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COMMERCIALIZATION OF BIOTECHNOLOGY SCIENCE MOLECULES TO MARKET – GLOBAL AND AMERICAN PERSPECTIVES

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Abstract

Biotechnology is a rapidly emerging domain that is impacting how we live and work daily. This paper delineates some of the major biotechnologies, their applications, and benefits to both societies and individuals. Challenges to commercialization to move biotech research from the lab to the marketplace are explored. The financial value of biotechnology is captured when the research breakthrough solves an economic societal challenge. The path is to commercialization is especially perilous for biotech due to its long lead time – measured in decades – and costs to transform the ideas into an innovation. Additionally, issues of intellectual property, patenting and licensing in the biotech industry are probed. Caveats on biotech's growth rate are examined and future prospects are prognosticated.

Introduction - Biotechnology Defined and Examples

There are many definitions for what the biotechnology industry is and is not. Biotechnology is a group of technologies that share two common characteristics – manipulation of living cells and their related molecules for

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commercial purposes [Keener et al. 2013]. Biotechnology began when James Watson and Francis Crick cracked the double helix code to reveal the structure of DNA that made a new biology [Gallwas, 2005]. Traditional biotechnology has been used for thousands of years to bake breads, make cheeses, brew alcoholic beverages, and breed better croups and animals. Modern biotechnology focuses on four main areas in health care: medicines, vaccines, diagnostics and gene therapy. Biotechnology, pharmaceuticals, and medical devices produce innovations for biomedical sector [Cohen and Hanft, 2007]. Modern biotechnology focuses on the modification of cells at the molecular level. For example, "Genetic engineering is a technique of removing, modifying, or adding genes to a DNA molecule to change the information it contains [Keener et al. 2013]." Genes are the chemical blueprints and genetic engineering uses biotechnologies to change the genetic makeup of cells, move genes across species boundaries to produce novel organisms [Union of Concerned Scientists, 2013].

Through genetic engineering, scientists can insert a gene into a plant to create biological defenses against specific diseases and insects. Xanthomonas oryzae is a bacterium which destroys rice corps. The International Laboratory for Tropical Agricultural Biotechnology transferred a Xanthomonas oryzae resistant gene from wild race to protect commercial rice from the disease. The genetically modified rice is currently cultivated on 24 million hectares globally [Keener et al. 2013].

Today, biotechnology aspects cover such area of innovations as: energy, food and drink chemistry, chemical engineering, materials, environment, genetics, medicine and biotechnology applications [Higgings et al., 1985]. Industrial biotech is a more specific segment of the biotech sector that includes any molecule that improves the efficiency of industrial processes such as textile, paper, pulp, and chemical manufacturing. Thirty per cent of the world's chemical and fuel needs could be generated by applying biotechnology process to renewable resources. For example, bio pulping reduces the electricity required for the wood pulping process by 30% [Keener et al. 2013].

Environmental biotechnology is concerned with the application of biotechnology industrialization, urbanization and other developments [Gavrilescu, 2010]. Environmental biotech is used in waste treatment and to prevent and to remediate environmental pollution. In many cases this process is fairly simple; bacteria are inserted into polluted areas where the bacteria digest the polluted waste into harmless by products. After the

bacteria consume the waste materials, the bacteria die off, and the ecosystem is restored to health.

Biotech methods also produce proteins for pharmaceutical purposes. For example, a harmless strain of *Escherichia coli* bacteria can be used to make insulin. Biotechnologies are being studied in gene therapies to explore treatments for diseases such as cystic fibrosis, AIDS, and cancer. Biotech is also used for DNA finger printing which is used to determine human and animal origins by geographical regions, as well as paternity [Keener et al, 2013]. According to a 2010 Pharmaceutical Research and Manufacturers' Report, there are 633 biotech medicines in human trials or under review by the US Food and Drug Administration [Son, 2013].

Biotech is broad field with many actual and potential commercial applications to food, agricultural, industrial, and medical fields.
For our discussion, we will adopt the following definition:

"*Biotechnology is a group of technologies based on molecular biology which enables scientists to genetically manipulate and replicate living cells, with a host of applications, in areas such as medicine, agriculture, food processing, and energy* [Argyres and Liebeskind, 1998].

This definition captures the core concept that biotechnology is the manipulation living cells at the molecular level to create commercial products for multiple industries.

Global and USA Biotechnology Industries

In 2012, the USA accounted for approximately 70% the 65 billion Euros ($84 billion USD) global biotechnology industry [Giovannetti & Jaggi, 2012]. Consequently, this section will focus primarily on the USA biotechnology industry.

The biotechnology industry in the USA is highly fragmented among nearly 3,800 organizations. The three major commercial organizations account for over 31% - Amgen, 14.1%, Genentech, 11.5%, and Monsanto, 5.8% - of the industry's 72 billion Euros ($93 billion USD) forecasted 2013 revenues [Son, 2013].

In 2009, global biotechnology firms reported a profit of 2.0 billion Euros ($2.6 billion USD) – 3.8% of revenues. This was the first profit recorded by the industry since its founding in the mid–1970s when Herbert Boyer and Stanley Cohen discovered to how to splice genes and consequently launched the global biotechnology industry. 2013 biotech industry profits are estimated at 3.8 billion Euros ($5 billion USD) – 5.3% of revenues. The revenues of American biotechnology companies are

forecast to grow from 72 billion Euros ($93 billion USD) in 2013 to 109 billion Euros ($142 billion USD) by 2018 [Son, 2013].

The 8.9% annual growth will be driven primarily by an aging population requiring additional healthcare resulting in a more favorable environment for new products. This demand pull will make it easier for biotech companies to raise additional investments for R&D and product commercialization. This should make it easier for the current American biotechnology firms to earn profits to facilitate their global growth.

USA biotechnology revenues are distributed among the following major market segments: biotech technologies, human health, agriculture, aquaculture, industrial, animal health, microbial, environmental. The major biotech sector revenues and related market shares are presented in the table 1.

Table 1 – Biotech by Major Sectors – Revenues and Market Share

Biotech Technologies	**2013 Revenues – Billions - Euros / $USD**	**% Market Share**
Human health	40.87 Euros - $53.01	57%
Agriculture / aquaculture	10.75 Euros - $13.95	15%
Industrial	8.61 Euros - $11.16	12%
Animal health / Microbial	5.74 Euros - $ 7.44	8%
Environmental	5.74 Euros - $ 7.44	8%
Total	71.71 Euros - $93.00	100%

Source: IBIS World, Son, 2013.

However, the industry is currently chaotic with many conflicts among the organizations developing and commercializing new biotech molecules and related products. These conflicts are so volatile that the industry borders on mayhem. The chaos is increasing due to intellectual property and related legal disputes – who owns what molecule for which application and market. This chaos will only increase in the near future as the commercial value of the intellectual property of biotech increases with the growing market and related applications.

Biotechnology's Intellectual Property and Commercialization Issues

Biotechnology is deeply grounded in fundamental science – because it is research based, biotechnology is much more deeply embedded

the university system than many alternative disciplines such as information technology and engineering. Consequently, most of biotechnology's research is in university labs. Until recently, commercial organizations did not engage directly in basic research and universities did not engage in commercialization of knowledge to create economic value. The wall between research and commercialization – between universities and business – became much more porous with the passage of Bayh-Dole Act in 1980 because it enabled universities to capture some of economic value of publically funded research.

Consequently, in most universities the discussion to patent or not to patent research findings is made in conjunction with the university's technology transfer office. This decision is frequently extremely complex because patenting involves revealing what is unique and novel. The patent disclosure gives the "secret" to competition rather than holding the research findings close to the researcher's lab. Furthermore, the patent system is both complex and costly. According to the US Patent and Trademark Office – it took an average of 33.6 months to award a biotechnology patent in 2011. The average cost of filing a patent, validation, and translation in the European Union is approximately 35,000 Euros (Biotechnology Industry Organization, 2012). The cost of patenting was further underscored by Alexander Weedon, head of business and legal affairs at UCL Business in London, who was cited in *Nature Biotechnology* (2012), "Obtaining a patent valid in most of Europe can cost up 100,000 Euros, the majority spent on validating the patent in each country and translation". Consequently, university offices of technology frequently use attorneys to find the pivot point among the conflicting facets of time, money, disclosure, and cumbersome academic and legal bureaucracies. In a practical sense, this means the scientific researcher must not only understand his/her scientific research domain but understand the commercialization process while functioning as a para legal attorney to protect the intellectual knowledge being developed.

Relative to commercializing other high tech knowledge such as information technology, biotechnology presents some very unique scientific and management challenges because of the challenging probability of success such a long development time between concept and product launch, and high initial costs.

Only one out of 5,000 to 10,000 biotech compounds created in labs are actually launched into the marketplace [Hamermesh and Higgins, 2007]. In contrast, Hansen [1995] points out that for 333 publically funded technology product ideas, only two new products were actually launched

into the marketplace to achieve one commercial success [Trzmielak and Zehner, 2011]. Still other studies have reported a 90% failure rate among biotech companies [Shaista et. al. 2006]. Biotechnology companies are "rolling the dice with long odds" of success but are willing to do so because of the potentially large economic and societal payoffs.

The time line to develop and commercialize a new biotech product is measured in decades rather than years or months for most technology products. Shaista et. al. [2006] reported, "On average, the entire biotech processes, from scientific discover to commercialization, can take up to 15 years." A 2011 [McDougall] study determined the time to commercialize some plant traits from discovery to first commercial application averaged about 13.1 years.

The time bound process may be depicted schematically as figure 1 presents.

Figure 1 – The Biotech Commercialization Process.
Source: Authors

Stage 1 is the basic research – the idea itself; stage 2 is the laboratory proof of concept – the idea actually works as conceptualized; stage 3 is invention of the product / service and involves not only the biotech molecule but its delivery system as well; stage 4 involves clinical trials to establish the molecules effectiveness and efficacy; stage 5 is the conversion of the invention into a biotech innovation located in the marketplace. The transition from invention to innovation involves interactions among the scientist, the university technology transfer office, the commercialization organization, and business elements such legal and venture capital organizations.

The lengthy process imposes a number of critical and time sensitive decisions on the biotech entrepreneur which they may or may not be capable of handling. For example, because biotech is heavily grounded in basic scientific research which is mostly undertaken in university research labs, the scientist-entrepreneur may have to devote an inordinate

amount of time to finding grants to support the basic research (stage 2). As the scientist-entrepreneur progresses through the invention phase, they will spend time dealing with technology transfer office as well as prospective non university organizations such as legal and investment organizations. Finally, when the molecule is the innovation – complete product stage (stage 5) – the scientist–entrepreneur must deal with spin–offs companies and venture capital investments.

The funding process is time consuming and requires the scientist entrepreneur to build multiple relations across many industries or potential applications throughout the process from idea to proof of concept to prototype to market launch. Individuals must be educated to the merits of the molecule at each step. Equally challenging is for the project to progress funding must be obtain from different sources – each with a requirement for different scientific data as well as a different time frame. Basic research is frequently funded through a 4 to 7 year scientific research grant but the time horizon of a venture firm to achieve commercial success is 3 to 5 years.

The cost of developing new technology products and launching them is significant. A rough rule of thumb is that for every one Euro invested in the cost of discovery of the principle, the cost of developing a prototype is ten times the cost of discovery, and the cost of market introduction is tenfold the cost of the prototype [Jolly, 1997]. A study by Tufts University Center for the Study of Drug Development [2006] estimated the average out of pocket cost (cash outlays) for the preclinical period was 153 million Euros ($198 million USD) plus another 277 million Euros ($361 million USD) in out of pocket cash outlays to secure clinical approval for a total of 431 million Euros ($559 million USD). The 2011 McDougall study reported that the cost of developing a new plant biotechnology trait introduced to the market place between 2008 and 2012 was approximately 105 million Euros ($136 million USD). Developing new biotech products is expensive and takes longer than pharm products but has a higher success rate of 30.2% compared to pharma's 21.5%.

As biotechnology has become more pervasive globally, questions and concerns about its intrinsic safety have surfaced – especially in Europe. In assessing the benefits vs. the safety of emerging technology, there are two types of risks: 1. the risks inherent in the technology itself and 2. The social – cultural context risks – which societal group benefits from the emerging technology and which group is harmed.

As example of the first type of risk, Keener et. al. [2013] point out "a biotech derived food with a higher content of digestible iron is likely to

have a positive effect if it is consumed by iron deficient individuals. Alternatively, the transfer of genes from one species to another may also transfer the risk of exposure to allergens…Individuals allergic to certain nuts; for example, need to know if the genes conveying this trait are transferred to other foods such as soybeans." Although these risks can be mitigated with additional research, it is difficult to predict the full societal effect of a new product until it enters the market.

In the USA, "type 1" inherent risks are evaluated by the Food and Drug Administration prior to commercialization. Keener et. al. [2013] conclude that "There is no evidence that genetic transfers between unrelated organism pose human health concerns that are different from those encountered with any new plant or animal variety. The (type one) risks associated with biotechnology are the same as those associated with plants and microbes developed by conventional methods."

Given the economic structure of modern societies which distances the food consumer from the food producer, many consumers are completely unaware that all foods they consume have been, in fact, genetically changed through traditional breeding methodologies. This illustrates a societal difference between US and European food consumers. Americans are much more accepting of genetically modified foods than Europeans. Americans seek information from scientific experts and place less trust in activists who oppose biotechnology. In contrast, Europeans place more trust in activists. However, some American food companies have modified their products to avoid biotech derived crops maintain positive consumer perceptions. Gerber Foods purchased its corn and soybeans from farmers that did not use genetically modified seeds [Keener et al, 2013]. Type 2 risks are less clear cut and eventually, every society determines what an acceptable type 2 risk is its own culture.

Applications of biotechnology are broad and the potential benefit to societies is great – especially for medicine and food production. However, the acceptance of growth of biotechnology within a particular nation and industry will depend on the balance between the commercial benefits and the evaluation of the necessary type 1 and type 2 risks for a particular society. As the world gains increased understanding of biotech's benefits, its commercialization will accelerate.

Unlocking Future Economic Value from Biotechnology Science

The biotechnology industry will grow from 15.5 billion Euros ($20 billion USD) [Bogdan, Viliger, 2008], 72 billion Euros ($93 billion USD)

in 2013 to approximately 109 billion Euros ($142 billion USD) in the next 5 years as it develops new commercial applications (Son, 2013). The growth will be driven by the aging of the USA population and resultant demand for medical treatments.

Most biotechnology startups will continue to emerge from university labs which research biotech phenomenon at fundamental scientific levels. Additionally, new startups will continue to be funded by licensing arrangements which also grant access of the startup to customers and distribution channels.

Licensing addresses the needs of the biotechnology startup which requires funding to continue its research. The licensee, normally, a large pharmaceutical company requires new products to fuel its product pipeline. The licensee wants to spread the new product risk over its product portfolio. Consequently, the licensee is not willing to pay a large sum initially [Villiger and Bogdan, 2009]. Rather, the licensee pays the biotechnology company some upfront money to recapture some of the economic value created to date by the scientist and milestone based money – as the scientist moves successfully toward translating the idea into an innovation – as well as royalties when the product is commercially marketed. New startups frequently seek a license from the university technology transfer office for any of several reasons, such as to ensure freedom to use a product line, to obtain exclusivity for a product line, and to become current quickly without the cost of internal research [Freeman, 2007]

Licensing is to the advantage of the biotechnology scientist-entrepreneur since it enables the scientist to do what he or she does best - focus on the frontiers of science without the constant distraction of raising cash. More importantly, by licensing the scientist-entrepreneur gains access to the pharma organization's market and distribution channels which are critical for economic success.

Consequently, the issues associated with patents and related intellectual property will continue to be even more important as more and more of the USA's biotech firms achieve economic viability and financial success. The increasing research investment in biotechnology and related intellectual property means the university offices of technology transfer and related attorneys will continue to define the relationships among the research, universities, biotech startups, and licensees. Given that the EU and US Courts are still defining precedents in the biotech space, some clarity may will emerge on when and how to best structure the highly complex licensing agreements.

Unlike the commercialization of most sciences, biotechnology must navigate a labyrinth of governmental regulation and its related expense. This regulation protects the public while simultaneously increasing both the cost and time to commercialize biotech breakthroughs. However, more and more government regulatory bodies are exploring ways to accelerate the safety verification and related approval processes as they gain more experience with biotechnology.

The biotech scientist's role is to create new knowledge. The role of the business manager is to husband the financial stewardship of an organization's assets. The differing "world views" between the scientist and business manager creates a great deal of tension. Dubinskas [1988] captures the intrinsic differences when he writes "In their grossest caricatures of each other, the complete adult realist managers, in their struggles with immediate economic necessity, must contend with immature scientists-dreamers. While from the other side of the table, the far sighted progressive scientists must protect their work (the basis of the firm's wealth) from myopic, and developmentally retarded managers!''

Formal academic programs to bridge the science – business chasm such as the scientist – professional program at the Keck Institute of the Claremont Graduate University are emerging. The single most important phenomenon will be the emergence of the biotech science – practitioners – a scientist who understands the research while appreciating the business professional talents necessary to transform an invention into an innovation which benefits society. The world's biotech scientists and business managers are tightly entwined in a symbiotic relationship to create societal benefits and economic wealth.

Conclusion

The next five years will see an explosion of biotechnologies to improve our lives and the biotech scientist-entrepreneur will manage the commercialization process much better than in the last five years as the global biotechnology industry continues to emerge and grow. Additionally, many of the legal issues and licensing processes will be more keenly defined making it easier and quicker to commercialize biotechnology knowledge.

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Abstrakt

Artykuł "Komercjalizacja wiedzy z zakresu biotechnologii – perspektywa amerykańska i globalna" pokazuje czym są i jaką wartość dla przemysłu stanowią nauki biotechnologiczne. Naukowcy z uniwersytetów amerykańskich prezentują również proces komercjalizacji technologii, w którym uwzględniają okres trwania poszczególnych etapów. Artykuł podkreśla rolę czasu w rozwoju technologii i produktów w sektorze biotechnologii oraz znaczenie licencjonowania w transferze wyników badań do przedsiębiorstw na rynku amerykańskim. Podrozdział monografii autorstwa W. B. Zehner, Dariusza M. Trzmielaka i J. A. Zehner jest

syntetycznym spojrzeniem na rynek globalny biotechnologii z perspektywy ostatnich kilku lat. Konkluzje zawarte w publikacji wyraźnie wskazują, że pomimo dużego ryzyka związanego z komercjalizacją biotechnologii rynki wciąż skłonne są inwestować w projekty badań, nowe technologie i produkty w analizowanym przez autorów artykułu sektorze. Dodatkowo podkreślona jest tendencja powstawania i rozwoju nowych segmentów rynku.