

b) PART 2 – Classification

1. The medical products subject of this document shall be classified as Class I, II, III, or IV, according to the intensive risk they represent to the health of consumers, patients, operators, or third parties involved. To classify medical products, the classification rules shall be applied.
2. In case of doubts in the classification after applying the rules described in Annex II, Anvisa shall be liable for classifying the medical product.
3. The classification rules herein described in Annex II may be updated according to the administrative procedures adopted by Anvisa, taking into consideration the technological progress and the information on the adverse effects caused by the use or application of a medical product.

c) PART 3 – Procedures for Registration

1. The registration of every medical product indicated in this document is hereby mandatory, except for those referred hereafter in items 2, 3 and 12.
2. Medical products submitted to clinical research are hereby exempt from registration, provided that they comply with the legal provisions of the competent health surveillance authority on the performance of this activity, prohibiting such products to be commercialized and used for other purposes.
3. New presentations of a medical product set already registered and in intact individual packaging are hereby exempt from registration, provided that its label and instructions for use contains the information about the registration of the corresponding medical products.
4. Anvisa shall grant the registration of families of medical products.
5. To apply for the registration of families of medical products classified as class II, III, or IV, manufacturers or importers shall submit to Anvisa the following documents:
 - Payment proof of the corresponding health surveillance fee;
 - Information to identify the manufacturer or importer and their medical product, described in herein Annexes III.A, III.B and III.C, stated and signed by their legal representative and technical manager;
 - Copy of the authorization given by the manufacturer or exporter overseas so the importer may commercialize the medical product in Brazil. When authorized by the exporter, the importer shall demonstrate the commercial relationship between the manufacturer and the exporter;
 - For imported medical products, proof of registration or free sale certificate (or equivalent document), granted by the competent authority in the countries where the medical product is manufactured and commercialized;
 - Proof of compliance with legal provisions set forth in technical regulations, such as Anvisa Legislation that regulates medical products.
6. Manufactures or importers that request the registration of medical products classified as class I shall submit to Anvisa the documents indicated in the aforementioned items 5(a), 5(b) and 5(e).
7. Anvisa shall evaluate the documentation submitted for *registro*, its alteration, or Revalidation and shall publish its decision on the Brazilian Official Gazette (DOU).
8. The evaluation of the documentation shall be carried out within legal conditions and periods set forth in health surveillance legislation.
9. To request the alteration of a medical product registration, manufacturers or importers shall submit, at least, the document required in item 5(a), Annex III.A completed and other documents required for the original registration of the product whose information has been modified.
10. To apply for the revalidation of a medical product registration, manufacturers or importers shall submit the document required in item 5(a) and the completed Annex III.A. This information shall be submitted within the period set forth in health surveillance legislation and the commercialization of such product shall not be interrupted until the expiration date of its registration.
11. When medical product registration holders, manufacturers or importers may request the cancellation of the registration by submitting the completed Annex III.A.
12. Accessories are hereby exempt from registration as long as they are exclusively manufactured to be part of a medical product with a registration whose technical report(Annex III.C) has information on such accessories. The medical product and its accessories shall have the same manufacturer. New accessories may be attached to the original registration by detailing the principles of their operation, actions and content, as set forth in item 9 of this Part 3.
13. The registration of healthcare products shall be valid for five years, after which it may be successively revalidated for the same period of time.

d) PART 4 – Compliance with Information

1. Any change made by manufacturers or importers in the information herein requested in item 5 of Part 3 shall be communicated within 30 days for Anvisa's approval, in accordance with the provisions of item 9 of Part 3.
2. Every announcement or publicity of medical products made in the consumption market shall strictly match the information submitted to Anvisa by their manufacturer or importer.

e) PART 5 – Administrative Penalties

1. As a health surveillance measure and when seeking well-grounded reasons, Anvisa shall suspend the registration of medical products in the following cases:
 - When the validity of any document herein addressed in item 5 of Part 3 is suspended for safety reasons and is duly justified;
 - When the non-compliance with any requirement herein made in Part 4 has been proven;

- When the product is being investigated by the competent health surveillance authority due to irregularities or defects found in the product or in its manufacturing process, representing a risk to the health of consumers, patients, operators, or third parties involved.
- 2. Anvisa shall cancel the registration of medical products in the following cases:
 - when there is proof that the information in any document herein referred in item 5 of Part 3 has been forged or when any of these documents has been cancelled by Anvisa;
 - When the product or its manufacturing process has been proven by Anvisa to be a risk to the health of consumers, patients, operators, or third parties involved.
- 3. The suspension of medical product registrations shall be published on the Brazilian Official Gazette (DOU) by Anvisa and shall last until the solution to the problem that originated the penalty has been communicated on the DOU.
- 4. The cancellation of medical product registrations shall be published on the DOU by Anvisa.^[8]

Challenging Faces In Export

In recent days, the USFDA has taken action for non-compliance of a regulatory framework to the Indian pharma industry. Notably, many domestic generic drug makers, including Sun pharma and Wockhardt, have faced the consequences. As the Indian pharma has a considerable proportion in exports, but still it has beset with challenges. The challenges include campaigns to harmful generic products, which are in the purview of violation of India's intellectual property rights formalities; suspected generic medicines coming out of India, with degraded quality standards; dependence on pharmaceutical raw material ingredients; and its pricing models compelling the exporters to fix the lower margins for their quality products. To ensure the tag of product made in India, bar-coding for all export products other than primary packaging which has made compulsory from July 01, 2015.^[9]

Recent Issues In Export

The European Union (EU) recently made its trademark law more stringent by introducing enforcement measures on goods in transit within its territories. This means that not only will goods with logos similar to the ones registered in the EU countries be disallowed from being sold in the bloc, but such items could also be seized by customs officials at EU ports and airports even if they are meant for a third country. "The new trademark legislation is unwarranted and unfair as the registration of a trademark is territorial and manufacturers in other countries may not have any idea that these exist," the official said. In its meeting with EU officials, the Indian team argued that a pharmaceutical manufacturer in India, selling items in Latin America or Africa, may be inadvertently using a logo similar to a registered trademark in the EU. "It is wrong to seize such items while in transit to other markets on the ground that it violates trademark protection given to a particular item in the transit country," the official said.^[10]

Some of The Recent Issues In Export

1. Restrictions to patentability for pharmaceuticals
2. Regulatory data protection
3. Import restrictions
4. Intellectual property protections
 - Patent application backlog
 - Ineffective patent enforcement
 - Regulatory data protection
 - Patent term adjustment for mailbox patents
 - Trademarks
 - Scope of patentable subject matter
5. Market access barriers
 - Price control regulation
 - Foreign currency access policy
 - Government price controls
 - Non production certificate
 - Government procurement
 - Government purchase and partnerships for development on production
 - Regulatory burden

Brazil

PhRMA and its member companies operating in Brazil remain concerned regarding discriminatory government pricing policies, patentability standards and enforcement, and regulatory data protection.

Key Issues of Concern:

- A. Patentability standards:** Amendments to the Brazilian Patent Law in the 1999 added Article 229-C, which inappropriately permits the health regulatory agency (ANVISA) to review all patent applications for pharmaceuticals products and/or processes, sometimes contradicting the patentability requirements established by Brazilian Patent Law and adopted by the Brazilian Patent Authority (INPI).
 - B. Regulatory data protection:** Although Brazil has enacted federal laws to ensure adequate data protection for veterinary and crop products, Brazilian law still does not provide adequate regulatory data protection (RDP) for pharmaceuticals.
 - C. Patent term adjustment for mailbox patents:** INPI issued a binding opinion in September 2013 followed by the filing of related lawsuits to entirely invalidate approximately 170 mailbox patents (primarily pharmaceutical patents), alleging that the products covered by those applications should not have been granted a minimum 10-year patent term as measured from the patent grant date.
 - D. Government price controls and taxation:** The current system is excessively complex and lacks transparency. The innovative pharmaceutical industry stands ready to assist the Brazilian Government in developing a transparent and consistent pricing mechanism that appropriately rewards the value of innovative medicines.
 - E. Partnerships for Development on Production (PDPs) 101 and Government purchasing:** There is no clear regulatory framework for the establishment of PDPs and Brazil lacks clear rules regarding the purchasing preferences offered to PDPs. The current PDP model limits competition and prevents Brazil's ability to foster local technology development in the pharmaceutical area. It also remains unclear how Brazil will apply a recently enacted government purchasing program that offers preferences to locally manufactured products and services in public biddings.
- 101.** The Brazilian PDPs follow the same principles of regular PPP agreements with adaptations designed to respond the specificities of the local pharmaceutical market

Intellectual Property Protections

1. Patentability Standards:

One of the most serious problems facing the pharmaceutical industry today in Brazil was created by Article 229-C, the 1999 amendment to the Brazilian Patent Law that authorizes the health regulatory agency (ANVISA) to review patent applications claiming pharmaceutical products and/or processes that may present a health risk. This review is in addition to and given equal weight as the examination conducted by the Brazilian Patent Office (INPI).

This dual examination is incompatible with Brazil's obligations under the antidiscrimination provisions of Article 27.1 of the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). In addition, ANVISA does not limit its role to the review the potential sanitary risk aspects of the patent application but also reviews the patentability requirements. ANVISA and INPI do not apply the same patentability review standards, thus generating uncertainty for patent applicants and undermining incentives for innovation.

In October 2009, the Federal Attorney General (AGU Office) issued an opinion recommending that ANVISA limit its role in the examination process to health and safety risks. As a result of that opinion, an inter-ministerial group was created to define the correct implementation of the decision released by the AGU Office. The inter-ministerial group recommended that ANVISA should analyze the patent application prior to INPI and only those applications that receive ANVISA's approval should be submitted to INPI.

2. Regulatory Data Protection (RDP)

The Brazilian Government still adopts a flexible interpretation of Article 39 of the TRIPS Agreement to allow Government officials to grant marketing approval relying on test and other data submitted by our member companies to prove the safety and efficacy of their products. While some positive steps have been taken to prevent inappropriate disclosure of these data held by the Government, additional efforts are needed to provide certainty that test and other data will be fully protected against unauthorized use to secure marketing approval for a fixed period of time.

Our member companies continue efforts to gain protection for their data through the Judiciary System, with limited success. The intense debate in the Judiciary demonstrates the lack of clarity in the Brazilian legal framework regarding RDP protection for pharmaceuticals. While the federal law 10.603/02 provides protection

for veterinary and crop products, the Brazilian legislation still does not provide similar protection for pharmaceutical products for human use, resulting in discriminatory treatment.

Overall, Brazil lacks adequate protection for data submitted for innovative biopharmaceutical products. period of data protection preventing ANVISA from relying on the innovator's data in approving a follow-on drug application is needed. Although there have been lawsuits seeking to secure a period of data protection for specific products, so far the cases are still pending in the

Brazilian Courts, leaving innovators without reliable regulatory data protection. A productive dialogue among U.S. and Brazilian authorities could lead to an appropriate RDP regime for pharmaceutical products in Brazil by assuring that the domestic legislation meets high standards.

3. Patent Term Adjustment for Mailbox Patents

In September 2013, INPI issued a binding opinion regarding the patent term for pharmaceutical patent applications filed between January 1, 1995 and May 14, 1997 (known as mailbox patents). Brazilian Patent Law 9,279/96 Article 40 provides that Patents will be given a 20-year protection from the date of filing (caput) and A minimum of 10-year protection will be given from the date of grant (paragraph one). However, in the event that a company's patent was filed in Brazil after the country acceded to the WTO, but before the Patent Law came into force (mailbox period) the mailbox patents Article 229 of the IP Law limited the patent term to 20 years from the filing without the minimum 10years of protection from the date that the patent was granted.

Approximately 170 mailbox patent applications for which INPI failed to complete its examination by December 31, 2004 as defined by Brazilian legislation were provided a minimum of 10 years patent protection under Paragraph One of Article 40. INPI's September 2013 opinion has the effect of revoking the granted 10-year minimum terms for those mailbox patents. The opinion, however, is not self-executing, and INPI has filed approximately 30 lawsuits in the Federal Court against the impacted mailbox patent holders seeking to invalidate their patents. INPI is seeking to invalidate the patents entirely or, in the alternative, to adjust the patent term expiration dates for the impacted patents to 20 years from the date of filing.

4. Patent Backlog

While PhRMA recognizes efforts underway at INPI to reduce the patent backlog, delays in patent grants have continued to worsen, undermining otherwise valid patent rights and incentives for companies to bring innovative products to Brazil. As of December 2013, INPI had a backlog of approximately 184,000 applications and estimated that the average time it took to receive a patent for a pharmaceutical product in 2013 was 10.2 years. Unfortunately, this is a significant increase from the average time for all patent applications of 5.4 years in 2011 and even 8.3 years in 2010. Although INPI states that it is committed to reducing the backlog by 2015 by hiring more examiners, this process follows the standard Government of Brazil hiring procedures, meaning that it is a complex and very slow track. Further, even though President Dilma authorized funding and positions have been filled in the last year, the newly hired examiners specialize in technologies other than pharmaceuticals or biotechnology.

The patent backlog for pharmaceutical patents in particular is further exacerbated by ANVISA's dual examination discussed above. As of December 2013, the average time it took for ANVISA to send a pharmaceutical patent application back to INPI with its decision on whether a patent can be granted was a little over one year.

Market Access Barriers

1. Government Price Controls and Taxation

A price control mechanism implemented with minimal input from the pharmaceutical industry allows price adjustments through a formula that excludes productivity gains. As a result, the average price increase is below the rate of inflation measured by the consumer price index (CPI). The methodology used to calculate the maximum annual permitted price increase does not reflect the characteristics of the pharmaceutical sector, and is the result of the application of an excessively complex and non-transparent formula. These restrictions are contrary to the free-market principles espoused by Brazil and create a less favorable environment for innovative pharmaceutical companies.

The Brazilian Government has already recognized the inaccuracy of the current price formula and began to assess possible modification in the legal framework that regulates the annual price adjustment. This movement gives the Brazilian and U.S. authorities a good opportunity to exchange mutual experiences and define a positive benchmark designed to promote free enterprise and also to discuss other and more effective mechanisms to promote access to medicines, such as the implementation of less regressive taxes on medicines at the federal and state levels which, combined, add 34% to the price of medicines (the highest tax burden on medicines in the world).^[55]

2. Government Purchase and Partnerships for Development on Production (PDPs)

The Brazilian Government issued the federal Law 12.349/10 granting preferences for locally manufactured products and services in public tenders. More recently, an amendment to Portaria MDIC 279/11 provided a list of pharmaceutical products eligible for preference margins and defined the parameters for its application in public purchases. While the issuance of Portaria MDIC 279/11 brought more transparency to the purchase process, it still fails in defining the compensation that according to the Law must be offered by those companies that benefit from this mechanism.

Regarding the PDPs greater transparency in the process of selecting technological partners is required. Today the terms and conditions for companies interested in participating in the PDPs processes are not public, which negatively impacts Brazil's ability to attract more competitive proposals. An industrial policy designed to stimulate alliances between national companies funded by the Brazilian Development Bank (BNDES) and international partners without the necessary background and/or certified sanitary processes is causing delays on the deliveries of some PDPs. In other cases, technology providers that entered into PDPs agreements with the Brazilian Government cannot offer the most updated technology and/or are simply not able to develop the technology at all. This model limits the competition and impedes Brazil's ability to foster local technology development in the pharmaceutical area.

3. Regulatory Burden

All participants in the pharmaceutical industry innovative and generic alike, face numerous challenges stemming from the deadlines currently enforced by ANVISA. While Brazilian legislation adequately addressed ethics, safety and efficacy standards, it did not

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provide a mechanism to ensure that ANVISA had adequate capacity to execute its assigned responsibilities. Ph.RMA and its members recognize that the current Board of Directors has demonstrated an awareness of this issue but this alone is insufficient.

The innovative pharmaceutical industry believes that a more efficient regulatory system in Brazil would require:

- More human resources and IT tools so that ANVISA could reduce timelines in analysis of line extensions and other petitions;
- More predictable processes, allowing companies to be prepared in advance, resulting in shorter "clock stops" and faster approvals;
- Introduction of an expedited process for line extensions (at least similar to the deadline for new products) providing faster access to post-approval innovations.

VII. Conclusion

The pharmaceutical products in different countries of Latin America have critical differences. Most countries required additional documentation that is not part of module 2-5 of the CTD, some of which might also be challenging to obtain. The primary challenges in drug exportation process observed and some key recommendation for success in the region is Knowledge of the drug exportation processes and submission content for particular country is essential for the effective planning and execution of global regulatory strategy

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