

# Thinking Small

U.S. patent officials and other regulators must get up to speed on the intricacies of tiny particles to avoid hindering the growth of nanotechnology.

By Lori Andrews and Julie Burger

At the everyday level of human experience, gold is a shiny inert metal and a medium of exchange. At the level of a nanoparticle, however, gold becomes a semiconductor, its color changes, and its melting point decreases dramatically as the particle size gets smaller. And small is the essence of nanotechnology—the manipulation and control of matter at the scale of 1 to 100 nanometers (a nanometer is 1 billionth of a meter), which capitalizes on the unique properties at this scale.

Nanogold is already used in home pregnancy testing kits in which the pregnancy hormone causes the gold nanoparticles to aggregate and appear red. It is also used to detect lead in water, to locate minute amounts of a protein linked to the early diagnosis of Alzheimer's in cerebrospinal fluid, and to target and destroy cancerous tissue.

But as the “gold rush” of nanotechnology converges with biotech to form a “biomolecular economy,” the very shape-shifting, boundary-crossing nature of this field that holds such promise also makes it a regulator's nightmare. Already, the U.S. Food and Drug Administration (FDA) and the U.S. Patent and Trademark Office (USPTO) are being criticized for their approaches as they attempt both to encourage and to impose order on the field.

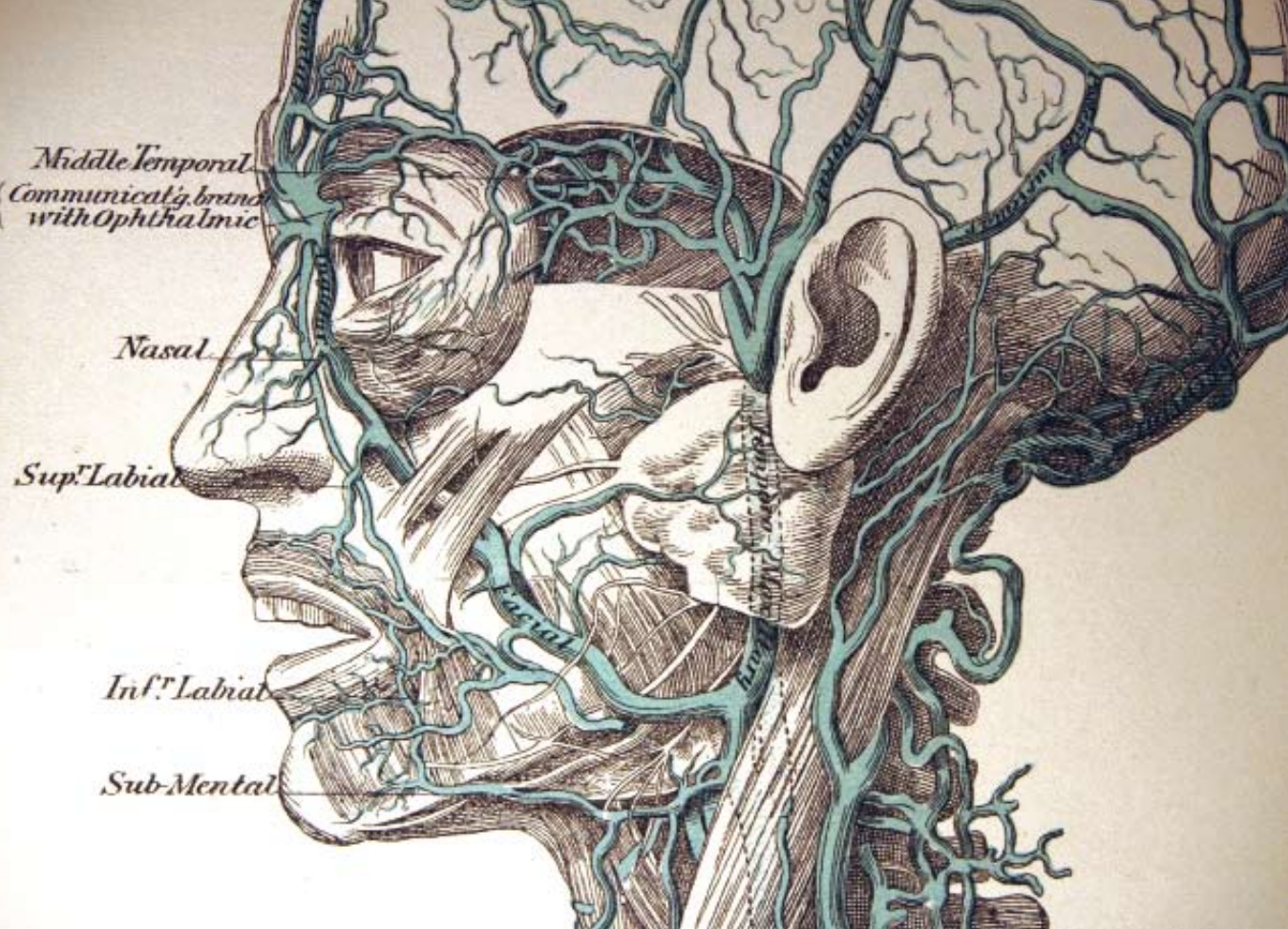
Consider, for example, the nano implications of the standard patent holder's right to demand royalties from anyone who “uses” his or her invention. Researchers at Carnegie Mellon University are currently working on nano-sized machines that could be inserted into the bloodstream to clear cholesterol from clogged arteries. Nanotechnology eventually may be used to help fight a person's cold or flu by introducing nano-sized devices or particles

into a person's bloodstream or airway that could hunt and destroy viruses. Depending on the nature of these devices, a person may need only to share saliva or blood to pass on his or her nanotechnology device to another.

Here's one hypothetical challenge for regulatory authorities: Let's say that a woman goes to visit her brother, who is a recent recipient of an injection of artery-cleaning nanobots. While talking, the brother sneezes, exhaling nanobots that are immediately and unwittingly inhaled by his sister. Now the nanobots begin coursing through her arteries, clearing them of plaque. For purposes of the Patent Act, the sister is “using” the nanobots, even though she did not intend to use them and, apart from breathing, did not take any action to start doing so. Under the patent statute, the sister is liable for infringement and could be required to pay a royalty.

Seem farfetched? Not really. Given the current application of law to biotechnology, enforcement might be even more stringent, as in the case in which a farmer was found liable because he had saved and planted seed from patented genetically modified (GM) plants that had blown onto his land. The court suggested that a truly innocent bystander who did not intend to use patented GM seed could avoid liability by acting to arrange for the seed's removal. This leaves open the possibility that a person who unintentionally is contaminated with a nanorobot would have to take action to have it removed, even if she never wanted it—or needed it—in the first place.

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blur, the old rules and procedures will not suffice.

The National Cancer Institute alone has implemented a five-year, \$144.3-million program to fund nanotechnology development to improve options for the prevention, diagnosis, and treatment of cancer. Federal funds are augmented by individual state investment in nanotechnology, about 40 cents for every federal dollar of investment. For 2008, President George W. Bush allocated \$1.44 billion for nanotechnology, an increase from \$1.35 billion in 2007.

Private investment in the field is also substantial. More than 1,200 American startups base their existence solely on the promise of technology at the nano scale. The National Science Foundation has predicted that the global market for nanotechnology-related goods and services will reach \$1 trillion by 2015, exceeding the combined economic impact of the telecommunications and information technology industries during the technology boom of the 1990s.

Government agencies and intellectual prop-

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erty policies will, for better or worse, constrain or encourage these developments. To get a patent, an applicant must prove that the invention is novel, non-obvious, and useful. Once a patent is granted, the patent holder can prevent anyone else from making, using, selling, or importing the invention. According to the principle of strict liability, a person or company doesn't have to intend to infringe to be liable. While these patent rules seem straightforward, applying them to the field of nanotechnology might lead to preposterous results, potentially creating a patent thicket or absurdly ensnaring innocent infringers.

Take the requirement that an invention must be novel. Nanotechnologies take advantage of the fact that smaller size alone gives substances novel properties. However, the FDA consid-

An illustration of the cerebral circulatory system. Nano-sized devices could one day be introduced into the bloodstream or airway to hunt and destroy viruses.



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A cellular view of a blood vessel from the circulatory system, which has an interior blockage. Researchers at Carnegie Mellon University are working on nano-sized machines that could one day clear cholesterol from clogged arteries.

ers the nano version of a chemical or product equivalent to the original larger version under the FDA approval process, so these smaller products would require no new pre-market approval testing. Yet, if the USPTO follows the FDA's lead and maintains that these nanotechnology products are equivalent to their larger counterparts, they would not be patentable.

Various nanotechnology products have been

found non-novel by the FDA and novel by the USPTO. NanOss is a bone implant that uses nanocrystals of calcium phosphate created from a patented precipitation process. The manufacturer, Ångström Medica, a privately held company located in the Boston area, claims that the nanocrystals, which will be reabsorbed by living bone, are very strong and resist cracking as compared to larger particles. It advertises the nanocrystals as duplicating "the microstructure, composition, and performance of human bone."

The FDA determined that NanOss is "substantially equivalent" to other resorbable calcium phosphate bone void filler devices because its intended use, design, and functional characteristics are substantially the same as previously approved devices, each of which was intended to fill gaps in bone, was not intended to be load-bearing, and consisted of calcium compounds. Yet the USPTO granted a patent

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on NanOss covering both the nanocrystals and the method of producing them.

Antimicrobial silver wound dressing is another product that employs nanotechnology, has FDA approval, and has been patented. NUCRYST Pharmaceuticals, a publicly held company in Wakefield, Massachusetts, uses a patented process to isolate silver-containing nanoparticles, which are then placed on a substrate of polyethylene mesh as atomically disordered nanocrystals. The substrate is used in wound and burn care products.

The FDA determined that the dressings are “substantially equivalent” to prior silver-coated dressings that release silver ions into wound sites to provide an antimicrobial effect. Yet NUCRYST holds numerous patents that cover the manufacturing process, as well as compositions of matter (including coatings, powders, and flakes) and uses that incorporate the technology.

If NanOss and nano-sized wound dressings are substantially equivalent to larger versions of the materials, as the FDA has found, an infringer might be able to challenge the patent on the grounds that the inventions are not novel. Alternatively, if these products are novel—and potentially create new risks—the FDA should be paying closer attention.

Public interest groups are petitioning the FDA to reconsider its position that the nano versions of products behave in the same way as the larger versions. In July 2007, an FDA taskforce recommended that the FDA seek public comments on which property changes in nano materials could lead to concerns about safety and efficacy. This is now playing out on our beaches and ski slopes, because the FDA determined that nano-sized particles of titanium dioxide and zinc oxide, ingredients commonly found in sunscreen, are substantially equivalent to their larger-sized counterparts. The small size of the nanoparticles gives sunscreen what seems to be a novel property—better absorbability, which reduces the white skin appearance that otherwise results from these compounds. But small size also raises health concerns.

As particle size decreases, there can be an increased evasion of the body’s natural defense



mechanisms. Inhaled or injected nanoparticles can enter the blood and lymph system and migrate to other organs, tissues, and the nervous system, raising concern that they may cause damage. Certain nanoparticles can also cross the blood brain barrier—a function which could be beneficial for drug delivery to the central nervous system, but which could also cause harm to neural tissue.

The FDA received a citizen petition from the International Center for Technology Assessment (ICTA) raising health and safety concerns relating to sunscreen products that contain nano-sized materials. In response, the FDA in August 2007 requested comments and data from the public about the safety and effectiveness of sunscreens with nanoparticles and how they should be regulated.

Faced with a new technology that creates challenges for business as usual, the USPTO seems to be granting rights to the same nanotechnology to several different entities—a sure recipe for disastrous litigation down the road.

According to the U.S. Department of Ener-

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The global market for nanotechnology-related goods and services is projected to reach \$1 trillion by 2015, exceeding the combined economic impact of the telecommunications and information technology industries during the technology boom of the 1990s.



Tall order: Jon Dudas, director of the U.S. Patent and Trademark Office, must simultaneously attempt to encourage and impose order on the highly complex business of nanotechnology.

gy, nanotechnologies “reach into electronics, biotechnology, medicine, transportation, agriculture, environment, national security, and other fields.” It is likely that a particular nanotechnology—such as a carbon nanotube or a quantum dot—will have uses in multiple fields, but the USPTO is not organized for analyzing multidisciplinary patents. Instead, it is divided into eight specific technology centers: biotechnology and organic chemistry; chemical and materials engineering; computer architecture,

software, and information security; communications; semiconductors, electrical and optical systems and components; designs; transportation, construction, electronic commerce, agriculture, national security, and license and review; and mechanical engineering, manufacturing, and products.

When an inventor submits a patent application, the USPTO routes it to the technology center with expertise in the particular discipline covered by the patent application. Because nanotechnology has such a broad scope, the USPTO does not have a single, specific technology center devoted to it.

Without specialization within the patent office, it is more difficult for examiners to gain experience with nanotechnology patents, more difficult for examiners to communicate with other examiners experienced with nanotechnology, and more difficult for the USPTO to educate personnel. As a result, nanotechnology patents may be issued that are overbroad, of poor quality, or invalid.

The ETC Group, a nonprofit environmental group, criticizes patents that claim one basic nanotechnology application but cover large portions of the periodic table. One applicant claimed proprietary rights to a metal-oxide nanorod made with any one of 33 different chemical elements. A quantum dot patent claimed semiconducting nanocrystals made from any of the elements contained within Groups III-V of the periodic table.

Columbia University economist Bhaven Sampat found that, between 2001 and 2003, 794 different primary patent examiners analyzed the 3,748 nanotechnology patents he identified in his study. This represented nearly one-fourth of the primary patent examiners employed by the USPTO during that time period. Similarly, in 2004, patent attorneys Donald Featherstone and Michael Specht reported that 142 examiners analyzed 206 nanotube patents. Less than one-quarter of these examiners examined more than one nanotube patent. Overlapping patents are already emerging for nanotubes, the cylinders made up of a layer of carbon atoms, either a single tube or multiple tubes within each other. In a 1991 article

in *Nature*, NEC Corporation researcher Sumio Iijma reported that he had created a carbon nanotube. Two years later, IBM filed a patent application that resulted in a claim for “[a] hollow carbon fiber having a wall consisting essentially of a single layer of carbon atoms.” The timing of the patent application raises questions as to whether it was truly novel given that such a compound had been discussed in a scientific journal several years earlier.

A study of nano patents published in 2005 by researchers from Arrowhead Research (a publicly traded nanotechnology company), Canon USA, and the NanoBusiness Alliance found 306 nanotube patents, including 10 patents claiming the nanotube itself and 20 patents on nanotube production methods, which could lead to litigation as various patent holders assert rights against each other.

The USPTO tried to deal with the issue of overlapping nanotechnology patents by holding meetings with industry representatives and creating a cataloging system which puts the label “Class 977” onto certain technologies related to “nanostructures.” The USPTO defines a nanostructure as “an atomic, molecular, or macromolecular structure that: (a) Has at least one physical dimension of approximately 1-100 nanometers; and (b) Possesses a special property, provides a special function, or produces a special effect that is uniquely attributable to the structure’s nanoscale physical size.”

The USPTO reviewed previously issued patents to determine retroactively which should be classified under 977. However, the 977 classification has many exceptions. For example, enzyme and protein complexes are generally excluded from 977. Viruses utilized for viral functions are categorized in separate classes, rather than 977. But, a virus utilized to form a nano structure is included in the 977 classification.

With funding from the National Science Foundation and the U.S. Department of Energy, we examined all nanotechnology patents issued from 1976 to 2006 that involved a particular nanotechnology—quantum dots. We found 307 such patents, with 6,769 claims. However, of the 307 nanotechnology patents claiming quantum dot technology we located, only one in five had been catalogued in Class 977, which might make it more difficult for patent examiners to locate relevant material about previously granted nanotechnology patents. This may be why duplicate patents are being granted to separate inventors on the same technology.



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It’s unclear what the future of nanotechnology will bring. The U.S. Department of Energy predicts nanotechnology will revitalize biotechnology and medicine. But overly broad patents—like IBM’s patent on the carbon nanotube—might create a patent thicket. The FDA and USPTO must come up to speed on the ABCs of nanotechnology—including Atomic Auto Film, Buckyballs, and Carbon Nanotubes—for the business of nanotechnology to go forward. **TOOLS**

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Antimicrobial silver wound dressings employ nanotechnology, have FDA approval, and have been patented. They work by releasing silver ions into the wound area, having an antimicrobial effect.