

Bioeconomy and the Global Economy: industrial policies and bio-innovation

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Abstract

The last decades have witnessed major growth in the bioeconomy. Emergence of the bioeconomy as a broad, creative and rapidly expanding part of the global economy coincides with the maturation of the established drug discovery system. This paper presents research evidence focused on the relationships between changes in the bioeconomy and changes in the global economy. It argues that new forms of governance and regulation are key to strengthen industrial policies needed for emerging and developing countries to take account of the complex interactions in life science innovation between technology, markets, regulation and civil society, which could significantly impact on global distribution of the industry.

Keywords: bioeconomy, global economy, pharmaceuticals, innovation, global health

1 Introduction

There is strong evidence that the post-1950s evolution of the pharmaceutical industry is maturing rapidly (Mittra and Williams 2007; Orsenigo and Tait 2008). It is becoming harder to find truly new drugs in spite of continuing high R&D expenditure. Pharmaceutical company profit rates are falling, although volumes are massive and keep big pharmaceutical firms in the top global companies worldwide (Mittra et al. 2010). Another indicator of instability is that large companies are constantly attempting to restructure: cutting in-house R&D units, such as Pfizer's decision in 2011 to close a set of R&D units (Mittra et al. 2011); shaving costs through mergers (Mittra 2007); outsourcing R&D to universities and specialist biotechnology firms; and, organisational changes such as encouragement of smaller 'fleet-footed' innovation units within big pharma companies. The pharma-production model has been increasingly tightly rigidified - increasing layers of regulatory enforcement, and industrial responses, resulting in restriction of innovation to a stage by stage, 'linear' innovative process with more and more sub-stages of clinical trials.

The relatively simple staged 'linear' drug discovery innovation model for highly regulated health markets, has given way to a complex mix of, often contradictory, drivers of innovation. The changes may herald a major transformation of health bio-innovation raising the question: Is a major restructuring of pharmaceuticals and health delivery on the cards (OECD 2009; Wield et al. 2013)? If the answer to this question is yes, it leads to two further questions:

- 2 Could these changes bring a broader more globally dispersed set of powerful agents, with resultant implications for the global economy? That is, will changes

in the global economy drive a broader range of nations to become bioeconomy players or will they be left behind?

3 To what extent can firms in emerging and developing economies take advantage of the transformations to catch-up in some segments?

Already there are some changes, perhaps most apparent in agro-biotechnology, where Brazil leads in first generation biofuels. In health, some developing countries, such as India and East Asian, have managed to move from imitation of off-patent drugs towards more complex generics production, including of biosimilars, as well as innovative vaccines (Kale and Little 2007; Chaturvedi et al. 2007; Huzair and Kale 2011; Wang et al. 2012). The push to develop new therapies for neglected diseases and for AIDS/HIV has also increased some capabilities in developing countries, including clinical trials capabilities.

The starting point for this paper is the rapidly increasing range of economic activities associated with the bioeconomy. By bioeconomy is meant economic output that involves three elements: biotechnological knowledge; renewable biomass; and integration across applications. Biotechnological knowledge is required to develop new products, such as biopharmaceuticals, vaccines, plant and animal products and industrial enzymes. This knowledge is highly R&D intensive whether ‘wet’ or ‘dry’, whether it focuses on genes, cells, tissues, organs or organisms; or indeed, bioinformatics, epidemiology and health databases. Renewable biomass can be obtained from primary sources (food crops, grasses, trees, marine algae) and from waste, but requires bioprocessing into products. Integration between knowledge and applications, is based on generic knowledge and value-chains that cross applications (OECD 2009: 22-23). Integration can encompass any or all of the following: primary production of living resources; health applications including pharmaceuticals, diagnostics, nutraceuticals and medical devices; and industrial applications such as bioremediation, chemicals, plastics and enzymes.

The paper will focus on health rather than the better analysed agricultural sector. Even so, health represents a huge range of economic activities. Crucially health brings together two, often separated, elements of the bioeconomy: on the one hand, health research and innovation on potential new therapies: most of which take 15 years or more to move from bright idea to new product or process. On the other hand, health policy and health services – that part of the bioeconomy focused on improving the efficiency of health delivery to different populations – drug costs, hospital costs, social care, access of the poor to health systems, and so on. Health policy tends less to integrate the processes by which new ideas become new therapies, rather beginning when the therapy is viable and asking questions about how to deliver it. There is little integration of health policy and health innovation perspectives, though we will summarise some of the exceptions. Improved integration of health applications such as these is essential if there are to be globally dispersed benefits as the bio-economy expands.

The paper begins by describing and drawing together some important transformations in the bioeconomy as a result of the structural consequences of the maturing drug discovery model. The paper goes on to analyse the implications for the global economy. It suggests that there

needs to be a re-evaluation of the complex co-evolution of science and technology and markets, with regulation and civil society influences which increasingly drive life science innovation in developing as well as advanced countries.

The paper is divided into four sections. In the next section, I address our first question. I summarise the main elements of the classic pharmaceutical innovation model, and the governance and regulatory system which drives it, and ways in which changes have brought a more complex, often contradictory series of drivers of innovation with opportunities for new innovation paths. Then, in section 3, I address question 2 by analysing the new actors, institutions and other driving forces to explore the chances that a more global dispersion might emerge from what has been, hitherto, largely a transatlantic (US-European) industry. Finally, in section 4, I turn to question 3 and explore whether catching-up this moving and increasingly diffuse target might bring future opportunities for local and non-transatlantic production, and the implications for industrial policy.

2 Pharmaceutical drug innovation models – old and new

In this section we begin with a firm-based analysis of the ‘old’ pharmaceutical innovation system, and then describe the broader more open and social approach which increasingly influences pharma innovation. The classic ‘old’ pharmaceutical drug discovery model is at the core of analyses of health innovation systems. The model, as practiced and honed over half a century is characterised by: identifying promising new blockbuster drugs; conducting large multi-phase clinical trials; and, an extensive marketing and sales presence. During the 1980s and 1990s, big pharmaceutical firms had relatively integrated and complementary R&D strategies (Mittra et al. 2010). The top ten firms were large multinationals, all based in the USA (companies like Pfizer, Bristol Myers Squibbs and Johnson and Johnson) or Europe (with Glaxo Smith Kline, Astra-Zeneca and Sanofi).

Two different arguments have emerged from analysis of the ‘old’ pharmaceutical industry innovation model. The dominant argument, and the one on which we focus in this paper, is that there is a crisis in pharmaceutical innovation, with low R&D productivity, excessive and ever-changing regulatory barriers and, as yet, weak translation of biology and biotechnology into a still predominantly chemicals-based industry. But an alternative argument, sitting alongside the first, is that the innovation system for pharmaceuticals has been exceptionally robust for over 50 years. Through massive changes in markets, increasingly heavy regulation, the lengthened drug discovery pipeline (now running at 15 years), the underlying business model of blockbuster drug innovation has held up rather well. The evolving regulatory system has helped cement its rigidity.

Indeed, analysis of the pharmaceutical sector suggests at first sight that the situation is still quite stable. Table 1 shows the top ten pharma companies in 2011, five being US- and five Europe-based. We also list the few biotech companies that have grown into mid-range pharma - Amgen, Genzyme, Genentech. The chances for new biotechs to grow to become independent companies are very low and chances have lowered over time as ‘low-hanging fruit’ were plucked – Genentech is now part of Roche and Genzyme part of Sanofi. Milne

and Tait report that, of the nearly 2,000 active biotech medicines in preclinical development in 2009, only 15% were owned by the top 20 pharmaceutical companies, ‘yet big pharma owns nearly 40% of projects in late development, and over 70% of the biotech medicines that have actually reached the market over the last 20 years’ (2009, p 734). The ‘valley of death’ of long development times involves too much risk for SMEs. Almost all of the top fifty companies come from the USA and Europe, with some few Japanese and one Israeli firm.

Table 1 about here

The biggest companies still depend hugely on blockbuster products. The pharmaceutical innovation model has been complexified, but is still based on a linear pipeline, driven largely by regulatory systems and the need to prove safety with clinical trials stages right along the pipeline. The rigidity freezes out newcomers who cannot fund the long lead times and extreme uncertainty of innovation, solidifying the top firms and constraining competition and change.

Interestingly, despite the promise of biological life sciences to transform drug production, the large pharmaceutical firms have not transformed themselves fully into biotechnology companies, in contrast to Monsanto in the agro-biotechnology sector. Indeed, so far there has been no pharmaceutical equivalent to Monsanto, that transformed the agro-sector from an agro-chemical based innovation model towards a biotech/seeds based model (Wield et al. 2010). The company’s unshakeable faith in its biotechnology, massive investment in seeds companies, together with the relatively the easier US regulatory systems for gm, allowed Monsanto to build its technological lead (Chataway et al. 2004).

In pharmaceuticals, from the 1990s, R&D pipelines began to narrow and the sector began to mature. ‘By maturity, we mean molecules had already been developed for easy targets and were now off-patent, and therefore no longer generating large profits, and industry was concerned about the long-term sustainability of conventional blockbuster R&D models’ (Mittra et al. 2011, 106).

However, since the 1990s, further challenges to the blockbuster model have emerged, key being decline in R&D productivity, high attrition rate of compounds, and rising overall costs of drug discovery (Mittra et al. 2011). Whilst the blockbuster linear innovation model still dominates, scientific and technological changes have taken place, or are beginning to impact on pharma R&D, such as: automated high-throughput screening; bioinformatics and systems; recombinant proteins; and pharmaco-genetics. Companies are also increasingly trying to cut costs by locating operations in emerging markets (China, India, Brazil, Russia). Some, like Novartis, have large generics subsidiaries. But still, these changes do not amount to a major disruptive driver of innovation change.

The pharmaceutical industry has responded with organisational changes to intensify the R&D process: with mergers and acquisitions; tighter links with universities; and, strategic alliances with biotechnology firms and other specialist innovators, including companies with niched therapies close to market. As the century drew to a close, these changes began to reshape the

R&D process, increasing economies both of scale and scope (Orsenigo and Tait 2008). Firms now coordinate a diverse range of open R&D activities (Mittra 2007).

To summarise, the pharmaceutical industry 'old' innovation model is showing symptoms of severe strain in terms of innovativeness, profitability and public image. The traditional business model is under question and more open innovation models are gradually taking on the blockbuster model. Scientific and technological progress is increasingly originating from universities, public research organisations and small specialised firms. An increasing number of new drugs have been developed through research and licensing agreements with these organisations and networks of alliances. Clinical trials are being increasingly outsourced.

As yet, there is no clear trajectory. Orsenigo and Tait have argued that there is a tendency towards a 'hierarchical structure where large corporations perform the crucial functions of integrators of the different fragments of knowledge and capabilities that are required to produce a new drug, surrounded by cohorts of new firms that acts as suppliers of highly specialised techniques' (2008, 395).

However, there are other trends, which I term 'new innovation trends', less influenced by the big blockbuster model of innovation. They are more influenced by a different sense of the relationship between health, particularly global health, and society. One significant driver is the increasing public feeling 'that the entire system of providing medicines and healthcare to those in need was deeply flawed, since it was so heavily biased towards rich markets and diseases' (Orsenigo and Tait 2008, 390).

These 'new' transformations include: first that biological-based therapies are increasing in importance over chemical ones. Biosimilars (generic competitors to early biologics now off-patent) are also beginning to emerge, with opportunities for emerging economies. Second, competition from emerging country producers has increased, beginning with generics, but now a more complex hybrid mix of a range of new forms of drug and vaccine products, from a range of countries (see Chataway et al. 2007 for the Indian case). These trends are both important for developing country local production capability which is increasing rapidly, albeit from a low base.

Third, there has been a large increase in new therapies as a result particularly of the FDA's orphan drug and fast track programs which promoted different (and prioritised) regulatory pathways. The proportion of new drugs and biological product approvals in the USA with orphan or fast track designation rose from 27% in 1998-2003 to 38% in 2004-2006 (Milne and Tait 2009). Fourth, massively increased attention has been paid to therapies that address the 'neglected diseases' of poverty and diseases that particularly affect the world's poorest countries. One result has been rapid growth in vaccine innovation and production.

The third and fourth trend, different though they are - one geared to mass diseases of global poverty, the other to complex rare diseases – share one common element: 'weak markets' that result in these therapies not having been, until recently, a major part of the pharmaceutical innovation trajectory. There are a range of public-private partnerships to attempt delivery of

new, often niche, products, including orphan drugs and product like vaccines for developing countries. These trends have given rise to growth in the number of global partnerships that integrate public, not for profit and private organisations, as with the International Aids Vaccine Initiative and Malaria Vaccine Initiative.

Fifthly, none of these trends fully take into account the need for massive changes to health services if health innovations are to improve health of whole populations. That is health innovation analysis is not linked to health policy analysis.

These data evidence that that the answer is ‘yes’ to our first question: Is a major transformation on the cards? We will now turn to our other questions: Can these changes bring a broader, more globally dispersed set of actors and with what are the implications for global economy? And, can firms in emerging and developing countries take advantage of the transformations to build capabilities and begin a process of industrial catch-up?

Section 3 New actors, institutions and drivers of innovation

In this section we use our research data and that of others to detail key changes and new actors, institutions and drivers of innovation. New governance and regulatory approaches are at the heart of such changes, and more are needed to open up innovation systems and processes. We assess whether and how these potentially disruptive technical and social innovations are likely to affect emerging and developing countries. We will characterise four types of change: first the possibility that innovation concerning rare diseases will drive the advance of innovations more generally and globally; second, the emergence of new public-private institutional arrangements to deliver innovative therapies for neglected diseases; third, increases in the volume and geographical distribution of chronic and non-communicable diseases that may drive innovation and bring opportunities for new countries; and, finally the emergence of new biomedical and health system industrial players, such as India, China, Cuba and Brazil.

These four typologies allow us to investigate significant drivers that include, sometimes significantly, those from emerging and developing countries. We will demonstrate not only that emerging and developing countries will be strongly affected by these changes, but also could become new drivers of innovation. Study of each type of change illustrates changes in innovation processes and practices, and the potential for global changes in health practices.

Rare diseases and fast track as rule changers in regulation

Promoting more open systems of innovation in the life sciences increasingly depends on radical revision of regulatory systems. Previous research (Chataway et al. 2006) has suggested that proactive regulation is more appropriate than reactive regulation that solely responds to adverse impacts and builds layer after layer of regulation clogging up the innovation process.

Rare disease regulation is, at present, the best evidenced case of proactive regulation (Table 2). The US Orphan Drugs Act 1983 waived FDA fees, gave assistance with development, and

brought a different regulatory system – seven years of exclusivity, including FDA not approving a marketing application for an identical drug to treat the same condition, even without patent protection. The results have been highly significant. Since 1983, 1,700 orphan designations have been granted, and about 300 orphan drugs approved. Fast Track designation, began in 1998, gives opportunity for priority review of applications for product development for serious or life threatening conditions.

These cases illustrate that the blockbuster innovation model can be changed by changing governance systems. New programmes made a significant contribution to breakthrough innovation. The US orphan drug programme was credited with getting fledgling biotechnology sectors off the ground in the 1990s (Milne and Tait, 2009). 72% of fast track applications and 50% of orphan drug designations are new molecular entities (not ‘me-too’ products). Both involve greater involvement of broader stakeholder groups, like patient interest groups. The Orphan Drugs Act came about in response to patient advocacy and the patient registers kept by patient groups are an essential part of the innovation process. The involvement of all key actors – industry, researchers and patients – is a key characteristic of the regulatory system.

At present, legislation affects advanced country innovation and health systems and is focused on niched therapies. But such programmes could be models to promote new health care technologies important for emerging and developing countries. One recent insight has been that research into rare diseases may offer learning that will improve drug pipelines and R&D productivity. Milne and Tait (2009), based on their empirical study, argue that indeed, the orphan drug/fast track ‘regulatory opening’ model is generalisable. The fast track and orphan drug approaches influence not only the need to bridge the market gap, but also provide a safe accelerated authorisation process. They conclude ‘one way to address the unmet medical needs in less developed countries is by enhancing and expanding incentive programs in more developed countries that combine elements of both fast track and orphan designations, together with prioritisation of neglected diseases’ (p 750).

Table 2 around here

Public-private product development partnerships for neglected disease eradication - rule changers towards open innovation

Public-private partnerships (PPPs) have been the key emergent organisational form in global health innovation since the 2000s. The International AIDS Vaccine Initiative (IAVI) is the most high profile, and a game changing social innovation, among a steadily increasing range of programmes to develop genetically engineered vaccines. Other PPPs include those to develop a malaria vaccine and a new vaccine against TB. PPPs emerged both because of constraints with previous innovation systems and also weak health systems. The problems were not just in the science but in ‘creating products and processes relevant to the developing world. Indeed, it is tragically obvious that the private sector in both pharmaceuticals and agriculture cannot or will not address the needs of the sickest and the poorest’ (Chataway and Smith 2006, 16). One statistic underlined the case of those advocating change – that 90% of

all medical research was targeted at problems affecting only 10% of the world's population – the 90/10 rule.

The new institutional approaches were based on the fact that on their own, public and private sectors were not be able to resolve the serious health inequalities that bring poor quality of life to so many people. Chataway and Smith (2006) also pinpointed that historically efficient institutional arrangements, such as the WHO and other UN agencies, had been increasingly disempowered and weakened in their historical role as global leaders and brokers of social innovation, as the neo-liberal policies of the 1980s and 1990s took root.

Study of the IAVI case showed the importance of factors such as: the history of previous relationships between partners, and how the tacit knowledge of working together can improve future partnership working. It also illustrated the importance of organisational and institutional evolution – IAVI learnt from its successes and mistakes. The approach partnerships took to markets, was key – the concept was developed as a way to get beyond market failure and risk.

The case also shows the importance of building capabilities, outside of core science nations. Although the science base of top global universities was crucial and continues to dominate, it quickly became apparent that other complementary capabilities were needed, and that these had to be distributed around nations with most of the HIV/AIDS cases: importance were building capacity in engaging those with the virus, and in setting up clinical trials. The need for distributed complementary expertise became apparent as the programme grew, and evolved from the high commitment to public engagement.

One example from East African fieldwork was that the IAVI funded a wide range of local research institutes (such as the Ugandan Virus Research Institute and Kenyan Aids Vaccine Initiative, which have a 'vision of vaccine research and trialling beyond HIV and beyond IAVI' (Rosiello and Smith 2008, 14). These results are a testament to a real flexibility within IAVI. 'The building and refurbishment of laboratories, the provision of funding for running expenses and the training and updating of scientists and technicians' knowledge' (Rosiello and Smith, 15). Rwanda, for example, had the vision of becoming a centre for vaccine clinical trials.

The IAVI, and those PPPs focused on global issues, have brought learning about institutional interactions increasingly seen as relevant to more mainstream pharma and health initiatives. In short, global health PPPs have not been a small and marginal experiment but a serious game changer, disrupting innovation norms. By the end of 2004 global partnerships, including PDPs, were responsible for nearly 75% of neglected disease drug discovery research (Moran 2005).

As experiments, they have brought insights to the study of innovation. Chataway et al. (2010) show their importance for the theoretical study of innovation brokers and integrators. Brokers bring together actors, sharing information and facilitating cooperation whilst integrators are hubs, often companies, that coordinate the activities of a distributed set of innovators.

Chataway et al. evidence that IAVI began as a ‘broker’ of innovation - it mobilised public and private organisations to work together to pool their different knowledge bases. But then, to develop potential vaccines, it began to include the innovation practices of an integrator – it built its own laboratories, for example and in some respects resembled a virtual pharma company. Chataway et al. also showed that the Malaria Vaccines Initiative (MVI) is further along the development route, which may be accounted for by the fact that it is closely linked to the health systems of the countries in which it operates.

In summary, at one level the PPPs confirm that knowledge creation and even knowledge circulation are risky activities requiring non-market as well as market activities. That is, after all, why nations support R&D and innovation activities. Neither is it new that innovation usually requires complementary knowledge bases not always found in one organisation, however large. But the global health PPPs illustrate that partnerships can be made to work and can better integrate health innovation with health systems and health policy.

Chronic disease drivers - as health system and generic drivers

The rise in volume of chronic disease is another major driver of new approaches, which has brought new organisations, though not, as yet, major new institutional innovation. Increased longevity, including from the rapid social and economic development of India, China, Brazil, and other emerging countries is already bringing large increases in the volume of people with diseases until recently characterised as diseases of advanced countries. Apart from increased lifespan, there are a range of contributory factors, including: tobacco use, decreased physical activity, and unhealthy foods. Diseases such as diabetes, coronary (mainly heart disease and stroke) , chronic respiratory, and some cancers are key chronic (non-communicable) diseases described as reaching epidemic proportions, accounting for 60% of all deaths worldwide, 80% in low and middle income countries (Daar et al. 2007). Developing countries have, reasonably enough, focused on infectious diseases such as HIV and malaria and not on the chronic diseases that dominate in advanced and emerging nations. But priorities are changing. The rise in chronic non-communicable disease growth and the need to manage it, is driving innovation, for example by cheapening medicines needed on a regular basis to control chronic diseases. This led to pressures for cheap generics, giving an opportunity for catch-up firms from developing countries. These, in turn, have used generics production capabilities to build more innovation capabilities first by imitation techniques, but increasingly using incremental and more disruptive innovation approaches (Kale et al. 2007).

Other innovations have, so far, not impinged greatly on emerging country capabilities. For example, the development of clinical decision support systems to routinize diagnosis and treatment; telehealth and health information systems, which are bringing significant changes to electronic diagnosis and treatment; and disease registries, from nutritional epidemiology to Generation Scotland’s focus on familial trends in chronic diseases (Haddow et al. 2008). This builds pressure to integrate the medical and health systems with innovation systems and some emerging countries are beginning to evolve their health systems to take account of them.

Promoting local innovation and catch-up

What possibilities exist for developing and emerging countries to become bioeconomy players? There is an enormous gap between big pharma and these new producers. Big pharma is separated from the next group by a large gap. So-called 'mid-pharma' companies are not that small with sales of \$billions a year. No developing country has a firm in the top 50 pharma companies, contrasting with a range of industry sectors where developing country firms are in the top group.

But health systems are key drivers and localised, there are market niches like generics and biosimilars, so there is potential for growth. What are the indications that innovation is possible outside of the top companies and North America/Europe?

Mackintosh et al (2008) bring together a range of cases from Africa, Asia and Latin America that show the invisibility, but crucial importance for pro-poor policies, of innovation for health. Wang et al. (2012) analysed the development of the biopharmaceutical industry in Taiwan, South Korea and China. They suggest that move of large firms towards building global innovation networks to work beside their global production networks has given emerging industrialising countries the opportunity to specialise in a set of activities and thus upgrade capabilities within value-chains. The classic developmental state approach to midwifery of new industry has not, until recently, leaned towards state leadership of public-private networks of the type increasingly needed for science-based biopharma industry. Wang et al. study the institutional arrangements in Taiwan, South Korea and China, with diverse transformation paths and consequent divergent development outcomes in the biopharma industry. In Taiwan, the state has focused on newly formed science firms rather than established generics firms. In South Korea, the emphasis has been more towards building a platform, with public-private partnerships and also a sector with both the large chaebols and SME development. China has a coherent holistic strategy that integrates policy on traditional local and foreign R&D as well as venture capital and science locations to cluster firms.

Resaie et al. (2012) characterise Brazilian and South African biopharma policy objectives as focused primarily on import substitution and lowering the cost of health products for local populations. They characterise Indian and Chinese policies as more oriented at nurturing 'an innovation eco-system and a vibrant bioeconomy' (p1). Our research (Chataway et al. 2007; Kale and Little 2007) details the development of the Indian pharma industry to its emergence as a leading internationally competitive supplier of generic drugs, as a movement along the R&D value-chain. We show that this gave Indian firms a solid base for development of competences in advanced innovation R&D.

This summary suggests that some developing country firms and nations are aiming to catch-up - some by imitating what exists already. Others are attempting to change the paradigm, albeit in a niched way. At the same they are all aiming at a moving target.

The key new changes we have mapped in this section are: new organisational arrangements that integrate cooperating public and private organisations to build new health innovation systems; chronic disease health research and management systems have the potential to integrate health systems; rare diseases that show the possibilities for smart and creative

regulatory and promotion policies; and, the increased scope for capacities to produce new products and also build new systems.

These changes evidence a positive answer to our second question. That is, changes in bio-based innovation do indeed present opportunities for a more globally dispersed set of actors, for firms and other institutions, in emerging and developing countries to become bioeconomy players. These have the potential to change the nature of drug discovery and production and their relationship with health policy. Such changes are possible not only in health for the poorest, but for health systems more globally.

Section 4 Implications for Industrial Policy

To address our third question and look at possibilities for firms to take advantage of changes to catch-up in the bioeconomy we focus on the potential for industrial policy and local production.

Our focus on local production in emerging and developing countries needs to be explained, as does our integrated analysis of health innovation issues with health policy issues as a sectoral innovation system. Often, health and development is studied only through the lens of developing countries as ‘recipients’ of health and medical technologies, not as producers. Developing health science, technology and innovation capacity is seen somehow as an impossible (even irrelevant) task compared to other sectors of innovation. It is seen as a hard sector to build but there is evidence from our research that much can be done. The changes we have mapped open up scenarios for firms in emerging and developing countries. They can take advantage, even lead, some of the innovative processes in the sector.

How can such opportunities be grasped? Our evidence suggests that there is relatively easier and relatively harder industrial policy potential, but that all options require a combination of firm strategy and broader public policy initiatives.

An example of relatively easy industrial change is that of the Indian pharmaceutical industry. A series of policy changes triggered the environment for ‘imitation’ that led to innovation. Chaturvedi et al. (2007) describe how the 1970 Patents Act in India impacted enormously on the technological evolution of India’s pharmaceutical industry since it opened the potential for reverse engineering and process innovation. This set the foundation for world-class generic drug production capabilities and then sub-contracting and technological licensing capabilities. Under different regulatory and economic reforms firms have co-evolved to become technologically more sophisticated organisations capable of catering to diverse global markets. Kale and Little (2007) show how Indian firms moved up the value-chain of pharmaceutical R&D.

In this case local policy synchronisation aimed at lowering the prices of key drugs for local populations allowed a whole industrial sub-sector to develop. Interestingly, this has not happened in other sub-sectors dependent on health innovation. Kale (2011) argues that the medical device sector in India has been held back by lack of synchronised institutional and

industrial policy development, in particular the lack of connection between industrial policy and a disregard for health service development.

The Indian pharma case above is a relatively easier one, because it did not depend on local health system improvement. Setting up health innovation synchronised with health systems seems to be harder, as the Indian case shows. The absence of a coherent health service in India is a barrier to innovation in medical devices, and much else. Examples from Cuba, Brazil and China give a sense of what can be done when policies are pulled together. Thorsteindottir (2007) examined the role of health systems in health biotechnology innovation in Brazil, Cuba and India as a way to identify the ways in which local health systems affect the innovation process. She found a mixed picture with only a proactive user-producer relationship in one country – Cuba. In the other countries she found that ‘the lack of active knowledge flow between users and producers seems to hamper the interactive learning between these groups that can foster innovation’. (p 671).

The harder industrial policy option, within increasingly integrated value chains, involves explicit integration of a whole range of institutional capability increases, including industrial policy ones – not just incentives that directly encourage firms to innovate, but intellectual property incentives such as those developed for orphan drugs and fast track; procurement policy incentives such as require a health service procurement system; regulatory changes, since radical innovation in health almost always feeds on regulatory rule changes; in short integrated industrial and health policy initiatives.

Conclusions

Recent growth of the bioeconomy is associated with significant changes in ways that drugs and medical therapies are produced, We have analysed changes in the ways drugs are produced via rare disease and fast track systems; also the extent to which public private partnerships have improved innovation of therapies for poorer regions, and so on. But we have also suggested that more will be required. For example, changes to the drug discovery system will require new forms of regulation and governance. Promoting more open, disruptive systems of innovation in the sector increasingly depend on radical revision of regulatory systems.

Health policy as a subject is more interested in development and global issues than are the subjects of medical science or health innovation. The weak systems of medical science and technology in many developing countries is seen as either ‘not the real problem’ or ‘as the weakness which results in health policy taking priority over health research and innovation’. So, although there are some emerging nations (such as India, China, Brazil and Cuba) which are developing sophisticated health innovation industries, in many countries, the assumption for ‘improved health’ is that new therapies will be produced somewhere else and ‘sent, donated, or otherwise funded’ for consumption by their populations.

We have asked the questions: can new actors be drawn into these changes? And will this bring opportunities for local production in emerging and developing countries. We have

shown that, although hard, it is possible. There is already good evidence of the potential. As Christensen et al suggest: 'lower cost business models emerge at the bottom of the market in simple applications and gradually move upmarket to disrupt the established competitors' (2009, xxxv). There is a real opportunity for developing country firms to do this in ways that established big pharmaceutical companies cannot.

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Table 1 Top Ten Pharma Companies (and leading biotech companies)

Company (Base)	Sales 2010 (\$bn) (unless noted)	R&D spend 2010 (\$bn)	Notes
Pfizer (USA)	58.5	9.4	
Novartis (Sw)	42.0	7.1	
Sanofi-Aventis (Fr)	40.3	5.2	
Merck (USA)	39.8	11.0	
Roche (Sw)	39.1	8.6	
Glaxo Smith Kline (UK)	36.2	6.1	
Astra-Zeneca (UK-Swed)	33.3	4.2	
Johnson and Johnson (USA)	22.4	4.4	
Eli Lilly (USA)	21.1	4.9	
Abbott (USA)	19.9	3.7	
Amgen (USA) – 13 th	14.7	2.9	
Genentech (USA) –	13.4*	N/A	Acquired by Roche. Sales data are from 2009
Genzyme (USA) – 29 th	4.0	0.9	Acquired by Sanofi-Aventis in 2011
Biogen – 36 th	3.5	N/A	

Source: Pharma Exec 2012, and the author

Table 2 Game Changing Innovations in Health Innovation

Changes in Innovation System	New Institutions, Rules	Impacts	Refs
Rare diseases as rule changers in regulation	Orphan Drugs Acts, Fast Track Legislation	New therapies, faster	Milne and Tait 2009
PDPs for neglected diseases	PPPs (IAVI, MVI, GAVI etc). New funding systems - Gates	Changed ambitions; changed priorities (eg of government donors; capacity building initiatives	Chataway and Smith 2006; Chataway et al. 2010
Chronic disease drivers for health systems and generics	Non-communicable disease institutions	Cheap therapies, better information systems	Daar et al. 2007
Developing country firm innovation and catch-up	Emerging country industrial policy, PPP pressure	More explicit industrial policies	Mackintosh et al. 2009; Wang et al. 2012; Resaie et al. 2012