



INTERNATIONAL
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2016 Top Markets Report **Pharmaceuticals**

A Market Assessment Tool for U.S. Exporters

May 2016



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Executive Summary

Encouraging and fostering U.S.-based innovative and generic industries is critical to the future of the U.S. economy and to improving healthcare outcomes for patients around the world. As growth rates slow in traditional markets, the development of new export markets is essential to sustain the pharmaceutical industry. The U.S. government therefore works to create export opportunities through a concerted effort to remove or diminish market access barriers and provide market information. Protecting the intellectual property of innovative pharmaceutical manufacturers, in particular, is vitally important for continued innovation and exports around the world and, in turn, provides the basis for eventual new growth for the generic industry.

The pharmaceutical industry is comprised of companies engaged in researching, developing, manufacturing and distributing drugs for human or veterinary use. New drugs have an enormous positive influence on global health, prosperity and economic productivity by saving lives, increasing life spans, reducing suffering, preventing surgeries and shortening hospital stays. Advances in medicine have eliminated deadly diseases and have brought other life-threatening conditions under control. Drug therapy is now an integral part of nearly every facet of healthcare, and new breakthroughs promise to revolutionize the treatment of non-communicable diseases.

The pharmaceutical industry is one of the most heavily regulated sectors in the world. Drugs are evaluated for safety, efficacy, manufacturing quality, misleading product claims and illicit inducements to choose a particular drug. Prices are regulated in many countries through their respective healthcare and insurance systems. While product success in the U.S. market is largely determined by open competition based on quality, safety and price, internationally, companies face a patchwork of uneven regulations, protectionist policies and price controls. These obstacles are increasingly being instituted in both developing and developed countries. Regulatory complexity and efforts to contain accelerating health costs are key challenges the U.S. industry needs to overcome.

This *Top Markets Report* examines over 50 different markets in terms of economic development, value of U.S. exports, aging populations, per capita pharmaceutical spending, degree of price controls, intellectual property protection and other factors that contribute to pharmaceutical demand growth. It then assesses key regulatory market barriers abroad that influence U.S. industry's export competitiveness and provides an estimated ranking of export markets by level of opportunity through 2017. The report provides commentary on the challenges and barriers facing U.S. pharmaceutical manufacturers going forward as well as opportunities for effective trade policy and export promotion activities on behalf of U.S. firms.

The following countries have been identified for in-depth case studies: Canada, China, South Korea and Turkey. These markets represent a range of countries to illustrate a variety of points and do not necessarily reflect the top markets overall.

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Overview and Key Findings

Introduction

The pharmaceutical industry is comprised of companies engaged in researching, developing, manufacturing and distributing drugs for human or veterinary use.¹ New drugs have an enormous positive influence on global health, prosperity and economic productivity by saving lives, increasing life spans, reducing suffering, preventing surgeries and shortening hospital stays. Advances in medicine have eliminated deadly diseases and have brought other life-threatening conditions under control. Drug therapy is now an integral part of nearly every facet of healthcare, and new breakthroughs promise to revolutionize the treatment of non-communicable diseases.

Understanding Pharmaceutical Industry Products

For the sake of simplicity and unless otherwise noted, ‘pharmaceuticals’ (or ‘drugs’, ‘medicines’) in this report refers to innovative and generic products, chemically-derived and biologically-derived products, and prescription-based and over-the-counter products. See below for a breakdown of pharmaceutical product sectors:

Pharmaceuticals (biopharmaceuticals, drugs, medicines) are defined as any substance intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease or any substance (other than food) intended to affect the structure or function of the body.² Drugs are produced in forms such as pills, tablets, capsules, vials, ointments, powders, solutions and suspensions.

Innovative (originator) chemically-derived drugs are developed through extensive R&D and clinical trials in both humans and animals. The innovator relies on patents, regulatory data protection and other forms of intellectual property rights (IPR) to justify the investment required to bring a product to market. The U.S. patent term is 20 years, and drugs are eligible for at least five years of market exclusivity depending on the time between patent validity and U.S. Food and Drug Administration (FDA) approval. The pharmaceutical industry is heavily dependent on the development of new molecules to replace the revenue stream of older drugs that are approaching the expiration of their patent terms. Pricing of new drugs is designed to cover past and future R&D expenditures.

Generic drugs are copies of innovative pharmaceuticals that contain the same active ingredients and are identical in strength, dosage form and route of administration. In the United States, upon either patent expiration or a successful challenge of relevant patents, a manufacturer can produce a generic drug as long as it meets FDA approval and bioequivalence standards.³ Generic companies typically focus on high volumes to earn profits, requiring efficient production methods and distribution chains.⁴

Generics that are sold under the chemical name are known as “commodity generics.” Commodity generics are often manufactured by more than one company and compete mainly on price. “Branded generics” are marketed by a drug company under its own label and typically command higher prices than non-brand generics.

Biologics (biotech drugs, biological drugs, biopharmaceuticals) include a wide range of products such as vaccines, therapeutic proteins, blood and blood components, tissues, etc. In contrast to chemically synthesized drugs, which have a well-defined structure and can be thoroughly verified, biologics are derived from living material (human, animal, microorganism or plant) and are vastly larger and more complex in structure. Biologic medicines are revolutionizing the treatment of cancer and autoimmune disorders and are critical to the future of the industry.⁵

Biosimilars (follow-on biologics) are versions of biologic products that reference the originator product in applications submitted for marketing approval to a regulatory body. Gaining regulatory approval in developed markets is far more complex for biosimilars than for chemical generics and may involve costly clinical trials. Those that succeed will also have to compete with the originator companies who are unlikely to exit the market. The biosimilars market is expected to increase significantly with an approval pathway now available in the United States.⁶ Prices of biosimilars may not be drastically cheaper than their patented counterparts.⁷

Over-the-counter (OTC) drugs are distinguished from innovative and generic drugs in that consumers do not need prescriptions to purchase them. OTC drugs are

considered by regulators to be safe for self-diagnosis and self-medication. In the United States, there are an estimated 100,000 OTC drug products marketed and sold in a variety of outlets, such as pharmacies and convenience stores.⁸ Sometimes drugs become OTC as a result of extensive market use that enables regulators to determine that the product is safe to dispense without a prescription. The innovator may also move to apply for OTC status upon patent expiration.

Active pharmaceutical ingredients (APIs) and excipients are ingredients in a medication. APIs are the compounds that make drugs effective. Excipients are the inert substances that give a medication its form, such as cornstarch (to make a tablet) or sterile water (to make a liquid), and serve as a delivery vehicle to transport the active ingredient to the site in the body where the drug is intended to exert its action. Other functions of excipients include keeping the drug from being released too early, allowing the drug to disintegrate into particles small enough to quickly reach the blood stream, protecting the product’s stability so that it will be at maximum effectiveness at time of use, and improving its taste and appearance.⁹ APIs and excipients must meet standards established by pharmaceutical standards-setting bodies (e.g., pharmacopeias), including purity, toxicity and absorption rates.

Key Findings: Top Markets and Methodology

This *Top Markets Report* examines 50 different markets in terms of economic development, value of U.S. exports, aging populations, per capita pharmaceutical spending, degree of price controls, intellectual property protection and other factors that contribute to pharmaceutical demand growth. It then assesses key regulatory market barriers abroad that influence U.S. industry’s export competitiveness and provides an estimated ranking of export markets by level of opportunity through 2017. Top markets for

pharmaceutical products continue to be developed countries in Western Europe, East Asia, and North America with high per capita spending on healthcare, growing elderly populations, and advanced regulatory systems. Though ranked lower, there are growing opportunities in developing countries like China as incomes and healthcare spending increases.

Methodology

Global industry information and data on total pharmaceutical sales, per capita pharmaceutical sales and percentage of patented drug spend are primarily sourced from Business Monitor International (BMI). Pharmaceutical export values are obtained from the Trade Policy Information System (TPIS). The ranking weighs heavily BMI’s Pharmaceutical Risk/Reward Index, a comprehensive metric that includes quantitative and qualitative factors that help determine the attractiveness of a market. Rankings of price controls are primarily sourced from a study by the Information Technology & Innovation Foundation.¹⁰ Other qualitative factors considered include U.S. Commercial Service industry rankings. See Appendix for more detail on methodology, data used, and full rankings.

Industry Overview and Competitiveness¹¹

Economic impact

Large, diversified and global, the U.S. pharmaceutical industry is one of the most critical and competitive sectors in the economy. According to the Pharmaceutical Research and Manufacturers Association (PhRMA), more than 810,000 people work in the biopharmaceutical industry in the United States across a broad range of occupations, such as scientific research, technical support and manufacturing. Directly and indirectly, the industry supports over 3.4 million jobs across the United States and added an estimated

Figure 1: Near-Term Pharmaceutical Export Market Rankings (2016-2017)

1	Japan	11	Sweden	21	Portugal
2	Belgium	12	Spain	22	Poland
3	Switzerland	13	Denmark	23	Greece
4	United Kingdom	14	Norway	24	Australia
5	Germany	15	Italy	25	Mexico
6	Austria	16	Taiwan		
7	Canada	17	Ireland		
8	Netherlands	18	Czech Republic		
9	France	19	South Korea		
10	Finland	20	China		

\$790 billion to the economy in 2014.¹² Although manufacturing jobs supported by the industry are expected to decline over the next decade due to continued productivity gains, it will remain an important source of high paying jobs, providing salaries way above the national average.

Figure 2: U.S. Snapshot

Population: 322 million

Population over 65: 48 million (15%)

Total healthcare expenditure: \$3.12 trillion (17.4% of GDP)

Government healthcare expenditure: \$1.49 trillion (47% of total)

Private healthcare expenditure: \$1.63 trillion (52% of total)

Total pharmaceutical sales: \$333 billion (1.9% of GDP; 10.7% of total healthcare exp.)

Per capita pharmaceutical sales: \$1036

Generic sales: \$70 billion (21% of total sales)

Patented sales: \$244 billion (70% of total sales)

OTC sales: \$19 billion (6% of total sales)

Research and development (R&D)

The pharmaceutical sector has consistently been one of the most R&D intensive industries in the United States. The research-based industry generally allocates around 15 to 20 percent of revenues to R&D activities and invests over \$50 billion on R&D annually.¹³ Although the United States remains the global leader in innovative R&D investment, producing more than half the world's new molecules in the last decade, its continued leadership cannot be taken for granted. R&D performed in the United States has become increasingly expensive relative to emerging economies in Asia, such as China and Singapore, where governments have enacted policies to attract investment and are poised for future growth. Conditions that limited R&D offshoring in the past, such as market proximity and availability of talent, are rapidly shifting.

Domestic market

The United States has one of the world's most supportive domestic environments for the development and commercialization of pharmaceuticals with minimal market barriers. Its strengths include an intellectual property system that rewards innovation through patent and data protection, a science-based regulatory system that is

Figure 3: Researched-based Pharmaceutical Companies

Research-based pharmaceutical companies operate under a challenging, high-stakes business model in which the failure rate is high. The R&D and regulatory review process for new drugs can often take over a decade and require hundreds of millions, if not billions, of dollars in investments. Around half of new medicines fail in the late stages of clinical trials, and even those that succeed often fail to make a profit. Only two of out of 10 medicines generate returns that exceed average R&D costs.¹ In the United States, more than 90 percent of biopharmaceutical companies do not earn a profit.¹

considered the most rigorous in the world, the world's largest scientific research base fostered by academic institutions and decades of government research funding, and robust capital markets. The United States attracts the majority of global venture capital investments in start-up biopharmaceutical enterprises.

In addition to a favorable IP and regulatory environment, U.S. laws allowing direct-to-consumer advertising creates immense demand for specific patented drugs.¹⁴ More importantly, the United States is the world's largest free-pricing market for pharmaceuticals. As a result, prices are comparatively high to make up for lower profits in other countries and to cover R&D costs. The United States also has high per capita incomes, unmatched access to healthcare, a large elderly population, a culture of end-of-life prolongation, high rates of chronic diseases and drug consumption and a strong consumer preference for innovative drugs. All of these factors contribute to it being, by far, the world's largest pharmaceutical market with \$333 billion in sales in 2015, about triple the size of its nearest rival, China. The United States will remain the world's most important market for the foreseeable future with healthy growth expected across all product sectors.

Industry trends

Fast growing segments of the pharmaceutical market include biologics and generics. Biologics now account for over a third of all new drugs in clinical trials or awaiting FDA approval.¹⁵ U.S. generic drug sales reached an estimated \$70 billion, representing a quarter of the global market, due to a large number of drugs going off-patent and healthcare reforms favoring

generics. Although generics make up only 22 percent of total prescription sales, its share of filled prescriptions has risen from 19 percent in 1984 to 88 percent in 2015.¹⁶ The high volume and low value reflects an extremely competitive sector with low-cost imports adding increasing pressure on domestic generics producers. It also points to high saturation in the U.S. generics market, underlining the need to expand abroad for future growth opportunities.

Meanwhile, the innovative pharmaceutical industry is currently facing unprecedented challenges caused by slower sales growth, expiring patents, increasing competition from generics, shorter product life cycles, tighter regulations, adverse media coverage and reputational damage, and a decline in the number of new innovative drugs under development. Many are concerned that, despite enormous expenditure on R&D, the industry is producing far fewer new drugs and effective therapies than it did decades ago while sales and administration costs are rising. This concern has been mitigated to some extent with successful drug approvals reaching record highs over the last couple years.¹⁷ The industry is adjusting to a more competitive environment by shifting manufacturing and other operations overseas, revamping research pipelines, reducing employment, particularly in sales but also in manufacturing and research, and organizing mergers and acquisitions (M&As).

A long string of M&As over the last few years has led to a more concentrated global industry with both innovative and generics companies engaging in acquisitions of all sizes. Large firms often purchase smaller, more focused innovator companies for new drugs to accelerate the R&D process. The lines between innovator and generic companies or between pharmaceutical and biotechnology companies have become increasingly blurred, and most major multinationals now incorporate both biologics and generics subsidiaries in their portfolios. As the prevalence of biosimilars grows, the high manufacturing and regulatory costs involved in developing these drugs further clouds traditional distinctions between innovative and generic business models and investment cycles.¹⁸

Trade

Most finished pharmaceuticals consumed in the United States are manufactured locally, particularly complex products such as biologics, or imported from Western European countries, such as Ireland, Germany and

Switzerland. The United States is a major hub for drug manufacturing, as imports account for only around a quarter of the market by value. Nevertheless, the sheer size of the U.S. market means that imports were valued at over \$86 billion in 2015, making it the world's largest importer of pharmaceuticals.

Figure 4: U.S.'s top five sources of imports of pharmaceuticals (2015)

1.	Ireland	\$15.2 billion
2.	Germany	\$14.5 billion
3.	Switzerland	\$9.4 billion
4.	Israel	\$6 billion
5.	India	\$6 billion

With \$47 billion in exports in 2015, pharmaceuticals rank as one the top exporting sectors for IP-intensive industries in the United States. The largest export markets include Belgium, the Netherlands, Canada, the UK and Japan. Projecting forward, the increasing use of low cost manufacturing bases for foreign-derived sales will inhibit the export potential of U.S. manufacturers, and patent expiries for high value export products will place negative pressure on value.¹⁹ Despite these pressures, high levels of R&D may provide new products for export growth in the long-term as will increasing penetration into emerging markets.

Figure 5: U.S.'s top five export destinations for pharmaceuticals (2015)

1.	Belgium	\$6.4 billion
2.	Netherlands	\$4.2 billion
3.	Canada	\$3.8 billion
4.	U.K.	\$3.7 billion
5.	Japan	\$3.5 billion

It should be noted that U.S. trade statistics do not fully reflect the globalized nature of the pharmaceutical industry, which procures ingredients and manufactures in locations based on cost and quality, among other factors. For example, most of the low value active pharmaceutical ingredients and excipients used in finished drugs in the United States are manufactured abroad, particularly in China and India.²⁰ Products and substances may cross borders at several points in the manufacturing chains. Due to product perishability and supply chain costs, foreign companies tend to have substantial manufacturing operations in the United States to better access the market. Likewise, there is significant U.S. industry production of pharmaceuticals in foreign markets, such as Ireland and Singapore, from

which companies export to third countries. There are also a growing number of product-based strategic alliances and joint ventures between U.S.- and non-U.S.-headquartered drug companies.

Global Industry Landscape

The worldwide market for pharmaceuticals is projected to grow from around \$1 trillion in 2015 to \$1.3 trillion by 2020, representing an annual growth rate of 4.9 percent. Several global demographic and economic trends are driving pharmaceutical consumption, including a rapidly aging world population and an associated rise in chronic diseases, increased urbanization and higher disposable incomes, greater government expenditure on healthcare and growing demand for more effective treatments.

Developed markets

The primary pharmaceutical export markets in the near-term will continue to be in the traditional strongholds of North America, Western Europe and Japan, which have high per capita spending rates on healthcare, strong IP protections and streamlined regulatory processes. Growth rates in these developed economies, however, are projected to hover in the low to mid-single digits due to stagnating national economies, tighter regulations, patent expiries and pricing pressure.

In an era of global fiscal austerity, the industry expects foreign governments, particularly in Europe, to continue to put pressure on drug prices through 2017 and beyond, as the high visibility of drug prices makes them a relatively easy target for healthcare providers trying to reduce costs. Even in the United States, the rapidly rising cost of healthcare is resulting in political pressures and regulatory efforts to contain costs that could significantly affect the industry's bottom line.

Comparative effectiveness determinations and value-based pricing are also starting to be mandated by some countries and insurers, who require evidence of cost savings or a clear clinical benefit before including new products in their formularies. Some have also entered into outcomes-based contracts with pharmaceutical companies. Such systems will force pharmaceutical companies to dramatically adjust their business models from simply selling medicines to managing outcomes and justifying costs. Doing so will require increased cooperation with the broader healthcare community throughout government, academia, hospitals,

technology providers and so on to build health management infrastructure and access data. In short, traditional business models are under huge pressure, and pharmaceutical companies will have to work much harder to earn profits going forward.²¹

Developing markets

Meanwhile, market growth is shifting toward emerging markets in Asia, Latin America and elsewhere, where pharmaceutical sales are forecast to expand at double digit rates. Further reforms of legislative systems, especially regarding patent protection and enforcement, as well as improving regulatory conditions, will make these markets increasingly attractive for U.S. industry.

Despite their impressive potential, developing countries pose immense challenges and risks for U.S. companies. To succeed, companies must choose markets selectively and devise tailored sales, marketing, acquisition and pricing strategies. Developed and developing markets often vary politically, culturally, socially and religiously in ways that affect pharmaceutical sales. They may vary, for example, in their use of traditional medicines or in the disease profile of the population due to different ethnic origins, diets and environments. Developing countries also possess very different economic attributes in terms of size, healthcare infrastructure, distribution chains and so forth. Adding to the complexity, companies must overcome a range of regulatory hurdles that differ greatly by country and type of product. A lack of transparency and capacity within regulatory systems, as well as weak or ineffectively enforced IP laws, are all too common.

Importantly, emerging markets differ from each other in their ability and political willingness to pay for innovative drugs. Consumers typically have to fund a larger share of their own healthcare costs as per capita government expenditure on healthcare is low. On average, low-income countries spend 4 to 6 percent of GDP on healthcare, compared to more than 10 percent of GDP for high-income countries, and current global economic uncertainties are likely to slow healthcare spending in the developing world in the near-term.²² Although growing pockets of wealthy patients willing to pay for high cost drugs provide opportunities for U.S. companies, it will take decades before even the most promising emerging markets can afford the latest treatments and prices prevalent in rich countries on a widespread basis.

Unsurprisingly, spending on cheaper, generic drugs is driving, and will continue to drive, most of the growth in emerging markets over the coming decade. While this bodes well for generics manufacturers, companies are not immune from increased price controls and other sales constraints imposed in these markets, which are already impacting revenues.²³ Moreover, companies will face increased competition from local manufacturers as well as a variety of trade barriers, as governments seek to promote domestic industries. The pharmaceutical sector is often targeted by protectionist or industrial policies as governments around the world view it as strategically important: it is non-cyclical, generally employs individuals at above-average incomes and ensures supplies of medicines to local populations.

Challenges and Barriers

Companies entering a foreign market face a plethora of challenges. Not only does each country have unique regulatory, marketing and reimbursement environments, but foreign government policies and practices can pose impediments to market expansion. The most commonly cited problems include regulatory review processes that are non-transparent; lack of effective protection and enforcement for intellectual property rights, which result in widespread sales of counterfeit medicines; burdensome reimbursement and pricing policies; and high tariffs. The following list elaborates on some, but not all, of the main issues facing U.S. companies in the pharmaceutical sector:²⁴

Regulatory approval

Differences in regulatory approval requirements can lead to duplicative testing and clinical trial requirements, delays in product approval and higher costs to manufacturers. Many regulatory agencies lack adequate training and resources to review submissions in a timely and consistent manner, creating enormous backlogs, approval uncertainty and market access delays. There may also be concerns related to the security and maintenance of confidential business information (CBI), such as clinical data that must be submitted for approval.

Patent approval

Similarly, patent backlogs and long, uncertain approval timelines are common problems worldwide. Because the term of a patent usually begins on the date an application is filed, approval delays can greatly reduce

Figure 4: Global Regulatory and Harmonization Initiatives¹

The U.S. Food and Drug Administration's (FDA) mission includes the mandate to "participate through appropriate processes with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements and achieve appropriate reciprocal arrangements." The FDA and its counterparts around the world have been working for years to harmonize regulatory standards through a variety of forums. Examples include:

International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH): Created in 1990, the ICH is the most influential regulatory harmonization initiative for medical products. The outputs of the ICH process include the Common Technical Document (CTD) and the Medical Dictionary for Regulatory Activities (MedDRA).

Asia-Pacific Economic Cooperation (APEC) Life Sciences Innovation Forum (LSIF) Regulatory Harmonization Steering Committee (RHSC): The FDA participates in the RHSC and its working groups, such as Supply Chain Integrity and Product Quality, Pharmacovigilance, Good Review Practices, Multi-regional Clinical Trials, Good Clinical Practice Inspection, Cell and Tissue-based Therapeutic Products, Biotherapeutic Products, etc.

International Pharmaceutical Regulators Forum (IPRF): The IPRF facilitates the implementation of ICH and other internationally harmonized technical guidelines for pharmaceuticals. Working groups have been established specific to: Gene Therapies, Cell Therapies, Good Clinical Practices (ICH E6), Biosimilars, and Nanomedicines.

Pan American Network for Drug Regulatory Harmonization (PANDRH): PANDRH supports regulatory convergence/harmonization in the Americas.

Pharmaceutical Inspection Cooperation Scheme (PIC/S): The PIC/S, comprised of regulators from 23 countries around the world, pursues the international alignment of pharmaceutical inspections through information exchange, training and harmonization of GMP standards and procedures among regulatory agencies.

World Health Organization (WHO): The FDA is involved in a number WHO programs, such as the PAHO/WHO Collaborating Center for Biological Standardization, providing expertise and research in developing WHO written standards and guidelines.

the value of granted patents. This is especially concerning to smaller firms, which tend to be more dependent on their intellectual property assets. Unfortunately, many countries lack patent term adjustment provisions or ways to address unreasonable patent examination delays.

Patentability

Whether through regulations or court decisions, many countries prohibit patents on important pharmaceutical innovations, such as new dosage forms or combinations that make it easier for patients to take medicines. Such incremental innovations are often essential for advancing treatments and add enormous value to patients. Furthermore, while pharmaceutical patents are typically filed and issued prior to clinical trials, a number of regulatory bodies require large, and some would say excessive, amounts of data requirements at the time of filing to prove patentability. These patentability restrictions are often applied solely to pharmaceutical products and discourage innovation.

Data supplementation in patent applications

In consideration of the time and expense required to gather data on pharmaceutical inventions, it is best practice for reviewing bodies to permit applicants to file supplemental data after a pharmaceutical patent application is submitted. Countries, however, are increasingly restricting the permissibility of post-filing data submissions, adding enormous uncertainty, costs and marketing delays for companies. Again, these restrictions are also often applied solely to pharmaceutical products.

Patent enforcement

An effective IP system should offer patent holders strong enforcement tools for defending against infringement. Such tools include patent linkage provisions, which give companies the opportunity to dispute infringing patents before they enter a market and damage their business. Many countries lack such early dispute resolution mechanisms and may even have polices that discourage companies from pursuing patent claims.

Compulsory licensing (CL)

CL refers to when a government allows someone else to produce a patented product or use a patented

process without the consent of the patent holder. It is one of the flexibilities on patent protection included in the TRIPS Agreement, which lists required conditions for issuing compulsory licenses, including non-exclusive nature, limited scope and duration, a right to remuneration that must be “adequate” and so on.²⁵ A number of countries, however, grant CLs without adequate justification on public health grounds, consultations with stakeholders or consideration of alternative options. CLs sometimes also appear to be used as an excuse to promote local manufacturing at the expense of foreign competitors. Governments periodically use the threat of CLs as leverage in pricing negotiations with manufacturers.

Regulatory data protection (RDP)

RDP complements patent rights by providing innovative companies protection for a limited duration against disclosure and unfair commercial use of the safety and efficacy data submitted to drug regulatory authorities. Given the time and expense required to produce such data, it is often extremely valuable intellectual property. RDP is particularly critical for biologic medicines, which may not be adequately protected by patents alone because of their inherent complexity. For this reason, the United States provides 12 years of RDP for biologics. Many countries, however, do not provide adequate, if any, RDP or provide protection only for small molecule treatments but not for biologics.

Pricing

Naturally, pricing is of paramount concern to pharmaceutical manufacturers. Artificially depressed prices set by governments can ultimately cripple drug supplies and reduce incentives for further investment in a market. While the U.S. government is sensitive to concerns related to cost-savings and the affordability of both generic and innovative drugs, it encourages transparency on pricing decisions and appropriate recognition of the value of innovative medicines. U.S. companies indicate that they are often not sufficiently consulted when governments make pricing decisions or determine the methodologies used to set prices. Unfortunately, lack of transparency, consistency and due process is widespread across the world and hinders business decision making.

Common price controls and cost-containment mechanisms used by foreign governments may include international reference pricing (IRP), whereby a government sets the price of a drug by comparing its

price from a basket of select countries, and therapeutic reference pricing (TRP), whereby a government designates medicines that treat a specified condition as therapeutically equivalent and sets a maximum reimbursement limit or reference price for that group. U.S. industry has asserted that the TRP process often assumes that all products used to treat the same condition are interchangeable without adequate scientific justification. Treating medicines that contain different ingredients as if they are identical solely based on the therapy they provide can harm patients, erode the benefits of patent protection, impede competition and inhibit future innovation.

Localization

Some trading partners, potentially in an effort to protect or develop their own domestic industry, limit or ban certain imported pharmaceuticals. Many also condition market entry on local content requirements or local manufacturing, exploit standards requirements to impose *de facto* bans on imports, require technology transfer or disclosure of business confidential information, impose procurement rules favoring local suppliers and so on.

Tariffs

Foreign tariffs, taxes and other fees also present significant market access barriers to U.S. pharmaceuticals. Not only do such expenses unnecessarily increase drug costs to patients, but they also often slow product delivery due to U.S. companies having to make payment on and credit complying transactions.

Counterfeits

A counterfeit drug is a pharmaceutical product that is produced and sold with the intent to deceptively represent its origin, authenticity or effectiveness. It may contain inappropriate quantities of active ingredients (or none at all), may cause bodily harm, may contain ingredients that are not on the label or be supplied with inaccurate packaging and labeling. Estimates on the size of the global counterfeit drug market range from \$75 to \$200 billion and can make up half of all drugs sold in some low-income countries.²⁶ Counterfeit drugs are a dangerous source of unfair competition and financial harm for both the innovative and generic industries. Counterfeits ultimately raise the price of medicines by requiring legitimate manufacturers to use considerable resources to ensure a safe supply chain for genuine pharmaceuticals. Existing government policies and enforcement efforts are often insufficient to address counterfeiting problems.

Country Case Studies

The following pages include country case studies that summarize export opportunities in selected markets. The overviews outline ITA's analysis of the U.S. export potential in each market. The markets represent a range of countries to illustrate a variety of points and not the top four markets overall.

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Canada

Canada is a leading market for U.S. pharmaceutical exporters and among the top 10 pharmaceutical markets globally. The market is supported by a growing elderly population, high per capita pharmaceutical spending and an advanced regulatory system. Shortcomings in intellectual property protection and the lack of uniformity across the country's provinces regarding drug reimbursement policies, however, are causing operational difficulties for U.S. companies.

Overall
Rank

7

Canada is the 10th largest pharmaceutical market in the world and the second largest in North America.²⁷ Pharmaceutical sales are forecast to grow from \$18 billion in 2015 to \$20.3 billion by 2020, representing an annual growth rate of 2.4 percent.²⁸ Per-capita consumption and spending on pharmaceuticals is one of the highest in the world.

As a result of economic growth and an expanding elderly population, healthcare spending in Canada has almost doubled over the last decade or so.²⁹ The total expenditure currently stands at around \$164 billion, or 10.7 percent of GDP, and is projected to reach \$190 billion by 2020. As the population ages, Canada's universal healthcare system will require extensive reforms to address long-term needs in terms of affordability and accessibility.³⁰

While Canada's public sector dominates total healthcare spending, federal/provincial/territorial public drug plans account for less than half of total pharmaceutical expenditures. Canada is second among OECD countries, behind the United States, in the participation of private insurers in drug spending.³¹ Because provinces/territories run separate public outpatient drug plans, coverage and eligibility vary tremendously by region.³² Navigating through the different pricing regimes and administrative complexity can present enormous challenges for companies.

Sales of generics, which account for 24 percent of the total market and 67 percent of prescription volume, are projected to grow from \$4.3 billion in 2015 to \$5 billion by 2020, representing an annual growth rate of 3 percent.³³ Canada has some the highest prices for generics in the world, in part because generics are not subject to the same pricing regulations as their

Figure 5: Canada Snapshot

Population: 35.9 million
Population over 65: 5.8 million (16.1%)
Total healthcare expenditure: \$164 billion (10.7% of GDP)
Government healthcare expenditure: \$116 billion (71% of total)
Private healthcare expenditure: \$47 billion (29% of total)
Total pharmaceutical sales: \$18 billion (1.18% of GDP; 10.6% of total healthcare exp.)
Per capita pharmaceutical sales: \$502
Generic sales: \$4.3 billion (24% of total sales)
Patented sales: \$10.8 billion (60% of total sales)
OTC sales: \$3 billion (17% of total sales)
U.S. pharmaceutical exports: \$3.8 billion

patented counterparts.³⁴ The generics market is expected to grow as the government promotes generics usage and as quality perceptions improve among patients. Patent expirations and improved regulatory pathways for biosimilars will also bolster growth in this segment.

Patented drug sales, which account for 60 percent of the total market, are projected to grow from \$10.8 billion in 2015 to \$12.1 billion by 2020, representing an annual growth rate of 2.3 percent. Although Canadian patients have traditionally exhibited a strong preference for patented drugs, government cost containment measures and heavy price regulation has slowed the rate of market growth. Moreover, the approval process for new drugs remains difficult, and both the number of approvals and access to new drugs are below the OECD average.³⁵

Disease burden

Typical of a mature economy, non-communicable diseases, such as diabetes, cancer, asthma and cardiovascular conditions, account for 97 percent of the total disease burden in Canada. Over 10 percent of the population has diabetes and 16 percent has pre-diabetes.³⁶ The number of new cases of cancer is forecast to increase by 182,000 in 2012 to 246,000 in 2025.³⁷ Approximately 8.5 percent of the population has asthma, which has been increasing in prevalence over the past 30 years, and around 4 percent of Canadians have heart disease.³⁸

U.S. exports and competitive environment

The United States exported \$3.8 billion of pharmaceuticals to Canada in 2015, representing around 33 percent of Canada's total pharmaceutical imports. Government cost containment measures and patent expiries have slowed U.S. pharmaceutical exports, which declined at an annual rate of 4 percent over the last five years.

Canada has been a significant manufacturing base for pharmaceutical companies. The domestic industry is made up of about 140 companies, of which over 50 are research-based, with the 10 largest multinational companies accounting for an estimated 60 percent of total sales.³⁹ The industry employs over 26,000 people and indirectly employs more than 100,000 people.⁴⁰

Due to intense competition from lower-cost foreign manufacturers, domestic pharmaceutical production has been declining at a 2.5 percent annual rate since 2008, and employment in pharmaceutical manufacturing has fallen by an average annual rate of 1.4 percent since 2006.⁴¹ The country is increasingly reliant on imported medicines, and drug imports overall are expected to maintain steady growth. Pharmaceutical trade between Canada and the EU, in particular, is expected to increase as they move toward a more unified regulatory environment. The U.S.-Canada Regulatory Cooperation Council (RCC) Pharmaceutical and Biological Products working group provides opportunities for greater regulatory harmonization between Health Canada and the U.S. Food and Drug Administration.⁴²

From 2011 to 2013, pharmaceutical R&D in Canada declined by 29 percent. In 2014, innovative companies spent a mere 5 percent of their Canadian revenues on R&D in Canada.⁴³ Despite government efforts to

encourage R&D investment through financing and tax incentives, rising operational costs and uncertainty regarding the IPR environment continue to create headwinds. Canada has one of the weakest pharmaceutical IPR regimes of any developed economy, and its unwillingness to reform or implement stricter intellectual property laws undermines the country's attractiveness as a location for investment.⁴⁴

Health insurance, drug coverage

Despite its universal healthcare system, Canada does not offer universal, public outpatient prescription drug coverage. Employers often provide private drug plans, and federal/provincial/territorial drug plans are available to certain elderly and low-income populations. Around a quarter of the population, most of whom are unemployed or self-employed, lack access to either public or private drug plans and must pay out-of-pocket for medicines.⁴⁵

Coverage and amounts of co-payments, deductibles and premiums in public drug plans vary tremendously by province, which have different funding levels and formulary and reimbursement systems. For example, elderly patients in British Columbia, New Brunswick, Prince Edward Island and Newfoundland pay between 0 and 35 percent of their annual prescription costs, but in Alberta and Nova Scotia, they pay between 35 and 100 percent. Over half a million Canadians, mostly in the Eastern provinces, have difficulty accessing necessary drugs, and 6 million people have inadequate access to pharmaceuticals or may struggle to pay for expensive treatments.⁴⁶

Regulatory approval, pricing, and reimbursement

The Health Products and Food Branch (HPFB) within Health Canada is the federal health agency responsible for approving and regulating drugs. The HPFB reviews new drug submissions for the purposes of safety, efficacy and manufacturing quality and issues marketing authorizations, also known as Notices of Compliance (NOC). Following the issuance of an NOC, HPFB's role is limited to post-market surveillance, inspections and investigations of the safety and efficacy of the drug.⁴⁷ NOC reviews take on average over 13 months for chemical compounds and 21 months for biologics.

The pricing and reimbursement process for innovative pharmaceuticals is controlled at three levels: by the Patented Medicine Prices Review Board (PMPRB), by

the Common Drug Review (CDR) and by the many federal and provincial/territorial bodies operating separate formulary and reimbursement regimes.

The PMPRB is a federal body designed to prevent excessive pricing by regulating the ex-factory price of patented medicines.⁴⁸ Innovative pharmaceutical companies are required to submit pricing information to the PMPRB before introducing a new product and on a semi-annual basis. The PMPRB first conducts a review to categorize a product based on its level of therapeutic improvement.⁴⁹ It then applies a price by comparing it to other medicines in the same therapeutic category; reference prices from France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States; and rates of inflation.⁵⁰ If it finds prices to be excessive, as it routinely does, the PMPRB can order a price decrease and even retroactive or punitive payments from the manufacturer.

Although the PMPRB has jurisdiction over an extremely broad range of pharmaceutical products,⁵¹ which remains a point of concern for U.S. companies, it cannot regulate prices throughout the distribution chain (i.e. from the wholesaler to pharmacies to patients),⁵² nor can it participate in price negotiations with federal and provincial drug plans.

The Canadian Agency for Drugs and Technologies in Health (CADTH) Common Drug Review (CDR) is intended to centrally harmonize the reimbursement review process among the provincial/territorial drug plans.⁵³ The CDR requires manufacturers to submit extensive data regarding the clinical and economic benefits of medicines seeking inclusion in public formularies. After a panel reviews the information and conducts pharmacoeconomic and cost containment assessments, the CDR issues a recommendation for inclusion on formularies and the level of reimbursement. The CDR process takes on average 8 to 9 months or around 6 months for biologics.

The CDR is often criticized over a lack of transparency, a poor appeals process and the absence of a specialized review pathway for orphan drugs. Because orphan drugs treat rare diseases in small patient populations, they often lack extensive data for traditional review and cost effectiveness analysis. However, the CDR does not allow for significant exceptions in the review requirements for such products.

After the CDR review, companies must then negotiate separately with each provincial and federal drug plan

for inclusion in the formularies. Although public drug plans typically follow and implement a CDR recommendation 90 percent of the time, manufacturers are still required to file separate and often duplicative submissions addressing issues specific to each plan. It generally takes around 6 to 7 months for a provincial body to decide whether or not to act on a CDR recommendation.

Challenges and Barriers to U.S. Exports

Heightened utility requirements

From 2005 onwards, Canadian courts began invalidating patents that failed to demonstrate “utility” because the original applications lacked evidence in the form of data from long-term clinical studies in patients. In Canada, innovators are now required to “demonstrate” or “soundly predict” the utility of a pharmaceutical as “promised” at the time of filing, meaning that a drug must be useful for exactly the purpose that is specifically promised at the date of patent filing.⁵⁴ This is impractical because companies must file for a patent early in the development process, usually well before clinical trial data is available.⁵⁵ Moreover, companies have no way of knowing what will be required to establish utility because it is interpreted subjectively and courts have set conflicting opinions on the matter. Moreover, Canada does not permit companies to submit post-filing data or evidence to demonstrate utility. The practical result is that pharmaceutical innovations have largely become un-patentable in Canada.

This “heightened” utility standard, which is unique to the world and applied only to pharmaceutical products, has caused 24 patents to be revoked over the last decade. All of the products affected were significant commercially, and damages from the premature loss of patent protection are estimated at \$766 million for U.S. companies alone.⁵⁶ Incongruously, every patent revoked on this basis had been approved by Health Canada and had been benefiting patients for years, undermining Canada’s justifications surrounding its ‘usefulness’.⁵⁷

Right of appeal in Patented Medicines (PM) Notice of Compliance (NOC) proceedings

Under Canada’s PM NOC regulations, generic drug companies are allowed to challenge innovators’ patents through a summary judicial review process in which patent owners have limited ability to dispute evidence

or provide arguments. Moreover, only generic manufacturers are allowed to appeal an unfavorable outcome. The innovator instead has to file a separate patent infringement case after the generic product enters the market, essentially restarting the process. It might take years before such patent infringement cases are tried, during which time injunctions to prevent generic market entry are rarely granted. Additionally, if a patent holder tries to prevent a generic manufacturer from obtaining market approval but ultimately loses, the generic manufacturer can claim compensation for lost profits and is often awarded damages from the innovator that are punitive in nature.

Standard for the Disclosure of Confidential Business Information (CBI)

Certain amendments in the recently enacted Bill C-17, *An Act to Amend the Food and Drugs Act*, appear to allow the Minister of Health to disclose confidential business information (CBI), such as clinical trial data submitted for market approval, without confidentiality protections. The language describing both the threshold for disclosure and the potential recipients is very broad, requiring only that “the Minister believes that the product may present a serious risk of injury to human health.” Although Health Canada released a guiding document in July 2015 that provided some reassurance to industry on the matter, the guidance remains non-binding.

Patent term restoration (PTR)

Despite a relatively long regulatory approval timeline for new medicines, Canada is one of the only developed nations providing no form of patent term restoration.⁵⁸ Although Canada has agreed to PTR provisions in the EU-Canada Comprehensive Economic and Trade Agreement (CETA) and the Trans-Pacific Partnership (TPP), statements made by the government suggest that PTR for unreasonable delays in the marketing approval process will be capped at two years, which is less than half of the maximum protection period in the European Union or the United States. Further, during this period, Canadian generics manufacturers may be permitted to make and sell patented products for export. The government has not yet issued any formal proposals for changes to the Patent Act or Rules to implement patent term extensions in CETA or TPP.

China

The pharmaceutical market in China is one of the most promising for U.S. exports in the long-term given its size and growth potential. Rising per capita incomes, an aging population, greater access to healthcare and regulatory reform are key drivers that will enhance the appeal of China's market to U.S. companies. Increasing price pressure and slowing economic growth, however, will impede sales in the near-term. Moreover, a number of serious regulatory concerns remain, including shortcomings in China's system for pharmaceutical registration and market approval. U.S. industry will continue to look to policy makers for assistance with these barriers.

Overall
Rank

20

China is the second largest pharmaceutical market in the world, forecasted to grow from \$108 billion in 2015 to \$167 billion by 2020, representing an annual growth rate of 9.1 percent.⁵⁹ Total public and private healthcare expenditure reached \$640 billion in 2015 and is expected to almost double to \$1.1 trillion by 2020, as the Chinese government rapidly expands universal insurance coverage.

Pharmaceutical sales currently amount to 17 percent of total health expenditures, or \$78 per person. In terms of the market breakdown, generics dominate with a hefty 64 percent of total sales. Low per capita spending and government policies favor rapid growth in the generic market, which is expected to surpass the United States in sales by 2017, when it is projected to reach \$80 billion.

Patented drugs amount to only 22 percent of total sales. Over the past decade, patented drug sales enjoyed strong, double digit growth rates. In the last couple years, government policy changes regarding reimbursement, tendering, hospital financing and sales promotion have significantly hindered revenues.

U.S. exports

U.S. pharmaceutical exports to China reached \$2 billion in 2015, up from \$617 million in 2010, representing an annual growth rate of 26.6 percent over the last five years. The United States is a leading source of pharmaceutical imports to China, comprising 11 percent of the total.

Figure 6: China Snapshot

Population: 1.38 billion
Population over 65: 131 million (9.6%)
Total healthcare expenditure: \$640 billion (5.9% of GDP)
Government healthcare expenditure: \$348 billion (54% of total)
Private healthcare expenditure: \$291 billion (46% of total)
Total pharmaceutical sales: \$108 billion (1% of GDP; 17% of total healthcare exp.)
Per capita pharmaceutical sales: \$78
Generic sales: \$68 billion (64% of total sales)
Patented sales: \$23 billion (22% of total sales)
OTC sales: \$16 billion (16% of total sales)
U.S. pharmaceutical exports: \$2 billion

Importing drugs to China is complex endeavor. While domestic manufacturers can sell directly to consumers, importers face a daunting, complex and highly fragmented distribution system made up of thousands of local distributors and wholesalers. Transportation quality and regulations vary by locality, and markups at various stages push up a product's final cost. Moreover, depending on the product, duties on imported drugs are high. Regulatory delays, IP violations, counterfeit medicines, price controls and a lack of transparency remain some of the most commonly cited barriers to better penetration of the Chinese market by foreign producers.

Competitive environment

China's generic market is dominated by a large number of low-cost, domestic manufacturers. The fragmented industry includes around 5,000 drug manufacturers, with the top 100 comprising just one-third of the market. Going forward, government policies aim to reduce industry fragmentation by imposing regulatory requirements that the China Food and Drug Administration (CFDA) estimates will shut down hundreds of sub-par, small manufacturers for lack of compliance.⁶⁰

Healthcare industries, particularly biopharmaceuticals, have been targeted by the Chinese government as a priority sector for industrial policies intended to create national champions.⁶¹ While these trends may improve some aspects of market access and regulatory reform, government policy goals are likely to increasingly advantage domestic companies over foreign multinationals.⁶²

Disease profile

In addition to China's large population and rising income levels, the chronic disease burden will remain a key driver of growth in the decades ahead. Changing diets and lifestyles, as well as air and water pollution, are contributing to staggering increases in the incidence of cancer, heart disease, diabetes and other chronic conditions. For example, China already has 110 million diabetics, three times the number in the United States, with many more undiagnosed.⁶³ In 2015, China reported 4.3 million new cancer cases, accounting for 20 percent of the worldwide total.⁶⁴ China's population over 65 will reach 170 million by 2020, creating immense demand for treatment and services for many years to come.

Healthcare reform

To meet these demands, China's healthcare reform program, which began in 2009, includes expanding insurance coverage to its enormous rural population and building thousands of community healthcare centers. Today, over 95 percent of citizens are enrolled in various public health insurance plans, which aim to achieve universal health insurance for the population.⁶⁵ Although coverage remains shallow, the central government is massively increasing its funding and continuing rapid reforms, including the merger of China's new rural cooperative medical scheme with its urban residents basic medical insurance scheme.⁶⁶

Ultimately, the long-term impacts of such developments should be positive for U.S. companies by expanding the depth of coverage for patients, particularly in lower-tier markets. The government's need to focus on cost savings and cut prices, however, is also increasing, creating uncertainty over reimbursement policies. Although the extent of China's macroeconomic problems remains unknown, the economy will likely continue to face significant headwinds and volatility over the next few years. The resulting budgetary constraints will inevitably produce further pricing pressure on drugs, particularly as frustrations over corruption, cost and access to healthcare continue to mount.

To be eligible for reimbursement under the national health insurance system, and therefore be affordable to the mass market, products must be on the National Reimbursement Drug List (NRDL). The NRDL has not been updated since 2009, however, and the process for inclusion on the list, as well as pricing policies, remains opaque and chaotic.⁶⁷ Moreover, new processes include the introduction of a bidding system in which branded generics compete directly on price with domestically-produced generics. Such bidding systems, which vary on a provincial and local level, are driving U.S. companies out of this market segment.⁶⁸

China's healthcare reform is also geared toward rooting out corruption by reducing the reliance of hospitals on a 15 percent mark-up on drug sales as a source of revenue. Until recently, this mark-up generated around 50 percent of hospital revenue, creating incentives for doctors to prescribe high-value medicines. While the gradual prohibition of this practice is positive for the industry in the long-run, it is causing a major drag on pharmaceutical company revenues.⁶⁹

In China, U.S. companies have long been reliant on selling more expensive, patented and branded generic drugs. Although patients predominantly pay out-of-pocket for medicine, they often ask for foreign brand products, partly due to perceptions of superior manufacturing quality. In addition, doctors in China have considerable prescribing power. As such, firms have relied heavily on promotional efforts among healthcare professionals to drive sales.

In 2013, UK-based GSK was fined \$489 million, a record criminal penalty in China, for allegedly bribing doctors and health officials to prescribe its medicines.⁷⁰ The fallout has caused industry-wide reputational damage and increased scrutiny of promotional practices.

Although foreign multinationals have largely ceased egregious sales tactics, domestic companies generally have not appeared to follow suit. Because doctors are extremely overworked and poorly paid, getting their attention for education on new therapies is difficult and corruption remains pervasive. Regardless, foreign companies are vulnerable to further crackdowns in this area and will need to develop strategies for selling drugs that avoid such risks.

The issues listed above are squeezing U.S. pharmaceutical companies in China, with revenue growth for many multinationals slowing from around 24 percent to under 5 percent over the last three years.⁷¹ To remain profitable, companies urgently need to bring new products to the market.⁷² Unfortunately, the China Food and Drug Administration's (CFDA) infrastructure and staff remain unable to approve products in a reasonable timeframe. The extent to which China will bolster CFDA funding, harmonize with global standards and enact necessary regulatory reforms in ways that benefit foreign as well as domestic companies remains to be seen.

Challenges and Barriers to U.S. Exports

Regulatory approval delay

Approval delays for pharmaceutical products have become the most pressing impediment to market access for foreign companies, creating enormous uncertainty over product launches and chipping away years of patent validity. From 2011 to 2014, CFDA concluded an average of around 5,000 application reviews annually, yet it accepted between 7,000 and 9,000 annually.⁷³ As a result, the accumulated backlog of applications is now estimated at around 17,000, and the approval timelines for both innovative and generic drugs can take more than seven years. To help address the problem, CFDA has successfully discouraged and thrown out a large number of deficient applications coming from substandard domestic manufacturers, and they have hired more review staff. Review efficiency has recently increased as a result. In 2015, CFDA completed reviews on 9,600 applications, compared to 5,260 in 2014.⁷⁴

Through various engagement opportunities, such as the U.S.-China Joint Commission on Commerce and Trade (JCCT), U.S. industry has raised with China its concern with long wait times for approval. At the 2014 JCCT, China made commitments to streamline its

approval process and eliminate the application backlog within 2 to 3 years.

Since then, China has rolled out a series of reforms and programs to reduce the current drug lag. Ongoing reforms signal national treatment concerns where foreign companies and imported products are treated differently than domestic products. For example, in a recent change in the CFDA review policy, innovative medicines manufactured locally in China are granted expedited priority review. Biosimilars from foreign companies remain blocked from the multi-regional clinical trial pathway and can only apply for clinical trials in China after receiving approval in the United States or European Union. This puts foreign biosimilar producers at a disadvantage to domestic firms and can result in additional market access delays of five years or more.

Regulatory data protection

During its WTO accession in 2001, China agreed to provide six years of regulatory data protection. Because of lack of clarity in its definition of “new chemical entity” (NCE) in its drug registration system, however, China interprets this commitment as only applicable when the drug is “new” to the world, as opposed to “new” to the regulatory authority. As such, Chinese domestic companies have been able to use U.S. innovators’ data to apply for marketing approval for drugs first developed by U.S. companies, often before they are able to bring the drug to the Chinese market. At the 2012 JCCT, China committed to define NCE in a manner consistent with international research and development practices, but it has yet to do so.⁷⁵

Definition of “new drug”

The definition problem resurfaced again in the August 2015 State Council Drug Reform Opinion and the November 2015 CFDA reform plan, which went into effect in March 2016 to revise the definition of “new drug” as an entity “new to the world” for regulatory approval purposes. This policy creates the possibility that a drug approved or marketed first outside of China may receive slower regulatory pathways and no market exclusivity in China. The “new drug” definition may also have implications regarding pricing, reimbursement and tendering decisions.

Patent linkage/enforcement

China lacks patent linkage rules to resolve disputes before infringing products are launched on the market. Chinese law requires that a product must actually be sold in the market before a patent holder can even bring an infringement action. Further, although China's laws theoretically allow for injunctive relief, in practice injunctions are rarely, if ever, granted in pharmaceutical cases due to procedural and practical barriers. Moreover, monetary damages awarded by Chinese courts have proven far insufficient to cover lost revenue or discourage infringement.

Data supplementation

Starting in 2001, China's State Intellectual Property Office (SIPO) disallowed patent applicants to file supplemental data and began denying patent protection to applicants that had been granted patents in the United States and elsewhere. China's Patent Re-examination Board then applied the change retroactively and invalidated existing drug patents that had been granted when supplemental data was allowed. At the 2013 JCCT, China agreed that they would allow filing of supplemental data and would note that this is their practice in their representations with the courts. In spite of this, recent court cases appear to violate the spirit of this commitment, and uncertainty remains on when supplemental data will be accepted.

Patent term restoration

The lack of patent term adjustment or restoration provisions to compensate for regulatory review and patent office delays is a serious problem given the review backlogs at SIPO and CFDA.

Transparency

Lack of transparency in Chinese regulatory development is widespread. U.S. pharmaceutical companies have had little opportunity to provide feedback or comment on unpublished process changes and new regulations. Even major amendments to its Drug Administration Law (DAL) have not been consistently released for public comment. At the 2014 and 2015 JCCT, China made commitments to publish relevant pharmaceutical regulations and measures in advance for public comment.

Counterfeit medicines

According to industry estimates, annual revenue losses to U.S. pharmaceutical companies due to counterfeit products in China run between 10 percent and 15 percent of the market, although the percentage could be higher. In the past few years, China has been stepping up enforcement efforts to combat fake medicines through regulatory reforms and enforcement. Still, criminal penalties remain insufficient, thresholds for wrongdoing are too high, and law enforcement is slow to act and is often protective of local industries. The production, distribution and sale of counterfeit medicines and unregulated active pharmaceutical ingredients (APIs) will continue to pose a threat to its trading partners for the foreseeable future.

Under current laws, China lacks effective regulatory control over the manufacture and distribution of APIs, creating regulatory loop-holes that endanger drug supply chains around the world. Chemical manufacturers only register with the CFDA if their product is intended for medical use. If they declare otherwise, CFDA has no authority to regulate them. Furthermore, CFDA does not monitor or inspect APIs intended for export, leaving importing countries and companies responsible for conducting due diligence.

South Korea

South Korea's rapid economic growth has fostered the development of a robust healthcare sector in a relatively short period. Rising incomes, a growing elderly population and increased health insurance coverage are catalyzing pharmaceutical sales. While the country has a sophisticated domestic pharmaceutical manufacturing industry, imports from the United States and Japan remain a significant part of the market. An uncertain and difficult pricing and reimbursement environment, however, may affect the export outlook for U.S.-based pharmaceutical companies going forward.

Overall
Rank

19

South Korea is the 13th largest pharmaceutical market in the world and the third largest in Asia.⁷⁶ Sales are forecast to grow from \$15.1 billion in 2015 to \$18.3 billion by 2020, representing a strong annual growth rate of 3.9 percent. Current spending on healthcare reached \$101 billion, or around 7.4 percent of GDP, which is very low for a developed country.⁷⁷ Still, South Korea boasts a world-class health system in terms of access and quality and is one of the few Asian countries whose population is able to afford innovative treatments.

Like other developed countries with growing public healthcare burdens, budgetary constraints are leading to cost containment measures. In recent years, the South Korean government has slowed pharmaceutical market growth through aggressive price cuts and tightening reimbursement criteria for both innovative and generic medicines. Reimbursement prices of generics are already approximately half the average for OECD countries.

Due to a large domestic generics industry and government policies to encourage usage, generics make up a comparatively large portion of the total market at 47 percent. Further government price cuts, stricter regulations on sales and rebates and intensified competition, however, are creating a difficult environment for generics companies moving forward.

The patented drug sector has seen steady growth above the global average, growing at an average annual rate of 4.1 percent over the last five years. Innovative treatments are introduced swiftly following approval, and the United

Figure 7: Korea Snapshot

Population: 50 million

Population over 65: 6.6 million (13%)

Total healthcare expenditure: \$101 billion (7.4% of GDP)

Government healthcare expenditure: \$52 billion (51% of total)

Private healthcare expenditure: \$49 billion (49% of total)

Total pharmaceutical sales: \$15.1 billion (1.12% of GDP; 15% of total healthcare exp.)

Per capita pharmaceutical sales: \$301

Generic sales: \$7.1 billion (47% of total sales)

Patented sales: \$5 billion (33% of total sales)

OTC sales: \$3 billion (19% of total sales)

U.S. pharmaceutical exports: \$934 million

States-Korea Free Trade Agreement (KORUS) contains provisions that, if adhered to, will strengthen the IP climate. Significant government subsidies and incentives are also being directed towards innovative companies investing in R&D. As with generics, however, government price cutting is dampening potential market growth.

U.S. exports

The United States exported \$934 million of pharmaceuticals in 2015, representing around 21 percent of South Korea's total pharmaceutical imports. Over the last five years, U.S. pharmaceutical exports have grown at an annual rate of 7.7 percent. With the KORUS deepening South Korea's reliance on U.S. medicine, the country will remain attractive to U.S. companies looking to pursue innovation and partnerships with local manufacturers in various parts

of the supply chain. Low pricing and reimbursement levels, as well as the lack of predictability and due process in reimbursement decisions, still remain the primary concerns for U.S. companies.

Competitive environment

South Korea's domestic pharmaceutical industry is relatively advanced and dominated by large generics firms. In recent years, the government has used subsidies, tax breaks, reimbursement policies and IP laws to promote R&D investment by both domestic and multinational firms.⁷⁸ The country now boasts a robust and growing R&D sector, particularly in biotech, with several locally-developed innovative drugs receiving approval in recent years.⁷⁹ With the establishment of an approval pathway for biosimilars in 2009, South Korea aims to become a global leader in biosimilar development and stem cell research. The country has a booming clinical trials industry, bolstered by a streamlined regulatory process and world-class medical facilities. Seoul is now one of the world's largest clinical research centers by trial numbers.⁸⁰

Demographics and disease burden

Due to a low fertility rate, South Korea's population over 65 is expected to increase from 13.1 percent of the total in 2015 to 15.8 percent by 2020. This aging population will sustain demand for pharmaceuticals given its high burden of non-communicable diseases, such as heart disease, obesity, cancer and diabetes. In 2012, South Korea recorded 220,000 new cancer cases, which is the leading cause of death.⁸¹ An estimated 8.7 percent of the adult population has diabetes, and 22 percent of all deaths are caused by heart disease.⁸²

Healthcare, reimbursement and pricing

South Korea provides compulsory, universal healthcare to all residents, regardless of citizenship, through the National Health Insurance (NHI) and Medical Aid Program. The NHI covers 97 percent of all residents and is funded by employers, employees and government subsidies. The Medical Aid Program is strictly government funded. The system is efficient in terms of providing high quality care with low administrative costs. It also relies on high co-payments from patients, set at 35 to 40 percent for drugs, and it is increasing reimbursement restrictions. Many individuals who require expensive treatments must therefore purchase additional private insurance.

Getting products listed on the NHI's reimbursable list is crucial for success in this market. As the only public insurer, NHI has an advantageous position in price negotiations, and the review process is complex. Drugs are assessed by two organizations, the Health Insurance Review & Assessment Service (HIRA) and the National Health Insurance Service (NHIS). HIRA first reviews a pharmacoeconomic analysis of a new medicine and sets a maximum price. NHIS then tries to negotiate down the maximum price with the manufacturer, taking into account projected sales volumes. The final price cannot exceed a basket of reference countries. The process takes about a year to 18 months before final ratification by the Ministry of Health and Welfare (MoHW). U.S. industry has raised a number of concerns about the predictability, methodology and transparency of this process, claiming that final price decisions often lack supporting data and scientific justification.

Once listed, drugs are subject to multiple price cuts for various reasons, such as punishment for illegal rebates, exceeding expected volume sales, fluctuations in reference country prices and automatic price reductions when drugs go off patent. The latter is of particular concern. Following patent expiry, the price of a generic drug is capped at 59.50 percent of the original drug's price. After a year, the cap is lowered again to 53.55 percent. But because new drugs are originally priced against a weighted average in a therapeutic category that includes generics, the patent-expiry price cuts cause a downward spiral in prices across the board. The result is that prices for new drugs are set lower than those of existing drugs.⁸³ Not only does this limit revenues for innovative manufacturers; it also depresses reference prices around the world.⁸⁴

The government's cost containment efforts also include cracking down on illegal rebates and promotional practices. South Korea has had a history of overpricing scandals and pharmaceutical firms providing kickbacks to boost drug sales.⁸⁵ In 2010, the government enacted legislation to regulate such behavior, which mostly targeted the business practices of domestic generics firms. Still, U.S. companies have noted that the regulatory language could be better clarified and more consistently enforced.

KORUS

KORUS entered into force on March 15, 2012 and contains provisions on facilitating high-quality health care and improving access to safe and effective

innovative and generic pharmaceutical products. KORUS requires the United States and South Korea to ensure fair, reasonable and non-discriminatory treatment and to provide predictability and transparency in the pricing and reimbursement process for pharmaceutical products. Importantly, it also strengthens patent protection, such as regulatory data protection and IP enforcement. Since KORUS has been implemented, South Korea has reduced tariffs, enhanced its regulatory transparency and attracted further investment from multinationals.⁸⁶

Challenges and Barriers for U.S. Exports

Pricing and reimbursement

U.S. companies continue to raise concerns that, contrary to KORUS obligations, South Korean regulations relating to pricing and reimbursement of pharmaceutical products - such as continued price cuts on innovative drugs - do not appropriately recognize the value of innovation and lack transparency.

Under KORUS, any new regulations affecting pricing and reimbursement of pharmaceuticals are to be published in advance for comment, and the South Korean government is to address significant, substantive public comments received and explain any substantive revisions made to proposed regulations in writing. The Ministry of Health and Welfare (MoHW), however, continues to make pricing and reimbursement policies with little transparency and opportunity for stakeholder input. Concerns remain that South Korea is, in practice, still not living up to its KORUS obligation to make available an independent review mechanism (IRM) for stakeholders directly affected by pricing and reimbursement decisions. Although the South Korean government argues it has

already adopted an IRM for stakeholders, U.S. industry stakeholders argue that the system now in place does not function in the intended manner.

In addition, there are concerns regarding recent policies that allow pharmaceutical companies with drugs first approved in South Korea to negotiate prices confidentially through a rebate system. Such loopholes tend to discriminate in practice against foreign companies. Additional pricing incentives for locally developed drugs are likely in the works and should be monitored carefully.

Patent enforcement

As part of KORUS, in March 2015, South Korea instituted a pharmaceutical patent linkage system. Known as the “Green List”, the system is designed to meet base requirements for deterring patent infringement prior to obtaining marketing approval for generic drugs. Its effectiveness remains to be seen, as the provision only provides for a nine-month sales stay, which may not be sufficient time to resolve a dispute, and sales stays are not automatic and could be denied.

Data submissions

U.S. companies remain concerned with South Korea’s continued resistance to align its domestic patent rules fully with international standards. In particular, the Korean Intellectual Property Office (KIPO) requires onerous data submissions for pharmaceuticals at the time of filing and does not allow supplemental data to be submitted during patent challenges. The result is that some products that are patentable in other countries cannot be patented in South Korea.

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Turkey

Turkey's pharmaceutical and healthcare market developed rapidly during the 2000s, driven by a modernizing economy, expanded universal health insurance, and a large and growing population. Over the last five years, however, government price cuts have severely undermined sales and profitability growth for both domestic and multinational companies. Moreover, the investment climate continues to suffer from regulatory approval delays, a lack of transparency and a weak IPR framework. Still, rising pharmaceutical demand due to positive, long-term demographic and economic trends holds promise for U.S. companies.

Overall
Rank

37

Turkey is the 29th largest pharmaceutical market in the world and the second largest in Central/Eastern Europe.⁸⁷ Sales are forecast to grow from \$7.6 billion in 2015 to \$9.8 billion by 2020, representing an annual growth rate of 5.2 percent. In 2015, Turkey spent \$39 billion on healthcare, or around 5.5 percent of GDP, which is average for a developing country. Healthcare spending is projected to reach \$50.9 billion by 2020, driven by a growing population, urban migration, rising affluence and the increasing prevalence of chronic conditions, such as diabetes, heart disease, cancer and dementia. Although public spending will continue to dominate the market, growing demand for higher quality care and market liberalization is spurring private healthcare spending, which is expected to rise from \$9 billion in 2015 to \$11.9 billion by 2020.

Although pharmaceuticals sales have risen steadily by volume over the last decade, they have dropped precipitously by value from \$11 billion in 2010 to \$7.6 billion in 2015. This is attributed to currency weakness and several rounds of government price cuts on drugs in response to budgetary shortfalls. In the near-term, continued cost-containment measures, as well as the complex regulatory environment and lengthy approval process, will hamper market growth.

In the long-term, Turkey provides considerable commercial opportunities for U.S. companies. The large population size and low per-capita pharmaceutical spending suggest enormous growth potential, particularly as universal insurance coverage deepens and private healthcare spending expands. Turkey's slow march towards regulatory harmonization with the

Figure 8: Turkey Snapshot

Population: 79 million

Population over 65: 5.9 million (7.5%)

Total healthcare expenditure: \$39.4 billion (5.5% of GDP)

Government healthcare expenditure: \$30.4 billion (77% of total)

Private healthcare expenditure: \$9 billion (23% of total)

Total pharmaceutical sales: \$7.6 billion (1.1% of GDP; 19.4% of total healthcare exp.)

Per capita pharmaceutical sales: \$97

Generic sales: \$2.8 billion (37% of total sales)

Patented sales: \$4.1 billion (53% of total sales)

OTC sales: \$.8 billion (11% of total sales)

U.S. pharmaceutical exports: \$108 million

European Union and continued sector modernization will make it increasingly attractive to innovative drug companies.

Sales of generics, which account for 37 percent of the total market, are projected to grow from \$2.8 billion in 2015 to \$4 billion by 2020, representing an impressive annual growth rate of 7.5 percent. Although subject to low prices and intense competition, the sector benefits from government policies favoring generic usage. Meanwhile, patented drug sales, which account for 53 percent of the total market, are projected to grow from \$4.1 billion in 2015 to \$4.8 billion by 2020, representing an annual growth rate of 3.4 percent. Despite increasing demand for innovative medicines, the sector faces headwinds due to patent expirations and challenging regulatory and pricing conditions. Still, the continued involvement of multinational firms in the market is a positive indicator of the segment's potential.

U.S. exports

The United States exported \$108 million of pharmaceuticals to Turkey in 2015, representing 3 percent of the import market. Over the last five years, U.S. pharmaceutical exports have declined at an annual rate of .6 percent. U.S. companies face numerous market access barriers in Turkey, including an unworkable government product inspections system, regulatory delays, a preference for the local generics industry and a poor intellectual property framework. Most significantly, the difficult pricing and reimbursement regime is causing companies to withdraw from the market. Nevertheless, Turkey's expanding population offers export growth potential if U.S. drug manufacturers are able to accept prices that are far below the European average and are able to turn a profit on the low margins available.

Competitive environment

Turkey's domestic pharmaceutical industry is highly fragmented and intensely competitive. The sector consists of over 300 local companies, most of which produce generics, and employs around 23,000 people. Around 70 firms manufacture pharmaceutical end-products in Turkey, mostly around Istanbul. Currently, the top 25 companies hold around 80 percent of the market share, but further consolidation is likely due to pricing pressure and lowered profit margins. R&D activities mostly concentrate on modifying existing molecules and adjusting dosages.

Turkey has the potential to be a pharmaceutical manufacturing hub. The workforce is young, with a large number of skilled science and engineering graduates, while wages remain comparatively low.⁸⁸ Its geographic position provides strategic access to markets in Central/Eastern Europe, North Africa and the Middle East. Yet, foreign direct investment has recently slowed, and Turkey remains heavily reliant on imports for both innovative medicines and APIs.

To address this trade imbalance, the Turkish government is keen to promote domestic production and R&D and has identified several areas, such as biologics manufacturing, where it is willing to provide subsidies and investment incentives.⁸⁹ Unfortunately, government price cuts in the domestic market have undermined these goals by severely weakening the viability of the domestic industry and discouraging international investment. The decline in domestic profitability has also resulted in product withdrawals,

dire shortages of life-saving medicines and a rise in unmet medical needs.⁹⁰

Healthcare, pricing and reimbursement

The Turkish government introduced universal healthcare to all citizens in 2004 and is the country's largest healthcare provider. The Ministry of Health (MOH) oversees national health policy and services, although the system is managed on a provincial level. While out-of-pocket spending on healthcare is considered low for a developing country, the system also suffers from overcrowding and poor facilities.⁹¹ Since 2012, citizens who make less than around \$150 a month are provided free access to healthcare services while those earning more pay a graduated social security premium. In its current form, the financing structure and budgetary outlays for healthcare are not sustainable in the long-term. In response to growing deficits, the government has resorted to ad hoc cost containment measures, including pharmaceutical spending caps and a rigid pricing policy.

Pharmaceutical pricing is regulated by the General Directorate of Pharmaceuticals and Pharmacies, which is part of the MOH, and the Pharmaceuticals and Medical Devices Agency. Turkey uses a reference price system by taking the lowest price available amongst France, Italy, Portugal, Greece and Spain. It then applies a 12 percent discount on the reference price and, on top of that, adds a further public discount of 28 percent for generics and 41 percent for innovative drugs.⁹²

For many years, the reference price was also then converted from Euros to Turkish Liras at a rate fixed in April 2009. As the Lira lost value in the following years, it resulted in a *de facto* price discount of more than 50 percent and billions of dollars in lost revenue for companies exporting to Turkey. Fortunately, legislation enacted in July 2015 has abolished the fixed exchange rate, and reference prices are now converted at 70 percent of the previous year's average Euro/Lira exchange rate.⁹³ Although the new system still does not reflect the true exchange rate, it at least gives companies the ability to raise prices following years of suppression.

Reimbursement decisions are the responsibility of the Reimbursement Commission, led by the Social Security Institution (SGK). The reimbursement system is based on a positive list whereby medicines are categorized according to active substance. Drugs are reimbursed up

to 10 percent above the cheapest medicine within the category, with consumers paying the difference if they opt for a more expensive drug.⁹⁴ By shifting the financial burden onto the patient, the system encourages usage of cheaper generics. It is, however, leading to a race to the bottom in pricing and a proliferation of low-cost, substandard medicines. It is also contributing to shortages and supply issues, as drugs become increasingly unprofitable.

Challenges and Barriers for U.S. Exports

Pricing and reimbursement

As described above, since 2009, Turkey has imposed a number of price cuts on generic and innovative drugs hindering market viability and access. Transparency remains an issue, as reimbursement criteria are not clearly defined and decisions lack sufficient explanations.⁹⁵ It is also time consuming. Reimbursement decisions take over a year to be finalized, and delays are not uncommon as the Reimbursement Commission meets only four times a year.

Good Manufacturing Practices (GMP) inspection requirements

In response to the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) requiring inspections of Turkish manufacturing sites, in 2010, Turkey began requiring U.S. and EU companies to have their pharmaceutical manufacturing plants inspected by Turkish authorities before being issued GMP certificates and receiving marketing approval for their products. According to U.S. industry, the MOH has not demonstrated the capacity to conduct these inspections in a timely manner, leading to excessive backlogs in processing GMP certificate applications and delayed market entry. Such issues hinder economic and scientific cooperation and put foreign firms at a disadvantage.

The Turkish government recently implemented “parallel submissions,” which would allow companies to apply simultaneously for GMP certification and marketing authorization but only for pharmaceutical applications deemed highly innovative. While a positive step, due to limited resources, products without this designation are inevitably subject to even longer delays.

Regulatory delays

The marketing approval process for pharmaceuticals can take more than 500 days, well beyond the 210 day limit as stipulated in Turkish law.⁹⁶ Combined with the GMP inspection backlog and long reimbursement decision process, a drug may take around three to five years to reach the market after regulatory submission. Yet Turkey provides no form of patent term restoration or mechanism to reconcile these delays.

Regulatory data protection (RDP)

Although Turkish laws provide for six years of RDP, in practice this protection is greatly limited.⁹⁷ This is because RDP is tied to the patent term so that data exclusivity ends when the patent expires, even if this is earlier than six years. The RDP term also begins on the date of marketing approval in Europe, which is inevitability many years earlier than in Turkey given its regulatory approval problems. Moreover, Turkey does not recognize RDP for combination products or biologics.

Patent enforcement

Patent protection for pharmaceuticals is a relatively new concept in Turkey, which first started granting it in 1999.⁹⁸ Turkey lacks an effective patent linkage system for resolving patent disputes, and courts lack technical expertise to hear patent cases. As a result, most administrative decisions do not receive appropriate judicial review and cases are ruled against the patent holder.

Localization

The government’s aggressive support for domestic pharmaceutical production has led to increasing localization concerns. Examples include preferential reimbursement arrangements for domestically produced products, the delisting of imported products from the reimbursement list, inspection requirements favoring domestic firms and more efficient regulatory approval pathways for locally manufactured products.

Transparency

Transparency remains problematic throughout Turkey’s regulatory system. For example, in February 2016, Turkey released a draft patent law with wide-ranging implications, including further restrictive patentability requirements for second usage and vague and

concerning language on compulsory licensing to satisfy domestic demand. Nonetheless, the government provided a mere nine days for public comment on the measure.

Addendum: Resources for U.S. Exporters

The U.S. Government has numerous resources available to help U.S. exporters: from additional market research, to guides to export financing, to overseas trade missions, to staff around the country and the world. A few key resources are highlighted below. For additional information about services from the International Trade Administration (ITA), please visit www.export.gov.

Country Commercial Guides

<http://export.gov/ccg/>

Written by U.S. Embassy trade experts worldwide, the *Country Commercial Guides* provide an excellent starting point for what you need to know about exporting and doing business in a foreign market. The reports include sections addressing: market overview, challenges, opportunities, and entry strategies; political environment; selling U.S. products and services; trade regulations, customs, and standards; and much more.

Basic Guide to Exporting

<http://export.gov/basicguide/>

A Basic Guide to Exporting addresses virtually every issue a company looking to export might face. Numerous sections, charts, lists and definitions throughout the book's 19 chapters provide in-depth information and solid advice about the key activities and issues relevant to any prospective exporter.

Trade Finance Guide: A Quick Reference for U.S. Exporters

<http://www.export.gov/tradefinanceguide/index.asp>

Trade Finance Guide: A Quick Reference for U.S. Exporters is designed to help U.S. companies, especially small and medium-sized enterprises, learn the basics of trade finance so that they can turn their export opportunities into actual sales and achieve the ultimate goal of getting paid on time for those sales. Concise, two-page chapters offer the basics of numerous financing techniques, from open accounts to forfaiting and government assisted foreign-buyer financing.

Trade Missions

<http://www.export.gov/trademissions/>

Department of Commerce trade missions are overseas programs for U.S. firms that wish to explore and pursue export opportunities by meeting directly with potential clients in local markets. Trade missions include, among other activities, one-on-one meetings with foreign industry executives and government officials that are pre-screened to match specific business objectives.

Certified Trade Fairs

http://www.export.gov/eac/show_short_trade_events.asp?CountryName=null&StateName=null&IndustryName=null&TypeName=International%20Trade%20Fair&StartDate=null&EndDate=null

The Department of Commerce's trade fair certification program endorses overseas trade shows that are reliable venues and good markets for U.S. firms to sell their products and services abroad. These shows serve as vital access vehicles for U.S. firms to enter and expand into foreign markets. The certified show/U.S. pavilion ensures a high-quality, multi-faceted opportunity for American companies to successfully market overseas. Among other benefits, certified trade fairs provide U.S. exhibitors with help facilitating contacts, market information, counseling and other services to enhance their marketing efforts.

International Buyer Program

<http://export.gov/ibp/>

The International Buyer Program (IBP) brings thousands of international buyers to the United States for business-to-business matchmaking with U.S. firms exhibiting at major industry trade shows. Every year, the International Buyer Program results in millions of dollars in new business for U.S. companies by bringing pre-screened international buyers, representatives and distributors to selected shows. U.S. country and industry experts are on site at IBP shows to provide hands-on export counseling, market analysis, and matchmaking services. Each IBP show also has an International Business Center where U.S. companies can meet privately with prospective international buyers, prospective sales representatives, and business partners and obtain assistance from experienced ITA staff.

The Advocacy Center

<http://www.export.gov/advocacy/>

The Advocacy Center coordinates U.S. government interagency advocacy efforts on behalf of U.S. exporters that are bidding on public-sector contracts with overseas governments and government agencies. The Advocacy Center helps to ensure that sales of U.S.

products and services have the best possible chance competing abroad. Advocacy assistance is wide and varied but often involves companies that want the U.S. Government to communicate a message to foreign governments or government-owned corporations on behalf of their commercial interest, typically in a competitive bid contest.

U.S. Commercial Service

<http://www.export.gov/usoffices/index.asp>

With offices throughout the United States and in U.S. Embassies and consulates in nearly 80 countries, the U.S. Commercial Service utilizes its global network of trade professionals to connect U.S. companies with international buyers worldwide. Whether looking to make their first export sale or expand to additional international markets, companies will find the expertise they need to tap into lucrative opportunities and increase their bottom line. This includes trade counseling, actionable market intelligence, business matchmaking, and commercial diplomacy.

The Global Healthcare Technologies Team

<http://www.export.gov/industry/health/>

The Global Healthcare Technologies Team is a specialized group within the U.S. Commercial Service that works to address issues and trade opportunities specific to the strong and growing healthcare sector, and to ensure you have the information you need to grow your business. The Global Healthcare Technologies Team is dedicated to enhancing the global competitiveness of the U.S. health industry, expanding its market access, and increasing exports. It

accomplishes this through a variety of resources and services for U.S. companies such as webinars, Gold Key and Platinum Key services. The team consists of trade specialists from throughout the U.S. and from U.S. Embassies around the world and provides market intelligence, business matchmaking, trade counseling, and regulations and customs navigation.

Discover Global Markets: Healthcare Connections -- Seattle, Washington, September 13-15, 2016

<http://export.gov/discoverglobalmarkets/healthcareconnections/>

The *Discover Global Markets* series of international trade conferences has been a highly successful and unprecedented effort designed to help U.S. businesses expand sales, penetrate new markets, and boost their bottom line through exports. *Discover Global Markets: Healthcare Connections* is the must-attend event of the year for medical device companies. Featuring global updates on healthcare opportunities, regulations, and best practices for success, this conference will equip you to compete and win internationally. You will hear directly from industry leaders and connect with international buyers, network with healthcare companies from around the country and get breaking news on country market intelligence. *Discover Global Markets: Healthcare Connections* will feature panels on opportunities in the medical device sector, diagnostics, health IT, global health, and more. U.S. Embassy-based industry specialists from around the world will give updates on country projects and regulatory framework.

Appendix 1: Country Rankings, Factors & Weighted Scores⁹⁹

Weighted Scores

Ranking	Country	BMI Pharmaceutical Industry 2016 Risk/Reward Index	U.S. Pharmaceutical Exports (2015)	Pharmaceutical Sales (2016 Forecast)	Pharmaceutical Sales, Per Capita (2016 forecast)	Percentage of Patented Drugs Spend (2016 Forecast)	Years of Data Exclusivity for Biologics	Extent of Price Controls (Low, Medium, High)	Total Score
	<i>Factor Weight</i>	0.45	0.1	0.1	0.1	0.05	0.1	0.1	1
1	Japan	94.4	55.1	87.9	98	97.5	80	50	84.5
2	Belgium	88.9	100.0	4.8	67	91.3	100	50	76.7
3	Switzerland	86.1	32.4	5.3	100	77.3	100	100	76.4
4	United Kingdom	100.0	56.8	32.7	71.2	67.3	100	0	74.4
5	Germany	86.1	35.9	43.3	75.7	78.5	100	50	73.2
6	Austria	88.9	10.4	5.4	99.6	86.7	100	50	70.9
7	Canada	91.7	58.9	14.5	57.8	69.1	80	50	70.8
8	Netherlands	80.6	65.3	4.7	43.6	68.1	100	50	66.0
9	France	88.9	21.4	30.5	66.7	73	100	0	65.5
10	Finland	86.1	0.1	2.1	70.9	86.3	100	50	65.4
11	Sweden	83.3	7.2	3.4	57	90.1	100	50	63.8
12	Spain	72.2	34.0	23.2	72	100	100	0	60.4
13	Denmark	83.3	1.2	2.0	66.3	83.2	100	0	58.6
14	Norway	83.3	0.2	1.5	58.6	86.9	100	0	57.9
15	Italy	61.1	39.2	19.4	46	92.7	100	50	57.6
16	Taiwan	63.9	5.6	4.0	26.6	75.3	50	100	51.1
17	Ireland	58.3	35.5	1.4	62.2	89.1	100	0	50.6
18	Czech Republic	61.1	0.1	2.2	36.7	55.3	100	50	49.2
19	South Korea	66.7	14.4	11.6	32.9	34.2	60	50	48.6
20	China	61.1	31.0	100.0	8.7	19.3	60	0	48.4
21	Portugal	52.8	0.0	2.5	42.7	84.3	100	50	47.5
22	Poland	61.1	0.5	6.8	26	31.7	100	50	47.4
23	Greece	50.0	0.2	3.7	55	74.1	100	50	47.1
24	Australia	69.4	12.6	7.7	47.3	77.3	50	0	46.9
25	Mexico	52.8	25.1	8.3	8.3	63.5	50	100	46.1
26	Hong Kong	63.9	3.2	0.9	28.5	61.9	0	100	45.1
27	Hungary	50.0	0.1	1.3	27.2	51.3	100	50	42.9
28	Singapore	50.0	6.3	0.0	15.6	63.2	50	100	42.9
29	Saudi Arabia	50.0	4.9	7.5	34.6	64.8	50	50	40.4
30	United Arab Emirates	58.3	1.9	2.1	41	78.8	0	50	39.7
31	Israel	38.9	2.8	1.1	30.2	62.8	50	100	39.1
32	Russia	41.7	3.0	12.8	11.7	18.7	100	50	37.4
33	Brazil	55.6	16.4	15.3	9.2	52.6	0	50	36.7
34	Chile	44.4	2.2	2.9	26.3	54.5	50	50	35.9
35	Malaysia	50.0	1.3	1.1	6.6	37.7	50	50	35.3
36	Argentina	38.9	8.0	4.1	13.8	65.2	0	100	33.3
37	Turkey	38.9	1.5	5.9	10.1	59.2	60	50	33.2
38	Colombia	33.3	4.3	1.9	5.8	37.5	50	50	28.1
39	New Zealand	25.0	0.6	0.1	23.6	79.6	50	50	27.7
40	Lebanon	30.6	0.4	0.8	34.5	55.4	0	50	25.1
41	Indonesia	22.2	1.1	4.5	1.2	17.5	0	100	21.6
42	Peru	19.4	0.8	0.6	4.2	35.6	50	50	21.1
43	Vietnam	19.4	0.9	3.3	4.4	17.9	50	50	20.5
44	Costa Rica	8.3	0.1	0.1	20.3	42.9	50	50	17.9
45	Thailand	22.2	2.5	3.3	6.6	31	40	0	16.8
46	Algeria	25.0	0.2	2.9	11	58.7	0	0	15.6
47	India	27.8	4.5	14.5	0	2.4	0	0	14.5
48	Philippines	13.9	1.4	2.2	2.4	26.6	0	50	13.2
49	South Africa	19.4	2.4	1.9	4.9	61	0	0	12.7
50	Egypt	8.3	0.8	3.2	4.3	56.5	0	0	7.4
51	Ecuador	8.3	0.4	0.8	11.1	36.3	0	0	6.8
52	Morocco	11.1	0.1	0.6	3.6	44.5	0	0	7.7
53	Pakistan	0.0	0.3	1.6	0	2.6	0	0	0.3
54	Bangladesh	0.0	0.0	1.4	0.2	0	0	0	0.2

Actual Values for Each Factors

Country	BMI	U.S.	Pharmaceutical	Pharmaceutical	Percentage of	Years of Data	Extent of Price
	Pharmaceutical Industry 2016 Risk/Reward Index	Pharmaceutical Exports, USD (2015)	Sales USD Billions (2016 Forecast)	Sales, Per Capita USD Billions (2016 forecast)	Patented Drugs Spend (2016 Forecast)	Exclusivity for Biologics	Controls (Low, Medium, High)
Algeria	50	\$0.23	\$4.13	\$102.20	52.0	0	High
Argentina	55	\$5.22	\$5.47	\$124.70	56.9	0	Low
Australia	66	\$8.21	\$9.61	\$395.10	66.1	5	High
Austria	73	\$6.79	\$7.01	\$817.80	73.2	10	Moderate
Bangladesh	41	\$0.11	\$2.40	\$14.70	7.5	0	High
Belgium	73	\$64.40	\$6.30	\$554.40	76.7	10	Moderate
Brazil	61	\$10.65	\$18.38	\$87.70	47.4	0	Moderate
Canada	74	\$37.95	\$17.42	\$480.20	59.9	8	Moderate
Chile	57	\$1.49	\$4.09	\$225.30	48.8	5	Moderate
China	63	\$20.05	\$115.46	\$83.50	22.1	6	High
Colombia	53	\$2.84	\$2.92	\$59.90	35.9	5	Moderate
Costa Rica	44	\$0.16	\$0.86	\$177.30	40.0	5	Moderate
Czech Republic	63	\$0.15	\$3.27	\$309.80	49.4	10	Moderate
Denmark	71	\$0.88	\$3.12	\$548.50	70.6	10	High
Ecuador	44	\$0.34	\$1.68	\$102.40	35.0	0	High
Egypt	44	\$0.57	\$4.47	\$47.90	50.3	0	High
Finland	72	\$0.17	\$3.24	\$586.00	72.9	10	Moderate
France	73	\$13.84	\$35.71	\$552.20	62.8	10	High
Germany	72	\$23.18	\$50.40	\$624.60	67.0	10	Moderate
Greece	59	\$0.20	\$5.00	\$457.80	63.7	10	Moderate
Hong Kong	64	\$2.14	\$1.79	\$243.10	54.4	0	Low
Hungary	59	\$0.12	\$2.28	\$232.50	46.4	10	Moderate
India	51	\$2.99	\$17.45	\$13.10	9.3	0	High
Indonesia	49	\$0.78	\$5.98	\$23.00	20.8	0	Low
Ireland	62	\$22.92	\$2.43	\$515.30	75.0	10	High
Israel	55	\$1.88	\$2.11	\$257.20	55.1	5	Low
Italy	63	\$25.33	\$23.01	\$384.70	77.8	10	Moderate
Japan	75	\$35.49	\$101.63	\$804.50	81.4	8	Moderate
Lebanon	52	\$0.35	\$1.75	\$292.10	49.5	0	Moderate
Malaysia	59	\$0.91	\$2.05	\$66.60	36.1	5	Moderate
Mexico	60	\$16.25	\$10.33	\$80.30	55.6	5	Low
Morocco	45	\$0.14	\$1.46	\$42.30	41.2	0	High
Netherlands	70	\$42.09	\$6.20	\$365.20	59.1	10	Moderate
New Zealand	50	\$0.49	\$0.93	\$204.10	67.8	5	Moderate
Norway	71	\$0.24	\$2.57	\$486.60	73.4	10	High
Pakistan	41	\$0.31	\$2.58	\$13.40	9.5	0	High
Peru	48	\$0.63	\$1.50	\$47.30	34.5	5	Moderate
Philippines	46	\$1.00	\$3.29	\$32.10	27.7	0	Moderate
Poland	63	\$0.43	\$8.61	\$223.10	31.5	10	Moderate
Portugal	60	\$0.09	\$3.69	\$358.40	71.4	10	Moderate
Russia	56	\$2.03	\$15.42	\$107.50	21.7	0	Moderate
Saudi Arabia	59	\$3.25	\$9.42	\$292.90	56.6	5	Moderate
Singapore	59	\$4.14	\$0.79	\$138.80	55.4	5	Low
South Africa	48	\$1.60	\$2.91	\$53.00	53.7	0	High
South Korea	65	\$9.34	\$14.10	\$279.20	33.4	6	Moderate
Spain	67	\$21.92	\$27.40	\$594.90	83.3	10	High
Sweden	71	\$4.70	\$4.68	\$474.90	75.8	10	Moderate
Switzerland	72	\$20.94	\$6.88	\$821.00	66.1	10	Low
Taiwan	64	\$3.71	\$5.33	\$227.70	64.6	5	Low
Thailand	49	\$1.67	\$4.55	\$66.70	31.0	4	High
Turkey	55	\$1.08	\$7.54	\$94.70	52.4	6	Moderate
United Arab Emirates	62	\$1.31	\$3.19	\$344.10	67.2	0	Moderate
United Kingdom	77	\$36.62	\$38.29	\$588.00	58.5	10	High
Vietnam	48	\$0.67	\$4.61	\$48.80	21.1	5	Moderate

Appendix 2: Classification Codes for Pharmaceuticals

The North American Industry Classification System (NAICS) is the standard used by Federal statistical agencies, such as the Census Bureau and the Bureau of Labor Statistics, to classify business establishments for the purpose of collecting, analyzing and publishing data related to the U.S. economy. Data on companies that produce drugs and biologics, such as geographic location and employment, are classified under NAICS 3254, “Pharmaceutical & Medicine Manufacturing.” Biotechnology research is captured under NAICS 541711, “Research and Development in Biotechnology.”

NAICS

3254	Pharmaceutical and Medicine Manufacturing
325411	Medicinals Botanicals
325412	Pharmaceutical Preparations
325413	In Vitro Diagnostics
325414	Biologicals
541711	Research and Development in Biotechnology

The Census Bureau defines In vitro Diagnostics (IVDs) as part of the pharmaceutical industry. Due to its regulatory and marketing characteristics, the Office of Health and Information Technology (OHIT) at ITA includes IVDs as part of the medical devices industry.

For the sake of simplicity and conformity, and because BMI uses HS codes 3001, 3002, 3003 and 3004 to calculate pharmaceutical market sizes and projections, this report uses HS code 30 – pharmaceutical products – to calculate export/import values. The Office of Health and Information Technology also uses the following HS codes to capture a broader range of pharmaceutical chemicals and products:

290551, 291822, 292146, 292214, 292219, 292231, 292241, 292244, 292250, 292411, 292424, 292512, 292520, 293221, 293311, 293333, 293339, 293340, 293341, 293349, 293351, 293352, 293353, 293354, 293355, 293359, 293372, 293390, 293391, 293399, 293430, 293490, 293491, 293499, 293500, 293610, 293621, 293622, 293623, 293624, 293625, 293626, 293627, 293628, 293629, 293690, 293710, 293711, 293712, 293719, 293721, 293722, 293723, 293729, 293731, 293739, 293740, 293750, 293790, 293791, 293792, 293799, 293810, 293890, 293910, 293911, 293919, 293920, 293921, 293929, 293930, 293941, 293942, 293943, 293949, 293950, 293951, 293959, 293961, 293962, 293963, 293969, 293970, 293990, 293991, 293999, 294110, 294120, 294130, 294140, 294150, 294190, 300110, 300120, 300190, 300210, 300220, 300230, 300290, 300310, 300320, 300331, 300339, 300340, 300390, 300410, 300420, 300431, 300432, 300439, 300440, 300450, 300490, 300620, 300630, 300660, 300680, 300692

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OTC medicine sales: The Nielsen Company, Consumer Healthcare Products Association (CPHA), BMI

Generic drug sales: Centers for Medicare and Medicaid Services (CMS), Generic Pharmaceutical Association (GPhA), local companies, BMI

Patented drug sales: Centers for Medicare and Medicaid Services (CMS), Consumer Healthcare Products Association (CHPA), BMI

Health spending, Govt. health spend, Private health spend: World Health Organization (WHO), BMI

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Office of the U.S. Trade Representative, *2016 Special 301 Report*, <https://ustr.gov/sites/default/files/USTR-2016-Special-301-Report.pdf>

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Generic drug sales, Patented drug sales: Canadian Generic Pharmaceutical Association (CGPA), Patented Medicine Prices Review Board (PMPRB), BMI

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Population, Population over 65: World Bank/UN/BMI

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- ⁹⁹ BMI Pharmaceutical Industry 2016 Risk/Reward Index, Pharmaceutical Sales, USDbn (2016 Forecast), Pharmaceutical Sales, Per Capita, USD (2016 forecast), Percentage of Patented Drugs Spend (2016 Forecast): BMI
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The BMI Pharmaceutical Industry 2016 Risk/Reward Index weighs market expenditure, market expenditure per capita, five-year projected sector value growth, urban-rural split of population, percentage of pensionable population, population growth, patent respect, policy support, approval expediency, economic diligence, policy continuity, lack of bureaucracy, legal diligence, and business transparency.

U.S. Pharmaceutical Exports, USD (2015): Trade Policy Information System (TPIS), HS 30

Degree of price control (in part): The Information Technology and Innovation Foundation (ITIF), J. John Wu and Stephen J. Ezell, *How National Policies Impact Global Biopharma Innovation: A Worldwide Ranking*, April 2016, http://www2.itif.org/2016-national-policies-global-biopharma.pdf?_ga=1.31130998.83834353.1460473341

Biologics data protection (estimated official numbers of years – level of data protection in practice varies depending on the country): Michael Best & Friedrich LLP, BRIC Wall, *Availability of Biosimilar Pathways and Data/Marketing Exclusivity Globally*, June 2014, <https://bricwallblog.wordpress.com/tag/biosimilar-pathway/>

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