



2016 Top Markets Report **Pharmaceuticals**

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

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		

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 \$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

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

Figure 3: Research-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

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 effect 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 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.

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.

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 policies 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.

¹ As defined by the Census Bureau.

² Food and Drug Administration, *FDA Glossary of Terms*, <http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm>

³ In general, a generic drug does not have to duplicate the clinical trial requirements for market approval with the exception of bioequivalence trials. See: *The Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch/Waxman Act)* as amended.

⁴ In general, it might take just two to three years and cost \$50 to 100 million to develop and market a generic drug.

⁵ Managed Care, Michael D. Dalzell, *In 5 years, >50% of top-selling drugs will be biologics*, October 2013, <http://www.managedcaremag.com/archives/2013/10/5-years-50-top-selling-drugs-will-be-biologics>

⁶ *The Patient Protection and Affordable Care Act* signed into law on March 2010 authorized the FDA to approve biosimilars, or follow-on versions of biologic drugs that were approved under the Public Health Service Act of 1944 or the Federal Food, Drug, and Cosmetic Act (FFDCA).

In 2015, Zarxio became the first biosimilar product approved by the FDA in the United States. Food and Drug Administration, *FDA approves first biosimilar product Zarxio*, <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm436648.htm>

⁷ The Wall Street Journal, Jonathan D. Rockoff, *Knockoffs of Biotech Drugs Bring Paltry Savings*, May 2015, <http://www.wsj.com/articles/knockoffs-of-biotech-drugs-bring-paltry-savings-1462458209>

⁸ Consumer Healthcare Products Association, *FAQs About the Regulation of OTC Medicines*, <http://www.chpa.org/FAQsRegOTCs.aspx>

⁹ International Pharmaceutical Excipients Council (IPEC) Americas, *Frequently Asked Questions*, <http://ipeccamericas.org/about/faqs>

¹⁰ 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

¹¹ Figure 2: U.S. Snapshot:

Pharmaceutical sales, Pharmaceutical sales per capita: Centers for Medicare and Medicaid Services (CMS), Consumer Healthcare Products Association (CHPA), BMI

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

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

See also: BMI, *United States Pharmaceuticals & Healthcare Report*, January 2016 (referenced throughout)

¹² Battelle/Pharmaceutical Research and Manufacturers of America (PhRMA), *The U.S. Biopharmaceutical Industry: Perspectives on Future Growth and The Factors That Will Drive It*, <http://www.phrma.org/sites/default/files/pdf/2014-economic-futures-report.pdf>

¹³ Pharmaceutical Research and Manufacturers of America (PhRMA), *Pharmaceutical Profile 2015*, http://www.phrma.org/sites/default/files/pdf/2015_phrma_profile.pdf

¹⁴ BMI, *United States Pharmaceuticals & Healthcare Report*, "Competitive Landscape," January 2016

¹⁵ EvaluatePharma, *World Preview 2015, Outlook to 2020*, June 2015, <http://info.evaluategroup.com/rs/607-YGS-364/images/wp15.pdf>

¹⁶ The Generic Pharmaceutical Association (GPhA), *Generic Drug Savings in the U.S. – Seventh Annual Edition: 2015*, http://www.gphaonline.org/media/wysiwyg/PDF/GPhA_Savings_Report_2015.pdf

¹⁷ Food and Drug Administration, *FDA and Accelerating the Development of New Pharmaceutical Therapies*, <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM439183.pdf>

¹⁸ BMI, *Special Report: Advances in the Biosimilars and Injectable Generics Market*, January 2016

¹⁹ BMI, *United States Pharmaceuticals & Healthcare Report*, "Structural Trends," January 2016

²⁰ The United States imports 80 percent of all APIs and 40 percent of all finished drugs.

Food and Drug Administration, *Drugs Imports Exports Compliance*, <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm348836.pdf>

²¹ Price Waterhouse Coopers, *Pharma 2020: Challenging business models*, <http://www.pwc.com/gx/en/pharma-life-sciences/pdf/challenge.pdf>

²² World Bank, *Health expenditure, total (% of GDP)*,

http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS?order=wbapi_data_value_2014+wbapi_data_value+wbapi_data_value-last&sort=asc

²³ Deloitte, *Global life science outlook: Adapting in an era of transformation*, <https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Life-Sciences-Health-Care/gx-lshc-2015-life-sciences-report.pdf>

²⁴ The following reports are excellent sources used throughout this section as well as in the country case studies: Office of the U.S. Trade Representative, *2016 National Trade Estimate Report of Foreign Trade Barriers*, <https://ustr.gov/sites/default/files/2016-NTE-Report-FINAL.pdf>

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

Pharmaceutical Research and Manufacturers of America (PhRMA), *Special 301 Submission 2016*,

http://www.phrma.org/sites/default/files/pdf/PhRMA_2016_Special_301_Submission.pdf

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