CRA Charles River Associates

POLICIES THAT ENCOURAGE INNOVATION IN MIDDLE-INCOME COUNTRIES

KEY FINDINGS

TIM WILSDON
JIM ATTRIDGE
EVA FIZ
SATOMI GINOZA

THE INTERNATIONAL FEDERATION OF PHARMACEUTICAL MANUFACTURERS AND ASSOCIATIONS (IFPMA) ASKED CHARLES RIVER ASSOCIATES (CRA) TO INVESTIGATE THE CONDITIONS NECESSARY TO ENCOURAGE INNOVATION IN MIDDLE-INCOME COUNTRIES. THE OBJECTIVE WAS TO EVALUATE THE POLICIES OF HOST GOVERNMENTS THAT ENCOURAGE INVESTMENT IN INNOVATIVE ACTIVITIES AND THE IMPLICATIONS FOR FUTURE INNOVATION POLICY.

We found that:

- All of the middle-income countries covered in our case studies have been investing in bioscience over the last five years.
- The continuing globalisation and fragmentation of the innovation process should make it easier for middle-income countries to increase their share of both public and private investment in all stages of research and development.
- There is a very different opportunity depending on whether we are considering large markets, such as China, Brazil and India, or smaller markets, like Colombia and Malaysia, therefore, they need to adopt targeted, consistent policies, tailored to their capabilities.
- Sustainable innovation requires co-ordination between health and industrial policy and between academia and the public and private sector institutions, as well as robust intellectual property protection.

Methodology

The report focuses on eight case study countries* (Brazil, China, Colombia, India, Malaysia, Russia, South Africa, and South Korea), which were chosen because they:

- Represented different geographic regions, and were seen as the most successful in developing innovative activities to-date in their region.
- Used a range of different policy approaches.
- Were varied in terms of whether they have a long-standing objective of developing an innovative industry, (particularly South Korea, which was included for this reason) as well as countries that had only relatively recently embarked on this.

In addition to reviewing the existing academic literature and government sources, we also undertook 25 interviews with government officials, academics, industry trade associations, and individual companies.

DEFINITIONS USED THROUGHOUT THE REPORT

What we mean by innovation

Innovation is defined as a multi-phased process, beginning with lab-based research leading to patentable inventions, moving into the stages of clinical research, which are then translated into safe, effective and commercially viable products, from which society gains a benefit in terms of improved health.

MEASURING INNOVATIVE ACTIVITY

Innovative activities can be measured in terms of:

- **Inputs** such as investment or number of people employed; or
- **Outputs** like patents, products in development or products ultimately commercialised

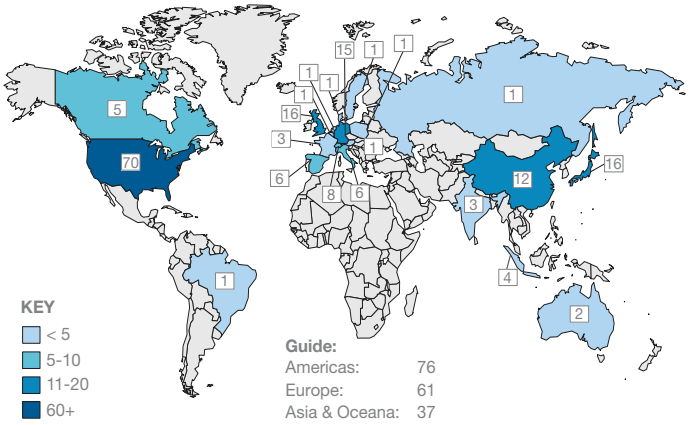
Innovation in middle-income countries, success to date

While pharmaceutical R&D is still heavily concentrated in high-income countries, there is a trend of such activities moving into middle-income countries. For example, between 2005 and 2010, the R&D spend by PhRMA members increased by 455% in Asia-Pacific (excluding Japan), 112% in Latin America, 303% in India. There has also been an increase in terms of innovative outputs in the case study countries. The number of medical science articles published increased dramatically between 2000 and 2010, with China and Brazil experiencing triple digit growth in publications. There has also been an increase in patents associated to these scientific outputs. In 2009, there were a total of 1339 PCT pharmaceutical patent applications summited by the eight case study countries. This represents an average annual growth rate of 17% between 1999 and 2009.

The majority of pharmaceutical R&D sites of international firms are located in the US and Europe (Figure 1). Of the case study countries, China is leading the list with 12 R&D centres. India (3), Brazil (1) and Russia (1) also host R&D centres of international pharmaceutical companies.

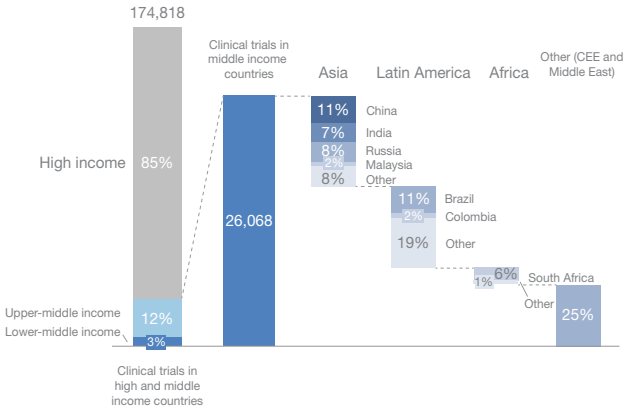
Clinical trial activity is undertaken in many locations. Middle-income countries host 15% of the clinical trials (Figure 2). Of the middle-income case study countries, China and Brazil have had the highest number of clinical trials to date.

Figure 1: Location of R&D hubs by international pharmaceutical companies



Source: CRA analysis based on public information of IFPMA members. Data collected for 20 companies as of August 2012

Figure 2: Total number of clinical trials conducted in middle and high income countries to date



Source: CRA analysis and www.clinicaltrials.gov. NB: South Korea is excluded due to its status as a high income country.

Figure 3: Relative performance of the case study countries

INNOVATION INDICATORS	BRAZIL	COLOMBIA	CHINA	INDIA	MALAYSIA	RUSSIA	SOUTH AFRICA	SOUTH KOREA
Total R&D spending	◑	◔	◑	◔	○	◑	◔	●
Biopharma-ceutical R&D spending	◑	◔	◑	◑	○	◑	◔	◕
Clinical trials	◑	◔	◕	◑	◔	◑	◑	◕
Employment in total R&D	◑	◔	◕	◑	◔	◕	◔	◕
Publications	◕	◔	●	◕	◔	◑	◑	◕
Patents	◑	◔	◕	◕	◑	◑	◔	◕
Novel medicines	◔	○	◑	◑	○	◔	○	◑

● Excellent performance ◕ Good performance ◑ Medium performance ◔ Poor performance ○ No information available

Source: CRA analysis

There has been some progress in the level of innovative activity in all of the case study countries. However, the extent of progress varies significantly (Figure 3).

- South Korea's biopharmaceutical R&D spending is clearly the highest but increasing in Brazil, China, India, and Russia.
- The number of clinical trials conducted has increased in China and South Korea. Only these two countries and India have Phase I trials account for over 10% of clinical trials.
- South Korea, China, and Russia have high numbers of people employed (although it is difficult to determine % in R&D).
- China, South Korea, India, and Brazil have high and increasing number of scientific articles published.
- South Korea and China, and India have patented and commercialised some locally developed novel medicines.

Lessons from innovation policies in the case studies

1. To develop innovative activity (particularly early stage research), governments must have a consistent long-term policy that is implemented effectively

All the case study countries have developed long-term policies regarding innovation in the pharmaceutical industry. These differ in terms of the focus, when they were applied (and if they were implemented), and their short-term objectives (Figure 4).

Given how recent some of these plans are it is difficult to draw strong conclusions about which of these have worked most successfully, but it is clear that they must be consistent policy if it is to provide the right signals regarding the future.

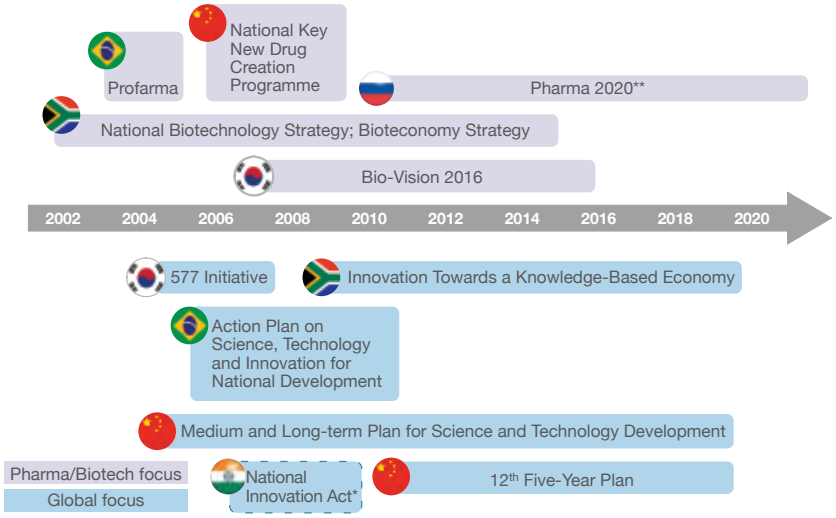
South Korea, which first initiated its innovation policy in the 1980s, demonstrates the value of consistently placing priority on developing a biotechnology industry, initially by investing in basic research and then through policies to encourage commercialization.

2. The capabilities to undertake different parts of the pharmaceutical industry value chain are different and hence so are the policy priorities

Although sharing some common components, the mix of policies that are needed to encourage early stage research and clinical trials differ (Figure 5). Countries have different characteristics in terms of population and market size as well as their comparative advantage in innovation. The policy priorities should therefore depend on the types of innovative activity that the country is trying to encourage. However, we found little evidence that manufacturing capabilities are necessary to develop successful innovative activity.

The medical infrastructure, population, and requirements to serve local markets are driving clinical trial activity in **India**, **Brazil** and **Russia**. The strength of the academic research centres and developing clusters in **China** and **South Korea** are seen as key to encouraging early stage research.

Figure 4: National innovation strategies



Source: CRA analysis. *The Indian National Innovation Plan was drafted in 2008 but it was not implemented. A new innovation plan expected to be announced in 2013 is being drafted. **Amendments to the programme were proposed due to budget concerns.

Figure 5: Elements to be encouraged to develop different types of innovation

EARLY STAGE RESEARCH	• World class research institutions • Highly trained workforce (retained or attracted back to the country) • Clusters of innovative companies providing support on core technologies (high throughput screening, gene sequencing etc.) • Partnership encouraging environment
CLINICAL TRIALS	• Efficient regulatory system for appraising clinical trials design • Supportive and well regulated system for enrolment • Strong medical schools and clinicians for designing • Managing and reporting trials design • Growing market receptive to innovation

Source: CRA analysis

3. There needs to be a high level of co-ordination between industrial and health policies

There is much discussion within policymakers and companies of whether they should focus on innovation for the global market or innovation for the domestic market. There are considerable differences in the case study countries in terms of whether they are focusing on global diseases (diabetes, cancer, cardiovascular) or diseases that are more prevalent in their markets.

In either case, in order to encourage both clinical trials and for early stage research a supportive domestic market is seen as important. A co-ordinated policy encompassing industrial and health policy is needed to support domestic innovation

The link between the growing market opportunity and the government's objective of developing an innovative sector is working together to make **China** a key location for innovation.

There appears to be increasing recognition within the government agencies in **South Africa** that purchasing strategy needs to be aligned to industrial strategy.

4. Intellectual property is a necessary but not sufficient condition for developing indigenous research and to develop a domestic innovative industry

The present innovation model is dependent on patents being observed to reward innovators, who take on risk in the innovation process. The impact of stronger intellectual property (IP) can be observed in many of the case study countries.

The level of protection influences the prioritisation of clinical trials in middle income markets and the location of basic research and preclinical research depends on the IP regime in the country. Although not sufficient, robust IP rules are required to encourage innovative activity.

Most interviewees reported that the IP system was an asset in encouraging domestic innovative activity. Changes in the IP system in **Brazil** were seen as significant in setting the foundation for innovative activity.

5. Sustainable innovation requires coordination between academia and the public and private sector

Once the basic infrastructure is developed, public investment in research is not enough to ensure a sustainable innovative product development and commercialisation industry. Partnership is vital for encouraging early stage research. The reasons are twofold:

- Innovative activities require a sustained, large amount of capital. As such public investment alone is insufficient to successfully develop and commercialise innovative products.
- The skills required to develop and commercialize drugs are different. The process is most efficient and successful when both public and private institutions work together.

Innovative activity in **South Korea** only developed when private investment was encouraged.

South Africa and **Brazil** have recognised the need to encourage partnership between academia, public research institutes and innovating private companies. In **China** there are successful examples of public and academic capabilities (e.g. the Beijing Genomics Institute) supporting private innovation.

6. The changing global business model is bringing new opportunities for middle-income markets

Changes in innovative global pharmaceutical business models brings both opportunities and challenges for middle-income countries:

- *Developing product portfolios to penetrate growing markets*: Low growth in the pharmaceutical markets in the west has created a need to look towards middle-income markets for additional revenue, which translates to a greater need to conduct clinical trial activities in those markets for marketing approval.
- *The biologic and biosimilars opportunity*: New research is increasingly focused on biologic medicines which require different skills and capabilities. This is likely to be beneficial for some middle-income markets who have the skills and appropriate experience; in others, this is likely to represent some additional hurdles.
- *Offshoring and outsourcing the value chain*: It has become standard practice for companies to relocate their manufacturing facilities to markets where the cost of production is lower. However, companies interviewed identified scientific capabilities as the most important factor (Figure 6) when choosing where to locate their innovative activities. The global industry is increasingly experienced in managing complex interactions between different suppliers in conducting early stage research and clinical trials. As middle-income countries develop their R&D capabilities they will have greater opportunity to be part of international firms' innovation process.

The advantages of outsourcing in **India**, refocusing on growth in **China**, and the opportunities to develop biosimilar competitors in **Brazil** demonstrate the increased opportunities.

High scientific standards and capabilities were identified as being more important than low cost. Poorly conducted clinical trials can be potentially expensive, either setting back or preventing a product's launch. The importance of scientific capabilities varies by innovation stage, with strong scientific capital being most important in the early stages of research.

Figure 6: Relative importance of factors affecting innovative activities

HIGH IMPORTANCE	• Medical schools operating to the highest international standards • Clusters of bioscience-based higher education institutions • Government health and industrial policies that are well-aligned • Consistently enforced systems of IP protection
MEDIUM IMPORTANCE	• A sound basic educational system • Collaborative international public-private partnerships (PPPs) • Market structures which facilitate effective and efficient diffusion of innovative medicines • Investment by domestic government
LOW IMPORTANCE	• Access to international markets • Low labour costs

Source: CRA analysis

About CRA and the Life Sciences Practice

CRA is a leading global consulting firm that offers business, financial and economic consulting services to industry, government and financial clients. Maximizing product value and corporate performance, CRA consultants combine knowledge and experience with state-of-the-art analytical tools and methodologies tailored to client-specific needs. Founded in 1965, CRA now has offices throughout the world. The Life Sciences Practice works with leading biotech, medical device and pharmaceutical companies; law firms; regulatory agencies; and national and international industry associations. We provide the analytical expertise and industry experience needed to address the industry's toughest issues. We have a reputation for rigorous and innovative analysis, careful attention to detail and the ability to work effectively as part of a wider team of advisers.

www.crai.com/lifesciences

Conclusions

Participation

All middle-income countries covered in our case studies are investing in bioscience strategies with the scale of investment reflecting national resources. The continuing globalisation and fragmentation of the innovation process should make it much easier for middle-income countries to increase their share of both public and private investment in both basic and clinical research on a piecemeal basis.

Innovation policy

There are very different opportunities depending on whether we are considering China, Brazil and India or smaller markets, such as Colombia and Malaysia. Policies need to be tailored to the countries situation. Not all countries have the market size or even the population that will encourage large scale clinical trials. It takes considerable time and investment to build up international standards research centres that are necessary for early stage research. Therefore a staged and targeted programme should be developed that builds capabilities over time in activities where the country can compete internationally. For middle-income countries to advance their participation in key facets of the innovation process, there are further improvements that will be needed in national regulatory frameworks in these countries to conform with generally accepted standards across developed markets.

Rewards

The combination of public and private inward investments over the past decade in South Korea and China, and to a lesser degree in India and Brazil, have greatly upgraded their domestic capabilities in basic and clinical research. There is every reason to believe, subject to further improvements in the regulatory frameworks, that this partnership will continue to flourish. From a national perspective therefore the first obvious pay-off for past investments are these assets, which with appropriate support from sound government policies going forward can be leveraged for decades to come to underpin competitive positions in the broader context of the globalization of innovation.

To develop the range of innovative activities from basic research to clinical development a jigsaw complex mix of policies are needed.

A key component to achieve this long term is to have a consistent policy framework, co-ordinate industrial and health policy, strong intellectual property and an environment that encourages partnership between the different stakeholders.

Contact

Tim Wilsdon
Vice President
twilsdon@crai.com

Dr. Jim Attridge
Senior Consultant to CRA
jattridge@crai.com

Eva Fiz
Consulting Associate
efiz@crai.com

Satomi Ginoza
Associate
sginoza@crai.com

CRA Charles River Associates

CRA International
99 Bishopsgate
London EC2M 3XD
United Kingdom

October 2012

ISBN 978-2-940498-18-5