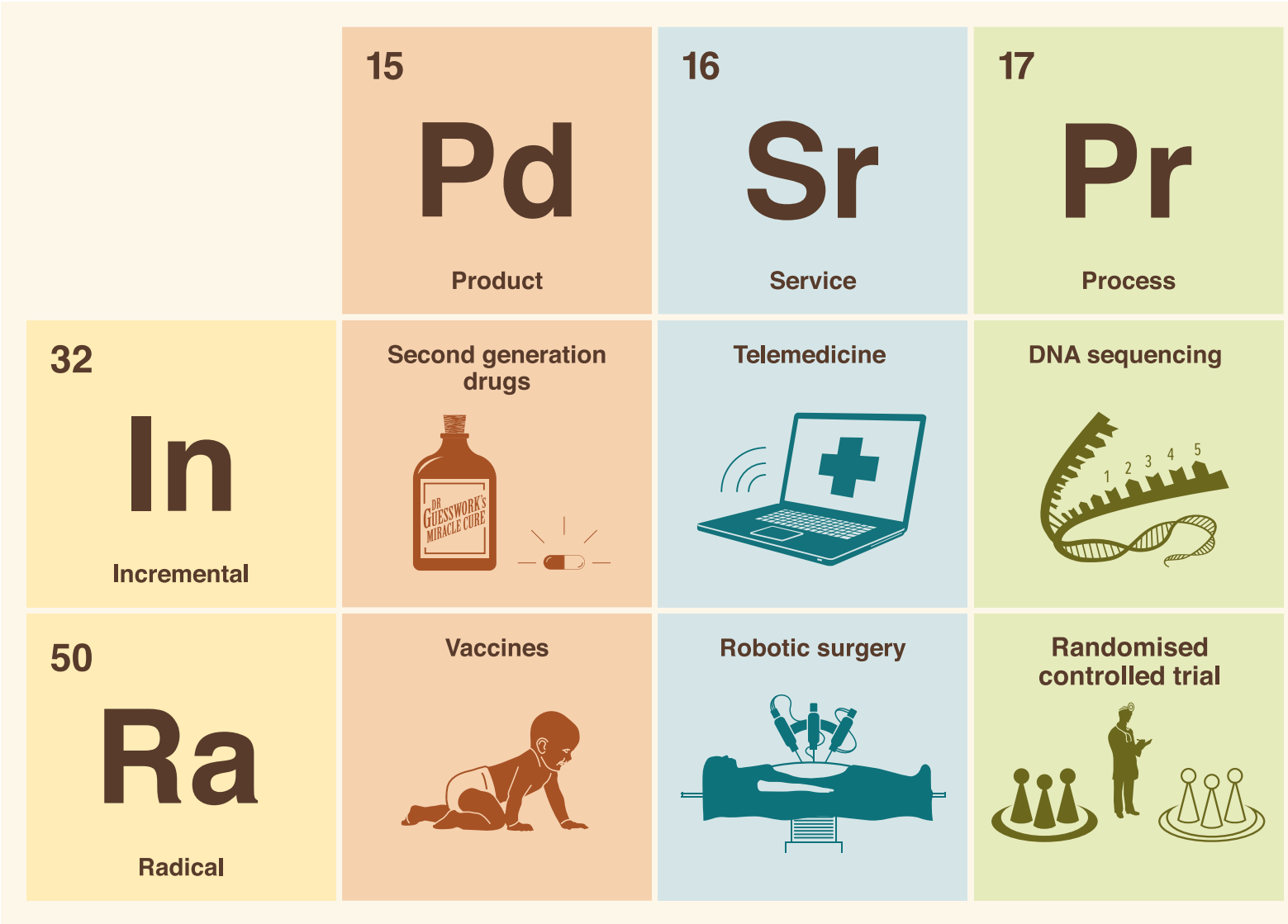
The Economist Intelligence Unit

Innovation in life sciences

An emerging markets perspective

A report by The Economist Intelligence Unit



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About this research

Innovation in life sciences: An emerging markets perspective is an Economist Intelligence Unit report. The findings are based on desk research and an interview programme conducted by The Economist Intelligence Unit. This research was commissioned by Dubai Science Park. The Economist Intelligence Unit would like to thank the following experts who participated in the interview programme:

- **Patricia Danzon,** professor of health care management, Wharton, University of Pennsylvania
- **Kirti Ganorkar**, senior vice president, business development, Sun Pharmaceutical Industries
- **Nilesh Gupta,** managing director, Lupin Ltd.
- **Christian Hogg**, chief executive officer, Chi-Med
- **Roger Humphrey**, executive managing director, life sciences, Jones Lang LaSalle
- **Kamalini Ramdas,** professor of management science and operations, London Business School
- **Satish Reddy,** chairman, Dr Reddy's Laboratories
- **Erika Ruiz,** promotion executive for the life sciences sector, Costa Rica Investment Promotion Agency
- **Karan Singh,** partner, Bain & Company, India
- **Irving Soto**, director of investment promotion, Costa Rica Investment Promotion Agency
- **Ramesh Swaminathan**, chief financial officer, Lupin Ltd
- **Dr Bicheng Yang**, director of communication and public engagement, BGI

The Economist Intelligence Unit bears sole responsibility for the content of this report. The findings and views expressed in the report do not necessarily reflect the views of the commissioner. Clint Witchalls was the author of the report. The editor was Adam Green.

Executive summary

The life sciences sector is capital intensive, high risk, and highly regulated. It is therefore little surprise to find that innovation is dominated by large incumbent firms from Western markets. Blockbuster brand drugs and advanced medical technologies still mostly come from companies in North America and Europe, with their long histories of innovation, strong domestic markets and access to talent. While companies from emerging markets have successfully gained ground and even leadership positions in areas such as electronics, cars and computing, the life sciences sector is one of the most impenetrable for newer market entrants due to scientific complexity and regulatory barriers.

However, it is eminently possible for emerging markets to become life sciences innovators. A handful of emerging markets have gained ground over the past three decades, becoming innovators in their own right. India, China, Brazil, South Korea, Costa Rica and Singapore all found a life sciences niche in a relatively short space of time in areas such as biologics, medical technology and health informatics. This report traces their trajectories from imitators towards innovators, explores the obstacles they faced, and identifies strategic lessons for countries seeking to nurture their own life sciences sector.

Key findings

The role of government in nurturing innovation is shifting away from intellectual property and towards direct R&D funding and incentives. India and Brazil became leading players in pharmaceuticals thanks to their governments' flexible stance on patents, which allowed national generics firms to grow and eventually transform into innovators themselves. Due to a trend towards tougher intellectual property (IP) protection, that option is less feasible for emerging markets at an earlier stage in life sciences development. In those cases, governments may need to focus on basic research investment and R&D promotion tools as their primary interventions.

Collaboration is vital to innovation, but is not common enough in emerging markets. Thanks to cultural ties and shared history, Western European and North American firms are more active collaborators in innovative research, patent applications and product development. Asian companies do have a history of collaboration, but predominantly through outsourcing partnerships with Western incumbents. Raising collaboration rates could bring about synergies. Two models coming into

vogue are in-licensing (India) and contract research partnerships (China).

Success does not depend only on size. Three giants of emerging markets life sciences—India, Brazil and China—benefited from large domestic markets. But Singapore and Costa Rica also found success in alternative models, showing that countries can build a leadership position by leveraging assets such as location and business climate.

Medical technology and health informatics is a promising avenue for emerging markets. Due to the challenges facing pharmaceuticals innovation, medical technologies and health informatics (such as DNA sequencing) might prove a more fruitful focus for newer arrivals to life sciences. Tangible breakthroughs are easier to achieve in this sector as compared with pharmaceuticals products, and there are easier routes to market.

Introduction

An innovation typology

'Innovation' is one of today's most popular buzzwords, describing everything from breakthrough immunotherapies for cancer to taxi-hailing apps. Governments speak of 'national innovation strategies', consultancies promise to help companies find their innovation 'sweet spot' and universities, from Zheijiang in China to Leiden in Belgium, have innovation research centres. But what does the word really mean? And how should countries that wish to become 'innovative' focus their energies?

Over many decades, economists and social scientists have developed different conceptual frameworks and models to define innovation, from the influential theories of Joseph Schumpeter (1883-1950) through to the typologies explored by contemporary academics such as Rajesh Chandy and Jaideep Prabhu (2011)[1].

Aravind Eye Hospitals: India's radical service innovation

India's incremental innovation can be readily found in the country's low cost generics industry. While these companies are 'copying' existing products, their operations require continuous, incremental 'process innovation' that has made India's generics among the cheapest and highest quality in the world.

The country has achieved more radical innovation in services. Kamalini Ramdas, professor of management science and operations at London Business School, cites Aravind Eye Hospitals as a paragon of such service delivery innovation. The not-for-profit hospital carries out more cataract surgeries than any other hospital in the world. Since first opening its doors in 1976, 2.5 million eye operations have been performed at an average cost of $25 per procedure. The hospital's founder, Govindappa Venkataswamy, was inspired by the 'McDonalds' formula of standardisation and reproducibility. Using an assembly line routine, nurses and other staff prepare each patient so that the surgeon doesn't waste any time in performing the operation. It is based on lean manufacturing principles, but applied to people. "There are massive innovations" in healthcare that "don't involve any new science", says Professor Ramdas.

[1] "R. Chandyand J. Prabhu (2011), "Innovation Typologies," in Wiley International Encyclopaedia of Marketing, Barry Bayus (ed.), John Wiley and Sons.

[2] A super generic drug is an improved version of an original drug which has lost product patent protection

In the life sciences, innovation covers a vast number of activities from landmark inventions like penicillin and X-rays, through to incremental innovations such as lower toxicity second generation drugs and 'super generics'[2]. It is most commonly associated with products, but it also applies to processes such as DNA sequencing, and services such as tele-health. In this report, we propose a matrix-based model of innovation that illuminates how emerging markets have participated in the life sciences innovation story. The model, which draws from concepts and ideas developed over decades of academic research, attempts to provide clarity for governments and companies in emerging markets that seek to nurture innovation their life sciences sector and want to identify niches (see Figure 1, page 7).

The matrix presented in this visualisation combines two types of innovation (radical and incremental, see left) with forms of innovation (products, services and processes, see right). *Radical innovations* are fundamental advances in our understanding of life sciences. Penicillin, vaccines, X-rays and the birth control pill are among the most commonly known examples—in this category we also include radical insights, such as germ theory. *Incremental innovations* are improvements on existing products, services or processes. Each time a new drug is released with fewer side effects or lower toxicity, for instance, it represents an important advance in human wellbeing.

As this model shows, both types of innovation—radical and incremental—apply to products but also to *processes* and to *services*. For example, the randomised controlled trial—a research method in which a treatment is randomly assigned to members within a group of volunteers—is one of the most momentous innovations in the history of medicine, allowing researchers to trace the impact of a therapy with greater statistical certainty than any other approach had allowed. Yet this innovation relates to a process, not a product. Similarly, the rise of tele-health transformed access to services for people once excluded from healthcare systems, but this was achieved by changing *service delivery*, not by inventing a 'product'.

Using this model, life sciences innovation in the emerging markets is clustered in certain 'combinations'. Incremental innovation has been most common in products (such as generic drugs), processes (such as DNA sequencing) and services (tele-health). This report also traces the emergence of radical product innovation in the likes of India, China and Brazil.

Figure 1. An innovation typology

'Innovation' is all the rage these days. But people increasingly use the term to mean very different things. Based on half a century of 'innovation' research, here is a visual typology of the forms and types of innovation, as found in the life sciences world. From vaccines to robotic surgery, this is our graphic framework showing the ways in which innovation really happens.

	15 Pd **Product**	16 Sr **Service**	17 Pr **Process**
32 In **Incremental**	**Second generation drugs** An incrementally improved version of a medicine e.g. slow release formula, reduced toxicity or fewer side effects.	**Telemedicine** Using telecommunications to help patients wherever they are – sharing electronic files, diagnosing on the web and monitoring patient recovery.	**DNA sequencing** The process of determining the precise order of nucleotides within a DNA molecule. Since first used in the 1970s, DNA sequencing has gone through incremental improvements in terms of speed and cost
50 Ra **Radical**	**Vaccines** Probably the most radical innovation in medical history. Vaccines work by giving a disease in very small doses, stimulating the body to produce antibodies that provide future immunity to the disease. Vaccines are the reason that once deadly diseases like polio, measles and tetanus have been eradicated from much of the world.	**Robotic surgery** Surgeons are increasingly using robots to assist them, through tele-manipulators or computer control. Smart instruments have reduced tissue trauma and provide steadiness beyond the capabilities of human hands.	**Randomised controlled trial** The RCT transformed the way we test medicines. It works by randomly allocating a medicine to one group and comparing with a control group who do not receive it.

Part One: Innovation drivers

Part one of this report identifies the drivers of life sciences innovation in key emerging markets over the last three decades. It focuses on three factors: government, market structure, and talent. We explore the government's role via policy interventions such as intellectual property laws, and direct engagement such as funding research and incentivising R&D. Market structures are examined, focusing on how local demand drives commercial growth, which in time gives companies the financial resources to invest in innovation. Finally, talent is explored as a key determinant of innovation.

Chapter 1: The Visible Hand

Over the past four decades, governments have nurtured the life sciences in a handful of emerging markets. India and Brazil's governments, for instance, played a catalytic role through their intellectual property policies, according to Nilesh Gupta, managing director of Lupin, the third largest pharmaceutical company in India by market capitalisation. "Just like Brazil, India took its time starting to accept foreign patents," he says. "It gave time for the industry to build and really be prepared for competition as it started coming in."

India's Patent Act in the 1970s did not recognise product patents, but did recognise process patents. This allowed Indian pharmaceutical companies to 'reverse engineer' or copy drugs from foreign firms that were still under patent protection. As long as Indian firms could prove they arrived at the copycat drug via a different process to the originator company, they would be granted a process patent, lasting seven years. Without expensive laboratories to fund, India's pharmaceutical companies could produce copycat drugs at an affordable price. Allowing local companies to produce 'generic' copies of existing drugs helped them to grow and acquire skills through 'learning by doing'.

From 1972 to 2004, under the process-patent regime, India's pharmaceutical industry grew from virtually nothing to the fourth largest in the world.[3] Many of India's major pharmaceutical companies emerged during this time.[4] By 2005 India's pharmaceutical market was worth $6 billion. By 2013, the market was worth $12 billion. According to McKinsey and Company, it is projected to be worth $55 billion in 2020.[5] Revenue generated from generics—which comprises 72% of the industry's total—gave companies the financial resources to invest in novel drugs (which now constitute 9% of revenue). Brazil's arc was similar. Between 1945 and 1996, Brazil did not recognise patents on pharmaceutical products. Domestic companies were similarly free to copy originator drugs.

As will be explored in this report, this policy stance created companies that—in more recent decades—have become more like innovators. Brazil and India followed a model that established pharmaceutical markets had used. For example, Switzerland did not have a national patent law until 1888 and, even then, lobbyists from the chemicals industry ensured the law only covered inventions that could be represented by mechanical models. This led a German legislator in the Reichstag to describe Switzerland as a "pirate state". A new patent law was introduced in 1907, but only protected chemical processes, not chemical products. It was this freedom from patent restrictions that allowed Switzerland's fledgling pharmaceutical industry of the day—which included the likes of Roche and Sandoz—to expand in the late 19th and early 20th century.

Direct funding for research and development

Beyond intellectual property policies, there are other ways that governments have nurtured life sciences industries (see Table 1). Of these, state funding of research, including investment in research infrastructure, is one of the more interesting areas.

The Chinese government has been supportive in terms of grants and developing infrastructure. Between 1996 and 2000, it invested $238 million in life sciences and biotechnology. Over the subsequent five years (2001 to 2005), the government more than trebled the available funds to $795 million. The twelfth five-year plan (2011 to 2015) was announced in 2011. Biotechnology was highlighted as one of six strategic emerging industries for research and innovation focus. To that end, the state earmarked $1.7 trillion in funding for biotechnology, of which $1.5 billion is for new drug development. In 2012, the US Department for Defense's Asia-Pacific Center for

[3] Haley & Haley (2011), "The effects of patent-law changes on innovation: The case of India's pharmaceutical industry". *Technological Forecasting & Social Change*. Vol. 79,4: 607–619

[4] They include Glenmark Pharmaceuticals (1977), Jubilant Life Sciences (1978), Sun Pharmaceuticals (1983), Dr Reddy's Laboratories (1984), and Aurobindo Pharma (1986).

[5] "India Pharma 2020: Propelling access and acceptance, realising true potential". McKinsey & Co.

Security Studies estimated that life sciences and biotechnology accounted for about one-fifth ($27 billion) of China's total R&D investment ($135 billion). The government also spent $1.8 billion on building biotechnology science parks.[6]

Singapore's government has also invested in the research ecosystem. Between 2000 and 2005, it injected $6 billion to kick-start the biomedical sciences industry, including building Biopolis, a biomedical R&D hub, setting up new research centres and attracting large international pharmaceutical companies to use Singapore as their base in Asia. The government has also fostered public-private partnerships by creating the Biomedical Sciences Industry Partnership Office which identifies research strengths in Singapore's universities, research institutes, hospitals and medical centres, and matches them with companies' interests.

In just 15 years, Singapore has gone from being a relatively insignificant biotechnology centre to one of the most highly regarded in the world. In *Scientific American's* 6th Annual Worldview Scorecard—a comprehensive country-by-country analysis of biotechnology—Singapore ranked second across all categories (productivity, intellectual property protection, enterprise support, intensity, education/workforce, foundations, and policy and stability).[7] Only the US scored higher.

[6] They include Glenmark Pharmaceuticals (1977), Jubilant Life Sciences (1978), Sun Pharmaceuticals (1983), Dr Reddy's Laboratories (1984), and Aurobindo Pharma (1986).

[7] "India Pharma 2020: Propelling access and acceptance, realising true potential". McKinsey & Co.

Table 1: State support for innovation

Fund science parks, hubs, and incubators
Offer grants and state-backed loans
Strengthen protection of intellectual property when the domestic market is sufficiently mature to withstand foreign competition
Bring regulation in line with international standards. For example, Brazil is in the process of harmonising its GMP (good manufacturing practice) for medical devices with international standards. The World Health Organisation (WHO) praised the CFDA (China's version of the FDA) for "being well on its way towards meeting the highest international standards for a regulatory authority"
Establish local content policy. Brazil's medical devices sector is strongly linked with the government's policy of promoting the use of locally made medical devices domestically
Provide tax breaks on R&D activities or capital goods equipment purchase/import

Source: WHO *Global Burden of Disease study*, 2013.

The Indian government, in contrast, has been a less active investor. "Government funds are available for doing innovation, but they are so small in size," says Kirti Ganorkar, head of business development at Sun Pharmaceuticals, the largest pharmaceuticals company in India. "Even if 100% of government funds were given to one company, you still couldn't do any basic research," he claims.

Other voices from Indian industry also claim the government needs to invest more. Drug development is high-risk. For every 25,000 compounds that start in the laboratory, 25 are tested in humans, five receive marketing approval and one earns back the amount invested. Venture capital firms may have the risk appetite to invest in promising late-stage products, but are less active in early-stage clinical research. And while equity financing is a route for firms in developed markets, raising an IPO in emerging economies may be a harder task.

"The government has to support it, because pharmaceuticals have a very long gestation period," says Mr Gupta at Lupin. "From the time that you start setting up a plant there is probably a four to five year window until you start making money," he argues, referring to generics which have a shorter gestation period than novel drugs. "This kind of waiting period is very rare in other industries, so you certainly need to incentivise and support the [life sciences] industry to grow it."

Mr Ganorkar would like to see the government play a bigger role in building up academic institutions too. "In the US and Europe, the basic research—like a new receptor or a new treatment or a drug—happens in academic institutions and then it comes to big pharma's hands," he says. "To do that, the government has to create a big institution along with the infrastructure. We [the Indian pharmaceuticals industry] cannot do it on our own."

Direct funding is not the only means of government support, however. Costa Rica

has shown the benefit of fiscal incentives for attracting companies that can contribute to the R&D profile. It has free trade agreements (FTAs) with over 50 trade partners and specific incentives to attract life sciences foreign direct investment (FDI). "There is a package of fiscal incentives that is part of our value proposition, and it has been a very solid package in terms of stability for more than 30 years. As a company, you have the certainty that what is stated in the law is what you will get as a company, with no negotiation: if you comply with the requirements then you are going to receive the benefits," says Irving Soto, director of investment promotion at the Costa Rica Investment Promotion Agency.

Chapter 2: Market dynamics

Market dynamics are the second driver of life sciences innovation. In India, intense competition has catalysed some process innovation to reduce costs. "There are about 10,000 pharmaceutical companies in India," says Mr Ganorkar at Sun Pharmaceuticals. "There are very competitive dynamics. If I make a product at 10 rupees and somebody makes the same product at 5 or 6 rupees, then I'm out of the market."

Low margins and intense competition have fostered incremental process innovation such as finding methods for increasing yields—the amount of product obtained in a chemical reaction—in active pharmaceutical ingredients (APIs). "When you start, maybe you are getting a yield of 50% to 60%," says Mr Ganorkar. "You keep on improving until you reach to 90% to 95% of the yield. That's one way of doing incremental innovation. As you increase your volumes, you also get efficiencies of buying the chemicals at an affordable price."

A second market dynamic affecting innovation is domestic demand. India, China and Brazil built industries because of the scale of their home market. Karan Singh, a partner at Bain & Company, says India used this local demand base to grow and, through retained earnings, later expand into foreign markets. Home markets have been even more powerful in China. Not only is its domestic pharmaceutical sector huge—the third largest in the world[8]—the government also provides health insurance for a large part of the population.

"The [Chinese] government is funding some level of national health insurance and reimbursements for drugs, and a lot of publicly financed healthcare providers or hospital systems prefer to buy Chinese drugs," says Patricia Danzon, professor of health care management at the Wharton School, University of Pennsylvania.

"When they have tenders, being a Chinese company probably helps. In that case, the Chinese industry has an advantage because more than any other country, both the size and the state of government commitment to paying for healthcare for its citizens really is ahead of other countries, with the possible exception of Brazil."

Brazil's healthcare system is universal and free for all citizens. Between 2001 and 2011, Brazil's per capita healthcare expenditure grew 14%, compared with 6% worldwide.[9] According to research firm IHS, Brazil's strong growth in the medical devices sector is due to an increase in the elderly population, and rising healthcare insurance coverage.[10] It is this combination of domestic market size, and the boosting of effective demand through healthcare insurance coverage, that allows these markets to generate profitable firms—a necessary condition for later investment in innovation.

Brazil's large market has substantially driven its medical technology industry. According to data from the Brazilian Health Ministry, the "health equipment" sector has been growing at over 7% a year since 2003 and is forecast to continue rising. Franco Pallamolla, the president of the Brazilian Medical Devices Manufacturers Association, ABIMO, anticipates that by 2020 Brazil will be one of the five largest manufacturers of medical, hospital and dental products in the word.[11]

Brazil's big players in medical technology include Fanem, a company that makes neo-natal, laboratory and hospital products, Ortosintese, a maker of orthopaedic implants, surgical tables and autoclaves, and Baumer SA, a maker of orthopaedic implants and prostheses. However, it is worth nothing that, in Brazil, two-thirds of the revenues in this sector are made by small and medium-sized companies. This is encouraging news for emerging markets which wish to enter the innovation game but do not yet possess large-scale domestic companies.[12]

[8] "Healthcare & life sciences in China—Towards growing collaboration", KPMG.

[9] Humphrey R. (2014). Life sciences cluster report, JLL.

[10] "Brazil's medical device market set to hit $13.1 billion by 2020", IHS.

[11] Jay Franco. (2011). "Brazil poised to enter world stage for medical device manufacturing". *Middle East Health*. p.54

[12] Humphrey R. (2014). Life sciences cluster report, JLL.

Small can be beautiful: Costa Rica and Singapore

While Brazil benefits from its large domestic market, medical technology—unlike pharmaceuticals—has advanced in smaller countries as well, suggesting that innovation dynamism does not necessarily depend on domestic market size alone. Although Costa Rica has a population of just 4.9 million, it is host to more than 60 medical device makers, including Covidien, Boston Scientific, Baxter Healthcare, Allergan and St Jude Medical. In 2012, Costa Rica exported $1.4 billion worth of medical equipment.[13]

Market size has helped, but in Costa Rica's case the defining factor has been proximity to lucrative regions—in particular the US. This means foreign firms like Abbott, Baxter and Boston Scientific can supply their domestic (US) market with medical devices from a free zone close its shores. Moreover, the likes of Baxter, Royal Scientific and Allergan focused initially on assembly and automation but over time leveraged the market access advantage to move further up the value chain in manufacturing. This evolution also brought 'cluster' effects with spill-overs between medical technology and electronics. "There is an excellent match and synergy between these two industries" says Erika Ericka Ruiz, promotion executive for the life sciences sector at the Costa Rica Investment Promotion Agency (CINDE).

Singapore is another example of a small country by market size that has made big strides in life sciences. While it has a universal healthcare system, its population is smaller than Costa Rica's (3.9 million residents). To compensate, it has pitched itself to foreign investors as a hub to the rest of Asia's healthcare markets.

Since 2000, the Singaporean government has been enticing international biopharmaceutical companies to use Singapore as a regional or even global manufacturing base, citing its robust supply-chain network with well-established links to Asia's markets as one of many inducements. The efforts have paid off. At least 50 biopharmaceutical companies, including Abbott, GlaxoSmithKline, Lonza, MSD, Novartis, Pfizer and Sanofi-Aventis, have built manufacturing plants on the island. Amgen opened its first biologics manufacturing plant in Asia in Singapore in 2014. The same year, AbbVie announced that it would build a $320 million bulk biologics manufacturing plant in Singapore, also its first in Asia. The plant is expected to be operational in 2019. Between 2000 and 2014, manufacturing output of biomedicine in Singapore increased from S$6.3 billion to S$21.5 billion. Biomedical manufacturing now accounts for 7% of the island's output.[14]

Singapore and Costa Rica both show that small emerging markets, measured by population, can develop a life sciences sector of global importance by leveraging access to surrounding markets using a hub strategy.

[13] MIT Observatory of Economic Complexity data. Available at: https://atlas.media.mit.edu/en/explore/tree_map/hs/export/cri/all/show/2012/

[14] Department of Statistics Singapore. Available at: http://www.singstat.gov.sg/statistics/browse-by-theme/trade

Chapter 3—Tapping talent

A third ingredient supporting life sciences innovation is human capital. India's pool of process chemists, and widespread English language skills, has been essential to its success. "We used the chemistry capabilities to reverse engineer and create generics," says Mr Singh at Bain & Company. "It is our legacy of strong chemistry talent coupled with the IP regime that led to the rise of the generics industry."

The story in China is more complex. In the past, many Chinese students who studied abroad, stayed abroad. One study, conducted in 2014, found that 85% of Chinese students who gained their doctorate in the US in 2006 were still there in 2011.[15] But there are signs that the brain drain could be slowing. "You've got quite a decent flow of returnees coming back to China," says Christian Hogg, chief executive officer of Chi-Med. "A lot of the CROs [contract research organisations] have brought back mainland Chinese pharmaceutical people who had gone to America to get PhDs." Chi-Med now employs 250 full-time scientists and staff at their Shanghai headquarters and its R&D pipeline includes biotech oncology products, a high growth area. "We've been able to use a very high quality group of returnees with global big pharma expertise to recruit, train, and essentially mobilise local talent. It's taken many years, but it's very effective," says Mr Hogg.

Strengthening local academic institutions is another way of reducing brain drain. Between 2001 and 2011, the Chinese government increased spending on universities six-fold, yielding impressive results. Between 2005 and 2012, published research articles from Chinese higher-education institutions rose by 54% and the number of patents granted increased eightfold. When deciding where to work, scientists are highly incentivised by the quality of talent that surrounds them.

A third leading emerging market for talent is Costa Rica. While the country has leveraged its geographical proximity to the US, it has also developed other competitive advantages in the form of its skilled workforce and the education system more broadly. "Our main asset is the quality of our labour force," says Mr Soto at the Costa Rica Investment Promotion Agency (CINDE). "We have worked our FDI strategy around this by focusing on companies that require a highly educated and very productive labour force."

A key contributor to this labour force has been a long-standing pro-education policy: education has been free and mandatory since as far back as the 1800s. Costa Rica also has a national learning institute providing free technology training, and companies have the right to require custom-made training for employees. There are also productive partnerships between industry and academia, notably collaboration between the national technical university and the University of Minnesota, culminating in Latin America's first Master's degree in the speciality of medical devices. This translates into high rates of job creation. In 2000, there were 8 medical technology companies producing 1,500 jobs. Today there are 60 life sciences companies generating 19,000 jobs, according to CINDE.

[15] *"A matter of honours: China is trying to reverse its brain drain"*, The Economist, Nov 22nd 2014.

Genomics in China: Create your own talent pool

BGI (formerly known as Beijing Genomics Institute) is the world's most prolific sequencer of DNA. The Shenzhen-based company sequences everything from viruses to humans. Its achievements include being the first to sequence the genome of the giant panda and the first to sequence the genome of an ancient human (from a 4,000-year-old permafrost-preserved hair).

BGI wants to create the world's largest database of sequenced genomes. To this end, the company employs about 2,000 PhDs, so finding and retaining talent is critical for the company's success. "In the process of developing major scientific and industrial projects, BGI has been exploring a new model of education and training to incorporate its own creative spirit and the project-oriented educational philosophy," says Dr Bicheng Yang, director of communication and public engagement at BGI.

Since 2009, BGI has created a number of joint undergraduate and graduate programmes in collaboration with universities in China and abroad. "BGI has been not only recruiting but also training a great number of outstanding young students in the fields," says Dr Yang. "Talent is always the source of innovation."

In December 2014, BGI, South University of Science and Technology of China and University of Copenhagen agreed to collaborate on establishing a specialised college. The international college will focus on cultivating "world-class, high-end talents" for the life sciences and bio-industry. The aim is not only to produce leading scientific research, but to boost the development of the bio-industry in China.

2 Part Two: Strategies, principles and lessons

Three decades since the lead emerging markets started developing their life sciences industries, there are valuable lessons to be learned from the strategies they have employed, the challenges they have faced and the obstacles they now confront as they seek to ascend the innovation value chain from incremental to radical. *Part Two* of this report explores the ascent of the lead emerging markets into areas such as biologics and biosimilars, focusing on the importance of state funding for research, and the need for greater collaboration within industry, before moving on to our lessons learned for the wider group of emerging markets wishing to build their capacities.

Chapter 4: Climbing the innovation ladder

The examples explored so far in this report pursued incremental innovation in products (largely generics), and have attempted more radical innovation in *processes* (DNA sequencing) and *services* (e.g. low cost cataracts surgery). But emerging life sciences players are increasingly looking to emulate the radical *product* innovation of the Western pharmaceutical companies as well. "Today the game is not about cost optimisation," says Mr Gupta of Lupin. "It's not about active pharmaceutical products or simple oral solid products. It is about the more complex products. It really is about innovation now."

India's move towards radical product innovation quickened in 2005, when the government reintroduced product patents creating opportunities for companies which had grown during the generics era. At that time, Shrikumar Suryanarayan, then president of research and development at Bangalore-based biotechnology firm Biocon, told the *Wall Street Journal*: "The winner used to be the guy who could copy faster. Now that has completely changed...Companies that don't innovate will die, especially in the pharmaceutical industry."[16]

According to *Nature*, the science journal, two forces are driving the product innovation trend in emerging markets: wide-scale adoption of the TRIPS agreement (which requires more strenuous levels of patent protection)[17], and enhanced government support for innovation.

One particular area of innovation is biologics —protein-based drugs made from living cells. A second is biosimilars—copies of biological drugs that have gone off patent, which tend to exhibit high molecular complexity and sensitivity to changes in manufacturing processes[18]. Biologics and bio-similars are a very different prospect to generics, requiring significant time, money and expertise to develop. But profits are potentially huge. Seven of the 21 top selling drugs in 2011 were biologics.[19]

China, India and Brazil are all building biologics and biosimilars industries, with India leading. Several firms have biosimilars at various stages of drug development. Dr Reddy's Laboratories, India's second biggest pharmaceuticals firm by revenue, has received approval from America's Food and Drug Administration (FDA) to start clinical trials for two biosimilars. Dr Reddy's Laboratories launched a biosimilar of the anti-cancer drug, Rituximab, in India in 2007.

India has used the strategies of its generics era to guide its entry into these new areas. Dr Reddy's uses the expertise of Indian returnees—mainly experts who had trained in Europe—to build up technology and expertise. They have continued to achieve the low cost outputs for which the industry is famed. Reditux—Dr Reddy's biosimilar of rituximab—initially sold at about 36% of the innovator's price. Growth strategies are also similar. "If you look at our journey with generics: we would launch them in India first at an affordable price using our technology, then we would take it to other emerging markets, also at affordable prices, and ultimately aim for the developed market," says Mr Reddy. "That's the same journey we will take with biosimilars." However, Reditux has yet to pass the stringent regulatory hurdles set in the US and the European Union.

China is also moving up the innovation value chain on biologics and biosimilars. The government has bolstered IP protection and 'GMP' (good manufacturing practices) compliance[20] and in 2011, the Shenzhen government set out its twelfth five-year plan to support research and innovation in six strategic, emerging industries, including biologics. Biologics enjoyed marked revenue growth between 2006 and 2010, according to the National Statistics Bureau of China (see Figure). Chinese firms, including Innovent Biologics and Henlius Biopharmaceuticals, now

[16] "India Senses Patent Appeal", Wall Street Journal, April 11th 2005.

[17] The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) is an international agreement that sets down minimum standards for intellectual property (IP) regulation and is applied to members of the World Trade Organisation.

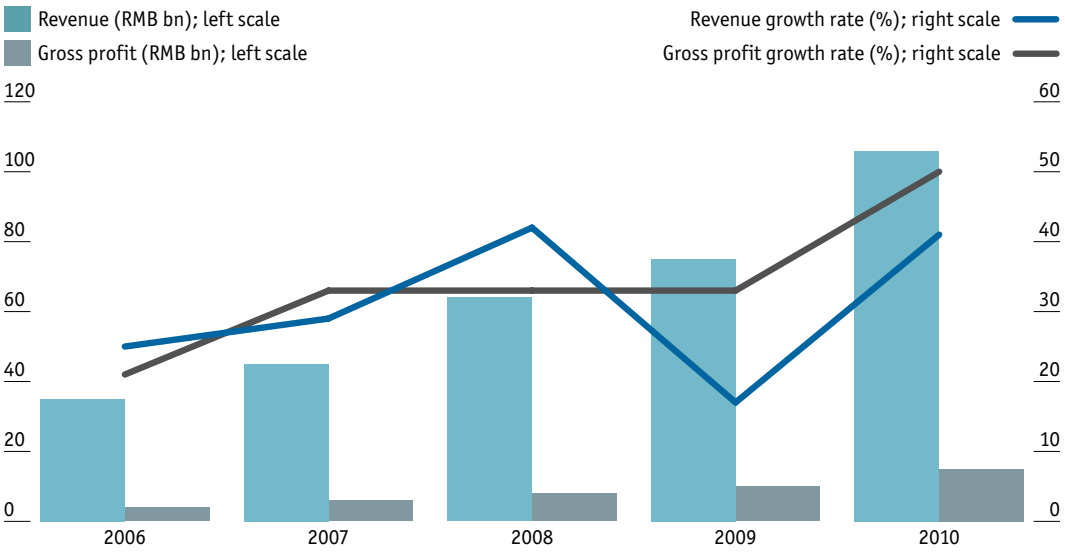
[18] Biosimilars are a type of biological product that are licensed by FDA because they are highly similar to an already FDA-approved biological product and have no clinically meaningful difference from the reference product.

[19] "Regulatory And and Cost Barriers Are Likely To Limit Biosimilar Development And Expected Savings In The Near Future", Health Affairs, June 2014 33:61048-1057.

[20] Humphrey R. (2014). Life sciences cluster report, JLL.

Chart 1

Biologics and biosimilars in China, 2006-10



Note. Data in December is excluded.
Source: NSBC.

have biosimilars in the pipeline and will seek marketing approval for their drugs in developed markets. However, this remains a challenge: so far, there have been biosimilars produced in China which are not recognised by drug regulators in developed markets, due to differing definitions.

Other Chinese attempts to climb the innovation value chain involve novel small-molecule drugs. Chi-Med's small molecule oncology drug, fruqintinib, will be submitted to regulators for approval next year. "We are setting the trend with regards to establishing innovative small molecule drug research and development operations in China," says Chi-Med's Mr Hogg.

Industry calls for basic research investment

Despite these advances, the life sciences still have some way to go in terms of radical product innovation rates. How could they gain ground? History shows that 'basic science'—defined as research with the sole purpose of developing knowledge, rather than developing products or applying knowledge to products—leads to the most dramatic innovations. Yet emerging markets are lagging here. "Asia should become a centre for basic research, but we are still far away from that reality," says Mr Ganorkar. "What you are seeing in South Korea and China, and what we are doing in India with biosimilars or slightly better generics, is really incremental innovation. We are still not where we need to be to do basic or breakthrough research."

Professor Danzon of Wharton agrees with this assessment. "To do something innovative, you need a base in cutting-edge basic science, because that's where the new ideas come from," she says. "At least at this point in time, it tends to be the countries which have a high enough level of revenue and a willingness of government to invest money." Professor Danzon says a number of non-US companies have hubs near Boston and Silicon Valley, where significant National Institute of Health (NIH) funding is directed, and where ideas are coming from.

Although China spends about 2% of its GDP on R&D, the focus is heavily skewed towards development[21]. About 84% of China's total R&D spending goes on product development, especially the development of clean energy and

[21] http://www.oecd.org/sti/inno/Note_MSTI2013_2.pdf

State-funded innovation: Highlights from the NIH

1955: NIH coordinates the first national cancer chemotherapy programme.

1968: Nobel Prize in Medicine awarded to Dr Marshall Nirenberg, head of an NIH Laboratory, for discovering the key to deciphering the genetic code.

1991: NIH scientists treated the first cancer patients with human gene therapy.

1996: NIH-supported scientists carry out first multicentre trial of bone marrow transplantation in children with sickle cell disease.

1999: NIH funds the discovery of HIV-1, the virus responsible for the global AIDS pandemic, and studies demonstrating effectiveness new treatments for preventing mother-to-child HIV transmission.

2002: A team of NICHD scientists developed the first vaccine against Staphylococcus aureus, a major cause of infection and death among hospital patients.

advanced grid technology. However, the Chinese government aims to raise the proportion of the R&D budget spent on basic research to 10% by 2020.[22] It is currently about 5% of total R&D spend, compared with 10 to 25% in developed countries.

Although India's R&D spend as a proportion of GDP is much lower than China's (0.9%), the share of the budget that goes towards basic research is larger. The share of R&D dedicated to basic research in India in 2012 was 26%,[23] which is slightly higher than France (25%), and ahead of the US (17%).[24] There is no data available on the share of Brazil, Singapore or Costa Rica's R&D spend directed towards basic research.

The investment can pay off. The US is perhaps the best example of the power of public funding for driving life sciences innovation. The NIH has been a major player in funding life sciences innovation in the US. While emerging economies may look on with envy at the NIH's roughly $30 billion annual budget,[25] they should not forget this is an organisation whose origin dates back to 1798, when it started with the modest goal of providing medical relief to sick and disabled men in the US Navy. Since then, it has evolved into a powerhouse which, through its competitive grant system, has nurtured some of the most important advances in life sciences including inventions that led to the elimination of rubella, whooping cough and pneumococcal pneumonia.[26] Over time, the US pharmaceutical industry's R&D spending outgrew that of the NIH, but the two work in tandem: the NIH supporting the basic science insights which the pharmaceuticals research builds upon. Crucially, NIH funding itself often leads to commercial success.

Not all emerging markets have the financial resources to fund basic research—but the evolution of the NIH from modest beginnings shows that such agencies can be developed over time, are key drivers of innovation and, perhaps most importantly, can complement the private sector by providing the insights on which private sector R&D can build.

[22] http://www.nature.com/news/china-goes-back-to-basics-on-research-funding-1.14853

[23] http://www.rdmag.com/articles/2012/12/bric-india

[24] National Science Foundation data - http://www.nsf.gov/statistics/seind14/index.cfm/chapter-4/c4s2.htm

[25] NIH Budget. Available at: http://www.nih.gov/about/budget.htm

[26] "Mother of Invention: How the Government Created "Free-Market" Health Care", Robert I. Field

Chapter 5: Collaborate to innovate

A second strategy for countries wishing to ascend the innovation value chain is promoting greater collaboration. Western European and North American countries show the most-frequent instances of international collaboration (i.e. at least one foreign co-inventor) on patent applications and Asian countries the fewest, according to a study by Jones Lang LaSalle.[27]

Roger Humphrey, executive managing director of life sciences at JLL, suggests two reasons that collaboration in Asia is not as high as it is in the West. One is the historic competition for territory and resources in Southeast Asia. The other is intellectual property law.

"Foreign collaborators, particularly in private industry, want assurance that their commercial interest in a patent will be protected," says Mr Humphrey. "The United States and Europe have had strong patent protections for many years, and that makes a difference in rewarding innovation and collaboration."

But Mr Humphrey says that where and why collaboration happens, and its impact on the marketplace, is a complicated issue. "The United States and Europe have dominated life sciences research since 1945, being home to leading academic institutions as well as the world's largest biopharmaceutical innovator companies," he explains. "Despite the fractures of World War II, there are cultural ties between the United States and Europe. Some would argue that their cross-border collaboration has advanced both basic research and the new product development more quickly than without collaboration."

Asian companies do have a history of collaboration, but predominantly through outsourcing partnerships. Some established firms in the West and Japan outsource the manufacture of APIs to Chinese and Indian firms. According to one estimate, India and China, supply over 40% of APIs used in the US.[28] Although this sector has enjoyed an estimated compound annual growth rate (CAGR) of above 17% for China and India, the margins on bulk pharmaceuticals are being eroded, both from within (inflation, rising wages, and currency appreciation) and without (competition from other emerging markets).

Perhaps a more fruitful area of collaboration, in terms of innovation, is in-licensing—companies entering sharing agreements over product licenses, and finding synergies enabling them to achieve in partnership what neither could achieve alone.[29]

"We have licensed new biologics for psoriasis from Merck," says Mr Ganorkar at Sun Pharmaceuticals. "This is exactly the reverse of what all other pharma companies are doing. Pharma companies develop new chemical entities and license them out to a big pharma or multinationals; we in-licensed new biologics from big pharma so that we are able to bring their product to the market." Mr Ganorkar says the company looks to in-licence pharmaceutical products in which they are not strong, and use this as a learning experience so they can create their own biologics in the future. Sun Pharma has also in-licensed an oncologic compound. "We are strong in synthetic chemistry where we are developing new chemical entities on our own," says Mr Ganorkar. "Wherever we have expertise, we develop new chemical entities on our own. Where we don't have expertise, we in-license products from small companies or big pharma and try to develop them and bring them to the market."

Ten years ago, Sun Pharma did everything alone. There was no collaboration with academic institutions or other companies. Since then, the company has changed tack and now collaborates with big pharmaceutical companies, small private companies, and research institutes in India and abroad. "Without collaborating, we can't innovate," says Mr Ganorkar. "Collaboration is a key because drug development or drug research

[27] "Life sciences cluster report", Humphrey R., JLL (2014).

[28] MDTV Alliance data. Available at: http://www.mdtvalliance.org/the-api-industry-at-a-glance/

[29] Products, often under development, licensed from one company to another.

now is not a monopoly of one company or a set of few people. It requires knowledge across different sets of people. That's why collaboration will be the way we will innovate in future."

Collaboration is also essential for Chi-Med, according to the firm's CEO. "While our research and discovery operations in China are terrific, when it comes to global development and, ultimately, when it comes to global commercialisation, partnerships are very, very important," says Mr Hogg. Chi-Med's strategic partnerships include deals with AstraZeneca and Eli Lilly. "That gives us so much more financial resource, and a capacity to move those programmes really fast in multiple indications," he explains. "These partners bring a great deal of capability, and global reach that we don't have."

Conclusion

From China to Costa Rica, progress in emerging markets life sciences has been impressive—but there are obstacles to overcome for these countries to innovate at the same rate as Western incumbents. For countries at the early stages of life sciences development, there are useful lessons to be learned from the last three decades.

Government remains vital, but its role is changing

Government activism over intellectual property helped Brazil and India build life sciences industries over time: companies were able to create copycat products under the protection of their governments' patenting policies. Learning-by-doing, and growing profits, enabled them to invest in more innovative activities later. "A lot of this science calls for deep pockets and Indian companies do not really have deep enough pockets to take on these uncertainties," says Mr Swaminathan, of Lupin. "It's only as Indian companies are becoming much bigger [that they are] willing to take the risk that is required to get on to the next frontier."

The problem for countries at an earlier stage in life sciences development is that the 'copy-cat to innovator route' is more challenging from a policy perspective. "In any field of endeavour, most people start by copying the greats, whether we're talking art or biotech," says Professor Danzon. "That's a game that countries can't play anymore, because all the countries of any significance have signed up to TRIPS.[30] That means they have to respect twenty-year product patents." Direct funding, however, is a form of state support for countries with sufficient resources. Experience of developed markets—and especially the US—is instructive.

State funding can deliver major gains for life sciences innovation, nurturing 'basic science' through grants and competitive award programmes which in turn incentivises private innovation. Such public investment in life sciences in Western countries is declining, even in the US which pioneered such approaches through the NIH. Cash-rich emerging markets can capitalise on this, and catalyse innovation through R&D-related grants. Allowing companies to patent discoveries that result from publicly funded research, as occurs in the US, has also been shown to promote innovation from public funding.

There are differing models for financing life sciences: the top-down approach, favoured by China and Singapore, and the bottom-up approach, favoured by India and Costa Rica. In the top-down approach, the government provides funding for science parks, research

[30] Trade Related Aspects of Intellectual Property Rights

and development (with a heavy emphasis on development), skills training and other aspects of the innovation system. In the bottom-up approach, the government removes obstructions (such as patent laws or tax exemptions on imports or exports) which allow the sector to flourish, but takes a lighter touch when it comes to funding.

In India, the generics industry funded itself through retained earnings and, in Costa Rica, foreign medical device companies brought their own cash with them. But funding the development of novel drugs or biologics development would not be possible for an emerging economy without significant assistance from the state. "If you're a small, poor country, the idea that you're going to be a powerhouse in biotech, it's just not going to happen," says Professor Danzon. Whether an emerging economy picks a top-down or bottom-up approach will depend on the life science niche they are looking to specialise in, and the depth of the state coffers.

Life sciences entrants face a tougher market

Countries seeking to nurture life sciences should look closely at how market dynamics will shape their growing industries. Is there a sufficiently sized market for a new healthcare industry to grow? If not, is the country located near to others that could offer a viable market? The combined populations of India, China and Brazil comprise nearly 40% of the world's population, with huge unmet medical need, both for communicable diseases but also, as the middle class numbers grow, non-communicable diseases, such as diabetes, cancer and cardiovascular disease. Most of the large pharmaceutical companies interviewed for this report focused on these domestic markets first, then progressed to selling their products in "semi-regulated" markets (such as the countries in the ASEAN group), before tackling more highly regulated markets. For countries without a large domestic market, such as Singapore and Costa Rica, the key is developing a hub and export approach to serve broader regions.

However, as with intellectual property, market saturation is more challenging. "If companies or countries are looking at markets like the US or Europe or Japan now, these are getting pretty saturated," says Mr Gupta. "There are at least 40 to 50 players that are targeting filings in each of these markets. So from that perspective, companies [looking to enter the field today] would have their work cut out for them."

Companies from China and India are hard for other emerging markets to compete with. Mr Singh of Bain believes the generics industry in India and China also has powerful competitive advantages "based on labour [wage] rates and the ecosystem" that will be difficult for a new entrant to beat. "Finding other areas where they [new entrants] can innovate—whether it's devices, whether it's looking at biologics, whether it's looking at new chemical entities—is something to consider now," he says.

Professor Danzon highlights medical devices as a potentially better bet for some emerging markets that are entering the industry. Evidence from Brazil and Costa Rica suggests that medical devices and technology can be viable sector for emerging market entrants—especially if they have strong basic infrastructure. Combined with changing norms in intellectual property protection, and lower barriers to entry, this is the most viable entry point for emerging markets in the life sciences space, as opposed to the generics pharmaceuticals approach pursued by the likes of India and Brazil in earlier decades. "Medical technologies and medical devices are a little bit easier because the investment required and the level of innovation required is not so extreme, and it's easier to produce something that is not in violation of existing patents but still has some value by doing something that already exists but doing it slightly better," says Professor Danzon. "It's easier to do that in devices than it is in drugs."

Build on specific competitive advantages

Countries need to look closely at their competitive advantages when deciding their entry route into life sciences. These could be natural assets like geography. Both Costa Rica and Singapore used proximity to large nearby markets (US, and Asia respectively) to encourage foreign investment in life sciences industries. This can be leveraged as an FDI-attraction measure, allowing companies to be immersed in regional markets which can help them develop tailored products and services with quicker routes to market. This is especially effective if there are free trade agreements with those markets, as Costa Rica shows.

A second competitive advantage is one that be built over time: local skills. The talent pool is a crucial enabler of innovation, and countries need to look at their existing skillsets prior to deciding which area to focus on. A high proportion of physicians, per capita, may suggest telemedicine or health tourism as possible areas to pursue. A surplus of data scientists may indicate potential for a vibrant e-health sector, while strong IT skills and reliable power supply might lend themselves to DNA sequencing.

China and India's API and generics businesses would have stalled without large numbers of chemists. Brazil's medical devices industry would have floundered without medical engineers. Costa Rica's medical technology sector succeeded largely thanks to the high quality labour force and partnerships between industry and academia. For a small city-state like Singapore, where there was not enough home-grown talent to fuel its nascent biomedical industry, the government focused on attracting foreign biomedical scientists to its shores with tax breaks and the perks of working in one of its well-funded, well-resourced science parks. For countries with a small population, talent can be maximised by developing an attractive working environment for the highly skilled. Emerging markets need to continually find ways of drawing the most talented workforce. Along with improving overall liveability indicators, additional incentives such as fast-track immigration procedures and perks could be considered. For example, tools to enable foreign scientists to set up their own research laboratories could help incentivise in-flows of appropriate skills.

Emerging markets wishing to strengthen their life sciences sector—and promote innovation—have both advantages and disadvantages. Positively, they can learn valuable strategic lessons from three decades of experimentation in the countries identified in this report. On the down-side, they are also finding a world that is more competitive, markets that are more saturated, and fewer policy instruments at their disposal. Nonetheless the progress made in lead countries, all of which had very different unique advantages and starting points, gives reason for optimism that a wider range of countries can secure for themselves a niche in this valuable industry.

Dubai Science Park (DSP) is the region's first free zone community that serves the value chain of the science sector, including science entrepreneurs, SMEs and multinational enterprises. Formerly known as DuBiotech and Enpark, it is home to over 280 science companies from across the value chain. DSP offers office, laboratory facilities and research infrastructure. The Park seeks to support innovation in the areas of human science, plant science, materials science, environmental science and energy.

DUBAI SCIENCE PARK

LONDON
20 Cabot Square
London
E14 4QW
United Kingdom
Tel: (44.20) 7576 8000
Fax: (44.20) 7576 8500
E-mail: london@eiu.com

NEW YORK
750 Third Avenue
5th Floor
New York, NY 10017
United States
Tel: (1.212) 554 0600
Fax: (1.212) 586 1181/2
E-mail: newyork@eiu.com

HONG KONG
1301 Cityplaza Four
12 Taikoo Wan Road
Taikoo Shing
Hong Kong
Tel: (852) 2585 3888
Fax: (852) 2802 7638
E-mail: hongkong@eiu.com

GENEVA
Rue de l'Athénée 32
1206 Geneva
Switzerland
Tel: (41) 22 566 2470
Fax: (41) 22 346 93 47
E-mail: geneva@eiu.com

DUBAI
Office 1301a
Aurora Tower
PO Box 450056
Dubai Media City
Dubai
United Arab Emirates
Tel: (971) 4 433 4208
Fax: (971) 4 438 0224
E-mail: kaywestmoreland@economist.com