USAID DEL PUEBLO DE LOS ESTADOS UNIDOS DE AMÉRICA | Programa MIDAS
Más Inversión para el Desarrollo Alternativo Sostenible

Comparative Study of Selected Government Policies for Promoting Transfer of Technology and Competitiveness in the Colombian Pharmaceutical Sector

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August 22-23, 2007

Bogota, Colombia

Project Overview

- Three basic components
  - Develop and present course on technology licensing in the pharmaceutical sector
    - Supplemented by presentation on regulatory framework for imports into the United States
  - Diagnostic of transfer of technology practices of four Colombian enterprises, development and implementation of action plans
  - Comparative study of policies of three countries comparable to Colombia to promote technology transfer and competitiveness of domestic pharmaceutical industry
- Components inter-related

Comparator Countries

- Brazil
  - population about 190 million, GDP of USD $1.65 trillion (PPP) and per capita GDP of USD $8,800 (PPP)
- Singapore
  - population of about 4.5 million, GDP of USD $141 billion (PPP), and per capita GDP of USD $31,400 (PPP)
- Mexico
  - population of about 109 million, GDP of USD $1.15 trillion (PPP), and per capita GDP of USD $10,700 (PPP)

As compared with

- Colombia
  - population of about 44 million individuals, GDP of USD $374 billion (PPP), and per capita GDP of USD $8,600 (PPP)

Key Characteristics of Global Pharmaceuticals Market

- Originator and Generics
  - 600 billion USD plus global sales
    - 500 billion USD sales of originator products
    - Originator market dominated by small number of large multinationals, principally based in US, Europe and Japan
    - 15% of originator revenue spent on R&D
- Originators typically do not out-license production and distribution of high-margin products to third parties, though some exceptions
  - Experience in Brazil and Colombia consistent with general rule
  - “Transfer of technology” opportunities limited in sense of in-licensing new patented drugs

Key Characteristics of Global Pharmaceuticals Market

- Producers of active pharmaceutical ingredients (APIs) and formulators
  - Quality of APIs important to quality of finished products
  - APIs production shifting to Asia – China, India, Singapore, Taiwan, Korea – part of fine chemical industry sector
- Regulatory quality control of manufacturing varies substantially between US-EU and developing countries
  - Differences in cGMP requirements as between US FDA and EU EMA (and lack of mutual recognition) and Latin American regulators
- Pharmaceutical regulatory control varies substantially among Latin American countries
  - Results in low level of intra-regional trade

Key Characteristics of Global Pharmaceuticals Market

- Major international generics producers have emerged outside US-EU
  - India (Aurobindo, CIPLA, Dr. Reddy, Matrix, Ranbaxy, etc.) took advantage of 10 year TRIPS Agreement transition and focused on improvements to API production processes
  - Israel (Teva) and Canada (Apotex) took advantage of patent expirations and challenged originators
  - International majors engaged in acquisitions throughout world, including EU
- Originators no longer ignore generics sector – promoting branded generics
- “Net” - world generics market increasingly competitive

Experience and Policy of Brazil

- Approximately 65-70% of market held by foreign multinationals
- 30-35% of domestic market held by locally-owned generics producers
- High balance of payments deficit in pharmaceutical sector
- Early introduction of pharmaceutical product patent (including pipeline) protection led to dramatic loss of domestic API production capacity
  - From supplying 55% of API market to less than 5%
  - Compare experience of India which took advantage of TRIPS transition

Experience and Policy of Brazil

- Domestic API producers suffer from high labor costs, tax discrimination in favor of imports, and public law requiring acceptance of lowest price bid (favoring Chinese and Indian suppliers)
- ANVISA inspects domestic API suppliers for GMP compliance, but not foreign suppliers, effectively according major cost advantage to foreign suppliers
  - National government formulators report serious import quality issues
  - ANVISA preparing to initiate foreign inspection program

Experience and Policy of Brazil

- Pharmaceuticals selected as one of four key industrial development targets
- PROFARMA program developed under BNDES
  - Loans to upgrade manufacturing facilities, including to meet ANVISA and US cGMP standards – 32 transactions, US$225 million to date
  - Financial support for mergers and acquisitions (e.g., Ache acquired Biosintetica using US$150 million loan to create company with US$750 million annual sales)
  - Loans and equity participation for R&D ventures
    - Up to 40% initial equity participation
    - Includes financing of laboratory and production facilities
    - 10 transactions totaling US$60 million to date

Experience and Policy of Brazil

- Government-owned manufacturing
  - FarManguinhos (Fiocruz) and state laboratories
  - FarManguinhos recently purchased a large “excess” manufacturing complex from Glaxo
- Industrial policy supports improvement of API manufacturing, but progress to adapt regulatory framework slow

Experience and Policy of Brazil

- Government support for R & D
  - Program at Federal University in Rio de Janeiro creating database of industrially useful non-infringing patent information
  - Researchers using federal funding authorized to own patents
  - Programs of Oswaldo Cruz Foundation (Fiocruz), including BioManguinhos
  - Research institute, Centro de Biotecnologia da Amazonia (CBA), established to investigate the industrial uses of Amazon forest biodiversity
- Patent Office (INPI) assessing scope and modalities of pharmaceutical patenting
- ANVISA formally assesses patentability of pharmaceuticals

Experience and Policy of Singapore

- Country perhaps best known for industrial policy efforts to promote pharmaceutical-related R&D
- Part of overall objective to increase R&D as percentage of GDP to match levels of highest small country R&D spenders
  - Singapore currently at 2.25% R&D, compared with close to 4% for Israel, Sweden and Finland. Singapore was at 0.89% in 1990
  - Current 5 year plan (2005-2010) calls for aggregate US$6 billion science and technology (S&T) expenditure

Experience and Policy of Singapore

- S&T promotion under direction of Agency for Science, Technology and Research (A*STAR)
- Biomedical Research Council (BMRC) to “coordinate support, direct and stimulate quality research in selected disciplines of science, engineering and biomedicine” is part of A*STAR
- Public funds used to construct “Biopolis” – US$350 million first phase, $50 million second phase (recently completed)
  - Complex houses several publicly funded biotechnological research institutes, as well as research divisions of two multinational pharmaceutical companies (Novartis and Glaxo)

Experience and Policy of Singapore

- Economic Development Board (EDB) plays complementary role to A*STAR/BMRC by seeking to attract private investment in the biotechnology sector to Singapore. The EDB has had a budget of USD $2.1 billion for the three five-year S&T Plans
- Significant support for public education, including support for Ph.D. candidates in the biotechnological sciences
- In the field of biotechnology, Singapore has targeted the hiring of leading researchers away from institutions in other countries by offering financial incentives

Experience and Policy of Singapore

- For start-up biotechnology companies, EBD provides capital under “Start-up EnterprisE Development Scheme (SEEDS)” program (which has invested in 149 companies over the past 4 years). Technical support is provided through A*STAR “Exploit Technologies” program
- Government seeks 2/3 level of private R&D expenditure nationally. Currently at 64%
- Promotes country as strong IP protection environment
  - Appears research institutes own patents for research undertaken with public funds, but researchers share in the proceeds from licensing of technology. Funding and assistance available for spin-offs
- Singapore is running US$10 billion per year “royalty” balance of payments deficit

Experience and Policy of Singapore

- Significant growth in “biomedical manufacturing” reported based on "a wider variety of active pharmaceutical ingredients produced”
- Some informed skepticism whether R&D sector can be publicly incubated through construction of Science Parks
- Too early to assess whether Singapore policy will succeed in creating self-sustaining R&D hub for pharmaceutical sector. Competition from throughout Asia growing

Experience and Policy of Mexico

- Since entry into force of NAFTA in 1994, Mexico's pharmaceutical sector dominated by foreign multinationals – 80% of sales by value
- Locally-owned producers all in generics sector
- Mexico's overall R&D as percentage of GDP 0.32% in 2002
- Mexico suffers annual trade deficit of US$2.1 billion in pharmaceuticals, and growing

Experience and Policy of Mexico

- "… there appear to be little or no sector-specific industrial policies to promote the pharmaceutical industry" (OECD, 2000 & 2007)
- Despite fairly strong patent protection, very low pharmaceutical R&D spending in Mexico, with 96% of patents held by foreign firms (OECD 2007)
- "The number of firms producing active ingredients has diminished in recent years: in 1987 there were 94 firms producing active ingredients, by 1994 this figure had dwindled to 48 and by 2005 there were only 26 companies" (OECD 2007, based on Ministry of Health data)
- Mexico illustrates risks of "no policy" for pharmaceutical sector

Colombian Experience and Policy

Manufacturing and distribution

- Total pharmaceutical market approximately US$2.6 billion in 2005 (Proexport data)
- Originators hold 60% market share, generics hold 40%
- 100% of originator market controlled by foreign multinationals
- Percentage of generics market held by locally-owned enterprises not certain. If assume 75%, amounts to $780 million/year sales

Colombian Experience and Policy

- Imports of US$735 million, exports of US$300 million, for trade deficit of US$435 million in 2006 (probably overstating value of pharmaceutical exports)
- Principal export destinations Venezuela, Ecuador, Panama and Peru
- All local enterprises “formulators”. No API manufacturing. APIs imported from China, India, Europe, US, etc.
- No plants approved or certified for cGMP compliance by US FDA or EU EMA, therefore no exports to these locations. Cost to achieve compliance would vary significantly among producers
- Substantial regulatory obstacles for exporting to Argentina or Brazil (e.g., compliance with ANMAT or ANVISA finished product requirements, including local plant inspections and variations in stability testing standards)

Colombian Experience and Policy

- No locally-owned pharmaceutical enterprises publicly listed on Colombia's stock exchange
  - Largely family-owned businesses
  - Replicates situation in Brazil
- Sales volume varies from high of US$250 million/year (inclusive of broader product line), to small-scale operations
- Comply with INVIMA inspection and certification requirements, providing cost advantages compared with some multinational imports. INVIMA reports quality concerns with finished products
- APIs can be purchased from non-FDA/EMA inspected sellers, providing potential cost advantage

Colombian Experience and Policy

- Local enterprises enjoy advantages of proximity to distribution systems, possible formal or informal advantages in public procurement
- Foreign products require registration with INVIMA, a complex and time consuming procedure
- If and as market is progressively opened to foreign generic competition, pressures will increase on locally-owned enterprises
  - International majors produce in larger and more technologically advanced scale, often with integrated API production
  - Global generics market highly price competitive, to extent major originators are moving manufacturing offshore to lower production costs

Policy Options for Manufacturing Sector

Policy Options for Private Sector

- Upgrade manufacturing facilities to meet cGMP standards adopted by the United States and Europe Union to enable exports to broader range of markets
- Increase scale and efficiency of production by consolidating operations, including by merger and acquisition
- Invest in the production of active pharmaceutical ingredients (APIs) relevant to Colombian and export markets, including through joint venture with foreign enterprises
- Engage foreign technical assistance for upgrading, etc.
- Assess use of public equity financing and/or public institution financing to accomplish these objectives

Policy Options for Manufacturing Sector

Policy Options for Government

- Provide development bank funding for upgrading of manufacturing facilities and capacities on financial terms designed to ameliorate cost burden to private enterprises, and ultimately to the public
  - Addresses public health objective of quality assurance
- Seek financial assistance from multilateral or national development aid sources to assist with such upgrading
- Promote consolidation of local industry with financial assistance, potentially along the lines of Brazilian development bank (BNDES) model

Policy Options for Manufacturing Sector

- Consider policy options to encourage private sector enterprises to offer shares on public equity market to further industry upgrading and consolidation
- Examine options for increasing vigilance with respect to API imports
- Pursue discussions with regulatory authorities in other countries, particularly in Latin America, regarding the harmonization or approximation of regulatory standards in the pharmaceutical sector, including mutual recognition of regulatory approvals
- Consider encouraging emergence of Latin American regional “champion” companies

Colombian Experience and Policy

Research and Development (R&D)

- Colombian R&D as percentage of GDP low (0.24% in 2000 per NSF data)
- Institutional infrastructure fairly well developed (e.g., Colciencias, regional institutions, universities)
  - Colciencias budget low (USD$15 million) (per World Bank study 2003 data) (more recent budgets increased)
  - Compare US National Institutes of Health (NIH) at US$28 billion, or Singapore S&T at USD$1 billion plus
- Public research institutes (e.g., CIDEIM) highly dependent on external funding sources

Colombian Experience and Policy

- Private pharmaceutical enterprise spending on R&D low
- Colombia rich in biological diversity
  - Not necessarily a panacea. So far R&D on biodiverse genetic materials slow to pay off
- Development of domestic originator industry expensive and carries significant risk
  - Cost of new drug estimates vary widely, US$100 million to US$1 billion plus
  - Developing countries have certain cost advantages (e.g., researcher salaries and clinical trials)

Policy Options for R&D

Policy Options for Government

- Encourage improvements in local generics sector enterprises with view to enabling private investment in R&D (e.g., Indian model)
- Seek to identify foreign countries and enterprises with scientific and financial capacity in the biotechnology sector that may have interest in joint venture R&D projects making use of Colombia's biodiverse resources
  - Management of rights ownership and output interests essential

Policy Options for R&D

- Initiate program to identify industrially useful patent information that may be employed without infringing patents
- Increase funding to public institutions conducting research on biological resources and diseases of particular relevance to Colombia
- Further make available financial assistance to ventures seeking to commercialize the results of Colombian research

Concluding Observations

- Challenge of maintaining and enhancing local capacity in pharmaceutical sector should not be underestimated
  - Local participation in industry by value of sales and manufacturing has substantially declined in a number of developing countries post-1995 (e.g., Brazil, Mexico, South Africa)
  - Consolidation of manufacturing a global phenomenon
- Key issue is whether pharmaceutical sector will be a government industrial policy priority
  - Considerations obviously involve public health policy and national security policy
  - Does each country in Latin America prefer to address the challenges alone? is there a basis for creating a regional policy with reciprocal benefits?