BIONANOTECHNOLOGY

GLOBAL PROSPECTS

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27 Patenting Inventions in Bionanotechnology: A Guide for Scientists and Lawyers*

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* This chapter reflects the current views of the author which are likely to evolve. Furthermore, they should not be attributed, in whole or in part, to the author's affiliation listed above, nor should they be considered as expressing an opinion with regard to the merits of any particular company or product discussed herein. Nothing contained herein is to be considered as the rendering of legal advice. This chapter will focus on U.S. patents and the U.S. patent system. The author may be contacted at: bawabio@aol.com.

27.1 INTRODUCTION

The high-risk, high-payoff global nanotechnology phenomenon is in full swing as innovations at the intersection of engineering, biotechnology, medicine, physical sciences, and information technology are spurring new directions in research, education, commercialization, and technology transfer. In fact, the future of nanotechnology is likely to continue in this interdisciplinary manner. One of the major impacts of nanotechnology is taking place in the context of biology, biotechnology, and medicine.* This arena of nanotechnology is generally referred to as bionanotechnology, and sometimes nanomedicine. These two terms will be interchangeably used in this chapter.

There are quite a few bionanotechnology-related products in the market with numerous other potential applications under consideration and development. Generally speaking, commercial bionanotechnology is at a nascent stage of development and its full potential is years or decades away. However, there are a few bright spots where development is progressing more rapidly. For instance, consider the recent advances in bionanotechnology-related drug delivery, diagnostics, and drug development which are beginning to alter the landscape of medicine and health care. In the future, significant technologic advances across multiple scientific disciplines will continue under the nanotech banner to be proposed, validated, patented, and commercialized. This will likely accelerate in the coming years.

There is enormous excitement regarding bionanotechnology's potential impact. However, one thing is critical in this regard. Securing valid and defensible patent protection is a must for any player interested in bionanotechnology commercialization. Although early forecasts for bionanotechnology commercialization are encouraging, there are a few bottlenecks as well. Some formidable challenges include legal, environmental, safety, ethical, and regulatory questions as well as emerging thickets of overlapping patent claims. In fact, patent systems are under great scrutiny and strain, with patent offices around the world continuing to struggle with evaluating the swarm of bionanotechnology-related patent applications. The emerging thickets of patent claims has primarily resulted from patent proliferation and secondarily from the continued issuance of surprisingly broad patents in bionanotechnology by the U.S. Patent and Trademark Office (PTO) (Section 27.9). Adding to this confusion is the fact that the U.S. National Nanotechnology Initiative's (NNI) widely cited definition of nanotechnology is inaccurate and irrelevant, especially with regard to bionanotechnology (Section 27.2). This has resulted in the inadequate preliminary patent classification system that was unveiled in 2006 by the PTO (Section 27.7).

These challenges are creating a chaotic, tangled patent landscape in various sectors of bionanotechnology where the competing players are unsure as to the validity and enforceability of numerous issued patents. If this trend continues, it could stifle competition, limit access to some inventions, or simply cause commercialization efforts in certain sectors of bionanotechnology to grind to a halt.

* Though nanotechnology is characterized by distinctively new technologies such as scanning probe microscopy and nanolithography, many experts refute the popular notion that it is a distinct industry or sector. It may be more accurate to consider it to represent a set of tools (e.g., scanning probe microscopy) and processes (e.g., nanolithography) for manipulating matter that can be applied to virtually all manufactured goods. Similarly, I caution against envisioning a "nanotechnology market," per se. Instead, one should focus on how nanotech is being exploited across industry value chains, from basic materials to intermediate products to final goods. In fact, I believe that most nanotech-related products developed in the next few years will remain within existing markets or established sectors, and thus will not be marketed as "nanoproducts."

Given this backdrop, it is hard to predict whether bionanotechnology will make small but valuable contributions to medicine and biotechnology or whether it will act as a catalyst for a vast technological and health-care revolution. One thing is certain: bionanotechnology is here to stay, and it will definitely generate both evolutionary and revolutionary products in the future.* However, if the full potential of this "revolution" is to be fully realized, certain reforms are urgently needed at the PTO to address problems ranging from poor patent quality and questionable examination practices to inadequate search capabilities, rising attrition, poor employee morale, and a skyrocketing patent application backlog. All players involved in bionanotechnology agree that a robust patent system is essential for stimulating the development of commercially viable products.

In spite of all these challenges and bottlenecks, governments around the world are impressed by nanotechnology's potential and are staking their claims by doling out billions of dollars, euros, and yen for research.† International rivalries are growing.‡ Political alliances are forming, and battle lines are being drawn.§

Governments, corporations, and venture capitalists in 2006 spent $12.4 billion on nanotechnology research and development (R&D) globally, up 13% from 2005.¶ In 2006, globally, government spending grew to $6.4 billion, up 19% from 2005.** Global spending in 2006 on nanotech products ($50 billion) far surpassed that spent on nanotech R&D ($12 billion).†† In 2005, nanotechnology was incorporated into more than $30 billion worth of manufactured goods.‡‡ U.S. federal funds are supplemented by state investments in nanotechnology (approximately 40 cents per U.S. dollar). The president's budget for 2008 allocated 1.44 billion U.S. dollars for nanotech as compared to 1.35 billion U.S. dollars in 2007.

Numerous nanotechnology market reports and economic forecasts are available, each varying in their statistics. Often, poor assumptions underlie the analyses, rendering the results highly questionable or largely irrelevant. Also, most market reports on nanotechnology rely on the flawed NNI definition of nanotechnology (see Section 27.2) to draw their conclusions. Therefore, the data reflected in these reports should be taken as indicating trends rather than reflecting absolute numbers. For example, according to the National Science Foundation (NSF), by 2015 the annual global market for nano-related goods and services will top $1 trillion, making it one of the fastest-growing industries in history. On the other hand, Lux Research, Inc., predicts that by 2014, $2.6 trillion in global manufactured goods may incorporate nanotechnology (about 15% of total global manufacturing output).§§

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* Although many sought-after innovations are decades away, a recent study claims that there are over 600 nanotech-based consumer products in the marketplace today (*See* A nanotechnology consumer products inventory—www.nanotechproject.org/index.php?id=44 [last accessed April 10, 2008]). Some examples of commercially available nanotech products include wrinkle-resistant khakis, super-light tennis rackets, and quick-drying paint.

† The passage of the 21st Century Nanotechnology Research and Development Act (Pub. L. No. 108-153) in 2003, which authorized $3.7 billion in federal funding from 2005 through 2008 for the support of nanotechnology R&D, is fueling the fervor over nanotechnology in the United States. This legislation resulted in the creation of R&D centers in academia and government. At present, there are over 50 institutes and centers dedicated to nanotechnology R&D. For example, the NSF has established the National Nanotechnology Infrastructure Network—composed of university sites that form an integrated, nationwide system of user facilities to support research and education in nanoscale science, engineering, and technology. Similarly, there are currently numerous government agencies with R&D budgets dedicated to nanotechnology.

‡ Edwards SA: *The Nanotech Pioneers—Where Are They Taking US?* Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany (2006); Van Lente MA: Building the new world of nanotechnology. *Case W. Res. J. Int. Law* 38(1), 173–215 (2006).

§ I am optimistic that current fears about self-replicating nanobots, the potential toxic effects of nanoparticles, and the focus on strict regulations or a nanotech moratorium, will eventually give way to intelligent public dialogue on the realistic impact of bionanotechnology.

¶ Reisch MS: Nano goes big time. *Chemical & Engineering News* 85(4), 22–25 (2007).

** *The Nanotech Report* (4th Edition). Lux Research, Inc., New York (2006).

†† *See supra Note* **.

‡‡ *See supra Note* **.

§§ Report: *Sizing Nanotechnology's Value Chain*, Lux Research, New York (2004).

27.2 CURRENT DEFINITIONS OF NANOTECHNOLOGY AND NANOMEDICINE—A SOURCE OF CONFUSION

The term *nanotechnology* is very much in vogue. However, one of the problems it faces is the confusion, hype, and disagreement among experts about its definition.* Nanotechnology is an umbrella term used to define the products, processes, and properties at the nano/micro scale. By manipulating atoms, scientists can create stronger, lighter, more efficient materials ("nanomaterials") with tailored properties. In addition to numerous advantages provided by this scale of miniaturization (over their conventional "bulk" counterparts), quantum effects at this scale impart additional novel properties. Many of the properties of nanomaterials are fundamentally different from those of their macroscopic/bulk analogues due to an increased surface area and quantum effects. As a particle's size decreases, a greater proportion of its atoms are located on the surface relative to the interior (core), generally rendering it more reactive. In fact, quantum effects coupled with surface area effects can affect optical, electrical, chemical, and magnetic properties of nanomaterials, which in turn can affect their *in vivo* behavior.

One of the most quoted, yet incorrect, definitions of nanotechnology is that used by the NNI†: "[n]anotechnology is the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications."‡ Clearly, this definition excludes numerous devices and materials of micrometer dimensions, a scale that is included within the definition of nanotechnology by many nanoscientists.§ Therefore, experts have cautioned against an overly rigid definition based on a sub-100 nm size, emphasizing instead the continuum of scale from the "nano" to "micro."¶

Various federal agencies are also grappling with the definition of nanotechnology. For example, both the U.S. Food and Drug Administration (FDA) and the PTO use the NNI definition based on a sub-100 nm scale. This definition continues to present difficulties not only for understanding nanopatent statistics,** but also for the proper assessment of nanotechnology's scientific, legal, environmental, regulatory, and ethical implications. This problem persists because nanotechnology represents a cluster of technologies, each possessing different characteristics and applications. Although the sub-100-nm size range may be critical for a nanophotonic company where size-dependent quantum effects are particularly important (e.g., a quantum dot's size dictates the color of light emitted therefrom), this size limitation is not critical to a drug company from a formulation, delivery, or efficacy perspective because the desired or ideal property (e.g., improved bioavailability, reduced toxicity, lower dose, enhanced water solubility, etc.) may be achieved in a size range greater than 100 nm. Numerous examples from the pharmaceutical industry highlight this important point

* Editors: Nanotechnology. *Nature Nanotechnology* 1(1), 8–10 (2006).

† What is Nanotechnology? The National Nanotechnology Initiative. www.nano.gov/html/facts/whatIsNano.html [last accessed April 10, 2008].

‡ A nanometer is one billionth of a meter, or 1/75,000th the size of a human hair. An atom is about one third of a nanometer in width. A nanometer is one-billionth of a meter. Here is the size of some common objects expressed in nanometers: a basketball is about 24 centimeters (240 million nanometers); a flea is about 1 millimeter (1 million nanometers); an anthrax bacterium is 1 micrometer (1000 nanometers); and a DNA molecule measures around 2.5 nanometers wide. A sugar granule is about 1 millimeter, and a single sugar molecule is about 1 nanometer.

§ Bawa R: Nanotechnology patenting in the U.S. *Nanotechnology Law & Business* 1, 31–50 (2004); Bawa R: Patents and nanomedicine. *Nanomedicine* 2(3), 351–374 (2007); Bawa R, Bawa SR, Maebius SB, Iyer C: Bionanotechnology patents: Challenges and opportunities. In: *The Biomedical Engineering Handbook* (3rd Edition). Bronzino JD (Ed.), CRC Press, Boca Raton, FL; 29-1–29-16 (2006); Morrow KL, Bawa R, Wei C: Recent advances in basic and clinical nanomedicine. In: *Medical Clinics of North America*, 91(5), 805–843 (2007). Bawa R, Bawa SR: Protecting new inventions in nanomedicine. In: *Foresight, Innovation, and Strategy: Towards a Wiser Future*. Wagner CG (Ed.), World Future Society Press, Bethesda, MD, 31–44 (2005); Bawa R, Bawa SR, Maebius SB, Flynn T, Wei C. Protecting new ideas and inventions in nanomedicine with patents. *Nanomedicine: Nanotechnology, Biology and Medicine* 1(2), 150–158 (2005).

¶ National Heart, Lung, and Blood Institute Programs of Excellence in Nanotechnology. http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-04-020.htm.

** Regalando A: Nanotechnology patents surge as companies vie to stake claim. *Wall Street Journal* June 18 Issue, A1 (2004).

(e.g., Abraxane's albumin-paclitaxel nanoparticles; Elan Pharma International's nanoparticles, and Kereos's anticancer particles).

Clearly, a definition based on physical limits tends to be an unorthodox way of defining a technology. Other technologies tend to be defined by a key technology or breakthrough: genetic engineering technology is based upon recombinant DNA, and the Internet is a collection of "bulletin boards" networked in a World Wide Web.

Furthermore, nanotechnology is nothing new. For example, nanoscale carbon particles ("high-tech soot nanoparticles") have been used as a reinforcing additive in tires for more than a century. Another example is that of protein vaccines that squarely fall within the definition of nanotechnology.* In fact, the scale of many biologic structures is similar to various "nanocomponents." For example, peptides are similar in size to quantum dots (around 10 nm), and some viruses are the same size as drug delivery nanoparticles (around 100 nm). Hence, most of molecular medicine and biotechnology can be classified as nanotechnology. In fact, biologists had been studying all these nanoscale biological structures long before the term "nanotechnology" became fashionable.† Given this confusion, I recently proposed a more practical definition of nanotechnology that is unconstrained by an arbitrary size limitation‡:

> The design, characterization, production, and application of structures, devices, and systems by controlled manipulation of size and shape at the nanometer scale (atomic, molecular, and macromolecular scale) that produces structures, devices, and systems with at least one novel/superior characteristic or property.

Naturally, disagreements over the definition of nanotechnology carry over to the definition of nanomedicine. At present, there is no uniform, internationally accepted definition for nanomedicine either. One definition, unconstrained by size while correctly emphasizing that controlled manipulation at the nanoscale results in medical improvements and significant medical changes, comes from the European Science Foundation.§

> The science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body.

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* Nanotechnology also aims to learn from nature—to understand the structure and function of biological nanodevices and to use nature's solutions to advance science and engineering. Evolution has produced an overwhelming number and variety of biologic devices, compounds, and processes that function at the nanometer or molecular level and that provide performance that is unsurpassed by synthetic technologies. When nanotechnology is combined with molecular biology, the potential applications at this frontier are widespread and sound like the stuff of science fiction. Given the complex biological machinery that exists in nature, it is hard not to conclude that complex machines on the nanoscale may be possible someday (Jones R: What can biology teach us? *Nature Nanotechnology* 1, 85–86 [2006]). The construction principles used in nanotechnology often originate in biology, and the goals are often biomimetic or aimed at the solution of long-standing research problems. At the heart of the approaches in this field is the concept of self-assembly. In fact, self-assembly of ordered elements is a defining property of life. Bionanotechnologists attempt to exploit the self-assembly and ordered proximity of nanoscale structures found in biology.

† However, note that the U.S. National Institutes of Health (NIH) emphasize that: "While much of biology is grounded in nanoscale phenomena, NIH has not re-classified most of its basic research portfolio as nanotechnology" (*See* www.becon.nih.gov/nano.htm [last accessed April 10, 2008]). The NIH identifies three broad areas that qualify as nanotechnology: "studies that use nanotechnology tools and concepts to study biology; that propose to engineer biological molecules toward functions very different from those they have in nature; or that manipulate biological systems by methods more precise than can be done by using molecular biological, synthetic chemical, or biochemical approaches that have been used for years in the biology research community."

‡ Bawa R: Patents and Nanomedicine. *Nanomedicine* 2(3), 351–374 (2007).

§ Nanomedicine—An ESF-European Medical Research Councils (EMRC) forward look report. European Science Foundation, Strasbourg, France (2004). Nanomedicine is, in a broad sense, the application of nanoscale technologies to the practice of medicine—namely, for diagnosis, prevention, and treatment of disease and to gain an increased understanding of the complex underlying disease mechanisms. The creation of nanodevices such as nanobots capable of performing real-time therapeutic functions *in vivo* is one eventual long-term goal here. Advances in delivering nanotherapies, miniaturization of analytic tools, improved computational and memory capabilities, and developments in remote communications will be integrated. These efforts will cross new frontiers in the understanding and practice of medicine.

Hence, I propose that the size limitation imposed in NNI's definition should be dropped, especially when it is applied to bionanotechnology nanomedicine. Furthermore, the phrase "small technology" may be more appropriate, because it accurately encompasses both nanotechnologies and microtechnologies. I believe an internationally acceptable definition and nomenclature of nanotechnology should be promptly developed in this context.

27.3 BIG PHARMA AND NANOTECHNOLOGY

Numerous market forces and challenges are dictating that new drug discovery, development, and delivery approaches be developed and implemented. There is a real and urgent need for drug companies to focus on technologies that support miniaturization and high throughput. Such approaches enable faster drug target discovery and drug development. They can also lead to a reduction in the cost of drug discovery, design, and development. Moreover, the current business model of drug companies (with their mammoth size and excessive reliance on blockbusters) is broken and is in need of repair.

Nanotechnology can enhance the drug discovery process via miniaturization, automation, speed, and reliability of assays. This is likely to result in a faster introduction of new cost-effective products to the market. For example, nanotechnology can be applied to current microarray technologies, exponentially increasing the hit rate for promising compounds that can be screened for each target in the pipeline. Inexpensive and higher-throughput DNA sequencers based on nanotechnology can reduce the time for both drug discovery and diagnostics. Although, these high-throughput screening technologies have led to an increase in the number of poorly water-soluble new chemical entities (NCEs), nanotechnology can also tackle such formulation problems. Nanoscience research has also resulted in a need for novel analytical technologies that can directly impact aspects of drug delivery, such as determining the efficacy of targeting, therapeutic outcome, and so forth.

Big pharma in today's global economy faces enormous pressure to deliver high-quality products to the consumer while maintaining profitability. It must constantly reassess how to improve the success rate of NCEs while reducing R&D costs as well as cycle time for producing new drugs, especially new blockbusters. In fact, the cost of developing and launching a new drug to the market, although widely variable,* may be upwards of $800 million. Typically, the drug appears on the market some 10 to 15 years after discovery.† Furthermore, only one out of five lead compounds makes it to final clinical use.‡ Annual R&D investment by drug companies has risen from $1 billion in 1975 to $40 billion in 2003, while new approvals have essentially remained flat, between 20 to 30 drugs per year.§ In fact, in recent years, NCEs accounted for only 25% of products approved by the FDA, with the majority of approvals being reformulations or combinations of already approved agents. Although the cost of drug R&D continues to rise, only 30% of drugs are able to recover their R&D costs. The weakened product pipeline issue is a global problem; the decreasing number of new drugs approved by the FDA and foreign drug agencies continue to haunt the drug industry. For example, FDA approvals have fallen by half since 1996, with only 20 approvals in 2005. Unique drug development models are being successfully developed by competitors to circumvent some of big pharma's patented branded drugs.¶

* DiMasi J, Hansen R, Grabowski H: The price of innovation: New estimates of drug development costs. *Journal of Health Econ*omics 22, 151–185 (2003); Adams C, Brantner V: Estimating the cost of new drug development: Is it really $802m? *Health Affairs* 25(2), 420–428 (2006).

† Anon R: Health Informatics into the 21st Century. *HealthCare Reports*. Reuters Business Insight February (1999).

‡ Erickson J: Translation research and drug development. *Science* 312, 997 (2006).

§ Sussman NL, Kelly JH: Saving time and money in drug discovery—A pre-emptive approach. In: *Business Briefings: Future Drug Discovery 2003*. Business Briefings Ltd, London, UK, 46–49 (2003).

¶ Owens J: Ethical medicine or IP dodge? *Nat. Rev. Drug Disc.* 6, 104 (2007).

In other words, while the above-mentioned trends and issues are creating novel challenges for the drug industry, they also represent an impetus for the drug industry as a whole to focus on nano-enabled R&D technologies.*

27.4 THE FUTURE OF BIONANOTECHNOLOGY

The potential future impact of bionanotechnology on society could be huge. Bionanotechnology could drastically improve a patient's quality of life, reduce societal and economic costs associated with health care, offer early detection of pathological conditions, reduce the severity of therapy, and result in an improved clinical outcome for the patient. The ultimate goal is obviously comprehensive monitoring, repair, and improvement of all human biologic systems: basically, an enhanced quality of life.

As of mid-2006, 130 nanotech-based drugs and delivery systems and 125 devices or diagnostic tests were in preclinical, clinical, or commercial development. However, the nano-pharma market is expected to significantly grow in the coming years. Analysts project that by the end of this year, the market for nanobiotechnology will exceed $3 billion, reflecting an annual growth rate of 28%.† One report predicts that the drug market for nanotech will pass $200 billion by 2015.‡ According to a 2007 report, the U.S. demand for nanotechnology-related medical products (nanomedicines, nanodiagnostics, nanodevices, and nanotech-based medical supplies) will increase over 17% per year to $53 billion in 2011 and $110 billion in 2016.§ This report predicts that the greatest short-term impact of nanomedicine will be in therapies and diagnostics for cancer and central nervous system disorders.

27.5 PROTECTING BIONANOTECHNOLOGY INVENTIONS: THE U.S. PATENT OFFICE AND CRITERIA FOR PATENTING

Globally, industries that produce and manage "knowledge" and "creativity" have replaced capital and raw materials as the new wealth of nations. Property, which has always been the essence of capitalism, is increasingly changing from tangible to intangible.¶ Intellectual property (IP) rights are a class of assets that accountants call intangible assets. These assets play an ever-increasing role in the development of emerging technologies like biotechnology, drug development, and nanotechnology. Modern IP consists of patents, trademarks, copyrights, and trade secrets. Patents are the most complex, tightly regulated, and expensive form of IP. They have the attributes of personal property—they may be assigned, bought, sold, or licensed.

* It is important to note that at this stage several obstacles beset nano-enabled drug R&D commercialization, including high production costs; the public's general reluctance to embrace innovative medical technologies without real safety guidelines; the relative scarcity of venture funds; few near-term commercially viable products; a general lack of knowledge regarding the interaction between nanomaterials and living cells (the issue of biocompatibility and toxicity of nanomaterials); big pharma's reluctance to accept and seriously invest in nanomedicine; production issues such as the lack of quality control, reproducibility, and scalability of most nanostructures of commercial interest; confusion and delay at the PTO (with respect to the burgeoning number of bionanotechnology-related patent applications) and FDA (with respect to a lack of clear regulatory/safety guidelines); pricing pressures due to high industry margins; a sharp decline in public confidence in the pharma industry generally; state and federal government's increased vigilance pertaining to hyperaggressive business practices (e.g., illegal drug marketing and improper drug pricing); and the media's continuing focus on the negative aspects of nanomaterials (environmental, health, and safety concerns are at the forefront).

† Report: *Nanobiotechnology Opportunities and Technical Analysis.* San Mateo, CA, Front Line Strategic Consulting (2003).

‡ Sesquehanna Financial Group LLP, Griffin Securities, Inc.

§ Report: *Nanotechnology in Healthcare.* The Freedonia Group, Inc. Cleveland, OH (2007).

¶ Intangible assets, as a portion of corporate market capital, are steadily rising.

Patent law is a subtle and esoteric area of law that has evolved in response to technological change. It has been modified numerous times since 1790, the year the first U.S. Patent Act was enacted.* This is due to new interpretations of existing laws by the PTO and by the courts, or by creation of new laws by Congress, often in response to new technology. Patent law, arguably one of the most obscure legal disciplines, is now at the forefront of bionanotechnology.†

Patentable inventions need not be pioneering breakthroughs; improvements of existing inventions or unique combinations or arrangements of old formulations may also be patented. In fact, majority of inventions are improvements on existing technologies. However, not every innovation is patentable. For example, abstract ideas, laws of nature, works of art, mathematical algorithms, and unique symbols and writings cannot be patented. Works of art and writings, however, may be copyrighted and symbols may be trademarked. Laws of the universe or discoveries in the natural world, even if revolutionary, cannot be patented. For instance, Einstein's Law of Relativity cannot be considered anyone's IP. For a U.S. patent to be granted, an invention must meet specific criteria as set forth in U.S. statutes (Table 27.1).

A U.S. patent‡ provides protection only in the United States, its territories, and its possessions for the term of the patent. It is estimated that 90% of the world's patents are issued through the three main patent offices—the United States, Europe, and Japan. Legally speaking, a U.S. patent is a document granted by the federal government (at the PTO§) whereby the recipient (or "patentee") is conferred the temporary right to exclude others from making, using, selling, offering for sale, or importing the patented invention into the United States for up to 20 years from the filing date. Similarly, if the invention is a process, then the products made by that process cannot be imported into the United States. All patented inventions eventually move "off" patent at the end of their patent term ("patent expiration") at which time they are dedicated to the public domain. This is the basis

* The Founding Fathers incorporated the concept of patents into the Constitution under Article 1, Section 8, Clause 8, whereby Congress was given the authority "[t]o promote the progress of science and the useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries." President Washington signed the first U.S. Patent Act on April 10, 1790. Title 35 of the *United States Code* codified the Patent Act of 1952, the Act currently in use. Since the granting of the first U.S. patent in 1790, more than 7 million patents have been issued by the PTO, a bureau of the U.S. Department of Commerce. In fact, 1790 was the first year of operation for the PTO and it issued only three patents. On the other hand, in the 2006 fiscal year, 183,187 patents were issued. For the past few years, the PTO has received over 400,000 patent applications annually. In 2006, the average pendency ranged from 25.4 to 44 months. The number of patent applications filed has been increasing, on average, by over 10% per year since 1996. Currently, there is an astounding backlog of over 1 million unexamined U.S. patent applications.

† It seems that in the new millennium, patent issues are making headlines on a daily basis. As the line between academia and industry becomes fuzzier, the axiom for success in science, "publish or perish," is being replaced with "patent or perish" or "patent and prosper." Universities are straying away from their "education mission" by focusing on patents for potential license revenue. I believe that patents are as important, if not more so, as publications on *curriculum vitae*, and have a major impact in academia on hiring, tenure, and promotion.

‡ A patent is not a "hunting license"; it is merely a "no trespassing fence" that clearly marks the boundaries of an invention. (For example, see *Brenner v. Manson*, 383 U.S. 519, 536 [1966]). In other words, a patent grant is a negative grant; it prevents other parties from using the invention without prior permission of the patent holder (which can be in the form of a license). This does not imply that the patent holder can automatically publicly practice (i.e., commercialize) the invention. Often, appropriate government regulatory approval is required.

§ The PTO issues three types of patents as defined by U.S. statutes: (a) utility patents for "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof"; (b) plant patents for "any distinct and new variety of plant" (i.e., asexually reproduced non-tuber plant varieties); and (c) design patents for "any new, original and ornamental design for an article of manufacture." (i.e., ornamental designs of an article of manufacture).

TABLE 27.1
Legal Requirements to Obtain a U.S. Bionanotechnology Patent

U.S. Patent Statute	Brief Description of Statue
35 USC § 102 Novelty requirement	Invention must be novel (i.e., sufficiently new and unlike anything that has been previously patented, marketed, practiced, publicized, or published).
35 USC § 103 Nonobviousness requirement	Invention must be nonobvious to a person with knowledge in the field related to the invention, meaning that the person would not automatically arrive at the present invention from a review of existing ones (i.e., trivial variations that are readily apparent to a person with knowledge in the field related to the invention cannot be patented).
35 USC § 101 Utility requirement	Invention must have utility (i.e., the invention has some use and it actually works or accomplishes a useful task).
35 USC § 112(1) Written description requirement	Invention must be adequately described to the public to demonstrate "possession" of the invention at the time of filing.
35 USC § 112(1) Enablement requirement, part I	Invention must enable a person with knowledge in the field related to the invention to make or carry out the invention without "undue experimentation" (i.e., to make the claimed product or carry out the claimed process).
35 USC § 112(1) Enablement requirement, part II	Invention must enable a person with knowledge in the field related to the invention to use the invention.
35 USC § 112(2) Clarity requirement	Invention must be described in clear, unambiguous, and definite terms.
35 USC § 112(2) Best mode requirement	Invention must set forth the best mode of making or using the invention, contemplated by the inventor at the time of filing of the patent application.

Note: USC stands for U.S. Code.

for low-cost generic drugs* that appear in the marketplace following expiration of the costlier versions of the patented branded drug.†

The basic rationale underlying patent systems, both in the United States and abroad, is simple enough: an inventor is encouraged to apply for a patent by a grant from the government of legal monopoly of limited duration for the invention. This limited monopoly or proprietary right justifies R&D costs by assuring inventors the ability to derive economic benefit from their work. In exchange for this grant, the inventor publicly discloses the new technology that might have oth-

* Generic Drugs: Questions and Answers, U.S. Food and Drug Administration, Center for Drug Evaluation and Research, http://www.fda.gov/cder/consumerinfo/generics_q&a.htm (last accessed April 9, 2008).

† Current U.S. patent laws allow granting a patent on new drug formulations that have been created from old drugs, for instance, via novel drug delivery systems (DDS). Nanotechnology could also allow reformulation of existing and orphaned compounds. These new reformulations may qualify as NCEs at the FDA and for patents at the PTO. In other words, "nanoformulations" of older drugs may be patentable as long as they fulfill all the criteria for patentability. Furthermore, innovative DDS or platforms may be patented on their own under current U.S. patent statutes. Innovative DDS could enable drug companies to devise novel drug reformulations of off-patent or soon-to-be off-patent compounds. This strategy could delay or discourage generic competition during the most profitable years of an innovator drug's life cycle, especially if the reformulated drug is superior to its off-patent or soon-to-be off-patent counterpart. This approach, in effect, stretches the product life cycle of an existing, branded, patented drug. This strategy, commonly referred to as "product-line-extension," is broad in scope and includes any second-generation adaptation of an existing drug that offers improved safety, efficacy, or patient compliance. In fact, successful reformulation strategies should focus on how to add value through added ease and convenience for the consumer. If this approach is successful, the innovative DDS or platforms can maintain market share even after generics appear in the marketplace. Another often-employed approach is to develop and patent a novel polymorph of the innovative drug compound prior to patent expiration. Yet another strategy involves generating patent protection from a competitor's formulation (patented or off patent), by analyzing the competitor's existing patent claims, then tweaking them and filing patents that circumvent the competitor's specific use or DDS.

erwise remained secret (an "immediate benefit" to the public) and allows the public to freely use, make, sell, or import the invention once the patent expires (a "delayed benefit" to the public). Hence, the new technology that is brought to light in the form of valuable technical information provides a continuous incentive for future innovation. In this way, society obtains a *quid pro quo* from inventors in exchange for the temporary grant of exclusive rights. Such an advantageous exchange stimulates commerce (a "long-term benefit" to the public). Patent protection is the engine that drives industry and the incentive for it to invest in R&D to innovate. Clearly, without such protection, most companies would avoid costly R&D, and society would be deprived of the many benefits thereof. However, it is critical that the scope or breadth of the patent issued by the PTO be just right; it should neither be unduly broad nor should it be too limiting. In other words, the invention granted a patent should just fit within the boundaries of that patent. Unfortunately, this is not often the case (see Section 27.9).

Obtaining a patent for an invention is often a long, expensive, and tedious process that generally involves the inventor, patent counsel, or practitioner (i.e., patent agent or patent attorney) and PTO staff (especially a "patent examiner"). Patent examiners are PTO personnel who review the filed patent application to ensure that it fulfils all pertinent requirements of the law (Table 27.1). This review process is commonly referred to as an "examination." The exchange of documents between the PTO and the patent counsel is broadly known as "prosecution." If the examiner believes that all requirements for a patent are met, then a "notice of allowance" is issued to the applicant. Following this, a patent is issued once the applicant pays an "issuance fee." Upon issuance, the entire contents of the patent application ("the file wrapper" or "prosecution history") along with a copy of the patent and all future documents pertaining to the patent, are made available to the public. The entire patent examination process, starting with the filing of the patent application to its allowance or final rejection, may take anywhere from 1 to 5 years, or longer. This depends upon variables such as the specific technology area within the PTO where the patent is being reviewed by the patent examiner and the time to process the paperwork that accompanies the patent application by the PTO clerical staff. As part of the patent prosecution, all applications filed on or after November 29, 1999, are generally published 18 months after filing (see also Section 27.7).

Because, for most patents, the patent term commences on the date of filing and ends 20 years thereafter, most commercially valuable bionanotech inventions are, in reality, in the marketplace prior to the actual patent grant date (unless regulatory approval is sought). Generally, it is impossible to predict the future commercial success or commercial viability of an issued patent. In part, this is due to the fact that most patents are filed at the PTO without any clear idea of whether the invention is commercially valuable. For example, in bionanotech, patent applications are continuously being filed on a large number of drugs, therapies, and devices even before it is known that they will be ruled safe and effective by the FDA. If litigation rates (which range from 1.5 to 2% of the issued patents) are any indicator of commercial value, then only a tiny fraction of patents are commercially significant. Although obtaining a patent does not ensure commercial success, economists view patenting as an indicator of scientific activity.* They argue that this is the basis for providing a nation with a competitive advantage, fueling its economy.

In recent years, however, patents have become the subject of much debate and controversy. In fact, there are plenty of antipatent players in the field who feel that patent laws (and most international treaties) are unfairly providing an economic advantage to some over others.† It has even been suggested that patent laws and IP are the products of a new form of Western colonialism designed to deny the developing world access to common goods. Issues like biopiracy and IP theft have been proffered as reasons for the unavailability of essential drugs to the poorest and neediest people in

* Merges RP: Commercial success and patent standards: Economic perspectives on innovation. *Cal L. Rev.* 76, 803–845 (1988).

† McGrath M: The patent provisions in TRIPS: Protecting reasonable remuneration for services rendered—Or the latest development in Western colonialism. *European Intellectual Property Review* 18, 398–453 (1996).

the world. Not surprisingly, those in the developing world support patent protection but prefer a regime that suits their own national interests. In this regard, they highlight the fact that although Western drug companies continue to cite the need to reward innovation as a justification for stronger patent laws or patent enforcement, the industry, in reality, continues to spend more on reformulating preexisting drugs and on expensive litigation to protect their current patents than to innovate.* Future struggles over patents on the international stage are almost certain to focus on multinational drug patents when they are revoked or challenged.†

The PTO does not police or monitor patent infringement and it does not enforce issued patents against potential infringers. It is solely up to the patentee to protect or enforce the patent, all at the patentee's own cost. The patentee may enlist the U.S. government's help via the court system to prevent patent infringement. However, PTO decisions are subject to review by the courts, including the Court of Appeals for the Federal Circuit (CAFC),‡ and rarely, the U.S. Supreme Court. Sometimes Congress intervenes and changes or modifies some of the laws governing patents. If a court deems a patent to be invalid, the patent holder is unable to enforce it against any party. However, suing an alleged infringer is a risky business because when a patent holder sues an alleged infringer, in certain technologies, there is a 50% risk that his own patent will be found to be invalid.

Based on my review of seminal CAFC patent decisions from the past decade or so, it is my conclusion that the CAFC has fostered the following: (a) expanded what can be patented under the patent statues; (b) lowered the threshold to obtain a U.S. patent; and (c) tilted its decisions in favor of patent holders. Clearly, this stance has resulted in stronger patent protection for patent holders. As a result, since the creation of the CAFC, the number of patents granted has increased at an annual rate of 5.7% as compared to less than 1% from 1930 to 1982.§ According to some experts, if this trend continues, it could stifle competition and limit access to some inventions. Moreover, this is contrary to the *quid pro quo* discussed earlier: it disturbs the delicate balance between the patent holder's limited-time monopoly over the invention on the one hand and the public's interest in accessing the invention's disclosure (from the public domain) on the other hand. Certainly, this could be the very reason why the Supreme Court is increasingly stepping in to hear more and more patent appeals of CAFC decisions. It is important to note that the Supreme Court, which has rarely reviewed patent decisions in the past, has heard at least five important patent appeals of CAFC decisions in the last 4 years alone, reversing all of them. One of these recent landmark rulings,¶ that broadly impacts bionanotechnology, allows drug companies to infringe drug patents held by others as long as the infringement is during the R&D phase (i.e., preclinical phase) of drug development and generates data (on the compound being tested) that may (or may not) be ultimately submitted to the FDA as part of the drug approval process. By these and other recent decisions, the Supreme Court may be trying to reestablish the balance between the patent holder and the public's interest, a certain flexibility that it may have viewed as eroding under the CAFC. It is critical that the CAFC refocus its efforts to provide greater clarity to patent law and render patent decisions that are more consistent. After all, this is its true mission.

One highly controversial yet important statistic worth briefly discussing is the patent grant rate (i.e., the patent application allowance rate). Because the PTO is often not very forthcoming in providing accurate patent statistics and data on this issue,** several legal scholars have published studies to gauge this figure. One widely cited estimate places the average PTO grant rate at 77% to 95%

* Saini A: Making the poor pay. *NewScientist* 193(2597), 20 (2007).

† Tremblay JF: Drug patents struggles in Asia. *Chem. Eng. News* 85(6), 11 (2007).

‡ The CAFC was created by Congress in 1982 with the aim of creating uniformity in the patent law, especially with respect to unpredictable, evolving technologies like biotechnology and nanotechnology. In reality, it has sometimes failed in this role by rendering inconsistent and contradictory patent decisions.

§ Jaffe AB, Lerner J: *Innovation and its Discontents: How Our Broken Patent System Is Endangering Innovation and Progress*. Princeton University Press, Princeton, NJ (2004).

¶ *Merck KGaA v. Integra Lifesciences I. Ltd. et al*. 545 U.S., No. 03-1237 (2005).

** Wegner H: The USPTO's 54% allowance rate. IPFrontline.com, Dec. 30, 2006, http://www.ipfrontline.com/depts/article.asp?id=13796&deptid=5 (last accessed May 4, 2008).

of filed patent applications for the years 1981 to 2005.* However, I agree with legal scholars who consider this estimate to be artificially high, because it is based on an inappropriate legal framework and somewhat flawed numbers.† In any case, it is immaterial as to what the exact figures are; the crux of the matter is that the PTO grant rates are rather high and this may indirectly reflect a less rigorous review of patent applications as compared to the other major patent offices. In other words, these high allowance rates may be partly to blame for the granting of poor-quality patents by the PTO.‡ (Other concerns are discussed in detail in Section 27.8.) In this context, it is interesting to note that the time taken for one million patents to be granted has greatly declined since the grant of the first patent in 1836.§,¶

27.6 SIGNIFICANCE OF BIONANOTECHNOLOGY PATENTS

Patents are critical to the bionanotech "revolution." When investors in nanomedicine or drug companies consider the merits of their investment, patent issues are one of the most important items they review. There is also ample evidence that companies, start-ups, and universities are ascribing ever-greater value and importance to patents. Increasingly, they are willing to risk a larger part of their budgets to acquire and defend patents. The process of converting basic research in bionanotech into commercially viable products is proving to be long and difficult. The development of bionanotech-related technologies is extremely research intensive, and without the market exclusivity offered by a patent, development of these products and their commercial viability in the marketplace would be significantly hampered.

Patents are especially important for start-ups and smaller companies because they may help in negotiations over infringement of their patents during competitive posturing with larger corporations.** In fact, patents may also protect the clients of a patent owner because they prevent a competitor from infringing or replicating the client's products made under license from the patentee. Moreover, patents provide inventors credibility with their backers, shareholders, and venture capitalists—groups who may not fully understand the science behind the technology. Generally, patents precede funding from a venture capital firm. For a start-up company, patents are not only a means of attracting investment, but also serve to validate the company's foundational technology. Therefore, start-up companies aggressively seek patents as a source of significant revenue. They cite the potential for licensing patents and the power to control emerging sectors of nanotechnology as major rea-

* Quillen CD, Webster OH: Continuing patent applications and the USPTO—Updated. *Federal Circuit Bar Journal* 15, 635 (2006).

† Ebert LB: On patent quality and patent reform. *Journal of the Patent & Trademark Office Society* 88(12), 1068–1076 (2006).

‡ In light of this discussion regarding patent allowance rates and patent quality, it is rather interesting to note the PTO's recent announcement of a 54% allowance rate for the past fiscal year (October 1, 2005 to September 30, 2006). In this regard, it is further worth noting that while the number of patent applications has continued to climb (creating a steady backlog that threatens businesses), the number of issued patents has declined in recent years. The most dramatic decline was in 2005 when a drop of 11% in the allowance rate was reported from the previous fiscal year. Do these figures imply a vast improvement in patent quality over the earlier years when allowance rates were much higher? Most experts would disagree. If this is not the case, then is it possible that numerous high-profile patent cases (like the recent BlackBerry case) have oversensitized PTO upper management, who are now actively engaged in artificially suppressing the high patent grant rate? If this is indeed the case, all this tinkering with numbers will have disastrous consequences for the entire innovation process. Moreover, it is clearly contrary to the basic tenet of the U.S. patent system: "[t]o promote the Progress of Science and Useful Arts." (U.S. Constitution. Article I, Section 8, Clause 8)

§ The first U.S. patent was issued in 1790, and the numbering system was established in 1836.

¶ Press Release, USPTO, USPTO issues 7 millionth patent. Feb. 14, 2006, http://www.uspto.gov/web/offices/com/speeches/06-09.htm (last accessed May 4, 2008).

** Often, larger competitors employ frivolous lawsuits to pressure smaller companies or start-ups whose patents stand in their way, or which they wish to acquire. Frequently, the cost in executive time and corporate money for the smaller company or start-up becomes so onerous that it caves in to a licensing agreement. One viable strategy to avoid being taken over is to license the patent to the large competitor, in whose interest it then becomes to protect its position by protecting and defending the patent.

sons for seeking patents on bionanotech-related technologies.* Moreover, venture capitalists will not support a start-up that relies on trade secrets alone. In sum, investors are unlikely to invest in a start-up that has failed to construct adequate defenses around its IP via valid, enforceable patents. Numerous technologies and techniques pertaining to bionanotech can be protected via a patent (Table 27.2).

A company seeking a dominant position in a particular sector of bionanotech may wish to review patent citations (i.e., patents cited in other patents). Patent citations can serve as a useful indictor of licensing potential: patents that are repeatedly cited are generally considered more commercially valuable.† One quarter of all patents receive no citations, and a mere 0.01% earn greater than 100 citations.‡ According to one study, a patent cited 14 times in other patents is, on average, 100 times more valuable than a patent cited only 8 times.§

Millions of dollars may be lost if a company fails to take the necessary steps to protect its patent assets. Securing valid defensible patent protection is vital to the long-term viability of virtually any drug or biotechnology company, whether nanotechnology is the platform technology involved or not. Often, loss of these critical assets is a result of both the researcher's excitement with his or her research as well as general ignorance about IP. In fact, experts agree that "patent awareness" (i.e., the knowledge that patents are intangible property that can be obtained and lost) is central to any business plan or strategy.¶ Furthermore, it is essential that managers and patent practitioners implement certain proactive measures to "box out" the competition (Table 27.3).** In other words, taking the correct preventive steps is critical to realizing the full commercial potential of an invention. Because nanomedicine interfaces with fields such as biology, physics, chemistry, engineering, medicine,

TABLE 27.2
Various Bionanotechnologies That Can Be Protected via a U.S. Patent

- Biopharmaceutics
  - Drug delivery
    - Drug encapsulation
    - Functional drug carriers
  - Drug discovery
- Implantable materials
  - Tissue repair and replacement
    - Implant coatings
    - Tissue regeneration scaffolds
  - Structural implant materials
    - Bone repair
    - Bioresorbable materials
    - Smart materials
- Implantable devices
  - Assessment and treatment devices
    - Implantable sensors
    - Implantable medical devices
  - Sensory aids
    - Retina implants
    - Cochlear implants
- Surgical aids
  - Operating tools
    - Smart instruments
    - Surgical robots
- Diagnostic tools
  - Genetic testing
    - Ultrasensitive labeling and detection technologies
    - High-throughput arrays and multiple analyses
  - Imaging
    - Nanoparticle labels
    - Imaging devices
- Understanding basic life processes

* Regalando A: Nanotechnology patents surge as companies vie to stake claim. *Wall Street Journal* June 18 Issue, A1 (2004).
† McKie S: Innovation asset management: Don't bottle up creativity. *Intelligent Enterprise*, Dec. 1, 2006, http://www.intelligententerprise.com/showArticle.jhtml?articleID=194500328 (last accessed June 10, 2008).
‡ Farrell C: Follow the patents. *BusinessWeek* January 8 Issue, 78–79 (2007).
§ See *supra* Note ‡.
¶ Forman D: IP storm clouds build on horizon. *Small Times* 21–24 (2004).
**Bawa R, Bawa SR, Maebius SB, Iyer C: Bionanotechnology patents: Challenges and opportunities. In: *The Biomedical Engineering Handbook* (3rd Edition). Bronzino JD (Ed.), CRC Press, Boca Raton, FL; 29-1–29-16 (2006).

TABLE 27.3
Legal Tactics Available to Bionanotechnology Companies Dealing with Patent Disputes

Predispute strategies	*Strategic patenting* to clearly box out the competition (i.e., patent-drafting guidelines used to obtain broad, enforceable patents that preempts the field).
	Patent interference practice to attack a competitor's patent application, thereby preventing overlapping patents from being issued.
Postdispute strategies	*Patent reexamination,* a procedure for legally challenging a competitor's issued patent.
	Cross-licensing of patents to peacefully coexist with a competitor.
	Patent infringement litigation to invalidate a competitor's overlapping claims.

TABLE 27.4
Inventor's Reality Checklist and Complex Marketing Factors

- Does the invention offer a unique solution to a real problem?
- Does it offer a measurable improvement over previous attempts to solve the problem?
- Is it a stand-alone product or part of an existing product?
- Can it be easily manufactured or integrated into an existing product or system?
- How big is the potential market?
- Is the market growing or shrinking?
- Is the market global? Can the invention be expanded into new markets as they evolve?
- Will the invention become passé before a prototype is designed?
- Who are the prospective investors, partners, or licensees in the field?
- What price will consumers put on its value?
- What are the estimates for commercialization and marketing?
- What are the incentives for the consumer to buy the product?
- Is federal regulatory approval required?
- How long will it take to bring the product to market?

and computer science, filing a patent application (or conducting a patent search) in this field may require expertise in these diverse disciplines. Hence, employing a qualified patent counsel (a patent agent, patent attorney, or a multidisciplinary team of lawyers) who understands the legal and technical complexities is a critical step in obtaining quality patents. Additionally, issued patents and other prior art* should be carefully evaluated and effective patent-drafting strategies devised accordingly. In 2005, the PTO proposed several sweeping changes in patent practice that could significantly alter the way in which bionanotechnology companies file and prosecute patent applications.† Therefore, companies may need to rethink their patent strategies in order to maximize their patent rights, including taking appropriate proactive action on pending patent applications prior to the actual implementation of these new rules. Additionally, many complex marketing factors may need to be carefully evaluated (Table 27.4).

* The phrase "prior art" refers to various sources of information that the PTO uses to reject a patent application. In other words, it is the "knowledge" that exists in the public domain prior to the date of the invention. Prior art is often in the form of a printed document that contains a disclosure or description that is relevant to an invention for which a patent is being sought or enforced. It can include documentary material like publications, prior patents, Web sites, or other disclosures that suggest that the invention is not new. It can also include evidence of actual uses or sales of the technology within the United States. Typically, prior art is submitted by the inventor during prosecution of his or her patent application.

† Notice: Changes to practice for continuing applications, request for continued examination practice, and applications claiming patentably indistinct claims. *Federal Register* 71(1), 48 (2006); Notice: Changes to practice for the examination of claims in patent applications. *Federal Register* 71(1), 61 (2006).

The phrases "patent value" and "patent quality" are distinct concepts; however, they are somewhat related. Both of these largely determine a patent's potential for commercialization, licensing opportunities, investor interest, and enforceability:

1. Patent quality is generally assessed by determining the degree to which a patent examiner has made proper, timely decisions about the validity and scope of protection during the examination process that are consistent with the legal ruling a court would make after comprehensive review of the same application.
2. On the other hand, the patent value of an issued bionanotechnology patent is often measured in terms of other factors ("valuation metrics"):
   a. The breadth and scope of the issued patent claims that affect others freedom to operate (i.e., the patent's originality)
   b. The number of potential competitors in that particular sector of nanomedicine
   c. Government fees ("maintenance fees") paid in order to keep the patent enforceable*
   d. The patent's applicability to other fields
   e. Licensing and litigation activity surrounding the patent
   f. The frequency by which that patent is cited by others (discussed earlier)
   g. Other IP held by the patent holder in that particular technology, including any blocking, pioneering, or upstream patents

27.7 KEY STRATEGIES FOR BIONANOTECHNOLOGY INVENTORS

There are certain key considerations and strategies that a bionanotechnology inventor and his or her company must follow in order to adequately protect an invention even before a patent application is drafted or filed. Some of these are discussed briefly below.

27.7.1 Avoid Any Early Publication or Any Public Disclosure

The inventor should refrain from publishing a description of, publicly presenting, submitting grant proposals for, or offering the invention for sale prior to filing a patent application. Often a company releases information on a new product, or discusses details during negotiations prior to filing a patent application. All of these activities create prior art against the inventor and can trigger a 1-year "on-sale bar." Note that one of the criteria for patentability in the United States is that the invention must be "novel" (Table 27.1) and not appear in the public domain in the form of prior art. According to current U.S. patent law, the inventor has 1 year to file for an application from the date that invention is known of or offered for sale (meaning that any public disclosure triggers a 1-year deadline to file a patent application in the United States). On the other hand, because this 1-year grace period is not offered by foreign patent offices, any publication or public disclosure will prevent the inventor from obtaining a foreign patent altogether, or prevent the inventor from realizing the full range of potential applications for which a patent is being sought overseas. In summary, a patent application should be drafted and filed as soon as possible after the completion date of the invention to realize its full commercial potential.

27.7.2 Consider Obtaining a Foreign Patent

Filing a bionanotechnology patent in a foreign country should be carefully considered and should largely depend upon commercial considerations. If there is an interest in expanding into foreign markets, then obtaining patents abroad should be seriously considered. Furthermore, even if the inventor does not plan to establish a market for the particular bionanotechnology invention in a foreign country, obtaining a patent there could be critical in securing licensing deals (and discouraging

* All utility patents that issue from a patent application filed on or after December 12, 1980, are subject to the payment of maintenance fees to the PTO to maintain them in force. Failure to pay maintenance fees on time results in the expiration of the patent.

unlicensed copying or use by foreign competitors). The danger of steering clear of foreign patent filing is that a competitor could commercialize the invention in a foreign country and capture valuable market share there. For example, an inventor who patents a novel dendrimer-based drug-delivery system only in the United States is essentially giving away the entire technology to other countries because the patent discloses the best method of making this novel system.

Most U.S. inventors seeking foreign bionanotechnology patents first file a U.S. patent application (known as the "national stage" application) and follow it with a patent application under the Patent Cooperation Treaty (PCT). The PCT is a multilateral treaty that was established in 1978. As of January 1, 2008, it has 138 member states. The PCT allows reciprocal patent rights among its signatory nations. In other words, it simplifies the patenting process when an inventor seeks to patent the same invention in more than one country. It should be emphasized that there is no "world patent." Inventors have a year after filing the national stage patent application to file in the foreign country under the PCT. Under PCT rules, inventors can specify particular foreign countries where they intend to seek patent protection for their bionanotechnology invention and may take 30 months (or more) from their original national stage application filing date (priority date) to complete all foreign application requirements under the PCT (international phase). This delay may provide the inventors with time to determine whether their bionanotechnology invention is commercially viable and merits patenting in several countries, thereby sparing them substantial effort and expense should they decide not to file overseas.

27.7.3 Beware of Pregrant Publication of U.S. Patent Applications

Today, as part of the application process, all U.S. patent applications are published 18 months from the earliest filing date (up to that point, during prosecution, they are kept confidential), unless the applicant "opts out" and foregoes foreign patent filing. Traditionally, applications filed at the PTO were kept secret until they matured into a patent. However, because of the American Inventors Protection Act (AIPA) of 1999, an application filed on or after November 29, 1999, generally loses its secret status when it is published. In effect, this implies that almost always a patent application, as filed, will eventually appear in the public domain (whether or not it is patented) and will be available to competitors.

27.7.4 Maintain Proper Laboratory Notebooks

Laboratory notebooks often contain valuable and critical information that may not be readily apparent to a company or its R&D facility. Therefore, it is critical that laboratory notebooks be maintained properly. This is especially important when working in research teams. Here, proper laboratory notes documenting the creative effort, maintaining confidentiality, and securing communication among the teams and filing for a patent promptly are essential steps that safeguard inadvertent or premature invention disclosure of one group's work by another group. Laboratory notebooks are also useful to patent practitioners to establish the date of an invention, especially in light of a competitor's challenge in court as to who invented first in what is known as "interference proceeding."

27.7.5 Conduct a Prior Art Search and a "Freedom-to-Operate" Search

It is highly recommended that a proper prior art search be conducted prior to filing a patent application. The purpose of this is to guage the competition. This may also assist the inventor to design around potential prior art. Moreover, because the patent owner does not automatically have the right to practice his/her invention, it may be wise to conduct a "freedom-to-operate search" of the issued bionanotech patent prior to investing in and commercializing it. Note that filing a patent application (or conducting a prior art or freedom-to-operate search) on novel bionanotechnology such as a nanoparticle drug delivery system may require expertise in diverse disciplines like biotechnology, physics, medicine, chemistry, and engineering. The quality and value of the issued patent (see Section 27.6 for details) will largely determine its potential for commercialization, licensing opportunities, investor interest,

and enforceability. Hence, employing qualified patent practitioners who understand the legal standards and the complexities of the technology at hand is a critical step to obtaining quality patents.

27.7.6 Educate Employees and Researchers

It is important that business and IP professionals within a company educate scientists to spot potential inventions during the R&D phase, as this may not always be apparent to them. In fact, a company should implement policies involving incentives where scientists are rewarded for reporting or submitting invention disclosures. This may be especially critical in a university setting where generating invention disclosures may be less of an incentive to researchers who are promoted or tenured based on their research grants. Scientists often overlook the fact that their inventions can be patented. Further, "patent awareness" may enable a researcher to pursue a particular research path that has a greater likelihood of leading to a patentable invention.

27.7.7 Require Strong Employment Agreements to Safeguard IP

Companies must require all employees to sign agreements that clearly specify that all company inventions, intellectual property, and proprietary information is company property and cannot be disclosed or exploited by any employee at any time. This could become critical if a former employee joins a competitor company or research laboratory. Similar agreements should be required of consultants and visiting scholars where all rights are assigned to the company or university. Nondisclosure agreements should be required during negotiations for venture capital or licensing discussions. Furthermore, confidential materials should be properly labeled and safeguarded; otherwise, value associated with specific information or invention may be lost or reduced.

27.7.8 Employ Standard Terminology While Drafting Patent Applications

The fact remains that bionanotechnology is an inherently difficult topic for discussion, in part due to the confusion surrounding its definition (see Sections 27.2 and 27.8). Although it is well recognized in patent law that a patent applicant can be his or her own lexicographer, it is recommended that an applicant should employ standard language in bionanotechnology patent applications whose meaning is well recognized in the pharmaceutical, medical, or biotechnology fields. Nondisclosure agreements should be required during negotiations for venture capital or licensing discussions. Furthermore, the language should be precise and the use of terms consistent throughout the claims and specification (avoid synonyms and be repetitive in the use of phrases when appropriate). This will prevent confusion at the PTO as well as prevent possible prosecution delay.

This can be especially advantageous later on if litigation arises. Note that it is possible that the patent will be the subject of litigation in the future (e.g., an infringement suit initiated by the patentee against a competitor or a suit for declaratory relief initiated by an accused competitor/infringer, asking a court to declare a patent invalid). The success of the litigation may hinge on how the patent was drafted. A poorly drafted patent will give an advantage to the competitor, causing significant aggravation and resulting in substantial litigation fees for the inventor. Therefore, while drafting patent applications, the drafter should anticipate that the patent might have to be defended in court. Moreover, poorly drafted patents can adversely affect patent issues like licensing potential, validity, and enforceability.

27.7.9 Relative Ease of Obtaining "Broad" Patents in Bionanotechnology

Broad patents continue to be issued by the PTO in bionanotechnology.* The overburdened PTO faces new challenges and problems as it attempts to handle the enormous backlog in bionanotechnology

* O'Neill S, Hermann K, Klein M, Landes J, Bawa R: Broad claiming in nanotechnology patents: Is litigation inevitable? *Nanotechnology Law and Business* 4(1), 595–606 (2007).

applications filed and the torrent of improperly reviewed patents granted. At present, all these factors favor obtaining broad patents in bionanotechnology. (See Section 27.9 for details.)

27.8 SEARCHING BIONANOTECHNOLOGY PATENTS AND OTHER PRIOR ART—ISSUES AND CHALLENGES

27.8.1 New Class 977 for Nanotechnology Patents

Due to the burgeoning number of new patent applications filed at the PTO and continued pressure from industry, in 2004, the PTO finally created a cross-reference classification scheme (also referred to as a cross-reference digest or art collection) for nanotechnology (designated as Class 977/Digest 1). The purpose of this class was described by the PTO on its official Web site in 2004*:

> [E]stablishing this nanotechnology cross-reference digest is the first step in a multi-phase nanotechnology classification project and will serve the following purposes: facilitate the searching of prior art related to Nanotechnology, function as a collection of issued U.S. patents and published pre-grant patent applications relating to nanotechnology across the technology centers and assist in the development of an expanded, more comprehensive, nanotechnology cross-reference art collection classification schedule.

It is important to note that this digest should not be construed as an exhaustive collection of all patent documents that pertain to nanotechnology.

The PTO currently expanded Class 977 into 250 subclasses. As of January 2008, the PTO has placed over 5000 U.S. patents in Class 977. However, these figures should only be considered a rough underestimate of the total number of nanotech-related patents. This is because the PTO has copied the NNI's narrow definition of nanotechnology (see Section 27.2) for classification purposes. This has resulted in a skewed patent classification system, especially with respect to bionanotechnology inventions. Furthermore, this classification scheme is neither sufficiently descriptive enough to accommodate many of the unique properties that nanotechnology inventions exhibit, nor does it address the interdisciplinary nature and range of technologies encompassed.

In conclusion, the PTO's efforts to provide a home for a few thousand U.S. patents via a skewed classification system defeats the very purpose for the creation of Class 977, namely: (a) to gauge the number of nanotechnology patent applications filed and patents issued, and (b) to assist patent practitioners as well as patent examiners in searching nanotechnology patent documents.

27.8.2 Searching Bionanotechnology Prior Art

There are various issues pertaining to bionanotech patent searching that are of concern. For example, some experts state that the PTO lacks effective automation tools to search prior art pertaining to bionanotechnology. Moreover, their databases may not be exhaustive. This problem may be particularly acute regarding nonpatent prior art. Although there has been a dramatic rise in bionanotechnology patent activity, most of the prior art still exists in the form of journal publications, technical reports, and book articles. Web sites and pregrant patent publications provide an additional resource. I believe that a large amount of this wealth of nonpatent scientific literature directed to bionanotechnology or nanomedicine predates many of the patents that have been issued and are currently issuing. It is possible that patent examiners lack access to some of this critical nonpatent information. This is possible either because the PTO does not subscribe to all relevant commercial databases, or because not all patent examiners are experienced searchers. As a result, patent examiners may miss discovering prior art (we have highlighted this in the case of carbon nanotubes [§]). The problem of access to nonpatent information is not unique to bionanotechnology

* New Cross-Reference Digest for Nanotechnology. U.S. Patent & Trademark Office, August 2004, www.uspto.gov/web/patents/biochempharm/crossref.htm

TABLE 27.5
Selected Prior Art Search Databases for Bionanotechnology

Issuing authorities' Web sites	U.S. Patent and Trademark Office (www.uspto.gov), the European Patent Office (www.epo.org), and the Japanese Patent Office (www.jpo.go.jp)
Thomson databases	Derwent World Patents Index, Delphion, Dialog, and Thomson Pharma
IFI CLAIMS patents database	Data on U.S. patents and current patent legal status
STN chemical abstracts database	Chemistry bibliographic data available from Chemical Abstracts Service, including patents and patent families
IMSWorld drug patents international database	Patent family data for commercially significant drugs
INPADOC	European patent search database
JAPIO	Patent abstracts of Japan
Engineering, technology, and scientific databases	INSPEC, EiCompendex, SCISEARCH, and Chemical Abstracts Service
Markets and business databases	Factiva and PROMPT

patent examination; it is seen in most technology areas.* Furthermore, the Internet usage policies of the PTO may prevent patent examiners from accessing all relevant databases to access information.† The issue here may be one of security because prior art searching on the Internet can run the risk of being tracked externally. Given these inferior search capabilities, I agree with the conclusion‡ that "the informational burdens on the examiner are clearly heavy—even before the examiner engages in the heavy lifting of interpreting the prior art."

Given this backdrop, it seems that patent examiners are basing decisions about the grant of bionanotechnology patent on limited information. It is scary to envision that their faulty decision making will shape a nascent industry for years to come. It appears that this information deficit has rendered examination unfocused and inefficient, resulting in the issuance of numerous "unduly broad" patents (Section 27.9).

Add to this confused state of affairs the general difficulty in searching bionanotechnology prior art. Because of its broad and often overlapping definition, searching and retrieving patents and publications is complicated relative to other technology areas. Different terms can refer to the same nanomaterial. For example, nanofibers, nanotubes, nanocylinders, buckytubes, nanowires, and fibrils all refer to carbon nanotubes.§ Because of this particular point, accurately mapping the patent landscape is also a real challenge. Patents or publications that are truly bionanotech-based may not use any specific nano-related terminology. In fact, patents or publications are often written "not to be found" in order to keep potential competitors at bay. On the other hand, there are business-savvy inventors and assignees who use key words incorporating a "nano" prefix into their patents or publications to better market their invention or concept. Therefore, part of the challenge in finding "true" bionanotechnology prior art while searching patent and commercial databases (Table 27.5) is the judicious use of key terms, patent classification codes, and alternative phraseology. Coupling this strategy with additional filtering (via a subject expert) is probably the most reliable way to uncover prior art.

* In view of all this, commentators have questioned the validity of issued patents in general. They state that a "granted patent" cannot be equated with "official government approval and certification of validity": "There can hardly be a patent agent who, privately, will not readily admit that he or she has got lots of things 'past the office' on flimsy grounds. In the nature of things, a patent office, however hard it tries can only be a coarse filter. Patents that pass the filter cannot be taken as necessarily valid." (Blackman M: Editorial. *World Patent Information* 29, 4–7 [2007].)

† Notice: Internet Usage Policy, 64 Federal Register 33,056,33,061, Dept. of Commerce (1999).

‡ Petherbridge L: Positive examination. *IDEA* 173, 182–183 (2006).

§ Harris D, Bawa R: The carbon nanotube patent landscape in nanomedicine. *Expert Opinion on Therapeutic Patents* 17(9), 1165–1174 (2007).

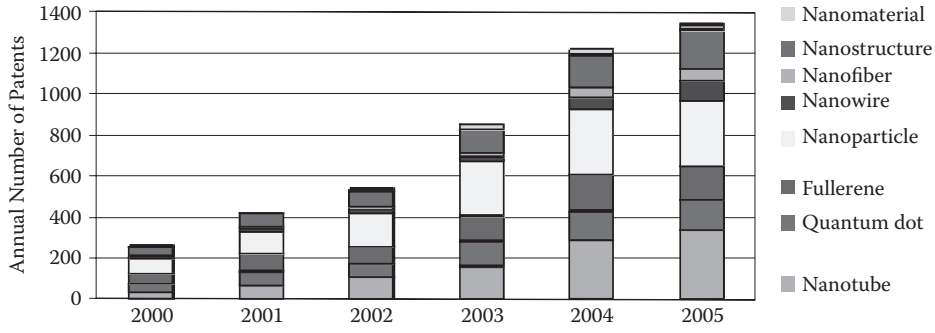

FIGURE 27.1 Nanomaterial-based U.S. patents issued.

27.9 BIONANOTECHNOLOGY PATENT PROLIFERATION AND PTO PROBLEMS—A RECIPE FOR DISASTER?

Federal agencies continue to grapple with nanotechnology.* The PTO is no exception. In fact, for more than a decade, all of the world's major patent offices have faced an onslaught of nanoscience patent applications.† The situation at the PTO is likely to worsen as more applications are filed and pendency rates further skyrocket. As companies develop products and processes and begin to seek commercial applications for their inventions, securing valid and defensible patent protection will be vital to their long-term survival. In the decades to come, with certain areas of bionanotechnology further maturing and promised breakthroughs accruing, patents will generate licensing revenue, provide leverage in deals and mergers and reduce the likelihood of infringement. The development of bionanotech-related products, which is extremely research intensive, will be significantly hampered in the absence of the market exclusivity offered by a patent. Due to the PTO's poor track record in handling issues like examination quality, skyrocketing patent pendency, out-of-control examiner attrition, and low morale, I note the following issues impacting bionanotechnology patenting.

27.9.1 A Chaotic Nanotech Patent Land Grab Continues

Due to the potential market value of bionanotech products, every entity in the international race for technological dominance—researchers, executives, and patent practitioners—views the collection and exploitation of bionanotech patents as critical. In fact, these players are making an effort to obtain the broadest protection possible for new nanoscale polymers, devices, and systems that have applications in biotechnology and medicine. Therefore, a sort of "patent land grab" (Figure 27.1) is in full swing by "patent prospectors" as start-ups and corporations compete to secure broad patents in nanomedicine during these critical early days.‡ This land grab mentality is also fueled by the

* Weiss R: Nanotechnology regulation needed, critics say. *Washington Post*, Dec. 5, 2005, A08, http://www.washingtonpost.com/wpdyn/content/article/2005/12/04/AR2005120400729.html (last accessed May 4, 2008) (suggesting that most federal agencies have not created nanotech-specific safety regulations and discussing EPA's nanotech program, with which companies that manufacture nanotech products may voluntarily choose to comply).

† Bawa, R: Patents and nanomedicine. *Nanomedicine* 2(3), 351–374 (2007); Van Lente MA: Building the new world of nanotechnology. *Case W. Res. J. Int. Law* 38(1), 173–215 (2006); Bawa R: Nanotechnology patents and the U.S. Patent Office. *Small Times* 4, IP8 (2004); Huang Z et al: Longitudinal patent analysis for nanoscale science and engineering: country, institution and technology field. *Journal of Nanoparticle Research* 5, 333 (2003); Bawa R, Bawa SR, Maebius SB: The nanotechnology patent 'gold rush.' *Journal of Intellectual Property Rights* 10, 426–433 (2005); Lawrence S: Patently absurd: Too many patents could kill nanotechnology. *Red Herring* November 20 Issue, 119 (2002); Jaffe AB, Lerner J: Patent prescription: A radical cure for the ailing US patent system. *IEEE Spectrum* 42, 38–43 (2005); Sabety T: Nanotechnology innovation and the patent thicket: Which IP policies promote growth? *Nanotechnology Law & Business* 1(3), 262–283 (2004).

‡ See *supra* pg. 325 Note *.

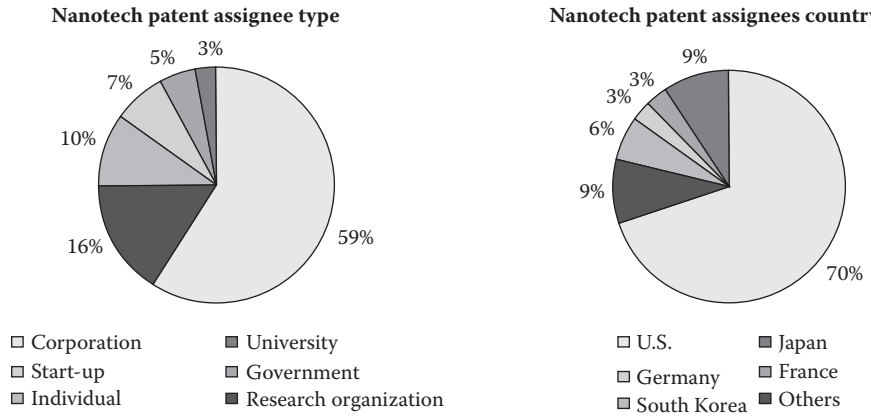

FIGURE 27.2 U.S. Nanotechnology patent demographics.

relative lack of products and processes in the marketplace. Companies feel that, to demonstrate confidence and sway venture capitalists, they must generate or claim IP. Some companies also feel pushed into claiming as much IP as possible due to fear that, if they lag behind in this effort, someone else will claim the broadest IP. Similarly, academic researchers feel this compulsion to file for bionanotechnology patents in order to bolster their reputation and *curriculum vitae*. Moreover, most inventors have quickly realized the opportunities of a disorganized PTO during these early days when they can secure broad patents on valuable upstream technologies with relative ease.

Certain general trends are being reported for nanopatents. With nanotechnology maturing further, the number of claims in the patent applications and the amount of scientific literature cited during patent prosecution is on the rise. This is significant because scientific publications are the most accurate indicator of scientific activity and productivity.* Another trend observed is that nanotechnology patent owners are eyeing commercial potential, and therefore, maintaining (i.e., paying maintenance fees) more of their patents.

However, these patent prospectors have to deal with an overburdened PTO, which historically has been slow to react to emerging technologies like biotechnology and software. In fact, the entire U.S. patent system is under enormous scrutiny and strain as the PTO continues to struggle with the evaluation of bionanotech-related patent applications. Some commentators have strongly voiced their concerns regarding the emerging patent thicket problem and its impact on global access to products.† Some of the concerns highlighted above are borne out by U.S. nanotechnology patent demographics from 2006 (Figure 27.2).

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* Ilakovac V et al: Reliability of disclosure forms of authors' contributions. *Canadian Medical Association Journal* 176, 41 available at http://www.cmaj.ca/cgi/reprint/176/1/41 (last accessed June 10, 2008); Pololi L, Knight S, Dunn K: Facilitation scholarly writing in academic medicine. *Journal of General Internal Medicine* 19(1), 64-68 (2004).

† Report: Nanotech's "second nature" patents: Implications for the global south. ETC Group, Ottawa, Canada (2005).

An extract from the report:

"Although industry analysts assert that nanotech is in its infancy, 'patent thickets' on fundamental nano-scale materials, building blocks and tools are already creating thorny barriers for would-be innovators. Industry analysts warn that, 'IP roadblocks could severely retard the development of nanotechnology.' Some insist that nano-scale technologies will address the most pressing needs of the [world's] marginalized peoples. But in a world dominated by proprietary science, it is the patent owners and those who can pay license fees who will determine access and price….The world's largest transnationals, leading academic labs and nanotech start-ups are all racing in the patent gold rush. Increasingly, universities are licensing on an exclusive basis. Nanotech's 'second nature patents' are positioning multinational matter moguls to own and control novel materials, devices and their manufacturing processes... Control and ownership of nanotechnology is a vital issue for all governments and civil society because nanomaterials and processes can be applied to virtually any manufactured good across all industry sectors… At stake is control over innovations that span multiple industry sectors … companies that hold pioneering patents could potentially put up tolls on entire industries." [Citations omitted]

27.9.2 Problems Plague the Patent Examination Process

Although the PTO budget has bloated to its current $1.6 plus billion mark, various examination problems continue to haunt it. One patent expert recently summarized the current crisis at the PTO*:

> The U.S. Patent & Trademark Office is under siege for issuing patents that should never have issued, and for excessive delays. Congress is considering changes such as a new opposition system for challenging patents when they emerge from examination.

A law professor is blunter in her criticism†:

> The United States patent system is broken and desperately needs fixing.… Why are so many bad patents being issued?… Under our current system, granting an application with little scrutiny takes less time than subjecting it to rigorous review.… The examiners are unable to perform more than a cursory search of their own [due to time constraints and lack of expertise]…Third parties—competitors and consumers—are generally excluded from the patent examination process, even though these parties have the greatest incentive to discover the prior art and disclose it to the Patent Office in order to prevent bad patents from being issued.

Indeed, questionable patent examinations at the PTO seem to extend across technology areas. Some of the shortcomings that impact bionanotechnology patent examination are examined briefly below:

- At present, the PTO lacks a dedicated examining group ("technology center" or TC) to handle applications on nanotechnology or bionanotechnology. Moreover, few examiners have experience in the rapidly evolving field of nanotechnology. Because bionanotech is interdisciplinary in nature, patent applications that are searched, examined, and prosecuted in one TC could and should be examined more effectively by a coordinated review of more than one TC. In reality, there is no such collective review and applications continue to be examined differently within each TC. Obviously, this approach does not provide a cohesive and uniform examination of applications because examiners in each of its eight TCs may rely upon case law, legal standards, and prior art that may be unique to their specific TC.
- Many bionanotech patent applications may not receive adequate examination during prosecution because of the patent examiner's inability to locate applicable prior art, especially nonpatent prior art. Therefore, as discussed in detail earlier (Section 27.8.2), it is accurate to conclude that patent examiners may sometimes be basing decisions about the grant of a patent on limited information.
- The PTO continues to be understaffed in numerous TCs, and it is plagued by high attrition. The agency's inability to attract and retain a talented pool of patent examiners is creating havoc. At hearings on Capitol Hill and in its Annual Reports, the PTO brass proudly touts hiring hundreds of new patent examiners each year to alleviate the backlog that is clogging the patent system. In fact, in this context, the Commissioner for Patents continues to highlight that the PTO will hire 1200 new patent examiners in the current fiscal year to alleviate the backlog that is clogging the patent system.‡ However, it fails to focus on the critical issue of "brain drain" resulting from an exodus of so many experienced patent

* Mcdonald D: Fighting the modern patent wars. *Intellectual Property Today* 14(1), 7 (2007).
† The Press Register. http://ipbiz.blogspot.com/2007/01/lafrance-on-jaffelerner-on-patent.html (last accessed June 10, 2008).
‡ Marasco CA: Overlooked opportunities in government. *Chemical and Engineering News* 85(11), 47–50 (2007).

examiners and other senior-level officials.* It would be desirable for the PTO brass to focus on retaining more of its seasoned employees and not put all its efforts into hiring new ones. These attrition rates are likely to be further exacerbated by poor morale and work conditions. According to many experts, patent examiners are underpaid (relative to U.S. law firm salaries) and overworked (as compared to their colleagues at the European Patent Office). They also have to review applications under unreasonable time pressures and skyrocketing patent pendency (discussed later). Arguably, the internal quality review process that monitors quality of patents allowed by patent examiners is fraught with a general lack of legal and scientific expertise on the part of reviewers.

- The PTO's funding problems are legendary. Congress's long-standing practice of "diverting" PTO user fees collected from patent applicants to the general budget have always caused much consternation. Naturally, stopping this practice would alleviate some problems at the agency. In February 2006, a bill was signed by the President that allows the PTO to spend all its projected collected fees, thereby preventing funds from bring diverted to other government programs. I hope that because of this law, the damaging drain on the agency's financial resources will finally end. It is also hoped that the PTO will now temper its annual practice of hiking patent fees.
- Even today, with all the quality initiatives underway, examiners are still rewarded on the quantity of their work, not the quality. An antiquated quota system is firmly in place. The patent examiner's production goals (quota) have not been adjusted in decades in spite of the increased complexity of patent applications, not to mention the substantial increase in the amount of prior art that the examiner has to search and analyze. Quality continues to take a back seat. Although, year after year, the PTO Annual Reports paint a much rosier picture. According to recent PTO statistics, the allowance error rate has hovered around 4%. This could imply that the PTO's own conservative estimates indicate that thousands of U.S. patents were "wrongly" allowed.†
- The PTO has failed to effectively engage outside legal or technology experts. Only a handful of experts from industry or academia have lectured on legal or technical issues unique to bionanotech. This reluctance to use outside expertise has further added to the information deficit. It is clear that the PTO lacks internal expertise in these matters, and its isolationist policy only compounds the problem. Moreover, patent examiners are not required to have advanced degrees in science or engineering. Possessing advanced degrees or advanced training, by and large, goes unrecognized at the PTO.
- Few training modules or examination guidelines have been developed to educate patent examiners in the complexities and subtleties of bionanotech. Similarly, no written guidelines specific to bionanotech are available for patent practitioners.

Given all these challenges, it is hard to predict with certainty how all these issues and challenges will play out with respect to bionanotech patenting or commercialization. We will have to wait and see whether this industry thrives like the information technology industry, or becomes burdened like the radio patent deadlock.‡

Congress is continuing patent reform hearings in an effort to quell questionable patents as well as to provide adequate safeguards against abuses to the patent system. One of the proposals under serious consideration is a "post-grant review" of patent applications. However, I agree with some patent experts that "[s]erious doubts exist whether a politically controlled PTO can guarantee the promise

* Many reports have highlighted the fact that the federal government is vulnerable to "brain drain" both because baby boomers are retiring and their potential replacements (most notably graduate students) do not view the government as their first choice of work.

† Hultquist S: Statistical musings. *Intellectual Property Today* 14(5), 48 (2007).

‡ Sabety T: Nanotechnology innovation and the patent thicket: Which IP policies promote growth? *Nanotechnology Law & Business* 1(3), 262–283 (2004).

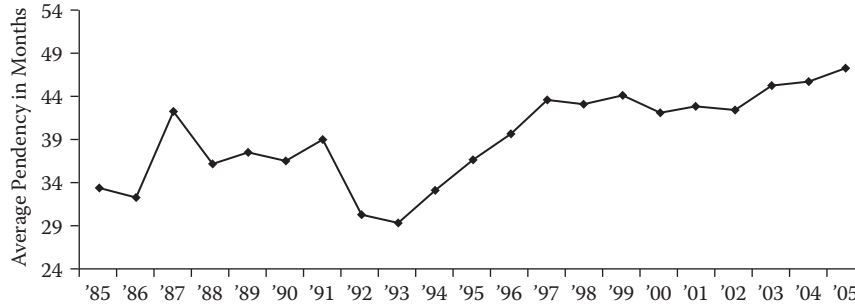

FIGURE 27.3 Nanotechnology patent pendency.

of the post-grant system that the patent community so desperately needs. ... [T]he patent community can hardly have confidence in a post-grant review system under the control of the PTO."*

27.9.3 The Nanotech Patent Onslaught Strains the U.S. Patent Office

For the past decade or so, there has been a dramatic increase in the number of new nanotechnology patent applications filed and patents granted (Figure 27.1) as well as an increase in published patent applications and scientific publications. This information overload has created numerous challenges for the PTO, an agency that traditionally struggles with this issue. Furthermore, this overburdened and inefficient agency has yet to implement a solid plan to handle the enormous growth in nanotechnology patent applications filed. This has resulted in added time to review patent applications (i.e., an increase in patent pendency) and concerns about the validity and enforceability of numerous issued patents (reflects a decrease in patent quality).

As stated earlier, the >1 million backlog of patent applications continues to build. A recent report puts the average nanotechnology patent pendency at 4 years† (Figure 27.3), a period that is simply too long for certain technologies that peak and are then obsolete in a few short years. This excessive delay has particularly serious business consequences for smaller companies and start-ups, as these entities rely heavily on venture funds for their success. Therefore, it was no surprise that these groups recently confronted the Undersecretary of Commerce regarding the high patent pendency of their nanotechnology inventions. Surprisingly, the Undersecretary blamed the excessive delays on nanotechnology companies, accusing them of poaching nanotech-trained examiners en masse from the PTO.‡ I find the Undersecretary's argument a sad excuse for inefficiency and incompetence.

Furthermore, surprisingly broad patents in bionanotech continue to be issued by the PTO.§ Obviously, this is partly the result of court decisions in the past two decades that have made it easier to secure broad patents. Laws have also tilted the table in favor of patent holders, no matter how broad or tenuous their claims. As a result, the PTO faces an uphill task as it attempts to handle the enormous backlog in applications filed. It also faces a torrent of improperly granted patents, many of which are likely to be "reexamined."

In this climate of patent proliferation, it is inevitable that in the near future there will be an increase in litigation. Most patent practitioners regularly highlight one or more of the following problems while discussing bionanotech patents:

- An improper rejection of a patent application due to an examiner's erroneous conclusion that the subject matter is not novel.

* Wegner H: Post grant review: is the PTO up to the task? www.ipfrontline.com/printtemplate.asp?id=15015 (last accessed June 10, 2008).
† *The Nanotech Report* (5th Edition). Lux Research, Inc., New York (2008).
‡ Editor: Poachers to blame for patent delays. *New Scientist* 194(2600), 23 (2007).
§ Bawa R: Patents and nanomedicine. *Nanomedicine* 2(3), 351–374 (2007).

- Issuance of an "overly broad" patent by an examiner that infringes previously issued patents and gives control over a broad swath of basic technology, allowing the patentee to unfairly exclude competition. This runs the risk of impeding important future downstream innovations.
- Issuance of a patent in spite of existing prior art that was overlooked by the examiner during patent examination.

Naturally, any of the above results is unacceptable to the nanotechnology community. Issuance of patents of poor quality, or too many invalid patents on early stage research (upstream technologies) is likely to cause enormous damage to commercialization efforts because it can result in one or more of the following:

- Suppressing market growth and innovation
- Causing loss of revenue, resources, and time
- Discouraging industry from conducting R&D and manufacturing
- Inducing unnecessary licensing
- Promoting a greater possibility of patent appeals and infringement lawsuits
- Stifling high-quality inventions (introducing noise into investment, valuation, and contracting decisions) and undermining the patent system
- Eroding public trust vis-à-vis bionanotech

One patent expert highlights the impact of poor-quality patents in economic terms*:

> Questionable patents can harm competition and hinder innovation by forcing market participants to pay licensing royalties, incur substantial legal expense to defend against infringement claims, engage in design-around efforts that raise costs and/or hinder product performance. . . . [A] patent holder can have real power even without being a true inventor because the systems for patent issuance and patent litigation are tilted in favor of patent applicants and patent holders. The result is that the patent system, while intended to promote innovation, instead places sand in the gears of our innovation engine.

27.9.4 Emerging Bionanotechnology Patent Thickets

Currently, there are too many players holding too many bionanotech patents; this has created the current fragmented, messy patent landscape. Most experts agree that this patent landscape is already producing "patent thickets" that have the potential of causing protracted legal battles. This is obviously an undesirable result and could easily stop bionanotech development in its tracks. Clearly, it poses one of the biggest threats to commercialization.

Patent thickets are broadly defined in academic discourse as "a dense web of overlapping intellectual property rights that a company must hack its way through in order to actually commercialize new technology."† Such patent thickets, a result of multiple blocking patents, naturally discourage and stifle innovation. Claims in such patent thickets have been characterized as broad, overlapping, and conflicting. Therefore, business planners and patent practitioners should steer company researchers away from such potential patent thickets. They may also need to analyze the patent landscape to gauge "white space" opportunities (i.e., no overlapping patents) prior to R&D efforts, patent filing, or commercialization activities (Figure 27.4). Classically, such an analysis of the number and quality of patents issued in a particular sector of bionanotech can highlight a particular

* Shapiro C: Patent system reform: Economic analysis and critique. *Berkeley Technology Law Journal* 19, 1017–1019 (2004).

† Shapiro C: Navigating the patent thicket: cross licenses, patent pools and standard-setting. *Innovation Policy Econ.* 1, 119–150 (2000).

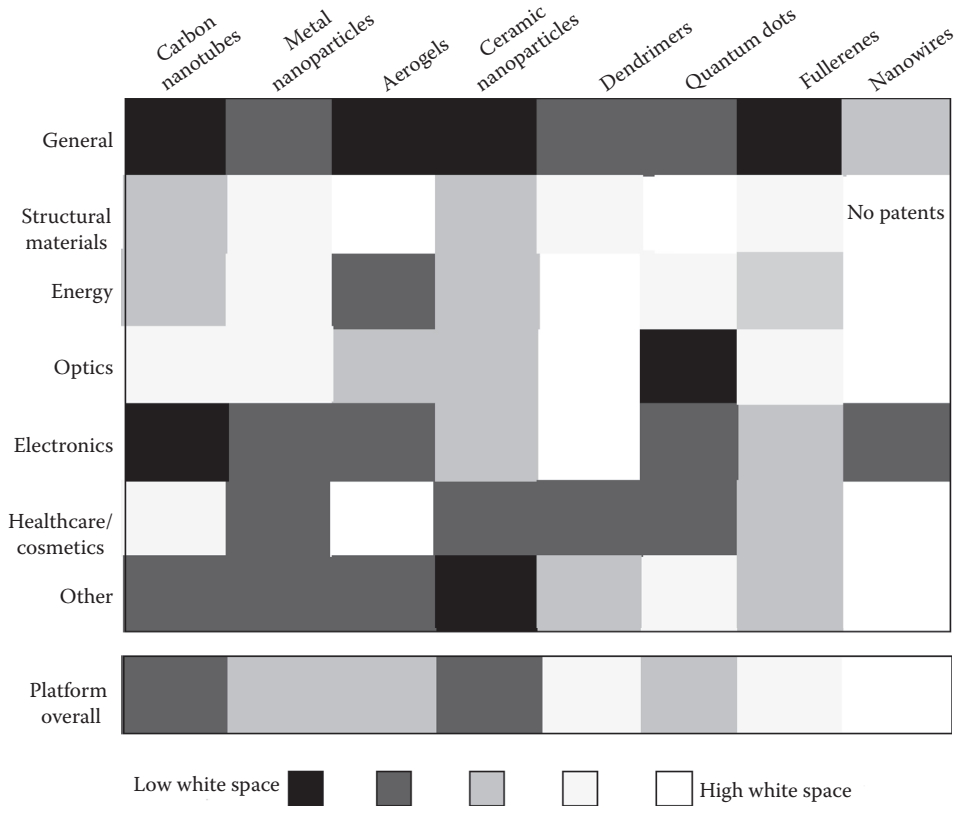

FIGURE 27.4 U.S. patent landscape analysis by nanomaterial platform.

technology trend, areas of high/low commercialization potential, and areas that indicate a high risk of market entry.

According to a widely circulated market study published in 2005,* nanoscience researchers around the world are steadily filing patents in the hope of creating "toll booths" that could slow future product development. Because there has been an explosion of overlapping and broad patent filing (and issuance of corresponding broad patents) on nanomaterials, it is likely that the companies that want to use these building blocks in products will be forced to license patents from many different players to implement their inventions. The report focused on five fundamental nanomaterials: carbon nanotubes, dendrimers, fullerenes, nanowires, and quantum dots. The study identified carbon nanotubes and quantum dots as of particular concern. The study noted that although fullerenes and nanowires are relatively free of overlapping patent claims, the other categories are quickly attracting patent applications. For example, the study found that a large number of patent claims for dendrimers have been assigned to recently acquired Dendritic Nano-Technologies, Inc. (Mount Pleasant, Michigan). It also noted that quantum dot patent claims tend to cover the materials themselves rather than specific applications and that the patent situation for using carbon nanotubes in electronics looks "messy." Although some dominant or pioneering patents on carbon nanotubes will expire in the near future, a classic patent thicket seems to be developing in the area of single-walled carbon nanotubes, where companies such as IBM (White Plains, New York), NEC Corpora-

* Nanotechnology gold rush yields crowded, entangled patents. Lux Research, www.nanotech-now.com/news.cgi?story_id=09134 (last accessed May 8, 2008).

tion (Tokyo, Japan), and Carbon Nanotechnologies, Inc. (Houston, Texas) are likely to aggressively stake out their claims.*

To analyze the perceived patent thicket in any bionanotech-related technology, a detailed legal review of the claim set from the patents in the thicket may be necessary before decisions regarding patent filings or substantial investment on commercialization are undertaken.

27.9.5 The Coming Bionanotechnology Patent Wars

Patent grants in bionanotechnology and nanomedicine-related inventions are likely to continue at a pace that is almost synchronous with funding. This is true on an international as well as national scale. The aggressive mentality described above has not only produced overlapping patents, but the race to patent anything "nano" has resulted in a flood of exceedingly broad upstream nanopatents. Although broad patents are generally awarded for pioneering inventions, they should never be allowed if prior art exists. Experts fear that bionanotech's constantly growing patent estate may actually retard innovation due to uncertainty over who is infringing on whose patent. Most experts directly blame the PTO for awarding numerous erroneously broad bionanotech patents.

Clearly, this proliferation of unduly broad patents and the resulting patent thickets will require litigation to sort out, especially if sectors of bionanotechnology become financially lucrative.† At the present time, it seems that nanotech companies in general are avoiding costly court battles. In fact, there is hardly any nanotech patent litigation underway in the United States. Companies sometimes avoid costly litigation to prevent exposing their own patents, some of which may be based on a poor review at the PTO and, thus, whose validity may be questionable. In any case, I believe that expensive litigation is as inevitable as it was with the biotechnology industry where extensive patent litigation resulted once products became commercially successful. The reason for this is simple: royalties may be collected by the patentee from potential infringers. However, in most patent battles, the larger entity with the deeper pockets will ultimately prevail even if the brightest innovative stars are on the other side. This situation is all too familiar to the business sector. It leads to higher costs to consumers (if and when products are commercialized), while deterring the innovation process.‡

Ultimately, companies introducing new products to the market will face considerable uncertainty regarding the validity of broad and potentially overlapping patents held by others. The ongoing land grab will definitely worsen the problem for companies striving to develop commercially viable products. In fact, bionanotech start-ups may soon find themselves in patent disputes with large, established companies, as well as between themselves. Start-ups may also become attractive acquisition targets for larger companies because takeover is generally a cost-effective alternative to litigation.

It is possible that companies may need to acquire costly licenses for patents from other companies in order to establish themselves. It is also possible that companies may use their patents to exclude rather than license out. Furthermore, those who do license may do so at an unreasonably high cost. However, I hope that none of these scenarios will come about. Instead, it is hoped that a more harmonious atmosphere will prevail, where (nonexclusive) cross-licensing agreements by start-ups and large corporations alike will become the norm. In my view, liberal patent licensing is another particularly effective strategy to maneuver through the patent thicket at this stage in the development of bionanotech, especially because the enforceability of so many patents is questionable. It should be noted, however, that when the total number of owners of conflicting intellectual

* Van Lente MA: Building the new world of nanotechnology. *Case W. Res. J. Int. Law* 38(1), 173–215 (2006); Harris D, Bawa R: The carbon nanotube patent landscape in nanomedicine. *Expert Opinion on Therapeutic Patents* 17(9), 1165–1174 (2007).

† O'Neill S, Hermann K, Klein M, Landes J, Bawa R: Broad claiming in nanotechnology patents: Is litigation inevitable? *Nanotechnology Law and Business* 4(1), 595–606 (2007).

‡ Lawrence S: Patently absurd: Too many patents could kill nanotechnology. *Red Herring* November 20 Issue, 119 (2002).

property is relatively small, cross-licensing has been the answer. But, when the number of owners of conflicting IP is relatively large, the transaction costs of cross-licensing may be too great for it to be effective. Also, critics consider cross-licensing as a settlement of a patent dispute that may not serve the public interest because cross-licensing (as compared to litigation) limits competition when it is between competitors, raising the spector of antitrust prosecution of these agreements as monopolies.

27.10 NAVIGATING THE BIONANOTECH PATENT THICKET

Following are some other proposals that may cut through the bionanotech patent gridlock and prevent widespread and wasteful litigation.

27.10.1 Formation of Patent Pools

The multiple-party patent thicket problem may be solved by the cooperative formation of "patent pools" by technologically competing entities. Patent pools are defined as legally permissible cooperative agreements whereby the members of the pool have access to the patents of the entire pool in exchange for a set price. However, it is uncertain at this stage whether patent pools will be a lawful, desirable, or beneficial answer to the patent thicket problem.

27.10.2 Government Actions to Encourage Nonexclusive Licensing

Some practitioners have also suggested that government must step in and use its existing authority under the Bayh-Dole Act to encourage nonexclusive licensing of foundational nanotechnology patents.* Under the Bayh-Dole Act of 1980, universities and small business entities may retain patent ownership rights if the research was funded by the U.S. government. The government retains a royalty-free license to any patented technology that is generated as a result of such funding. Naturally, the Bayh-Dole Act will assist bionanotech companies in the same way it helped biotechnology start-ups—by promoting the transfer of university-owned patents funded by government grants to the private sector, given that academia has become increasingly aggressive in patenting its bionanotech-related research.

27.10.3 Other Government Actions

Government action, such as the imposition of compulsory licensing of upstream and/or foundational patents that have been financed by public funds, may assist in breaking up dominant patent monopolies. Enforcement of antitrust and competition laws by the government may encourage more cooperation between the various players as well as stimulate active cross-licensing and patent pooling.

There are, of course, other strategies available to prevent or navigate patent entanglements, both before and after the patent issues.† Companies could also focus on trade secrets as a supplement to patents. A greater willingness on the part of the patent applicant to provide prior art, particularly nonpatent prior art, would be helpful to the patent examiner.

* Sabety T: Nanotechnology innovation and the patent thicket: Which IP policies promote growth? *Nanotechnology Law & Business* 1(3), 262–283 (2004).

† Harris D, Miller J, Bawa R, Cleveland JT, O'Neill S: Strategies for resolving patent disputes over nanoparticle drug delivery systems. *Nanotechnology Law and Bus,* 1(4), 101–118 (2004); Bawa R, Bawa SR, Maebius SB, Iyer C: Bionanotechnology patents: Challenges and opportunities. In: *The Biomedical Engineering Handbook* (3rd Edition). Bronzino JD (Ed.), CRC Press, Boca Raton, FL; 29-1–29-16 (2006).

27.11 CONCLUSIONS, CAUTIONS, AND RECOMMENDATIONS

Securing valid and defensible patent protection is critical to the bionanotech "revolution." Although early forecasts for commercialization are promising, the emerging patent thicket in this arena of nanotech could be a major stumbling block.* It is almost certain that the enforceability of numerous U.S. bionanotechnology patents (like e-commerce patents previously) will be a major problem in the future. Furthermore, due to the substantial annual increase in costs associated with maintaining and enforcing issued patents, enforceability may also be a problem when the patent holder lacks the resources to maintain or enforce the patent against potential infringers. On the other hand, valid patents stimulate market growth and innovation, generate revenue, prevent unnecessary licensing, and greatly reduce infringement lawsuits.

The PTO continues to be under enormous strain and scrutiny. Reforms are urgently needed to address issues ranging from poor patent quality and questionable examination practices to inadequate search capabilities, rising attrition, and an enormous patent backlog. Numerous influential entities, ranging from government to nongovernment organizations, have recently become more vocal in their criticism of the PTO. They have produced authoritative reports with detailed recommendations regarding overhauling the PTO and the U.S. patent system.† These reforms are urgently needed in order to ensure a better balance between innovation and competition.‡ Without these reforms, the cursory patent examination that is currently in place coupled with patent proliferation and patent backlog that already exceeds 1 million will result in the issuance of too many invalid and unenforceable bionanotech patents. This will continue to generate a crowded, entangled patent landscape with few open-space opportunities for commercialization. For many companies, navigating this minefield will be an unattractive option.

Ownership of technology in the form of patents is one thing, deriving sufficient economic value therefrom is a different issue. Obtaining undeserving patents and profiting from the threat of litigation rather than providing beneficial bionanotech products runs counter to the foundations of our patent system. Therefore, if the current dense patent landscape becomes more entangled and the patent thicket problem worsens, it may prove to be *the* major bottleneck to viable commercialization,§ negatively impacting the entire bionanotech revolution. For investors, competing in this high-stakes patent game may prove too costly.

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* Bawa R: Patenting nanomedicine: A catalyst for commercialization? *Small Times* 5(8), 16 (2005); Bawa R: Will the nanomedicine "patent land grab" thwart commercialization? *Nanomedicine: Nanotechnology, Biology and Medicine* 1, 346–350 (2005); Bawa R: Patents and nanomedicine. *Nanomedicine* 2(3), 351–374 (2007).

† Report: *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy.* Washington, DC: Federal Trade Commission, (2003); Merrill SA, Levin RC, Myers MB (Eds): *A Patent System for the 21st Century.* National Academies Press, Washington, DC (2004); Mittal AK, Kootz LD: *Improvements Needed to Better Manage Patent Office Automation and Address Workforce Challenges.* Report GAO-05-1008T, U.S. Government Accountability Office, Washington, DC (2005); Report: *US Patent and Trademark Office: Transforming to Meet the Challenges of the 21st Century.* National Academy of Public Administration, Washington, DC (2005).

‡ Patent reform bills are currently pending in Congress. Similar measures have failed in the past 3 years as the information technology industry and big pharma have battled over the finer points of these bills. (See Sandburg B: Patent reform bill gets cool reception from Rx industry; damage cap is worry. *F-D-C Report* 69(17), 8–9 (2007); Hess G: Patent reform stalls in Senate. *Chemical and Engineering News* 86(22), 40–43 (2008).

§ Bawa R: Patenting nanomedicine: A catalyst for commercialization? *Small Times* 5(8), 16 (2005); Bawa R: Will the nanomedicine "patent land grab" thwart commercialization? *Nanomedicine, Nanotech. Biol. Med.* 1, 346–350 (2005).