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Outsourcing to Asia

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Overview of Asia and its Pharmaceutical Market

Demographics

Country	Population	Population Growth (2004 est.)	GDP (PPP)	Per Capita Income (PPP)	Life Expectancy (Years)
China	1,298,847,624	0.57%	\$6.449 trillion	\$5,000	71.96
Hong Kong	6,855,125	0.65%	\$212.2 billion	\$28,700	81.39
Philippines	86,241,697	1.88%	\$390.7 billion	\$4,600	69.60
Indonesia	238,452,952	1.49%	\$758.1 billion	\$3,200	69.26
Japan	127,333,002	0.08%	\$3.567 trillion	\$28,000	81.04
Malaysia	23,522,482	1.83%	\$207.2 billion	\$9,000	71.95
Singapore	4,353,893	1.71%	\$109.1 billion	\$23,700	81.53
South Korea	48,598,175	0.62%	\$855.3 billion	\$17,700	75.58
Taiwan	22,749,838	0.64%	\$528.6 billion	\$23,400	77.06
Thailand	64,865,523	0.91%	\$475.7 billion	\$7,400	71.41

Source: CIA World Fact Book 2004

Healthcare Statistics

Country	Number of Hospitals	Doctors per 1000 Person	Per Capita Spending on Healthcare (US\$)
China	330,348	1.69	30
Hong Kong	103	1.4	N/A
Philippines	1,652	N/A	33
Indonesia	1,089	0.14	19
Japan	169,556	1.91	2,908
Malaysia	360	0.7	101
Singapore	28	1.39	4,107
South Korea	21,686	1.35	584
Taiwan	18,265	7.42	677
Thailand	1,392	0.32	71

Source: Compiled from various sources by PBI

Size of Asian Pharmaceutical Markets

Country	Pharmaceutical Market Size
China	US \$23 billion
Hong Kong	US \$1.5 billion
Philippines	US \$300 million
Indonesia	US \$350 million
Japan	US \$53 billion
Malaysia	US \$210 million
Singapore	US \$400 million
South Korea	US \$6.3 billion
Taiwan	US \$2.5 billion
Thailand	US \$1.5 billion

Source: Compiled from various sources by PBI

Overview of Asian Pharmaceutical Market

- Over 30% of new expenditures on healthcare worldwide is attributable to Asia
- Spending is driven by:
 - Aging population
 - Increasing life expectancy
 - Increasing incidence of major diseases
 - Increasing health consciousness
 - Higher disposable income

Introduction

What is being outsourced?

- Pharmaceutical companies are choosing to outsource:
 - Clinical trials
 - R&D
 - Manufacturing

Outsourcing Clinical Trials

- Costs of clinical trials in Asia much less than in US/Europe
- Asian population exceeds 4 billion and is genetically diverse
- Many of these people have never received medication to treat their conditions
- These patients are more suitable for trials because they have not been influenced by previous treatment
- Some Asian countries now offer incentives to clinical trial volunteers
 - Example: India provides volunteers with free medication and often better medical attention than what they would receive at an average hospital

Outsourcing Clinical Trials: A Company Example

- Asian setting can make clinical trials easier, faster and more efficient
- Example: Germany's Mucos Pharma GmbH
 - Hired Indian company to find 650 out of 750 volunteers needed for a clinical trial
 - Indian company found the patients within 18 months visiting only 5 hospitals
 - Mucos Pharma spent nearly twice as long visiting 22 hospitals to find the remaining 100 patients in Europe

Downsides to Outsourcing Clinical Trials

- Standards and regulations may not be as high as in the US/Europe
- Not all medical procedures uniform within some Asian countries
- Testing is not always sufficiently documented
- Some Asian countries have restrictions on the type of clinical trials that can be carried out
 - Example: India does not allow companies to conduct Phase I clinical studies for drug safety

Outsourcing Clinical Trials: India Regulatory Update

- In the past, a drug had to undergo clinical trial one phase higher in another country first, before the previous trial phase could be conducted in India
- October 2004 Announcement:
- MOH plans to amend Drugs and Cosmetics Act to allow foreign and domestic companies to conduct clinical trials in India and other countries simultaneously
 - Applies to Phase II and II trials only
 - Phase I trials not included, since Phase I trials test drug safety
 - Clearances to conduct trials will be granted on a case-by-case basis
 - Foreign companies will not be permitted to conduct clinical trials solely in India
 - MOH will set up special group to monitor clinical trials

Outsourcing R&D

- Drug companies are under intense pressure to contain R&D expenses
 - Fewer new drug discoveries, rising drug prices and competition from generic drugs
- PhD chemist at a U.S. CRO with 10 years experience costs \$250,000/year (including salary, benefits, overhead, etc.)
 - PhD chemist in India (with 10 years experience) costs \$30,000 – \$40,000/year
 - PhD chemist in China (with 10 years experience) costs \$40,000 - \$60,000/year

Outsourcing R&D

- Concern still exists over communication and timeliness problems but the situation is getting better
 - Some Asian CROs can claim business efficiency equivalent to U.S.-based CRO.
 - Communication typically done through email with 10-12 hour time difference taken into account
 - Many CROs now have in-house videoconferencing facilities

Outsourcing R&D: A Company Example

- Roche opened new global R&D center in Shanghai in Nov. 2004
 - Expected to be a world-class R&D center for new pharmaceuticals in 3 to 5 years
- CEO says: China not only an important sales market, but also a vital R&D center
- Roche Group has invested more than \$300 million in China and has maintained double-digit growth in sales output

Downsides to Outsourcing R&D

- Lack of Intellectual Property Rights
 - This situation is improving, but not great
- Logistics of moving raw materials and finished compounds between laboratories, overseas collaborators, and drug companies can be burdensome

Update: Patent Protection in India

- Previously:
 - India granted “process patents”
 - Another drug inventor could patent the same product as long as it was created by a “new” process
 - A tiny modification in the synthesis of a molecule would justify a new patent
- Passed a new patent law March 23, 2005
 - Sellers of already-approved generic drugs in India will now have to pay licensing fees
 - Generic drug producers can apply to copy a patented drug, but only after it has been on the market for 3 years
 - Generic producer may have to pay “royalty fees”
 - The patent owner can object to the copying

Patent Protection: A Company Example

- Novartis, a Swiss drug manufacturer, asked Indian manufacturers to stop producing a generic form of their leukemia drug, Glivec
 - Indian companies had been selling it for \$2,700/year
 - After stopping Indian production, Novartis priced the drug at \$27,000/year

Outsourcing Manufacturing

- Cost of labor very low, but quality of work typically getting better
- Some Asian countries (India, the Philippines, Singapore, etc.) have many workers with fluent English
- Large pool of talent in Asia with education and ability to run manufacturing plants equaling U.S. complexity and quality
- Asian manufacturers are becoming more sensitive to FDA regulations, ISO and other international standards

Outsourcing Manufacturing

- Companies involved in high-tech manufacturing or innovative research can often obtain special tax breaks or exemptions
- Examples:
 - China - special economic zones for companies in the same industry offering favorable tax conditions
 - Malaysia - Pioneer Status and Investment Tax Allowance incentives provide tax exemptions for first few years of establishment

Special Economic Zones (SEZs)

China

- Traditionally located in the southern and coastal regions of China. More areas now being designated by the government
- SEZs offer significant tax concessions during early life of a project
 - Income tax can be exempt during first 5 years of operation
 - Exemption “start” date begins when company reaches a specified percentage of production capacity
 - Incentives vary from region to region – research and comparison is necessary
- Carefully examine conditions placed on SEZ incentives
 - Export quotas or price ceilings may be too restrictive

Outsourcing Manufacturing: A Company Example

- Divi’s Laboratories (Hyderabad, India)
 - Manufacturer of active pharmaceutical ingredients and advanced intermediates
- Built a 1000m³ GMP fine chemicals plant on 300 acres of land for US\$25 million in the mid-1990’s
- In the US, the same facility would have cost US\$250-\$400 million
- Labor costs in Hyderabad are about 1/10 of those in the West

Outsourcing Manufacturing: A Company Example

- Respironics Inc., a US medical device company (Murrysville, PA)
 - Set up manufacturing facilities in China and the Philippines
 - Contracts out components to Hong Kong
 - China and Hong Kong provide Respironics with a substantial number of well-trained and experienced workers, many of whom are fluent in English

Outsourcing Manufacturing: A Company Example

- Hikal, an Indian company and originally an agrochemical producer which expanded into the pharmaceutical industry
 - Acquired a pharmaceutical ingredient plant in Bangalore, India in 2001
 - Overhauled the entire facility, implemented GMP standards, obtained USFDA approval

Outsourcing :A Company Example

- Actavis, an Icelandic pharmaceutical company, purchased Lotus Laboratories in Bangalore, India for approximately \$25 million
 - Actavis will have access to technical expertise offered by Indian employees
 - Lowers R&D expenses
 - Actavis now looking to source:
 - API's and finished dosage forms
 - Formulation development
 - Clinical trials
 - Manufacturing

Outsourcing Manufacturing: China Regulatory Update

- July 1, 2004
 - GMP required for all drug manufacturers
- January 1, 2006
 - GMP required for IVD reagents (administered as drugs)
- January 1, 2007
 - GMP required for medicinal gas manufacturers
- January 1, 2008
 - GMP required for crude drugs for Chinese medicine
 - How manufacturer processes and contains prepared slices of drugs, including the cleaning, cutting and steaming processes

Outsourcing Manufacturing: China Regulatory Update

- September 2004: SFDA issued *Interim Provisions for Drug Safety Credit Classification*
- Applies to foreign and domestic drug companies, including manufacturers, distributors, R&D units
- Officials will conduct inspections of facilities and assign one of four categories based on compliance with drug regulations:
 - 1) Initial compliance or made improvement and is now in compliance
 - 2) Received one warning due to non-compliance
 - 3) Received second warning due to non-compliance
 - 4) Received multiple warnings; no effort to comply
- Companies with low credit ratings →
 - Subject to higher level of supervision; more frequent inspections
- Companies with high credit ratings →
 - Less inspections; priority in administrative approval processes

Sourcing in Asia

Overview of Sourcing in China

- More US medical companies are now outsourcing manufacturing to reduce their costs
- Many drug manufacturers in China have made significant improvements in medical technology and product quality
- Identifying the right factory in China can be a challenge for a US company

Identifying Product Manufacturers

- Use the Internet and trade catalogues
 - Will provide you with an initial list of manufacturers
 - Numerous websites that provide sizeable lists of manufacturers and often include contact information and a brief description of each manufacturer
 - This type of search should only be *a starting point* and should not be considered a thorough investigation
- Once several potential manufacturers have been identified by the Internet/catalogue search
 - Examine each manufacturer's respective website
 - To establish an accurate idea of the company, both websites (English and Mandarin) should be viewed by a person fluent in both languages
 - Foreign companies should keep in mind that some of the information on the Internet or an individual manufacturer's website could be misleading or inaccurate

Initial Planning and Communication

- After compiling a list of potential manufacturers, contact each one directly
 - Emails and phone calls
 - Can be used to answer initial questions and confirm the manufacturers' production capabilities
 - Can the manufacturer produce your products to your specifications and required standards?
 - Even if the Chinese manufacturer has an English speaker, it is best for the foreign company to have a bilingual speaker available
 - Begin building a relationship

Determining the Price

- If you have a "standard" product –
 - Price quote should be fairly straightforward
- If your product has somewhat unique features or specifications, or if you are requesting atypical quantities –
 - General price quote may not be very useful
 - May be necessary to ask the manufacturer for an itemized quote
- Keep in mind:
 - Many Chinese manufacturers tend to use metric units and may not be familiar with inches or pounds
 - The manufacturer may only honor their price quote for a limited amount of time
 - Factor in other expenses, such as:
 - International and domestic shipping
 - Customs duties
 - Possible travel expenses for visiting the manufacturer

Know the Difference: Trading Companies vs. Factories

- Trading companies act as a “middleman,” purchasing products from a local manufacturer and selling the products to a foreign buyer
- Trading Company Advantages:
 - Tend to have a wide variety of products available for purchase
 - A foreign company with numerous product lines may be able to use one trading company for most of their products
 - Can often purchase products for better prices since they already have well-established relationships with local manufacturers
 - Usually easier dealing with a trading company since they tend to have more experience communicating with foreigners and working with foreign companies
 - Trading companies offer short-term profits and generally business relationships with these companies can be established in less time
- Factory Advantages:
 - Foreign company can develop a long-standing relationship with a local Asian manufacturer
 - Have more control over product design and quality
 - Hopefully more leverage on prices as the relationship and volumes grow
 - Trading companies could cut off foreign company’s supply at any time

Due Diligence Before the Site Visit

- At this point in the manufacturer investigation, some major problems should have already surfaced
 - May still be smaller issues that could cause potential problems
- Prior to visiting a local Chinese factory or making a final decision on which factory to visit, due diligence should be conducted by a local person in that country
- Investigation should involve:
 - Confirming that the factory exists and has the necessary business licenses/registrations
 - Make sure they comply with required labor laws and working conditions
 - Operations should meet the standards of the foreign company
 - If factory uses a great deal of manual labor, as opposed to machinery, quality control could potentially be an issue
- Buyers Beware:
 - A local Chinese company could claim to have a very large manufacturing operation with hundreds of workers
 - In reality → it is a trading company with a few people acting as go-betweens in a small office space
 - Or, a Chinese manufacturer could initially offer excellent and speedy service, while actually experiencing financial trouble and frequent power outages

Visiting the Factory

- After factory investigation is complete, foreign company should arrange to visit the factory and begin solidifying the business relationship
- Face to face communication is necessary →
 - Crucial to developing a good working relationship
- During the visit:
 - Spend time with the key people at the factory
 - Ask to see business, SFDA and GMP licenses in their offices
 - If any licenses are missing, this may indicate that the factory lost their license or never held one at all.
 - Ask whether the factory has passed any international requirements (GMP, ISO 13845)
 - Get a sense of the factory's financial background and status
 - If a factory is owned by a single person, it is best to determine the source of the factory's initial funding when possible

Examine the Regulatory Requirements

- Chinese drug manufacturers exporting to the US are required to meet specific US FDA regulations
- These regulations can cause compliance problems for Chinese manufacturers, making it difficult to source from certain factories
- Any Chinese drug manufacturers that export to the US must register with a US Agent and provide this information to the FDA

Negotiating the Contract

- Be concise
 - Specify how long the price quote is valid for
 - Shipping terms should be well-defined
- Important to include a dispute resolution clause in the contract
 - Though it is best to solve sticky issues and problems via direct face-to-face meetings
 - Clause should define the law to be applied, arbitration is almost always a better option in China rather than a lawsuit

Establish a Quality Assurance System

- Best method for ensuring product quality is to implement a quality assurance system in China
 - Depending on the shipping terms defined in the contract, the purchaser may have to pay 100% of the cost of the products at the foreign country's dock
 - It is preferable to inspect the products prior to shipping
 - It is possible to hire a local quality control company to conduct an inspection
 - Many local Chinese manufacturers will not object to a visit from their customer's own quality control team
 - Higher costs
 - May be more reliable and easier to arrange in some instances
 - Good idea to select multiple samples from a production run for testing prior to paying 100% of the purchase
 - If the local Chinese manufacturer is aware of these planned visits or tests, they may be more conscientious of the factory's quality control methods from the start

Important Cultural Issues When Doing Business in Asia

Cultural Issues

- It is important to understand the cultural and business norms that are unique to a specific country or ethnic group

Western Approach

- *Do a deal
- *Maximize short-term profits
- *Assess competitive capabilities
- *Be frank
- *Make changes fast

Eastern Approach

- *Build relationships
- *Establish long-term foundations
- *Assess integrity and trust
- *Don't deliver bad news
- *Move when ready

Understanding the Chinese

- Chinese mentality
 - Importance of family
 - Concept of “face”
- Conducting effective business
 - Introductions
 - Negotiating
- Little things that mean a lot
 - Gifts
 - Body language
 - Conversation

Understanding People in India

- Hierarchy (caste system) plays a large role in Indian society
- Relationships and trust are key to successful business
- Language
 - Different regions have different dialects
 - English commonly used for international business
- Meetings
 - Should be arranged well in advance
 - Greet the most senior person first with a handshake
 - Exchange business cards
 - Use formal titles, Dr., Mrs., etc.
 - Start with informal conversation – small talk
- Negotiations
 - Can be slow; Middle East mentality
 - Can be very confrontational

Understanding Southeast Asians

- Intercultural communication – differentiate Chinese from locals
- Conducting effective business
 - Personal connections
 - Negotiating with locals – more harmonious
 - Do not point – seen as a threatening gesture
 - Dress conservatively
 - Do not touch anyone's head
 - Do not point feet towards another person

Cultural Issues

- For each other Asian country you must know the local religious traditions and other unique cultural factors
- Not all Asian countries share the same Asian attitudes, values and mindset (India is very different than China)
 - Must pay close attention to the particulars of each individual country
 - Pearl Harbor

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