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Editorial Commentary

Will the nanomedicine "patent land grab" thwart commercialization?

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Commercial nanomedicine is at a nascent stage of development. Although the full potential of nanomedicine is years or decades distant, recent advances in nanotechnology-related drug delivery, diagnosis, and drug development are beginning to change the landscape of medicine. Site-specific targeted drug delivery (made possible by the availability of unique delivery platforms such as dendrimers, nanoparticles, and nanoliposomes) and personalized medicine (a result of advances in pharmacogenetics and pharmacogenomics) may be on the horizon. Early forecasts for nanomedicine commercialization are encouraging (Table 1 [1-4]). Will these advances in the laboratory result in viable commercial products that benefit society, or will certain bottlenecks and unforeseen issues prevent their introduction to the marketplace?

Several variables will determine whether advances in the laboratory will translate into multiple opportunities for the consumer. Early-stage nanomedicine commercialization will be hampered by large-scale production challenges, high production costs, the public's general reluctance to embrace innovative medical technology without real safety guidelines, a scarcity of venture funds, few near-term commercially viable products, a well-established micrometer-scale industry, the pharmaceutical industry's reluctance to embrace nanomedicine, and the absence of clear regulatory guidelines. Furthermore, the confusion at the US Patent and Trademark Office (PTO) with respect to the burgeoning patent applications for the innovations of nanomedicine contributes to the problem. There is also confusion and disagreement about the classification and definition of nanotechnology. Government agencies such as the Food and Drug Administration and the PTO use a rigid definition based on a scale of less than 100 nm—a definition originally proposed by the National Nanotechnology Initiative (NNI). However, this NNI definition of nanotechnology presents difficulties not only for understanding nanopatent statistics [5], but also for the proper assessment of its scientific, legal, environmental, regulatory, and ethical implications. This problem exists because nanotechnology represents a cluster of technologies, each of which may have different characteristics and applications [6-8]. Moreover, this size limitation of less than 100 nm is not critical to a drug company from a formulation or efficacy perspective, because the desired or ideal property (eg, improved bioavailability, reduced toxicity, lower dose, enhanced solubility) may be achieved in a size range greater than 100 nm. Numerous examples from the pharmaceutical industry highlight this important point (eg, Elan Pharma International's nanoparticles; Kereos, Inc. anticancer formulations). Hence, the size limitation imposed by the NNI should be revised, especially with respect to nanomedicine. Similarly, the PTO's flawed definition of nanotechnology, which is essentially copied from the NNI, has resulted in a skewed preliminary classification system, particularly with respect to nanomedicine- and bionanotechnology-related inventions. In light of this confusion, a more appropriate and practical definition of nanotechnology, unconstrained by size, is as follows [9]:

> "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."

The critical role of patents to the nanomedicine "revolution" cannot be underestimated. When investors in nanomedicine or pharmaceutical companies consider the merits of a particular investment, patent issues are one of the most important items that they review. There is also ample

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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, exercise, and defend patents.

Patents are of great importance to start-ups and smaller companies because they may help in negotiations over infringement during competitive posturing with larger corporations. In fact, patents may also protect the clients of a patent owner, because they may prevent a competitor from infringing or replicating the client's products made under license from the patentee. Moreover, patents provide credibility to an inventor with his or her backers, shareholders, and venture capitalists groups, who may not fully understand the science behind the technology. For a start-up company, patents are a means of validating the company's foundational technology to attract investment. Therefore, start-up companies are more aggressively seeking 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 reasons for seeking patents on nanotech-related technologies [5]. Experts agree that "patent awareness" (ie, the knowledge that patents are intangible property that can be obtained and lost) is central to any business plan or strategy [10]. Few venture capitalists are likely to support a start-up that relies on trade secrets instead of patents. Generally, patents precede funding from a venture capital firm. In short, investors are unlikely to invest in a start-up that has failed to construct adequate defenses around its intellectual property.

For more than a decade all of the world's major patent offices have faced an onslaught of nanomedicine-related patent applications [5,6,9,11-16]. This situation is probably going 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 nanomedicine further maturing and the promised breakthroughs accruing, patents will generate licensing revenue, provide leverage in deals and mergers, and reduce the likelihood of infringement. The development of nanomedicine-related products, which is extremely research intensive, will be significantly hampered in the absence of the market exclusivity offered by a US patent.

The Bayh-Dole Act of 1980 will also assist nanomedicine-related companies in the same way it helped biotechnology start-ups—by liberalizing the transfer of university-owned patents funded by government grants to the private sector. Because of the potential market value of these products (Table 1), researchers, executives, and patent lawyers are making an effort to obtain broad protection for new nanoscale polymers and materials that have applications in nanomedicine. Therefore, a sort of nanomedicine "patent land grab" is in full swing by "patent prospectors" as start-ups and corporations compete to secure broad patents during these critical early days [5,9,11-15,17-25].

Table 1

"By 2014, 16% of goods in health care and life sciences (by revenue) will incorporate emerging nanotechnologies [1]."
"Sales of nanomaterials for use in nanobiotech applications generated revenues of $750 million in 2004. . .projections for 2011 are more than $2 billion [2]."
"Venture funds are preferentially going to nanobiotechnology, with 52% of the $900 million in venture capital funding for nanotechnology in 1999 to 2003 going to nanobiotechnology startups [3]."
"The market for nanobiotechnology has existed for only a few years, but it is expected to exceed $3 billion by 2008, reflecting an annual growth rate of 28% [4]."

However, these patent prospectors are confronted with an overburdened PTO [22], which has historically been slow to react to new technologies such as biotechnology and software [5,6,9,11,18,24-32]. In fact, the entire US patent system is under enormous scrutiny and strain [24-28,31,34], as the PTO continues to struggle with the evaluation of nanotechnology-related patent applications [5,6,8-15,18,20,24,35-40]. Therefore, "the jury is out" as to whether the nanomedicine industry will thrive like the information technology industry or become burdened like the radio patent deadlock [23]. However, patent grants globally in nanotechnology and nanomedicine-related inventions are likely to continue at a pace that is almost synchronous with funding [5,6,9,11-16] (Figure 1).

According to a recent report from Lux Research [24], almost 4000 US nanopatents have been issued as of late March 2005, with another 1777 patent applications pending. This report concludes that nanoscience researchers around the world are steadily filing patents with the hope of creating "toll booths" for future product development. Because there has been an explosion of overlapping and broad patent filing on nanomaterials, it is probable that companies that want to use these building blocks in products will be forced to license patents from many different sources 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 report 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 Dendritic Nano-Technologies, Inc. (Mount Pleasant, MI). It also noted that quantum dot patent claims tend to cover the materials themselves rather than specific applications, that the patent situation for using carbon nanotubes in electronics looks "messy", and that "the common assumption that carbon

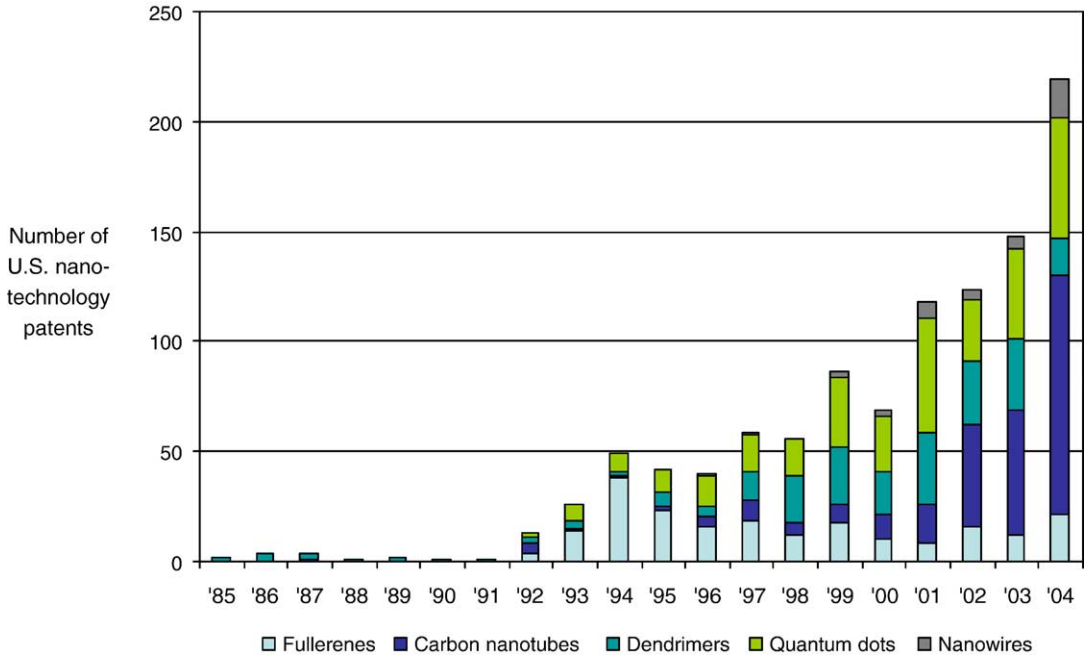

Fig 1. US nanotechnology patent trends by technology sector. (Courtesy of Lux Research, New York, NY, and Foley & Lardner, Washington, DC).

nanotube patents are both numerous and overlapping across all important application categories is incorrect" (Figure 2). Although some dominant or pioneering patents on carbon nanotubes will expire in the near future, a classic "patent thicket" (defined below) seems to be developing in the area of single-walled carbon nanotubes [21], where companies such as IBM (White Plains, NY), NEC Corporation (Tokyo, Japan) [5], and Texas-based Carbon Nanotechnologies, Inc. (Houston, TX) [21] are likely to aggressively stake out their claims. However, to analyze the perceived patent thicket in carbon nanotube technology, a detailed legal review of the claim set may be necessary before substantial investment for commercialization is made [41]. Universities are also becoming increasingly aggressive in patenting their nanomedicine-related research, with the hope of generating licensing revenue. For example, carbon nanotubes are a subject of extensive research activity at the university level.

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" [42]. Such patent thickets, as a result of multiple blocking patents, are considered to discourage and stifle innovation [42]. Claims in such patent thickets have been characterized as "often broad, overlapping and conflicting—a scenario ripe for massive patent litigation battles in the future" [18]. Therefore, business planners and patent practitioners—namely, patent lawyers and patent agents—should steer company researchers away from such potential patent thickets. They may also need to analyze the patent landscape to gauge the "white space" opportunities (no overlapping patents) prior to R&D efforts, patent filing, or commercialization activities (Figure 2).

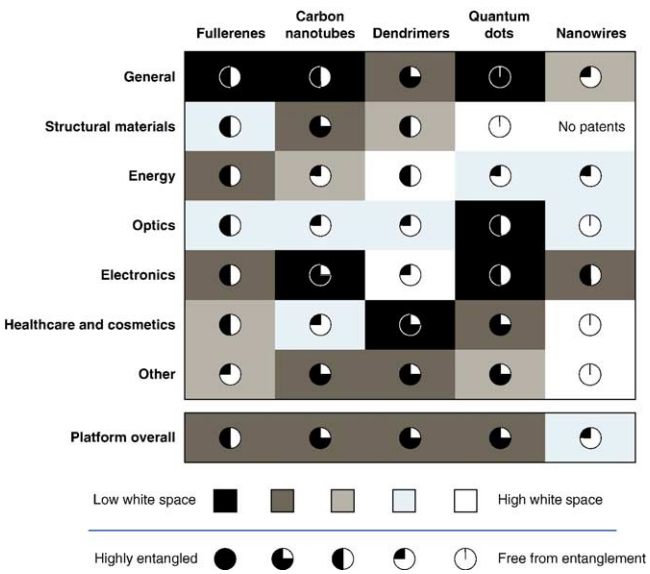

Fig 2. US patent thicket analysis by nanomaterial technology sector. (Courtesy of Lux Research, New York, NY, and Foley & Lardner, Washington, DC).

This aggressive mentality has not only produced overlapping patents, but the race to patent anything "nano" has produced a flood of "unduly broad" nanopatents. Broad patents are generally awarded for "pioneering inventions." Clearly, such a proliferation of unduly broad patents will ultimately produce patent thickets that will require litigation to sort out, especially if sectors of nanomedicine become financially lucrative. Given such a patent landscape, expensive litigation is as inevitable as it was with the biotechnology industry, where extensive patent litigation resulted once the products became commercially successful. In most of the

patent battles the larger entity with the deeper pockets will rule the day even if the brightest stars and innovators are on the other side. In the future the nanomedicine start-ups will become attractive acquisitions for larger companies, since takeover is generally a more cost effective alternative to litigation. Ultimately, this situation is all too familiar to the business and patent communities, in that it leads to higher costs to consumers, if and when products are commercialized [5], as well as deterring the innovation process itself [22].

Furthermore, most experts agree that the stage is set for a wave of cross-licensing agreements by start-ups, and bundles of intellectual property for specific nanomedicine applications licensed by groups of large corporations. Generally, when the total number of owners of conflicting intellectual property is relatively small, cross-licensing has been the answer. However, when the number of owners of conflicting intellectual property is relatively large, the transaction costs of cross-licensing may be too great. At this point, this multiple-party patent thicket problem may be solved by the cooperative formation of patent pools by technologically competing entities. Apart from this, are other strategies available to scientists and nanomedicine companies to navigate patent entanglements [20].

Ultimately, companies introducing new products to the market will certainly 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, nanomedicine start-ups may soon find themselves in patent disputes with large, established companies, as well as between themselves. Therefore, it is critical that reforms be undertaken at the PTO in order to ensure a better balance between innovation and competition [27,28,33,34], particularly in the nanomedicine space. Otherwise, cursory patent examination at the PTO and the resultant issuance of invalid nanomedicine patents will certainly generate a crowded, entangled patent landscape with few open space opportunities for commercialization. If such a dismal patent climate persists, investors are unlikely to invest in risky nanomedicine commercialization efforts. For them, competing in this high-stakes patent game may prove to be too costly. In fact, this patent thicket problem in nanomedicine may prove to be the major bottleneck to viable commercialization, negatively affecting the whole nanomedicine enterprise.

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