Pharmaceuticals – International Regulatory and Policy Environment

USA

The United States (U.S.) is one of world's largest markets for pharmaceuticals and the world leader in biopharmaceutical research. The U.S. firms conduct 80%[7] of the world's research and development in biotechnology and hold the intellectual property rights to most new medicines. In 2010, the pharmaceutical sector employed approximately 272,000 people[8], and those manufacturers spent US$67.4 billion on research and development in 2010.[9]

The U.S. market is the world's largest free-pricing market for pharmaceuticals and has a favourable patent and regulatory environment. Product success is largely based on competition in product quality, safety and efficacy, and price. U.S. government support of biomedical research, along with its unparalleled scientific and research base and innovative biotechnology sector, make the U.S. market the preferred home for growth in the pharmaceutical industry.

Some of the key aspects of the domestic environment enabling pharmaceuticals sector growth are as follows:-

- Research and Development Schemes (R&D): Five federal agencies – the National Institute of Health (NIH), the US Agency for International Development (USAID), the Department of Defence (DoD), the Centre for Disease Control and Prevention (CDC) and the US Food and Drug Administration (FDA) – contribute funding and infrastructure, as well as their own unique capabilities and expertise, to R&D in the United States. Financial support is driven by three agencies – NIH, USAID and DoD – which are responsible for 87%, 6% and 6% respectively of US government funding for global R&D in pharmaceuticals. Some of the programmes that have driven R&D in the USA are:

Scheme	Details
Small Business Innovation Research (SBIR)	**Objectives**: The SBIR Program includes the following objectives: • Using small businesses to stimulate technological innovation • Strengthening the role of small business in meeting Federal R/R&D needs • Increasing private sector commercialization of innovations developed through Federal SBIR R&D, • Increasing small business participation in Federal R/R&D, and • Fostering and encouraging participation by socially and economically disadvantaged small business concerns and women-owned business concerns in the SBIR program.
	Structure of scheme: The program is structured in three phases: • Phase 1: The objective of Phase I is to establish the technical merit and feasibility and potential for commercialization of the

[7] Select USA : "The Pharmaceutical Industry in the United States"
[8] Bureau of Labor Statistics
[9] Pharmaceutical Research and Manufacturers of America (PhRMA)

	proposed R/R&D efforts and to determine the quality of performance of the small business awardee organization prior to providing further Federal support in Phase II. Support normally may not exceed US$150,000 total costs for 6 months. • Phase 2: The objective of Phase II is to continue the R/R&D efforts initiated in Phase I. Funding is based on the results achieved in Phase I and the scientific and technical merit and commercial potential of the project proposed in Phase II. Only Phase I awardees are eligible for a Phase II award. Support normally may not exceed: US$1,000,000 total costs for 2 years. • Phase 3: The objective of Phase III, where appropriate, is for the small business concern to pursue with non-SBIR funds, the commercialization objectives resulting from the Phase I/II R/R&D activities. In some Federal agencies, Phase III may involve follow-on non-SBIR funded R&D or production contracts for products, processes or services intended for use by the U.S. Government.
Small Business Technology Transfer program (STTR)	**Objective:** • The objective of STTR was same as that of SBIR with few differences. First, under SBIR Program, the Principal Investigator must have his/her primary employment with the small business concern at the time of award and for the duration of the project period, however, under the STTR Program, primary employment is not stipulated. Second, the STTR Program requires research partners at universities and other non-profit research institutions to have a formal collaborative relationship with the small business concern. At least 40 percent of the STTR research project is to be conducted by the small business concern and at least 30 percent of the work is to be conducted by the single, "partnering" research institution.
	Structure: Like SBIR, STTR program is also structured in similar 3 phases
Cooperative Research And Development Agreements (CRADAs) and Material Transfer Agreements (MTAs)	The purpose of CRADA is to make Government facilities, intellectual property, and expertise available for collaborative interactions to further the development of scientific and technological knowledge into useful, marketable products.CRADAs provide an exciting opportunity for National Institutes of Health's (NIH) investigators to join with their colleagues from industry and academia in the joint pursuit of common research goals. Government scientists can leverage their own research resources, as well as serve the larger mission of NIH, to facilitate the development and commercialization of health-care pharmaceuticals and products. Companies also can leverage their own R&D efforts while collaborating in state-of-the-art NIH research. A MTA generally is utilized when any proprietary material is exchanged, and when the receiving party intends to use it for his/her own research purposes. Neither rights in intellectual property nor rights for commercial purposes may be granted under this type of agreement. MTAs define the terms and conditions under which the recipients of materials, provided by either the NIH scientist or the

	other party, may use the materials. Included in the MTA are the requirements that the materials be used for research purposes only and that the materials cannot be used in human subjects. The NIH also requires that all materials received by their scientists originating from humans be collected under 45 CFR 46, Protection of Human Subjects.

Source: National Institutes of Health, USA

- Taxation and Fiscal Incentives

Research Tax Credit	Under IRC Section 41, business taxpayers may claim a tax credit for their spending on qualified research above a base amount. The incremental design is intended to give firms an incentive to spend more on research than they otherwise would. The credit lowers the after-tax cost of undertaking qualified research above the base amount: one dollar of the credit reduces that cost by the same amount. The research credit is composed of five separate and distinct non-refundable credits: a regular research credit, an alternative incremental research credit (or AIRC), an alternative simplified incremental credit (or ASIC), a credit for contract basic research, and a credit for contract energy research. All five are due to expire at the end of 2009, and the AIRC is unavailable in 2009. A business taxpayer may claim no more than the basic and energy research credits and one of the remaining three in a single tax year. The drug industry is a leading beneficiary of the research credit: in 2006, it claimed $902 million in research tax credits, or 12% of the total amount of such claims by all industries.
Orphan Drug Credit	Under IRC Section 45C, a firm may claim a tax credit equal to half the cost of human clinical trials for drugs intended to treat rare diseases; such drugs are also known as orphan drugs. The credit indirectly subsidizes the cost of capital for investment in the development of such drugs, as human clinical trials, which are conducted in three phases, constitute the most time-consuming and costliest step in the new drug development process. The statutory provision defines a rare disease or condition as one likely to afflict fewer than 200,000 individuals residing in the United States, or one likely to afflict more than 200,000 such individuals but for which there is no realistic prospect of recovering R&D costs from U.S. sales alone. The credit applies to expenditures for the supplies and the wages and salaries of researchers used in clinical trials for orphan drugs, but not for the structures and equipment used in the trials. It is a permanent provision of the tax code and a component of the general business credit, and thus subject to its limitations. Since the orphan drug credit was enacted in 1983 as one of a series of measures aimed at stimulating increased investment in the development of new drugs to treat rare diseases and conditions, at least 325 such drugs have gained regulatory approval in the United States.
Possessions and Puerto Rican Economic Activity Tax Credit	The drug industry was a major beneficiary of what was known until 1996 as the possessions tax credit under IRC Section 936.Under the Small Business Job Creation Act of 1996, the credit was revised and reborn as the Puerto Rican Economic Activity Credit (PREAC) under

	IRC Section 30A; it expired on December 31, 2005. In 2005, the industry was able to reduce its federal income tax liability by more than 2% by using the credit; drug firms accounted for 53% of the total amount of the credit claimed by all industries. When the PREAC was available from 1997 to 2005, corporations chartered in the United States could exclude from federal taxation as much as 40% of their income from business operations in Puerto Rico, the U.S. Virgin Islands, and other U.S. territorial possessions. To take advantage of the exclusion, a firm had to derive 80% of its overall gross income from business operations in one or more of these possessions, and 75% from the active conduct of a business there. There is some evidence the drug industry responded to the possessions tax credit by establishing a substantial manufacturing presence in Puerto Rico. According to a 1992 report by the then General Accounting Office, a total of 26 drug firms owned manufacturing operations there in 1990. The firms realized an estimated tax savings of $10.1 billion that year from those operations, which produced 17 of the 21 most commonly prescribed drugs in the United States in the early 1990s

Source: Federal Taxation of the Drug Industry and Its Effects on New Drug Development: CRS Report for Congress

- *Regulatory environment*: The industry is regulated by FDA, which includes testing, approval, production and marketing of drugs and biologics. However, the level of scrutiny varies according to the type of product and level of potential risk. New drugs and biological are subject to the rigorous evaluation to prove safety and efficacy for its intended use. Other organizations that develop drug quality and registration standards include U.S. Pharmacopoeia , the International Conference on harmonization of technical requirements for Registration of Pharmaceuticals for Human Use(ICH) and the World Health Organization(WHO)

China

China's pharmaceutical industry has seen rapid growth over the last few decades, especially since the economic reforms in 1978. The pharmaceutical industry's drug discovery has evolved from pure imitation to innovation supported by the government policies. At present, the Chinese pharmaceutical industry, especially bulk drugs and active pharmaceutical ingredients (API) are highly competitive and among the largest in the world.

The economic reforms in the early eighties have contributed towards development of China's pharmaceutical industry. Prior to the reforms, the government had control over the production plan, and supply &distribution of the pharmaceuticals made by the state owned pharmaceutical manufacturers. There was no patent law in China until 1985, as a result of which there was direct imitation of drugs from foreign companies. Pharmaceutical factories were encouraged to imitate patent drugs from foreign countries by reverse engineering and focus on expanding the pharmaceutical synthesis capacity.

After the economic reform, China started to develop its comprehensive pharmaceutical policies on control assurance, production and distribution regulation, advertising control, promotion of R & D on new medicines, pricing control and management of pharmaceuticals produced in China and imported from overseas. The government played an important role by laying new regulations and decrees regarding drug production and distribution, which enabled state owned pharmaceutical companies to become more market oriented. The Chinese government has also contributed in development of drug R&D capabilities by creating an innovation-oriented environment.

Government's Role in Evolution of China's Pharmaceutical Industry

Period	Phase type	Key features	Government policies
1949-1985	Pure Imitation	• No patent laws were present	• China's pharmaceutical companies could legally copy any drugs from foreign countries. Thus, pharmaceutical factories were encouraged to imitate patent drugs from foreign countries through reverse engineering. • Government allocated funds to establish several large-scale state-owned pharmaceutical enterprises to produce antibiotics, sulfonamides, and antipyretic analgesics.
1985-1993	Innovative Imitation	• Patent law was introduced in 1985 • Companies could still imitate existing drugs, but they had to conduct low-level innovations to develop new synthesis methods or new dosage forms	• China started IP protection by enforcing its first patent law on April 1, 1985. • In order to encourage innovations in the pharmaceutical industry, the Chinese government carried out a series of major national investment projects, such as the Spark Plan and the 863 Program, to give enterprises financial support for technology innovations. • "Provisional Regulations of the National Hi-tech Industry Development Zone Policies" (1991) provided tax benefits to hi-tech companies, including pharmaceutical companies.
1993-2008	Imitative Innovation	• The 1992 patent law granted full patent protection to drugs, as a	• To comply with TRIPS and prepare for entering the WTO, China amended its Patent Law in 1993

			result of which the pharmaceutical companies could not imitate existing drugs without modifying their molecular structures. Thus, they focused on developing "me-too" drugs which have minor structural differences from existing drugs	and 2000 respectively and revised the "Detailed Rules for the Implementation of the Patent Law" • The Chinese government implemented the 973 Project and National Science and Technology Major Project successively to encourage technology innovations. • A series of tax exemption policies were enacted to spur technology innovations through reducing income taxes, value-added taxes, and business taxes related to technology innovations.
2008 onwards	Independent Innovation	•	Since the 2008 patent law, drug patent protection in China has become more comprehensive and stronger, making it difficult to imitate existing drugs. Hence, pharmaceutical companies can stay competitive only by conducting independent innovations by discovering NCEs.	• In 2008, the Chinese State Council issued "National Intellectual Property Strategy Compendium", asserting that China would be transformed into a country with high level of creating, utilizing, protecting and administrating intellectual properties by 2020. • The new patent law adopted the international standard of novelty examination to conduct drug patent review and approval so that innovative drugs made in China are competitive in the global market. In terms of drug patent administration, new clauses of parallel importing, compulsory licensing and drug trail and application exemption (Bolar exception) are added. To enforce drug patent protection, the new patent law increased administrative penalties for patent violations. • Strict regulatory policies have been formulated to control the market approval and pricing of drug products. While strict procedures and criteria are set by law to review and approve new drugs,

the Chinese government opens a special "green channel" for new drugs independently developed by domestic organizations and orphan drugs

- The Chinese government has activated a national program, Major New Drug Creation, proposing a budget of almost one billion dollars to support domestic pharmaceutical companies to develop new drugs with independent IPR.
- The government has been steadily increasing funding to support drug R&D activities of the domestic pharmaceutical industry.
- The Chinese government applied tax reduction for high technology industry, including pharmaceutical industry. Pharmaceutical firms are eligible for exemption of income and sales taxes for their drug R&D expenses.

Source: 'From Imitation to Innovation: A Study of China's Drug R&D and Relevant National Policies', Journal of Technology Management & Innovation

Government support: taxation and other incentives

The Chinese government provides strong incentive programmes to support the domestic pharmaceutical industry. These incentives include tax reliefs, direct funding opportunities, as well as the development of numerous technology parks. China spends nearly 4.7% of GDP on health care (2004), of which roughly 44% of the expenditure is on pharmaceuticals, which is one of the highest shares of pharmaceutical expenditure in total health expenditure in the world, compared to an average of around 15% in the OECD countries.[10]

Details of various government support measures are provided hereunder.

a) ***Direct funding***: Chinese government's national innovation policies and the IPR policy have played an important role in fostering China's drug R&D. The government runs a national program 'Major New Drug Creation' which includes budget allocation of almost one billion dollars to support domestic pharmaceutical companies in developing new drugs with independent IPR. The funding for this project is expected to increase to about US$ 4.3 billion by 2020[11].

[10] Economic Intelligence Unit: Asia Economic Outlook
[11] Journal of Technology and Management, 2011, Vol 6, Issue 2

b) ***Tax incentives:*** Pharmaceutical companies in China are eligible for various tax incentives for conducting R&D and other operations. The below table illustrates various tax incentives available to the industry.

Incentive type	Key features
High/New Technology Enterprise (HNTE) incentive	• Enterprises qualifying as HNTEs are entitled to reduced CIT of 15% (as against general 25%). • Newly established HNTEs in five SEZs and Pudong New Area can enjoy tax holiday of 2 years followed by 3 years of 50% reduction in CIT.[12]
CIT super-deduction	• To encourage R&D activities, companies, including pharmaceuticals, are allowed an extra 50% expense deduction for eligible R&D costs. Such eligible R&D costs include expenses incurred through the development of new technology and products. They also cover salary expenses for R&D personnel, and the depreciation of instruments and equipment used for R&D purposes.
Income tax exemption for the transfer of technology	• The portion of income derived from the transfer of technology during a tax year not exceeding RMB5 million can be exempt from CIT. The portion exceeding RMB5 million is eligible for a 50% reduction in CIT.
Tax concessions/ refunds	• Additional tax concessions or refunds can be granted if the profits generated are reinvested in the form of a capital increase or capital investment in another Chinese enterprise. As a rule, a refund amounting to 40% of the tax paid on reinvested profit may be claimed. Companies investing in export-oriented or technologically advanced companies may even claim refunds of 100%.

Foreign Investment measures

China has emerged as an attractive market to many multinational pharmaceutical companies owing to its large market size, increasing government spending on healthcare, government reform plans to restructure the highly fragmented industry, emphasis on encouraging innovation, and improved intellectual property protection.

Moreover, the government provides various tax and other incentives to foreign investors in the sector. Although foreign enterprises are subject to 30% corporation tax and additional 3% local corporation tax, the foreign companies generally end up paying lower than full corporate tax due to various tax

[12] China's Pharmaceutical Industry –poised for giant leap, KPMG

exemptions. The foreign companies enjoy similar tax concessions as domestic companies in the Special Economic Zones.

Quality compliance

China's State Food and Drug Administration (SFDA) has been making constant efforts to upgrade quality of drugs produced in China. A new set of Good Manufacturing Practices (GMP) in China came into effect in March 2011, which upgrades drug quality standards of the country at par with international standards, thereby making Chinese drug companies internationally competitive.

Intellectual Property Rights

For a long period, the foreign pharmaceutical companies faced a major bottleneck in China due to the rampant theft of their intellectual property through patent infringement and counterfeiting. As a result, the US companies accounted for less than 10% of China's total pharmaceutical imports between 1998 and 2000. However, the Chinese government has in recent times taken various steps in protecting international patents. In 2005, China and U.S. reached an agreement on intellectual property protection. China has also agreed to implement the Trade Related Intellectual Property Agreement of the Uruguay Round. According to local news sources, the foreign companies can now file compensation claims ranging from $400 million to $1 billion against companies that copy patented medicines.