

SPECIAL



SEGMENT

The Nano-Bio Convergence and New Regulatory Challenges

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ABSTRACT

Drawing parallels between biotechnology and nanotechnology is no new exercise—tremendously broad in their potential, dizzying in their promise, and each successively dubbed The Next Big Thing, both fields have nonetheless traveled the same bumpy road commercially. Just as many investors in biotech ventures still await tardy payoffs, recent years have seen a bust where a boom in nanotechnology was supposed to be. However, as nanotechnology applications increase in their sophistication and cross into the biotech sector, the fortunes of biotech and nanotech are becoming intertwined rather than merely parallel.

INTRODUCTION

Drawing parallels between biotechnology and nanotechnology is no new exercise—tremendously broad in their potential, dizzying in their promise, and each successively dubbed The Next Big Thing, both fields have nonetheless traveled the same bumpy road commercially. Just as many investors in biotech ventures still await tardy payoffs, recent years have seen a bust where a boom in nanotechnology was supposed to be. However, as nanotechnology applications increase in their sophistication and cross into the biotech sector, the fortunes of biotech and nanotech are becoming intertwined rather than merely parallel.

One area where the great possibilities posed by biotech and nanotech converge, of course, is medicine. A classic, if a bit clichéd, vision of the future of nanotechnology involves armies of microscopic, disease-fighting robots coursing through patients' veins; a shorter-term likelihood is the advent of treatments such as the nanotech-enabled, cancer-fighting, modified plant virus developed by researchers at North Carolina State University.¹ The viability of such developments depends on a healthy supply of capital to propel them into the marketplace. At the moment, the supply on the nanotech side appears tenuous.

Even if nanotechnology's advocates are correct in their insistence that the industry's perceived struggles are merely the result of inflated and unrealistic expectations, the symptoms of an ailing nanotechnology sector are there. In the past year, the French government announced a five-

year, €107 million bailout of its nanotechnology industry; NanoDynamics attempted the latest in a series of failed IPOs; and even the term "nano" has fallen out of favor with some venture capitalists seeking to distance themselves from concerns hovering over the field. With promises of riches so far going unfulfilled, the pressing question is: why hasn't nanotechnology lived up to the hype?

POTENTIAL APPLICATIONS OF NANOTECHNOLOGY

An examination of nanotechnology's plight must consider what its properties and potential applications are that shape nanotechnology's role in the market. Compared to other examples of breakthrough technologies, nanotechnology has less to do with semiconductors and more to do with plastics. Whereas semiconductors were a concrete product in the particular field of electronics, nanotechnology's promise is in its fundamentally new approach to building things in general, and its applicability seems to be theoretically limitless. Cyrus Mody, a specialist in nanotechnology history at Rice University, notes that "[s]ome proponents talk about nano[tech] as being like electricity—i.e., when you go to the store, you don't buy electricity, but electricity is in or enables pretty much everything you do buy."² Products currently for sale that utilize nanotechnology include water and stain resistant clothing, clear zinc oxide sunscreens, Samsung's "Nano Silver" antibacterial washing machines, ultra responsive golf balls and self-cleaning glass.

As illustrated by these examples, many nanotechnology

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applications are used to improve existing products, and the industry's services are often grafted on top of or interwoven with other industries. As with plastics, nanomaterials in and of themselves are not valuable—it is their potential use in a wide variety of other industries that gives them value. As a result, nanotechnology is spread horizontally across the market rather than standing alone as a vertically integrated industry with one key end product in mind. “Industry,” in fact, could be termed a misnomer for nanotechnology. According to the Tim Harper, CEO of Cientifica, a nanotechnology consulting firm, “It is a technology and no more an industry than physics or chemistry.”³

REGULATORY CHALLENGES ASSOCIATED WITH NANOTECHNOLOGY

This practical difficulty faced by the nanotechnology sector is reflected in the debate over how the Food and Drug Administration (“FDA”), responsible for regulating a vast swath of the collaborative efforts between biotech and nanotech, should regulate products containing nanomaterials. The FDA's policy currently remains largely the same toward nanotechnology products as toward the rest: the FDA regulates “products, not technology.” That is to say, the FDA determines the testing protocol for a particular product based on its classification into a product type rather than on the technology that it employs. The FDA straightforwardly states on its website that “the existing battery of pharmacotoxicity tests is probably adequate for most nanotechnology products that we will regulate. Particle size is not the issue.”⁴

The assertion that particle size is not the issue is rather semantic—certainly, it is the safety risks that nanoparticles pose that concern the FDA, but it is their size that creates the risks. First, at the tiny scale of nanoparticles, the ratio of surface area to volume increases drastically. With more reactive sites of the molecule thus exposed, the particle may have greater reactive potential, and therefore greater potential for toxicity, than its macroscopic cousin. Second, due to their size, nanoparticles can more easily permeate biological membranes, making them more readily absorbed and widely dispersed throughout the human body. Third, some nanoparticles are actually so small that they are subject not to the laws of classical physics but of quantum mechanics, under which various properties of the substance may change significantly. Each of these qualities presents a novel risk to consumer health.

The potential for harm is not solely hypothetical. One study, for example, found that the use of nanoscale zinc oxide and titanium dioxide—ingredients used in sunscreens—can lead to DNA damage in skin cells.⁵ At the nanometer scale, both substances become highly photo-reactive and can produce harmful free radicals when

exposed to ultraviolet rays.

However, advocates for nanotech contest both the legitimacy of the science behind some such studies and the sincerity of those who cite them as the principal grounds for their opposition to the rise and proliferation of nanotech. Here, nanotechnology once again crosses paths with biotechnology, in that “nano[tech] is seen as prone in some way to the same worries as genetically-modified organisms.”⁶ Although opposed to the nanotech “military-industrial-academic complex” for a variety of reasons, organizations that cut their teeth on the fight over GMOs “see their biotech case as only having gotten traction when they focused on the toxicological and environmental [risks] from GMOs—and therefore they've cut out the middleman and gone directly to those issues with nanotech.”⁷

It is in this context that the FDA's relatively passive approach to the emergence of nanotechnology in the consumer marketplace has drawn fire from public health watchdogs, who argue that the inimitable risks presented by nanotechnology require a new, separate regulatory framework. In response, the FDA's Nanotechnology Task Force issued a report in July of 2007 asserting “the need for timely development of a transparent, consistent, and predictable regulatory pathway,” and stating that the challenges posed by nanotechnology “may be magnified” in part “because nanotechnology can be used in, or to make, *any* FDA-regulated product.” (emphasis added).⁸ The question of the adequacy of the existing testing protocol is far

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beyond the limited scope of this article. More germane is the question of whether a separate regulatory framework for nanotechnology products is even logistically feasible.

The FDA's current regulatory scheme funnels products into various testing centers, each with expertise in a particular type of product. Combination products—“product[s] comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic...and produced as a single entity”—illustrate the process well. Assignment of primary regulatory responsibility of a combination product is made based on a determination of the product's primary mode of action, defined as “the single mode of action of a combination product that provides the most important therapeutic action of the combination product.”⁹ The center to which the product is assigned—either the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, or the Center for Devices and Radiological Health—will then evaluate the product for approval based on that particular center's guidelines.

As such, the way the FDA regulates nanotechnology (or any other technology) mirrors the way nanotechnology applications are developed and consumed: case-by-case, product byproduct, across a wide array of industries.

Nanotechnology-specific testing protocols could either be implemented area by area within the existing framework or performed in a new, centralized testing center through which any product flagged as nanotechnology would have to pass on its way to approval. The different but congruent drawbacks to each option may demonstrate why nanotechnology's rise to commercial prominence has proved elusive.

The first option, to establish nanotechnology-specific tests across the existing framework, could dilute the FDA's expertise with the technology by scattering the procedures throughout the various testing centers. The second option, to create a separate testing center for nanotechnology products, could leave the center without the necessary product-specific expertise to evaluate how safely the nanotechnology functions within the particular product. The problem is that the risk posed by a nanotechnology product depends both on what the nanotechnological component of the product is and on what the product itself is. Conceivably a nanomaterial applied topically could be safe while the same material ingested or injected would not be.

This logistical difficulty encountered in regulating nanotechnology may reflect an inherent inefficiency within the nanotechnology industry that has slowed its commercial development. The age-old adage to do one thing and do it right is hard to follow in the case of nanotechnology, where the product by nature lends itself to a myriad of uses. Furthermore, the practice of nanotechnology is far enough out on the cutting edge that the pool of sufficiently sophisticated research and development bodies may be spread thin by the number of sectors seeking to implement the technology. Consequently, the horizontal orientation of the nanotechnology industry may create similar problems for the industry as it does for those who regulate its products: centralization of expertise in nanotechnology itself might limit its range of use, whereas maximizing the breadth of nanotechnology's applications could hurt the quality of the products by diminishing expertise.

The effect of this dilution of expertise can also be seen in nanotechnology's intellectual property landscape, where "in many cases, the use of a novel nanomaterial is covered by a patent from a company that possesses application know-how but doesn't have access to the best material source."¹⁰ Platform companies, the business model increasingly in favor with big-money investors in nanotech, are specifically designed to combat this phenomenon by amassing a large array of widely applicable technology and building strategic partnerships to exploit it.¹¹ Implicitly acknowledging that expertise in nanotech is a limited resource, a position paper by industry stalwart Nanosys states that "Nanosys leverages the market expertise and complementary technologies of our strategic partners, while our partners leverage the unique technical and

market opportunities enabled by nanotechnology *without having to become nanotechnology experts themselves.*"¹² (emphasis added)

Similarly, the diffuse profile of the nanotechnology field poses problems for companies seeking to protect their intellectual property rights because it can be difficult to draft a patent application that captures and shields the full spectrum of such broadly cross-disciplinary inventions. The most popular solution implements, on a smaller scale, the principle behind nanotech platform companies: patent attorneys charged with protecting nanotech IP rights are pulling together multidisciplinary patent-drafting teams made of experts from the various fields where IP rights may lie. This arrangement illustrates in microcosm that the future of nanotech business may lie in the construction up and down the production ladder of units that serve as centralized clearinghouses for information.

However, revisiting the analogy between biotech and nanotech, it is worth noting that attempts to create biotech "clusters"—artificially centralized business regions—have largely failed to pay off. Whether the nanotech sector bears structural similarities to its biotech counterpart inherently or because it was designed that way, leaders in nanotechnology development need to be creative to avoid past pitfalls.¹³

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To return to the regulatory level, the U.S. Patent & Trademark Office ("USPTO"), caught in the same quandary as the FDA, currently employs the same strategy in reviewing nanotech patents as the FDA does in regulating nanotech


products—it has funneled nanotech-related patent applications into its existing patent examination departments, rather than creating a separate entity to process such applications. However, also like the FDA, the USPTO is taking steps to grease the information exchange within the organization in regards to nanotech matters. One such centralized information depot is a cross-reference art collection of existing nanotech patents.¹⁴

SUMMARY

Although it is heartening to see that the USPTO considers nanotechnology worthy of special consideration, it remains to be seen whether the measures taken will be sufficient to handle the immediate challenges created by the wave of IP claims in this nascent field. Without judicious and diligent oversight, the field of nanotechnology could become clogged with overbroad or overlapping patents—the proverbial "patent thicket"—and possibly bogged down in litigation over conflicting rights. The IP landscape around the carbon nanotube, an iconic nanomaterial used as a drug delivery structure (among many other applications), is ripe for such a battle.¹⁵

So, while some nanotech companies have begun to

address the practical problems of their business, uncertainties in the regulation and the IP protection of nanotechnology continue to shake the faith of investors whose support could fund more ambitious initiatives. Liability concerns are particularly prevalent in some of the areas where nanotechnology's promise is greatest, such as medicine (see, for instance, a 2006 petition by the International Center for Technology Assessment formally requesting an FDA recall of all sunscreens employing nanotechnology).¹⁶

Across the board, the unusually wide range of applications for nanotechnology raise the debate of whether to regulate and protect nanotechnology products on a case-by-case or product-by-product basis or to route the industry through some centralized oversight process. In this sense, the very fact that nanotechnology is so widely applicable has hamstrung its commercial progress, and the difficulties of regulating the industry can be viewed as both a reflection and a cause of its struggles. 

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