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Getting Serious About Biotech:
Challenges and Opportunities
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The scientific discovery of DNA by Francis Crick and James Watson in the mid 20th century has had profound implications that have not only transformed the world of science, but also the way in which economic development is sought at the turn of the millennium. Today, gene splicing, cloning and other procedures heretofore conceived of as exclusive to academia are being discussed in corporate boardrooms and public hearings while scientists and engineers-turned-entrepreneurs have become the leaders of a blossoming industrial sector that focuses on the technologies of life or biotechnologies. The rapid growth of this relatively novel industry has been fueled by the increasing market opportunities and the promises of riches and economic expansion that lie ahead with each new scientific breakthrough.

This distinct marriage of science and economics has become one of the fastest growing sectors of advanced and developing economies and consequently the new focus for economic development practitioners at diverse levels. The list of cities and regions that have jumped on the biotech bandwagon is expanding fast. In the United States, for example, a survey of 77 local and 36 state economic development agencies reported that 83 percent listed biotechnology as one of the top two targets for industrial development (Cortright and Meyer, 2002, p.6). Similarly, it has been reported that several state governments in India have invested large sums of capital in an attempt to encourage the growth of the sector which they expect will employ a million skilled persons and generate annual revenues of \$5 billion by 2010 (siliconindia.com, 2005).

Puerto Rico is not exempt from the list of countries that have included the biotechnology sector as a top priority for future industrial and economic growth. In recent years, numerous initiatives aimed at growing the high-technology sector (such as the creation of industry clusters and research centers) have been announced. For the most part, these efforts have been slow to gather speed, yet more recent developments have brought to light local prospects for the biotechnology industry. Big pharmaceutical and biotechnology firms like Eli-Lilly and Amgen have announced multi-million dollar investments to expand local operations¹. Citing regulatory and human resources advantages, top executives are looking at Puerto Rico as a favorable destination for the manufacturing of blockbuster drugs and new products. These events have made local government officials take proactive measures to support and build on the new opportunities as they embark upon a paramount challenge to become one of the new 'hotbeds' of the global biotechnology industry.

This brief will focus on presenting a series of ideas and suggestions, based on the examination of: trends within the global biotechnology industry, local capa-

bilities and lessons from the field. Our main objective is to perform a cursory examination of some key issues that will place the prospects for the emerging Puerto Rican biotechnology industry in perspective and will serve as a guide post for future policy development.

Outline of the Biotech Industry

As is often the case with concepts that are shared by multiple communities and sectors, there is little consensus on how to define 'biotechnology'. For our purposes, we will use a broad explanation set forth in a recent study published by the Brookings Institution: "Biotechnology is the application of biological knowledge and techniques pertaining to molecular, cellular and genetic processes to develop products and services." (Cortright and Meyer, 2002, p. 6). Bearing in mind this definition, it is no surprise that the biotechnology industry comprises a diverse group of commercially-focused entities that partake in knowledge and science-intensive endeavors; from agriculture to medical and health applications, the field is quite broad and interdisciplinary. In order to narrow down our focus, in this section we will concentrate on analyzing general industry trends while also paying special attention to the health and medicine segments within the US, since they represent the largest share of the global industry and are the most relevant when analyzing Puerto Rico's potential development.

The inner workings of the biotechnology industry are highly complex and sophisticated. Although the scope of work resembles that of the pharmaceutical industry, biotechnology companies engage in more expensive and riskier product development. This is due in part to the unique scientific processes that are followed and to the fact that a large portion of the projects pursued involve life-threatening or other serious diseases where alternative treatments have not yet been discovered. Estimates from the Biotechnology Industry Association (BIO), indicate that for every drug that goes into the market, four do not. As is the case in the pharmaceutical industry, the process of discovering a new drug and its eventual launch into the market is a long and costly process that could take up to 16 years and cost up to \$800 million given that rigorous testing and clinical trials have to be performed in order to assure safety and trustworthiness (Rosenberg, 2004, p. 4).

The industry is also highly dependent on intellectual property since knowledge is the essential ingredient behind the discovery of new products and applications. Top-notch scientists and research institutions are understood to be the motors behind industry growth. Thus, research and development (R&D) accounts for a large portion of the total expenditures incurred by biotechnology firms. Figures from recent years denote that the US biotechnology industry as a whole reported a 31% increase in R&D spending, from \$15.7 billion in 2001 to \$20.5 billion in 2002. An impressive \$101,200 was spent on R&D, per employee, by the top 5 biotechnology companies in the US in 2002 (BIO, 2004, p.4).

Assuming risk, finding talent and consuming time can add up to millions of dollars. This is a fact that many biotechnology firms have become aware of as they

search for ways to finance operations. For the most part, pre-venture funding for pure medical and health-related research that might lead to the discovery of new drugs comes from several federal government sources like the National Institutes of Health and the US National Cancer Institute, to name two. Yet, as researchers have noted, the most important source of start-up capital is organized and enduring venture capital, which, in many cases provides several rounds of financing for firms that cover numerous periods until the product reaches the marketplace. (Cortright and Meyer, 2002, p.21). In 2003, over \$3 billion were invested by venture capital firms in US biotech industries. This figure represented close to 20 percent of all the funds invested in the US biotechnology industry for that year (BIO, 2004, p.7).

As the medical and healthcare-oriented biotechnology industry matures, two distinct groups of competitors can be identified: emerging and top-tier operations. Their classification is largely based on firm size and capacity to develop and take products to market. Emerging firms are usually small, undercapitalized operations that can only take discoveries and processes through a certain point of the development pipeline and usually end up partnering or are bought out by larger firms that can bear the costs of clinical trials, manufacturing and marketing. Most of their operating expenses go towards R&D since their core competency is discovery and research of new drugs. One important characteristic to note is that very few, if any, make a profit; their survival is mostly based on the business opportunities that their products can provide down the road. On the other end of the spectrum are the top-tier operations, known for rolling out blockbuster drugs and reporting high profits (this category includes companies like Genentech, Amgen and Biogen Idec). Given that their core competency lies in the actual manufacturing and deployment of new products, these firms spend proportionally less on R&D and are relying more on emerging firms for new discoveries. Although top-tier firms are also subject to the long process of drug discovery and development, their cash position allows them to fill gaps in their pipeline through the acquisition of drugs that have already been discovered by other smaller firms. Collaboration amongst biotechnology firms of diverse sizes and between biotechnology and pharmaceutical firms has become more commonplace, making the field more specialized as each segment concentrates on its core competencies.

Finding Fertile Ground for Biotechnology

The location of biotechnology activity has become a key issue for researchers interested in deciphering industrial growth and economic development. Similar to what transpired during the early days of Silicon Valley and Route 128, numerous states and localities have begun to draft blueprints and development agendas that will make them the premiere locations for biotechnology firms. As was also the case in the 80's and 90's the dreams of many will crumble and few will be able to claim success in the race to host innovation and knowledge-driven industries. Their failure will be more the result of local capacity than scarcity of information on the matter since there is sufficient scholarship on the issue of what it takes to become a successful high-technology enclave. Amongst the most notable, are studies that stress the importance of institutional frame-

works that promote both collaboration and competition amongst firms (Saxenian, 1994) and others that spell out the dynamics of industrial clusters (Porter, 1998).

As can be expected, there is not one explanation of what makes countries and regions thrive or fail in attracting and nurturing high-technology firms and achieving competitive advantages within a specific industry. Nonetheless, there is agreement on the basic elements that have been present in all successful regions, which include: top-notch universities and research centers, access to sources of capital and venture financing and an environment for innovation supported by proactive public policies and strategic state involvement. It is worth mentioning that, as experience has shown, success is not solely dependent on the existence of the aforementioned elements, but that it is highly probable that the absence or ineffectiveness of any of these factors will lead to dismal results.

Although most of the knowledge garnered on the subject has focused on the information technology industry, specific analyses on biotechnology have generated similar findings. Two major reports (Cortright and Meyer, 2002; DeVol, et. al, 2004) focused on analyzing the emergence and composition of biotechnology clusters and centers in the US, confirm much of what was mentioned earlier regarding the inputs for growth. As Cortright and Meyer (2002) suggest when explaining the preeminence of nine leading biotechnology regions: “[They] are leaders because they have two necessary elements for industry growth: strong research capacity and the ability to convert research into successful commercial activity” (p.3). Correspondingly, when analyzing a similar group of biotechnology centers, De Vol, et. al. (2004) explain that:

Though there are many economic factors expediting the formation of these biotechnology clusters and sustaining them, the fundamental building blocks are pools of talent, human capital and their respective capacity to fulfill the technical and operational requirements. Location still matters only if it has vast capacity to attract talent that yield a tremendous amount of intellectual property (IP) (p.4).

Each report develops its own metrics and methodology when determining which regions or metropolitan areas have been more adept at attracting and sustaining biotechnology industry activity. Despite differences in the rankings, there is agreement on the primacy of known high-technology regions like San Francisco-Oakland, San Diego, Boston-Worcester and Raleigh-Durham, amongst others. Not surprisingly, the Cortright and Meyer report, where the unit of analysis is the census-defined Metropolitan Statistical Area (MSA), includes the San Juan-Caguas-Arecibo Consolidated Metropolitan Statistical Area (CMSA) and is included in the listing of those areas where there is “No Significant Biotech Research or Commercialization”. A closer look at some figures helps to explain why the CMSA is included in this category.

Puerto Rico's Biotechnology Infrastructure

Following the analysis set forth by the reports mentioned above, we collected some data on several indicators that would help assess our place within the highly contested race to become an attractive locale for the biotechnology industry. Although most of the metrics analyzed were previously reviewed by Cortright and Meyer for the San Juan-Caguas-Arecibo CMSA, we wanted to update some of the figures and make a more generalized analysis². It must be made clear from the outset that, for the most part, Puerto Rico lags behind most US jurisdictions that aim to become biotechnology centers.

One of the frequently cited metrics when analyzing knowledge-intensive and innovation driven industries is the number of registered patents. Looking at some of the principal biotechnology/pharmaceutical patent classifications, it becomes clear that although we are home to a number of successful pharmaceutical/biotechnology firms, the type of work undertaken in these branch operations is not focused on R&D. Rather, it primarily emphasizes manufacturing and other related activities. As Table I indicates, from 1999 to 2003 only 8 patents have been registered under the 424 and 514 classifications, which are described as "Drug, Bio-Affecting and Body-Treating Compositions". This figure placed us at the bottom of the list for US states and jurisdictions³. During the same time period we did not register any patents under other biotechnology-related classes utilized in the Cortright and Meyer report.

Table I

Puerto Rico: Biotechnology Patents					
Class 424 and 514: Drug, Bio-Affecting and Body Treating Compositions					
1999	2000	2001	2002	2003	Total
2	0	1	2	3	8

Source: US Patent and Trademark Office

With regards to the research infrastructure, from 1999 to 2003, a total of 86 PhD's in the life sciences fields were granted by local academic institutions (see Table 2). This is a very small figure when compared to most US states, especially those where a high concentration of pharmaceutical and biotechnology industries are evidenced. At present, only 4 academic institutions are granting doctoral degrees in the life sciences. Notwithstanding, administrative officials at the UPR Mayaguez Campus have voiced an interest in establishing a PhD program in biotechnology in the near future.

Table 2

Puerto Rico: Number of Life Sciences PhD's Awarded					
1999	2000	2001	2002	2003	Total
11	12	30	16	17	86

Source: NSF, WebCASPAR

The flow of federal funds to research institutes and academic institutions also serves as a metric of research activity and capacity. According to Cortright and Meyer, these funding sources serve as pre-venture financing streams for the creation of new biotechnology knowledge (p.21). Although total dollar amounts are not as large when compared to other jurisdictions in the US, Puerto Rico has seen considerable increases in its share of National Institutes of Health (NIH) grants during the past years (see Table 3). As expected, the vast majority of funding has gone to the University of Puerto Rico, specifically to the Medical Sciences and Río Piedras Campuses. It must be noted that not all the funds received are earmarked for pure and applied scientific research since a considerable number of awards are utilized for developing the needed infrastructure for future or existing projects.

Table 3

NIH Funding to Puerto Rico				
2002	2001	2000	1999	1998
\$65,937,444	\$44,278,458	\$40,849,173	\$32,936,671	\$26,305,715

Source: US National Institutes of Health

Conversely, venture capital (VC) deal flow in Puerto Rico has been very slow and non-recurrent. Aside from an increase in deal flow during 2000-2001, VC has not been one of the main funding sources for start-up industries in Puerto Rico. Furthermore, start-up firms in Puerto Rico have been even less reliant on this type of funding according to a recent analysis by A.T. Kearney (2004) for the Puerto Rico 2025 initiative (p.226). Moreover, reports by PricewaterhouseCoopers reveal that only two VC deals have been reported in the local biotech industry. Notwithstanding, capital investments to finance expansions by major biotechnology companies operating in Puerto Rico have been quite substantial, adding up to over 1.6 billion in 2003 alone (Commonwealth of Puerto Rico, 2003). Atop the list are companies like Amgen, Abbott Biotechnology and Dupont Pharmaceuticals. This mix of significant capital investments by major corporations and sluggish VC performance could be interpreted in many ways but primarily demonstrates lack of financing opportunities and commercialization of local research. This, in turn, helps to explain the dearth of indigenous commercial biotechnology activity since, as Cortright and Meyer (2002) explain “by far the most important source of start-up capital for the biotech industry is organized venture capital: private investments made by professional fund managers, typically specializing in a related set of technologies” (p.21).

Before making any definitive judgments regarding local biotechnology capacity, a more detailed analysis must certainly be performed and other variables must be included in that assessment. Nonetheless, as mentioned earlier, the metrics presented in this section provide an initial point of reference that demonstrate, not just the challenges faced, but also the opportunities present. Puerto Rico’s high-technology and health related manufacturing experience, regulatory framework and other aspects provide some clear benefits that can be capitalized, yet as examples from other nations that have become emerging biotechnology hubs demonstrate, the path to prosperity requires that other advantages be leveraged.

Lessons From Abroad

Although most of the focus on the biotechnology industry is centered on the US- in part due to the fact that it is the home base and birthplace of the largest multinational pharmaceutical and biotechnology firms- the spotlight is now being shared with a group of countries that have garnered an important share of the global biotechnology market. In Puerto Rico, most of the attention has been traditionally placed on Ireland and Singapore as the leading competitors in our efforts to attract foreign high-technology corporations and become leaders in the manufacturing field. By many standards these comparisons are anachronistic given that both countries have reached much higher economic and industry development levels, and therefore should be considered more as models than competitors.

The list of countries that are fast becoming global contenders in the biotechnology industry is expanding rapidly and includes places like: India, Brazil, Cuba, China and South Korea to name only a select few. Interestingly, some of these economies once considered “developing” are now touted as “emerging”. Their rapid rise, especially within the global biotechnology market, has been a result of deliberate measures taken to improve the economic development infrastructures and inputs to industry growth.

Although each story is unique, some countries share similar accounts of the approaches taken to jumpstart their local biotechnology industry. One of the main points of convergence cited in recent academic literature on developing countries (Thorsteinsdóttir, et. al., 2004b) is the focus on local health needs. In India and Brazil, for example, the development and manufacture of a meningitis B vaccine and recombinant human insulin to attend to local health necessities, has served as a successful starting point for local biotechnology activity. Success has also been attained through the expansion of basic scientific research carried out in local universities and research institutes. Through concerted efforts to improve the educational system and establish systems of knowledge sharing between academia and industry, applied research discoveries have arisen and evolved into commercial opportunities. As Thorsteinsdóttir, et. al. (2004) have pointed out in a examination of the biotechnology prospects of seven developing countries:

All the countries in this study have relatively good schools, at least for a subset of their citizens. Good education has enabled their experts to understand the potential of biotechnology and seize new opportunities offered by the technology at the same time that their policymakers, business people and the general public have recognized the importance of biotechnology and have supported its development. (p. DC 49)

The role of national and state governments has also been crucial. Most countries whose biotechnology sector is gathering steam established supportive policies decades earlier and followed these amidst changes in political regimes. In Brazil, the Ministry of Science and Technology and the National Research Council began supporting research endeavors since the 1970's through the

creation of specific research programs on genetic research and tropical diseases. Similarly, India's national and state governments have been the main source of funding for health biotechnology. Conscious of the investments needed to support the industry, in 2003-2004, the national government alone allocated 2,730 million rupees (\$59 million) for biotechnology. Such was the importance and vision, that their sixth Five Year Plan (1980-1987) emphasized health biotechnology as a tool to tackle India's development needs (Thorsteinsdóttir, et. al., 2004, p.DC 32).

The Indian case also illustrates the advantages leveraged from the pharmaceutical industry. Having hosted numerous pharmaceutical manufacturing operations for years, local industrialists saw an opportunity to take advantage of expiring drug patents (and a lax domestic policy that allowed generics manufacturers to copy drugs for consumption in local and unregulated markets) to produce indigenous "me-too" products for local and worldwide consumption. At present, companies like Ranbaxy and Dr. Reddy's Laboratories, who have become notable generic drugs producers, are utilizing their acquired capacities and experience in the process and production side to begin venturing into biopharmaceuticals and biogenerics. India's biotechnology industry is also growing thanks to the rise of contract research and manufacturing organizations (CRO's and CMO's) and bioinformatics corporations. Within this segment, Indian companies have been able to take advantage of the lower costs of operations and manufacturing, their skilled and trained workforce that speaks English, a sizeable patient population, specialty hospitals, vast experience in software development and a well developed public R&D infrastructure (Thorsteinsdóttir, et. al., 2004; Jayaraman, 2004). Today, India has the twelfth most successful biotechnology sector in the world measured by number of firms (Ernst & Young, 2004).

Brazil shares a similar experience with Puerto Rico when analyzing the presence and impact of multinational pharmaceutical operations. Although it boasts the 11th largest pharmaceutical market in the world and is home to several big pharmaceutical multinationals, the patenting and innovation rates of these operations are quite low. Most multinationals are focused on the manufacturing of bulk materials and "fill and finish" tasks that add jobs to the economy and certain skills to the workforce, but are not conducive to new knowledge that enables a considerable upward movement in the value chain nor promote the discovery of new products that could spur biotechnology start-ups. Notwithstanding this scenario, indigenous biotechnology operations have emerged in recent years (thanks in part to the efforts by public and private sector actors mentioned earlier). In 2001, Brazil boasted 354 biotechnology firms of which approximately 70% were local private firms, 25% were multinationals and 5% were state-owned firms. This represented an impressive increase from 1993 when 76 firms were dedicated to biotechnology (Thorsteinsdóttir, et. al., 2004).

The Road Ahead for Puerto Rico

One thing that Puerto Rico has not lacked is grandiose ideas about where our economy should go. From tax incentives to growth poles to clusters, the catalog of economic development strategies pursued is quite deep and expansive.

Yet, during the last decades, these theoretical exercises have failed to deliver any plausible results, making many people wonder what can be done to remedy our current state of affairs. Today, the talk of the town is “biotechnology”- a new buzzword that has had its share of headlines and sound bytes across the globe. As has been argued in this brief, it is essential that we assess what realistic possibilities exist for Puerto Rico, taking into account the existing economic and social infrastructure. From our perspective, we are perhaps 10 to 15 years behind some of the major biotechnology hubs, but there are also some underlying opportunities that could help us leapfrog towards a more competitive stance.

As stated previously, our experience as a manufacturing enclave for big pharmaceutical corporations should be considered an advantage in various respects but must not be interpreted as the defining piece of evidence sustaining the argument that we are now ready to take on the biotechnology market. Our recent economic experience shows that the linkages between non-local manufacturing operations (especially pharmaceutical) and our economy are quite low (Dietz, 2003), and thus have not promoted an intensive technology transfer process (CEPAL, 2005, p.101). The lack of R&D conducted locally serves as further evidence for this argument. In the late 1990’s Puerto Rico spent close to 0.24 percent of GDP on R&D and by 2001, this figure had dropped to 0.14 percent. (AT Kearney, 2003, Slide #141). Furthermore, it can be argued that due to the tax and accounting regimes that helped pharmaceuticals locate to Puerto Rico under the auspices of Section 936, an incentive to manufacture and export high value added products and a disincentive for performing R&D was created. Although a formal study has not been realized, these trends have led researchers to conclude that the local innovation system is underdeveloped and presents a lack of integration (CEPAL, 2005, p.102). Policy efforts to support R&D and the development of local systems of innovation have been almost non-existent and although a specific policy on science and technology was adopted in 1996, it has not yielded any significant results.

Regardless of these experiences, specific actions to begin growing local biotechnology capacity have been undertaken recently (Lama Bonilla, 2005; Martínez, 2005). In January of 2005, the Puerto Rico Industrial Development Corporation (PRIDCO) and the University of Puerto Rico (UPR) announced the construction of Puerto Rico’s first bioprocess & workforce development pilot plant financed through a joint investment totaling \$12.5 million. According to PRIDCO and UPR officers, the plant, which will be located in Mayaguez (home to the Island’s largest engineering school and only biotechnology program) will provide the infrastructure for biotechnology firms to work on development and process projects with the hopes of eventually attracting the R&D side. The facility will also function as a training ground for students and current industry employees. The establishment of this plant coupled with the creation of a \$100 million science and technology research trust and the recent announcements of new expansions from local US biotechnology corporations are all positive advancements. Notwithstanding, these efforts must be seen as the tip of the iceberg or starting point of larger efforts to grow local technical and knowledge capacities. If monetary investments are any indication of commitment and desire, our efforts do not coincide with our dreams when compared

to the Singaporean \$1.5 billion infrastructure fund for biotechnology and the recent \$3 billion bond approval by California voters to advance stem cell research in the state.

In the coming years, Puerto Rico needs to take proactive steps to link its budding research infrastructure and manufacturing centers with successful efforts abroad. The recent founding of the first comprehensive cancer research center in Puerto Rico (Brower, 2004) that will undertake projects in several areas in conjunction with the M.D. Anderson Cancer Center in Houston, Texas is a step in the right direction that should be emulated in other sectors. The center will not only be nurtured by a working relationship with a renowned institution but will also perform important research endeavors that will have an impact on local health needs. As has been described earlier, this is an approach that has rendered results for several developing countries interested in pursuing biotechnology.

Other opportunities lie in utilizing our manufacturing experience and regulatory knowledge to attract corporations interested in moving from research to development and production of new and existing products. If the cards are played right, Puerto Rico could build the institutional and physical infrastructure for conducting reliable and cost-effective clinical trials and process development improvement. These capabilities could serve as the starting point for future indigenous R&D efforts. Alliances with groups such as the New York City Bioscience Initiative could prove to be ideal given the needs and offerings that both localities can provide each other. New York City is fast becoming a biotechnology cluster with approximately 30 biotechnology corporations opening operations each year. For the most part, due mostly to the cost of space, operations being lured to New York City are heavily focused on R&D. In the coming years, a number of these will have products ready for the trials and manufacturing phases, and Puerto Rico could emerge as a desired location that supplies their needs. In this respect, there are clear advantages of having been a manufacturing enclave for the pharmaceutical industry and producers of some of the most popular blockbuster drugs sold worldwide. Nonetheless, this will not happen serendipitously and many measures need to be taken to assure that a synergic relationship between New York City's and Puerto Rico's biotechnology sectors emerges and that an effective technology transfer process is effectuated.

The private sector will definitively play a vital part yet, especially in the initial stages, there is also an expanded role for governments at diverse levels. In the coming years, we must be aware of an important piece of advice conveyed by the sociologist and expert on industrial development, Peter Evans: "State involvement is a given. The appropriate question is not 'how much' but 'what kind'" (1995, p.10). If we aim to get real on the biotechnology front we must advance a series of analytical exercises focused on assessing our capabilities and disadvantages, which in turn will lead to specific policies and signal the beginning of a transparent dialogue where not only economic, but ethical and moral issues tied to future endeavors, are discussed with all partners.

Notes

1. On a recent visit to Puerto Rico, Amgen's CEO announced that a \$1.2 billion investment for operations expansion is underway in the Juncos plant. He also noted that, as a consequence, the Puerto Rico operations will be producing \$10 billion in sales for the company. (Lama Bonilla, 2005)
2. Although we are mirroring some of the metrics used by Cortright and Meyer, in some cases we do not utilize the same data sources. Thus, ours is not a formal update or comparison but rather a snapshot of the biotechnology infrastructure in Puerto Rico. We expect to make a more formal analysis in a future publication.
3. For the purposes of this initial analysis, US states were used as the benchmark due primordially to the availability of comparable data.

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