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Strategies for Resolving Patent Disputes Over Nanoparticle Drug Delivery Systems

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Strategies for Resolving Patent Disputes Over Nanoparticle Drug Delivery Systems

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ABSTRACT

Some of the earliest products commercializing nanotechnology could be drug delivery systems. Nanoparticle-based delivery systems would allow faster drug absorption into the human body and would have other unique properties minimizing side-effects. As companies seek to bring new therapies to market, there are certain to be a number of disputes over potentially overlapping patents. In this article, IP lawyer Drew Harris and his colleagues explore the major issues faced by a nanobiotech company as it deals with cross-infringing patents. Specifically, they cover the legal tactics available to companies dealing with patent disputes at the different stages of competition, including: (1) patenting strategies to obtain broad, enforceable patent coverage that preempts the field; (2) patent interference practice to attack a competitor's patent application; (3) patent re-examination, a procedure for challenging a competitor's issued patent; (4) cross licensing of patents to co-exist with a competitor; and (5) patent infringement litigation. While this article is tailored towards nanoparticle drug delivery systems, these strategies may also be used to resolve other nanotechnology patent disputes.

INTRODUCTION

There have been few nanotech patent disputes thus far, mainly because most companies have yet to commercialize their nanotechnology discoveries. That is about to change, as companies are now bringing nanotech products to market. Nanoparticle-based drug delivery

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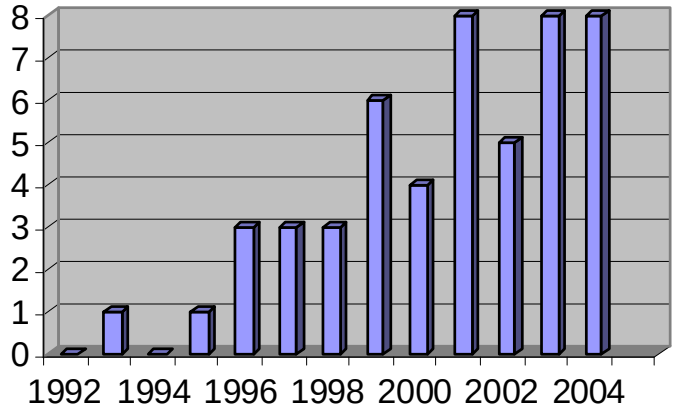
systems may be among the first types of products to generate serious nanotech patent disputes as the multi-billion dollar pharmaceutical industry begins to adopt them. These new drug delivery systems would allow faster drug absorption, controlled dosage releases, and shielding from the body's adverse reactions—enhancing the effectiveness of already existing drugs. Researchers are also investigating novel treatment approaches based on nanoparticles, such as using them to carry chemotherapy drugs and specifically target cancerous cells.

The market impact of nanoparticle drug delivery systems on the pharmaceutical industry will be widely felt, ranging from new specialized treatments for exotic diseases to reengineering common over-the-counter pain relievers. These new delivery systems will even disrupt the generic drug market, since pharmaceuticals can repackage their brand name drugs with expired patents along with newly patented delivery systems, so that generic drugs can no longer claim to be brand name equivalents. According to a report by Front Line Strategic Consulting, the market for nanobiotechnology will exceed $3 billion by 2008,[1] a good chunk of which will likely come from drug delivery systems.

In light of the potential market value of nanoparticle-based drug delivery systems, researchers, executives, and patent lawyers are in a patent "land grab," trying to snatch up broad patent rights on different nanoparticle compositions and methods of use. As *Figure 1* depicts, a recent study of patent activity for nanoparticles in drug delivery shows a clear increasing trend in issued patents.

FIGURE 1: TREND IN ISSUED PATENT INVOLVING NANOPARTICLES



Source: Presentation on the U.S. Patent Landscape of Nanoparticles for Drug Delivery by Susan J. Mack, Esq. Reprinted with permission.

Some companies are already marketing their patented drug delivery systems. For example, Elan Corporation is marketing their proprietary "Nanocrystal" technology, which delivers drugs in particles around 200 nanometers in size, covered by a stabilizer coating. Elan's press releases announce that their Nanocrystal technology has already been granted approval for use in drugs by Merck and Wyeth, as well as having been licensed to other pharmaceuticals such as Roche and Aventis.[2]

While Elan and its drug delivery business unit, Nanosystems LLC, have a sizeable portfolio of composition and method of use patents for their Nanocrystal technology, they and other nanobiotech companies bringing new drug delivery systems to market will face considerable uncertainty regarding

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[1] *See* FRONT LINE STRATEGIC CONSULTING, NANOBIOTECHNOLOGY, OPPORTUNITIES AND TECHNICAL ANALYSIS (April 2003), *available at* http://www.navigantconsulting.com/lifesciences/flsmr3.htm#nano.

[2] The relevant Elan Corp. press releases are available at http://www.elan.com/DrugDelivery/Announcements.

broad and potentially overlapping patents held by others. As others have previously noted, the U.S. Patent & Trademark Office's lack of expertise with the interdisciplinary nature of nanotechnology has led to many patents with overlapping claims.[3] As a potential example, the pending U.S. Patent Application No. 20040076586 makes the extremely broad claim of "a pharmaceutical composition comprising a nanoparticulate drug delivery vehicle and a pharmaceutically active agent." The application, entitled "Compositions and Methods for Delivering Pharmaceutically Active Agents Using Nanoparticulates," asserts a March 28, 2002 priority date based its provisional application.

This ongoing patent land-grab will worsen the problem for companies trying to commercialize their nanotechnology research now. As nanobiotech startup companies may soon find themselves in a patent dispute with established pharmaceuticals or the multitudes of newer biotech firms, their executives and lawyers should carefully consider their strategic options.

In this article, we seek to provide a roadmap of strategies to nanobiotech companies involved in patent disputes. We describe strategies that a company can use to proactively avoid getting into a patent dispute, such as (1) strategically drafting clearly described patents that preempt the field, or (2) attacking potentially overlapping patents before they are ever issued. The article also covers three potential strategies once a dispute occurs, in order of increasing cost. These include (3) requesting a patent re-examination by the patent office, (4) cross licensing patents, and (5) patent litigation.

While this article describes these strategies in the context of overlapping claims regarding nanoparticle-based drug delivery system, they are also applicable to resolving other kinds of nanotechnology patent disputes.

TABLE 1: STRATEGIES FOR RESOLVING PATENT DISPUTES

Pre-Dispute Strategies	1. ***Strategic patenting*** to clearly box-out competition
	2. ***Interference practice*** to prevent overlapping patents from being issued
Post-Dispute Strategies	3. ***Patent re-examination*** to inexpensively challenge a competitor's patent
	4. ***Cross licensing patents*** to peacefully co-exist
	5. ***Patent litigation*** to invalidate a competitor's overlapping claims

I. BACKGROUND ON NANOPARTICLE-BASED DRUG DELIVERY SYSTEMS

New drug delivery systems based on nanosized structures offer significant advantages over current systems. First, delivering drugs in smaller particle size increases the total surface area of the drugs, allowing for faster dissolution into the bloodstream or other liquids. This faster dissolution translates into faster absorption by the human body, and thus faster performing drugs. For example, Nanosystems LLC's U.S. Patent No. 5,718,919 (issued Feb. 17, 1998) describes a composition of nanoparticles of ibuprofen along with a surface modifier. Ibuprofen, commonly sold as Advil or Motrin, can be delivered as a quicker, longer-lasting pill.

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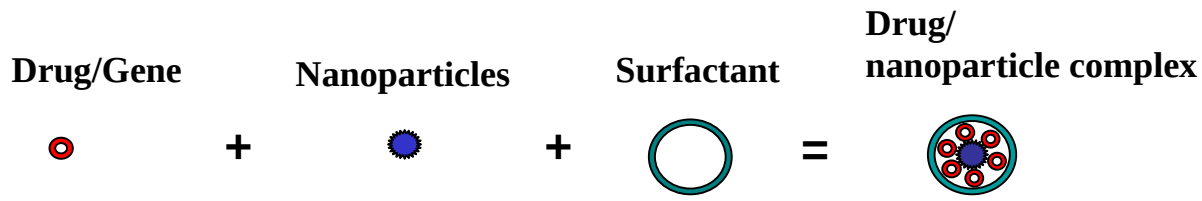
[3] *See* JOHN MILLER, ET AL., THE HANDBOOK OF NANOTECHNOLOGY BUSINESS, POLICY, AND INTELLECTUAL PROPERTY LAW 68-74 (2004) (describing the issues of broad and overlapping claims in issued nanotechnology patents).

The enhanced absorption also means that drugs that would normally have to be intravenously injected into the body in liquid form could instead be taken orally as a pill or even as a nasal spray. Many of the drugs taken orally have to be combined with some other form of solvent, ranging from lipids to bile salts, to assist with dissolution and bodily absorption. This creates drug delivery problems such as the stability and purity of the delivered drug, as well as potential toxicity for some people. New nanoparticle drug delivery approaches would reduce or eliminate the need for such co-solvents.

New delivery systems would also increase the efficiency of drugs by increasing their "bioavailability." As a higher percentage of the drug compound can be quickly absorbed by the body, the overall dosage can be reduced. This lowered necessary dosage reduces the potential side effects of many drugs. Furthermore, drugs that have side-effects due to triggering an immune system response can be "wrapped" in a nanoparticle coating, preventing the immune system from recognizing and reacting to a foreign substance.

FIGURE 2: ASSEMBLING OF A DRUG-LOADED AND COATED NANOPARTICLE



Courtesy of NanoDel Technologies GmbH

Another exciting use of this nanoparticle coating is a controlled release of the drug. Drugs could be coated with a nanoparticle surface that breaks down according to controlled parameters, allowing the drug to be released over a long period of time, or just when necessary. BioSante Pharmaceuticals is developing a surface-coating approach they call "calcium phosphate-based nanotechnology" ("CAP"). Biosante is the holder of Patent No. 6,355,271 (issued Mar. 12, 2002), which describes methods of preparing and using calcium phosphate particles as "controlled release matrices for biologically active material." BioSante is currently testing its CAP technology in animals for long-acting injectable insulin, as well as inhaled and oral insulin.[4] Other researchers have been trying to develop implantable devices made of copolymer-nanoshell composites that release drugs when exposed to infrared light.[5]

Nanoparticles can also be used to create a whole new class of drugs, rather than merely be used as vehicles to deliver preexisting ones. The Scripps Research Institute is developing a new class of antibacterial peptides. Nanotubes are formed by self-assembly of cyclic peptide nanoparticles. With appropriate design, these nanotubes insert themselves into bacterial—but not mammalian—cell membranes. The nanotubes create pores in the cell membrane, resulting in rapid bacterial cell death and great reduction in infection.

As a review of select nanoparticle drug delivery patents shows (see *Figure 3*), there are several advantages to using nanotechnology in delivering medicine. Pharmaceutical companies and nanobiotech startups are racing to develop novel approaches, and patenting everything they can along the way.

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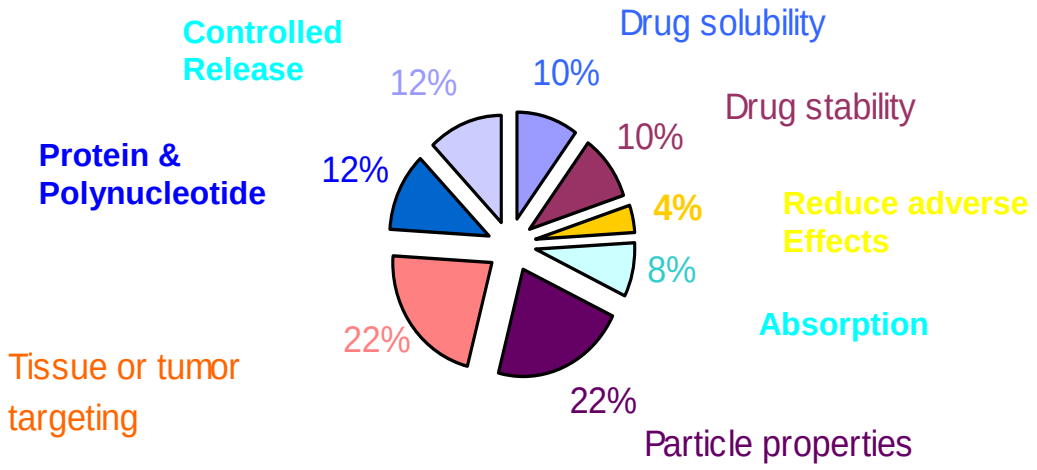
[4] *See* BIOSANTE, PRESS RELEASE PHARMACEUTICALS PRESENTS STUDY RESULTS FOR TRANSMUCOSAL INSULIN ADMINISTRATION, Nov. 8, 2004, *available at* http://www.biosantepharma.com/newshtml/110804pr.html.
[5] *See generally* Celia M. Henry, *Drug Delivery*, 80 CHEM. & ENG'G NEWS 39 (Aug. 22, 2002).

FIGURE 3: GOAL OF SELECT NANOPARTICLE DRUG DELIVERY PATENTS ISSUED 1992-2004



Source: Presentation on the U.S. Patent Landscape of Nanoparticles for Drug Delivery by Susan J. Mack, Esq. Reprinted with permission.

II. STRATEGIC PATENTING TO "BOX OUT" THE COMPETITION

1. The Ease of Obtaining Broad, Overlapping Patents in Nanotechnology

The first way to resolve a patent dispute is to prevent it from happening in the first place by having broad, clearly described patents that box out the competition.

There may be strategic reasons to be less clear in describing a claimed invention—an examiner might allow a broader claim, or a competitor might fail to fully understand the relevance of the patent until it is too late. However, this strategy will also create more potential disputes over the patent. Examiners may grant invalid patent claims because they did not review potentially relevant prior art, or may grant later overlapping patents. Other companies may unintentionally infringe the patent, rather than just ask for a license, resulting in unnecessary infringement litigation. Companies seeking to avoid costly patent disputes should strive for clarity while seeking the broadest patents possible.

Because nanotechnology is in its infancy, filing nanotech patents has become a "patent land grab." Since the prior art is sparse-to-nonexistent for many of the new discoveries in nanoscience, broad patents are being issued by the U.S. Patent & Trademark Office ("PTO"). This is especially true in areas such as nanopharmaceuticals and nanobiotechnology, since the PTO's current staff lack the cutting edge knowledge to completely understand these inventions. This problem is exasperated by the fact that the PTO still faces an enormous backlog of nanotechnology patent applications. While the PTO has recently created an individualized classification for nanotechnology patents, given the current structuring of the PTO (with Congress siphoning off money from patent fees to fund its general coffers), the PTO cannot pay going market rates for employees with cutting edge, highly skilled backgrounds. Adding to this problem is the practice of companies providing cryptic descriptions of their inventions in an attempt to "bury" their patents to obtain broader claims. With unclear descriptions or claims, the PTO examiner is

often unable to find and identify all relevant prior art. The result of these problems has been a torrent of improperly reviewed patents being granted.[6]

These broad, overlapping nanotech patents are converting the patent system from a stimulator of innovation to a creator of litigation and uncertainty.[7] The current "patent proliferation climate" affecting nanotechnology generally will certainly extend to nanopharmaceuticals and nanobiotechnology. Since nanobiotech companies have no choice but to participate in the patent land grab, their patents should minimize future patent disputes by claiming broad subject matter while clearly signaling to patent examiners and competitors the scope of their claims.

2. Maintaining Proper Lab Notebooks

A strategic patenting approach starts even before an invention is discovered. Scientists and researchers need to be schooled in the ways of spotting potential inventions and documenting them. Policies regarding proper laboratory notebook documentation are often critical to resolving patent disputes.

Since discoveries and inventions often come about in unpredictable ways, it is important for nanobiotech startups to document each step of their research, which is often done in laboratory notebooks. The company should have a clear policy for its researchers to ensure that each measurable step of progress is well-documented. That way if anything ends up being patentable, the dates for its conception and reduction to practice will be documented. These dates will become crucial if and when two competing entities lay claim to the same invention.

3. Avoiding Early Publication or Any Public Disclosure

Often a company releases information on a new drug treatment under development, or discusses details during negotiations with pharmaceutical companies prior to filing a patent application. Companies should be very careful when doing so.

In general, companies 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. Such early disclosure may trigger the one-year "on-sale bar." A patent applicant has one year to file for an application from the date that an invention is first published, publicly displayed, used by others, or offered for sale.[8] Public disclosure in any of these forms triggers a one-year deadline to file a patent application in the U.S.

4. Obtaining Foreign Patent Protection

Public disclosure can also undermine a company's ability to obtain foreign patent protection. Since foreign patent offices do not allow for a one-year grace period as does the U.S., *any* publication or public disclosure could prevent the inventor from obtaining foreign patents altogether.

Whether or not a company should file a patent in a foreign country should be based largely upon realistic market considerations. This may include the desire to launch a product directly into foreign markets, but even if the inventor has no intention of establishing a business abroad, foreign patent protection should still be part of a long-term competitive plan. Benefits include potential licensing deals

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[6] For more information about the state of the PTO's review of nanopatents, see Raj Bawa, *Nanotechnology Patenting in the US*, 1 NANOTECH. L&B. 31 (2004); Raj Bawa, *Nanotechnology Patents and the U.S. Patent Office*, 4 SMALL TIMES IP8 (2004).

[7] *See generally* ADAM JAFFE & JOSH LERNER, INNOVATION AND ITS DISCONTENTS (2004).

[8] 35 U.S.C. § 102(b) (2004).

in other countries as well as the discouragement of importing unlicensed foreign goods. Failing to patent abroad can result in a loss of valuable market share abroad as well as having to deal with the headache of foreign companies selling "gray" market goods in the U.S.

However, foreign patent protection is not cheap. Outside of the United States, countries charge around $5,000 a year on each pending patent. The translation fees alone to secure a patent in Japan can run $12,000 to $20,000. Nanobiotech companies must decide whether market demands justify the price of international patents.

U.S. inventors planning on filing abroad should file an application under the Patent Cooperation Treaty ("PCT").[9] Filing in accordance with PCT rules allows inventors a one-year grace period from the time of filing the national stage patent application in which to file in foreign countries that have joined the PCT. PCT rules provide a mechanism by which the inventor can specify in which particular foreign countries he or she intends to seek patent protection. The inventor then has thirty months (or more) from the time of filing the original national stage application to fulfill all the requirements of each of the foreign patent offices in which he or she filed. The real advantage to this extensive time period is that it gives the company an amount of time to determine whether their invention is commercially viable and warrants the further expense of fulfilling the further requirements for patenting in the designated foreign countries.

5. Filing Quick and Dirty Provisional Patents

To obtain maximum patent protection worldwide, a nanobiotech start-up can choose to file a "quick and dirty" provisional patent applications as soon as they realize new inventions. Provisional applications contain a description of the invention, but do not include claims. After filing for a provisional application, a start-up has one year to file a non-provisional application.

Provisional patent applications are a relatively new concept which allows an inventor to make a claim on an invention by filing documents without actually going through the tedious process of drafting claims. The main benefit is that the filing date of the provisional application acts as a priority date for filing the patent in other countries under the PCT. After the company has filed a provisional application, it does not have to worry that publication and other disclosures will automatically disqualify it from obtaining foreign patent protection.

While some companies and institutions favor filing provisional applications with an organized specification—and in some case, even with draft claims—others do not want to slow down their researchers. Instead, they file simple documents with just an engineer's description and no specification or claims—hence the name "quick and dirty" provisional applications.

6. Conducting a Prior Art and "Freedom-to-Operate" Search

A key step to drafting broad claims that preempt the field is to fully understand what else is in the field. It is imperative to conduct a thorough prior art search before filing a patent application. Knowledge of existing patents allows the patentee to write patent claims which "carve between" competing patents. In addition, since patents do not automatically provide the right to practice the underlying invention, it is wise for a company to conduct a broader "freedom-to-operate" search prior to investing and/or commercializing the claimed invention. This consists of researching other patents and

[9] The PCT is a multilateral treaty established in 1978 among more than 120 nations that 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."

products which, while not identical, are similar or related enough to create the possibility of a patent dispute. A list of databases to search is included below in *Table 2*.

TABLE 2: PRIOR ART SEARCH DATABASES[10]	
Issuing Authorities' Websites	Including the U.S. Patent & Trademark Office (www.uspto.gov), the European Patent Office (www.european-patent-office.org), and Japanese Patent Office (www.jpo.go.jp)
Thomson Databases	Providing various patent databases, including Derwent World Patents Index, Delphion, and Thomson Pharma
IFI CLAIMS Patents Database	Providing data on U.S. patents and current patent legal status
STN Chemical Abstracts Database	Provides coverage of the chemistry bibliographic data available from Chemical Abstracts Service, including patents and patent families
IMSWorld Drug Patents International Database	Provides patent family data for commercially significant drugs
INPADOC	European patent search database
JAPIO	Patent abstracts of Japan
Engineering, Technology & Scientific Databases	Including INSPEC, EiCompendex, SCISEARCH, and Chemical Abstracts Service
Markets & Business Databases	Including Factiva and PROMT

As a further note, the filing of a patent application or the conducting a prior art or freedom-to-operate search will most likely require the assistance of skilled engineers and attorneys well-trained in multi-disciplinary areas including biotechnology, physics, medicine, chemistry, and engineering. Therefore, handing over ones patent application to a person lacking a piece of this multifaceted puzzle of knowledge may result in a company forfeiting much in the terms of the bread and enforceability of the patent. This will in turn impact the patent's (1) commercialization opportunities, including licensing, (2) investor interest, and (3) may even result in the patent being found to be unenforceable. Therefore, employing well-qualified—technically minded yet creative—patent counsel is of critical importance.

7. Using Standard Language When Drafting Patent Applications

Many patent disputes are caused because the patent does not use standard language that clearly signals what the patent covers. Nanotechnology is an inherently difficult topic to discuss, in part due to growing proliferation of "nano-" terms, as well as the confusion surrounding the definition of this new area of technology.[11] Often different words can all be used to describe the same thing—for example, nanoparticle, nanoparticulate, and nanocrystal could all be used to describe a solid state cluster of atoms with certain properties. Further compounding this problem is the well-recognized principle in patent law that applicants can be their own lexicographer; they can create new terms to describe the disclosed

[10] For more tools for researching prior art, see also Raj Bawa, *Nanotechnology Patenting in the US*, 1 NANOTECH. L&B 31, 40 (2004).

[11] There is confusion on the definition of nanotechnology, particularly the scale of products. While the U.S. National Nanotechnology Initiative has arbitrarily defines nanotechnology as "anything involving structures less than 100 nm in size," this definition excludes numerous devices and materials of micron dimensions, a scale that is included within the definition of nanotechnology by many scientists.

invention. While fanciful naming may be fun for engineers and may add hype to the marketing of the invention, it is recommended that an applicant employ language that is well-established in the field of endeavor.

Additionally, the language should be precise and the use of terms consistent throughout the claims and specification. This would include the avoidance of synonyms as well as the unnecessary repetition of phrases to prevent confusion and the inherent prosecution delay caused by a confused PTO examiner having to determine the meaning. The more confused the examiner is, the more likely he or she will look into an increasing number of prior art areas, which will most likely lead to the narrowing of claims, or in the extreme, the denial of a patent.

Further, if the patent were ever to become the subject of a lawsuit for infringement, the success of this suit may hinge on how the patent was drafted. A poorly drafted patent will give an advantage to the competitor, causing significant aggravation and substantial litigation fees for the inventor.

8. Be Prepared for Pre-Grant Publication of U.S. Patent Applications

In the last few years, the PTO has changed the way it publishes patent applications. Currently, as part of the standard application process, each patent application is automatically published eighteen months from the date of filing, unless the applicant opts out and foregoes foreign patent filing.[12] Therefore, regardless of whether the disclosed invention is granted a patent or not, its confidential status will be gone within a year and a half. This furthers the PTO's stated objective of granting potential patent protection to the inventor in exchange for turning over the underlying ideas to the public domain.

What this means is that competitors will be able to review ones patent application and potentially challenge it through the interference proceedings described below. Companies should be prepared for reaction from competitors when their patent applications reach the eighteen month publication date.

9. Require Strong Employment Confidentiality Agreements

As a final note, a strategic patenting policy should also make use of trade secret protection to prevent similar research or patenting activity by competitors that may lead to disputes. Nondisclosure and non-competition agreements, which if drafted within the accepted realms, can safeguard against company researchers from disclosing or using technology to further their own personal agendas. Additionally, agreements should be required of consultants and visiting scholars that ensure that all rights to discussed technologies fostered internally are assigned to the company. Furthermore, confidential materials should be properly labeled and safeguarded; otherwise, value associated with specific information or inventions may be lost or reduced.

III. INTERFERENCE PRACTICE: ATTACKING A COMPETITOR'S PATENT APPLICATION

1. Monitoring Issued Patents and Published Applications

As noted above, pending patent applications are published after eighteen months. Companies should be monitoring relevant patent applications and issued patents to look out for potential disputes. When companies find overlapping subject matter in another application, they can file a request with the PTO for

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[12] Traditionally, applications filed at the PTO were kept secret until they matured into a patent. However, as a result of the American Inventors Protection Act ("AIPA") of 1999, an application filed on or after November 29, 1999, loses its secret status if and when it is published.

an interference, which entails having the patent office make a determination between two conflicting patent applications as to who was the first to conceive and reduce to practice the underlying invention.

This proceeding exists because the U.S. system awards patents based on a system of "first to invent" in marked contrast to that of most other countries, which have adopted a "first to file" patent system. Under the "first to file" system, the first entity to file a patent application on a given patentable subject matter is entitled to have the patent. However, under the U.S. "first to invent" system, the first person to invent receives priority. The first to invent is based on the first to conceive of the idea so long as the idea is reduced to practice without any unreasonable delay.

Since the PTO is backlogged and it often takes about three years to obtain a patent from the date of filing, oftentimes two patent applications covering common subject matter will have review times which are coterminous with one another. When this happens, an interference proceeding can be initiated so that the PTO can "flesh out" which inventor was the first to conceive and reduce to practice the invention. This can be initiated at the request of either party, or by the PTO itself.

Because examiners work independently of one another, there is no built-in monitoring system within the PTO for determining when an interference should be raised on its own initiative. Therefore, unless two similar applications by chance cross the desk of the same examiner, the chances for a PTO-initiated interference are very slim. Therefore, the more common scenario that one of the patent applications is published or issues as a patent, and the other party becomes aware of it and then requests an interference. In making such a request, the party can challenge multiple applications or patents which it deems to be in conflict with its own application.

2. Interference Proceedings

Once an interference proceeding has begun at the PTO, each party must submit evidence in support of the conception and reduction to practice of the invention. This evidence critically includes inventor's records documenting the date of conception of the invention, including: (1) lab notebooks, (2) correspondence between inventors, (3) prototypes, and (4) computer models. Further, to adequately document these materials, it is imperative that the inventor routinely and methodically date and sign these materials in front of a witness. This is crucial because during the actual proceeding for the interference, the testimony of the witness will often carry more weight than that of the inventor.

Once an interference is requested, an administrative patent judge presiding over the case will designate one party the "senior party" and the other the "junior party," based on which has the earlier filing date. Consequences stem from these designations, including a placement of the evidentiary burden on the junior party. This results in the junior party having the burden of proving that its conception occurred first. This can amount to a tremendous burden as "hindsight is 20/20," and the documented evidence is sometimes just not there. Therefore, the importance of filing an application as early as possible can be beneficial not only in avoiding prior art, but also in shifting the burden of proof in an interference proceeding.

Once all of the evidence has been submitted to the patent office, the administrative patent judge, who is a member of the Board of Patent Appeals, reviews the information and decides which party was the first to invent. Should one party want to challenge this ruling, an appeal may be made first to the Board of Patent Appeals and Interferences, and subsequently to the United States Court of Appeals of the Federal Circuit. Should one want to challenge the Federal Circuit's ruling, the party must file a petition to the U.S. Supreme Court.

IV. PATENT RE-EXAMINATION: A METHOD OF CHALLENGING A COMPETITOR'S ISSUED PATENT

To challenge the validity of an issued patent, a party can file for a re-examination of the patent. This practice often takes place in situations where one party did not file an application, but does not believe that a competitor's issued patent is valid. This most likely this occurs after a patent holder sends a letter to another to "cease and desist" making, using, or selling the underlying inventions claimed by the patent. If the recipient of the letter believes that the patent should be invalidated, it can file for a re-examination instead of filing a lawsuit for declaratory relief as to the patent's validity. The main reason for doing this as opposed to litigating is the significantly cheaper cost. In fact, re-examination was first established in 1980 in an effort to provide a lower cost alternative to litigation.

The advantage to using re-examination is that a patent examiner with a scientific background would be the one making the invalidity determination, instead of a judge, who in most cases, has no scientific training. Further, if the re-examination is granted, then the trial can be "stayed," i.e., put on hold pending the outcome of the re-exam. However, the defendant is pretty much stuck with the conclusions of the re-exam; if the patent survives re-exam, then the defendant cannot challenge it at trial using any of the prior art it provided as a basis of the re-exam. In the event that the patent is completely invalidated, then the defendant has put an end to the lawsuit's claims for patent infringement.

1. Anonymous *Ex Parte* Re-Examination

Further there are two types of re-examinations: *ex parte* and *inter partes*. In an *ex parte* re-examination, any party, including the patent holder and outside parties, can seek re-examination of an issued patent. However, this re-examination must be based on issued patents or printed publications. The term "publication" is broad and extends beyond a book or published article to include any disclosure that is publicly accessible. This definition would embrace such sources as websites and catalog offerings. In submitting the request for re-exam, the party must set forth its arguments in much detail in the request. However, a key benefit to going this route is that the requesting party may remain anonymous throughout the proceeding.

After the request is filed, the patent office must determine within a three month period whether a substantial new question of patentability exists. In making this determination, the PTO looks to see if "there is a substantial likelihood that a reasonable examiner would consider the prior art patent or printed publication important in deciding whether or not the claim is patentable."[13] If such a determination is made, re-examination of the patent will take place. However, if not, then the decision is final and non-appealable.

In the event that a re-examination is ordered by the patent office, the patentee is given the opportunity to file a statement concerning the new question of patentability within two months of the request. At this point, the patentee may submit amendments or file new claims to be considered. However, copies of these statements and amendments are provided to the anonymous party requesting re-examination. Also, the requesting party is given two months to file a reply to the patentee's statement.

Following the *ex parte* re-examination, the patent office issues a certificate cancelling any claim determined to be unpatentable, confirming any claim determined to be patentable, and incorporating in the patent any new claim or amended claim determined to be patentable.

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[13] MANUAL OF PATENT EXAMINING PROCEDURE § 2242 (2004).

2. Appealable *Inter Partes* Re-Examination

A second form of re-examination exits known as *inter partes* re-examination was recently established just in 1999. While it has not been used as much as the PTO hoped, given that companies do not want to be the PTO's "guinea pig" for this relatively new procedure, it does provide a different mode of re-examination.

While this procedure is similar to *ex parte* re-examination in that any party can make a request for it, it differs in that this party's identity is not kept confidential by the PTO. Also, while the prior art to be considered is the same for both procedures (i.e., prior patents and printed publications), *inter partes* re-examination differs from regular re-examination in that the third party requester will receive copies of any communications between the patent office and the patentee, and vise versa. In addition, the third party is permitted to submit timely comments to any communications sent by either the PTO or the patentee.

After the patent office has reached a final decision in an *inter partes* proceeding, either the patent owner or the requester may appeal an adverse finding to the Board of Patent Appeals and Interferences, and on up, as is the case in interferences. This differs significantly from *ex parte*, in which no appeal is possible.

V. CROSS LICENSING PATENTS: A METHOD FOR CO-EXISTING WITH A COMPETITOR

When overlapping subject matter exists in patents, an efficient and often mutually beneficial method for resolving such patent disputes is to consider cross licensing agreements.

A recent example of a successful cross licensing agreement as a means to settle a technology dispute involved two emerging companies, namely, BioCrystal Limited, and Crystalplex Corporation. Each company owned technology associated with producing fluorescent semiconducting nanocrystals and nanobeads that are used in detecting low-abundance molecules in research and diagnostics. In the cross licensing agreement, BioCrystal provided Crystalplex with the right to use its proprietary technology related to nanocrystal-encoded beads and a nanocrystal-enhanced filter set. In return, Crystalplex provided BioCrystal with the right to use, via a sublicense, its proprietary alloyed nanocrystal technology.[14]

As a result of the technology exchange in the BioCrystal-Crystalplex cross licensing agreement, both parties are now collaborating on efforts to extend the market reach of their fluorescent biomolecular assaying platforms. Toward this end, the cross licensing agreement also allows for joint product distribution of their nanocrystal and nanobead technology.

1. Benefits of Cross Licensing

As BioCrystal and Crystalplex may have discovered, one of the primary reasons for entering into a cross licensing agreement is that each party gains access to nanotechnology that may be necessary for continued development and commercialization of their individual technologies. In this regard, cross licensing agreements between two otherwise competing parties provides a means for the exchange of intellectual property with the potential (typically for at least one of the parties) to receive payment for their part of the technology. Apart from outright payment for the license, an additional benefit that the

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[14] *See* NANOTECHCAFE.COM PRESS RELEASE, *BioCrystal and Crystalplex in Broad Cross-Licensing Pact*, Nov. 1, 2004, *available at* http://www10.nanotechcafe.com/nbc/articles/view_article.php?section=CorpNews&articleid=150911.

parties may obtain from the cross licensing agreement is the receipt of income due to the other party's ongoing commercialization of their technology.

Another not-so-obvious benefit of cross licensing agreements is that each party may garner "free advertising" via news releases regarding the other party's research efforts and product line. More specifically, such news releases may advertise the other party's technology as being incorporated into the product line. Furthermore, each party to the cross licensing agreement typically gains strength when teamed with the other party to lock out competition from other entities developing similar areas of nanotechnology.

2. A Cross License Agreement Represents Two Grants

In its broadest sense, a cross licensing agreement incorporates two licensing agreements in a single document. More specifically, typical cross licensing agreements between two parties represent the grant of a first license of technology from Party A to Party B, with part of the consideration being the grant of a second license of technology from Party B back to Party A. Because the terminology used in the cross licensing agreement is the same as would be used in two separate agreements, combining the license agreements into the single document increases efficiency in drafting the licensing agreement as well as removes uncertainty with regard to the rights and liabilities of each party. Each party to the cross licensing agreement becomes both a licensor and a licensee, with all of their rights and the liabilities being conveniently contained within a single document.

3. Initial Assessments Prior to Entering into the Cross License Agreement

Prior to entering into the cross license agreement, each party should assess the capability of the other party in performing its share of the terms of the license agreement. For example, each party should assess the ability of the other party to fully exploit the technology that it is receiving as well as the ability of each party to provide any consideration as part of the technology exchange. Such consideration may be in the form of additional technology or it may take a monetary form, such as an up-front or lump sum payment, or future scheduled payments.

Each party should also determine whether it is best to enter into an exclusive or non-exclusive grant of the rights to their technology. If one party is unsure as to whether the other party will fully exploit the technology that it is receiving, a non-exclusive license agreement may be the more prudent vehicle. In a non-exclusive license agreement, other entities that are not party to the cross license agreement may be in a better position to commercialize the technology and thereby add to revenue that can be generated. In extremely competitive or emerging technology areas such as nanotechnology, granting exclusive rights in both directions may help to block outside competitors from gaining market share.

The duration of the cross licensing agreement is another important factor to consider for each party. Typically in one-way license agreements involving patents, the license agreement runs until the expiration of the last-to-expire of the licensed patents. However, in rapidly developing technology areas such as nanotechnology where products may become obsolete in short periods of time, the actual duration of the cross licensing agreement may fizzle prior to the expiration of any licensed patents such that the specification of a time limit is a mere formality.

4. Parts of a Cross Licensing Agreement

In many legal documents, a principal cause of conflict between parties is uncertainty as to the meaning of certain terms and language. Likewise, in cross licensing agreements, differing interpretations as to language laying out each party's rights, duties and liabilities may result in conflict. Specifically in

the case of nanotechnology where there is much confusion regarding the meaning of certain terms, it is essential that any language is clear regarding the rights that are being granted by each party. It is preferable to err on the side of verbosity in describing exactly what each term means and examples are highly recommended where it is anticipated that the definition of certain terms in the agreement may be unclear.

A. Define the Licensed Technology

The cross licensing agreement should clearly state which patents are to be included in each grant. Furthermore, the cross licensing agreement should specify whether any patent applications and related technology are to be included in each grant. Even further, the cross licensing agreement should consider whether continuation applications, continuation-in-part applications, and/or divisional applications which may be developed down the line, should be included in each grant.

The language of the cross licensing agreement should also clearly spell out which rights are being granted including a clear indication as to whether a party has the right to make, use, sell, or import products that incorporate the technology claimed in patents. In this regard, each party to the cross licensing agreement should consider whether it wishes to reserve some of those rights for itself, such that they may themselves practice the technology that is transferred to the other party.

B. Transferability of Rights

Each party to the cross licensing agreement should consider whether the rights and duties of the cross licensing agreement are assignable to a successor of each licensor. Many license agreements include a clause stating that the licensee's rights automatically terminate in the case of any attempted assignment of such rights without consent of the licensor. Such language is included in the cross licensing agreement to prevent technology from falling into the hands of another competitor.

C. Patent Validity Contests

Most license agreements provide that a licensee may contest the validity of a patent that is the subject of the license agreement as long as the licensee has a reasonable justification for contesting validity. Cross licensing agreements are no exception and may include similar language that specifies the course of action to be followed in the event that a dispute arises regarding patent validity. For example, the cross licensing agreement may include a clause that requires any dispute to be first submitted to binding arbitration.

D. Representations and Warranties

Most license agreements include a clause which discloses that each party has the right to grant the technology that is covered by their patents. In the case of a cross licensing agreement wherein the grant of rights of at least one of the parties is exclusive, such language may state that the licensor has not made any prior grant to other parties. In addition, license agreements may also include language which describes the course of action to be followed in the event that new technology is developed based upon the transferred technology. For example, the cross licensing agreement may indicate that the licensor is required to apply for patent protection on such new technology but that the licensee has the option to obtain an additional license on the new technology that is covered by such after-acquired patents.

E. Indemnification

Indemnification clauses in license agreements typically protect a licensee against infringement of patents of a third party. Such indemnification clauses absolve each party against responsibility for any liability or damages that may arise out of the use of the technology. Fortunately, in emerging

technologies such as nanobiotechnology where the number of competing entities is relatively small, it is likely that each entity involved in the particular technology area is also aware of the nature of the activities of other entities developing similar technology. Therefore, it is easier for each party to a cross licensing agreement to foresee the extent to which the transferred technology will be utilized, allowing the parties to evaluate the potential for infringement of a third party's patent.

F. Improvements in the Licensed Technology

As mentioned above, nanotechnology is in its infancy and therefore improvements are occurring at a relatively fast pace. Each party to a cross licensing agreement is therefore highly likely to make improvements on any technology that is the subject of licensed patents. Therefore, the cross licensing agreement should lay out the steps to be followed in the event that patents are applied for on the improved technology. The language of the cross licensing agreement should also specify which of the parties is responsible for handling the prosecution of the patent applications and should address the apportionment of fees incurred during prosecution.

For example, the cross licensing agreement may specify that where the licensee develops technology based on a licensor's original technology, the licensor, as owner of the original technology, is responsible for handling the prosecution of any new patent applications. Furthermore, the cross licensing should specify which party has rights to new technology that is covered by a new patent. Alternatively, the cross licensing agreement may specify that prosecution expenses may be split by both parties with ownership rights also being distributed evenly to both parties.

G. Boilerplate Clauses

Because certain clauses are commonly included in many types of business agreements, such clauses are referred to as "boilerplate" clauses. Such clauses may address choice of law, arbitration, notice, and other issues. *Table 3* below summarizes these common boilerplate clauses.

TABLE 3: COMMON BOILERPLATE CAUSES	
Integration	Integration clauses prevent another party from interpreting a cross licensing agreement based on external documents or conversations.
Choice of Law	Choice of law provisions are typically included because of differences in commercial law in different states. In the case of a cross licensing agreement wherein each party may be from a different state, it is especially important to stipulate which state's laws are to be applied in resolving disputes.
Arbitration	The arbitration clause may include language which requires that both parties present a detailed description of the dispute, and present such description to the opposing party and if no agreement can be reached within a set period of time, then the dispute shall be forwarded for arbitration. Arbitration clauses typically include language specifying an association, such as the American Arbitration Association, whose rules and protocol are to be used in resolving disputes.
Notice	Notice clauses pertain to how and when one party has received indication the other party of a desire to terminate an agreement, exercise an option in the agreement, or inform the other party of a dispute. Language in such notice provisions typically specifies the name and address of a contact to which such notice is to be given and additionally includes a specification as to when such notice is deemed to be received by the other party.
Patent Marking	Patent marking provisions may specify that the failure of one party to mark

	the patent number on goods produced under the patent may prevent the licensor from collecting damages for infringement in a suit by a third party on such patents. When more than one licensed patent is involved, the language may require that the licensee agrees to mark all the licensed products that are sold.
Severability	A severability clause may be necessary in a cross licensing agreement because general contract law holds that an entire agreement may be voided if any provision thereof is invalid or void for any purpose.
Force Majeure	A *force majeure* clause may also be included in the cross licensing agreement to protect each party in the event of a natural or manmade disaster that occurs and which is outside the control of either party. Such a clause typically excuses performance by at least one of the parties.

It is important for both parties to the cross licensing agreement to realize that most, if not all, of these licensing terms are up for negotiation. Counsel for each party has a duty to consider their client's current position as well as the client's long-term needs, and negotiate accordingly. Properly drafted, a cross licensing agreement can create a symbiotic relationship between both parties and provide a low-risk way for the parties to exchange intellectual property so that each may exploit their own technology as well as collaborate on jointly developed technology.

VI. LITIGATION: A FINAL WAY OF RESOLVING PATENT DISPUTES

Nanobiotech companies will also need to handle patent litigation issues—either as a plaintiff, enforcing its own patents against a competing product; or as a defendant, answering a claim that its product has infringed a competitor's patent.

To date, there has been very little patent litigation in the nanotechnology area.[15] This is not surprising since there are as yet few nanotechnology products on the market. One rare example of litigation in the nanopharmaceutical arena was Caliper Technologies' 2002 lawsuit against Molecular Devices Corporation, alleging infringement of Caliper's U.S. Patent Nos. 6,287,774 and 6,472,141. These patents, which cover methods and systems for performing a variety of assays, relate to the microfluidic "lab-on-a-chip" technology that Caliper was bringing to market. Rather than undergo the uncertainty and expense of trial, the companies settled in 2003.[16]

It is expected that in the next few years there will be an increasing amount of patent litigation, particularly as more drug delivery systems based on nanotechnology come to market and companies begin to assert their patents. These initial nanotechnology patent litigation cases could be brought by large pharmaceutical companies or small nanobiotech startups, and will likely raise new questions of patent law unique to nanotechnology. Unlike with biotechnology, however, for which virtually a whole new body of law developed, experts do not expect the development of a "nanotech" patent law. Instead, it is expected that some aspects of existing law will evolve to account for the special features of nanotech inventions. Only time will tell how the patent law will change to embrace these new technologies.

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[15] Some of the rare examples of nanotech patent litigation include Ultratech, Inc.'s lawsuit against Tamarack Scientific Co. for infringement of semiconductor lithography claims in U.S. Patent No. 5,621,813; and Veeco Instruments Inc.'s lawsuit against Asylum Research Inc. alleging infringement of five patents regarding atomic force microscopes.

[16] *See* NANOTECHWIRE.COM, *Caliper Technologies Settles Patent Infringement Suit Against Molecular Devices*, Nov. 4, 2003, *at* http://nanotechwire.com/news.asp?nid=534&ntid=125&pg=1.

1. Costs of Litigation

What is certain, however, is how expensive patent litigation is. It is estimated that only about two percent of all issued patents end up generating more revenue than the cost of obtaining the patent. Of these select patents, only some will amount to being worth the price of litigating them in court. A typical patent litigation can cost on average in excess of one million dollars per claim. This is due to the market hourly rates for skilled patent attorneys, ranging on average from between $300 and $500. These rates are typically higher than those charged by non-IP attorneys due to a high demand for experienced patent attorneys who often have advanced engineering degrees in addition to a law degree. In addition to high attorneys' fees, there are exorbitant discovery costs and fees for expert witnesses.

A nanobiotech startup company can choose certain methods of financing its suit which avoid some of the upfront costs, such as a contingency fee arrangement where the plaintiff company will give a percentage of any future judgments or settlements to the attorney as payment for representation. However, this arrangement depends on finding an attorney willing to take on the considerable risks associated with this type of payment. In deciding whether to accept a contingency fee case, the attorney will likely both assess the patent's validity and likelihood of being able to prove infringement. If the attorney believes that the knowing and willful infringement could be proved, which permits the recovery of triple the actual damages, this would be an incentive to take on the case at a lower percentage rate. However, if the suing company is only seeking an injunction blocking the alleged infringer from making, using, or selling the patented invention (as opposed to collecting damages), this would preclude the use of a contingency arrangement.

Additionally, the ability of the defendant to pay for judgment if there is a successful verdict is a crucial factor in deciding whether to pursue litigation. Often the client or attorney will first conduct an asset search on the alleged infringer to see if there is an ability to pay which exceeds the projected cost of litigation. This would also be useful to assess the ability of the defendant to afford a legal defense. If the defendant is cash-rich, then a lengthy lawsuit prolonged by several appeals is likely. Thus, when considering litigation as a strategy for dispute resolution, the considerable cost of patent litigation should be foremost in mind.

2. Risk Management

Even if a company decides not to pursue this final option for resolving a patent dispute, there is always a chance it may be dragged into a lawsuit regardless. As part of a larger risk management plan, companies bringing nanotechnology products to market should maintain an ongoing assessment of the potential of being sued for patent infringement. Ideally, companies should regularly seek to obtain non-infringement opinions, which are written opinions from patent attorneys that assess whether a product could be deemed to infringe of any relevant patents. Such an ongoing review is also a valuable resource for the company's inventors, as it provides information on other companies' patents so that the inventors can create innovations which design around the existing patents.

Finally, nanobiotech companies may wish to obtain intellectual property infringement insurance, which covers the costs of defending against a patent infringement suit. This type of insurance is very specialized and separate from a typical commercial liability insurance policy, which almost invariably excludes coverage for patent infringement. Typically such coverage can be obtained as part of a package of liability insurance, but is usually offered by only a limited group of insurance companies.

While such a risk management audits, lawyers' opinions, and infringement insurance represents a significant cost to a nanobiotech start-up, it may be than "an ounce of prevention can be worth more than a pound of cure" when it comes to the huge uncertainties and expense of patent litigation.

CONCLUSION

Patent disputes are a certainty with nanotechnology—especially in the nanopharmaceuticals industry—and companies trying to bring innovations to market will need to be prepared for them. This article offers five strategies to either prevent or resolve patent disputes. Smart companies should think carefully about their patenting strategies, and should monitor published patents in case they need to initiate a PTO interference proceeding. When companies get embroiled in a patent dispute, they typically resolve the dispute by requesting a re-examination, entering into a cross licensing agreement, or as a last resort, suing for patent infringement.