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**Claiming Nanotechnology: Improving USPTO Efforts at
Classification of Emerging Nano-Enabled Pharmaceutical
Technologies**

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By Jordan Paradise *

I. INTRODUCTION

¶1 Touted as ushering in “the next industrial revolution”¹ over ten years ago, nanotechnology is now positioned to enable tremendous advances in virtually limitless scientific and technological fields. Unique and novel properties at the nanoscale have powered innovations in medicine and health care, environmental remediation, electronics, mechanics, energy, optics, computing and information technology, industrial manufacturing, and a vast array of marketed consumer goods. However, as nanotechnologies advance, so do a barrage of familiar questions that have vexed past technologies such as biotechnology, genetics, and stem cell research: how should knowledge and applications of the science and technology be integrated into marketed products, how will consumers access information about these products, how and to what extent should resulting inventions be protected, and who will serve as the gatekeeper?

¶2 The unique and far-ranging properties of nanostructures and nanotechnologies have particularly facilitated breakthroughs in the pharmaceutical and medical device realms. The interface of nanotechnology, biotechnology, and genetics have increased bioavailability, introduced more precise targeted drug delivery and release, decreased adverse side effects, and enabled cutting-edge cancer treatments. Due to the high-stakes characteristics of the pharmaceutical industry—national and multinational corporations, high upfront research and development costs, rigorous clinical trials and data requirements, a thriving generic drug market, and intense competition—patents are particularly critical to innovation and market protection.²

¶3 Not surprisingly, innovations at the intersection of nanotechnology and medicine have inundated the United States Patent and Trademark Office (USPTO) with the resulting patent applications. Patents that couple genetic sequence information,

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¹ See, e.g., Press Release, White House, National Nanotechnology Initiative: Leading to the Next Industrial Revolution (Jan. 21, 2000), http://clinton4.nara.gov/WH/New/html/20000121_4.html.

² See Jordan Paradise, *The Devil Is in the Details: Health Care Reform, Biosimilars, and Implementation Challenges for the Food and Drug Administration*, 51 JURIMETRICS J. 279 (2011) [hereinafter Paradise, *The Devil Is in the Details*]; Jordan Paradise, *Reassessing ‘Safety’ for Nanotechnology Combination Products: What Do ‘Biosimilars’ Add to Regulatory Challenges for the FDA?*, 56 ST. LOUIS U. L.J. (forthcoming Dec. 2011).

biological information, and the enabling properties at the nanoscale for diagnosis, treatment, and long-term patient assessment are the next frontier in health care and medicine. Along with great promise, nanotechnology innovations undoubtedly signal looming patent battles as products reach the market.³ As the U.S. health care model moves toward targeted and personalized medicine utilizing emerging technological advances, where drugs and medical interventions are tailored to individual biological make-up and genetic propensity, the pharmaceutical industry will need patent protections more than ever to stake out product identity and market share.

¶4 Recognizing the scope and commercial importance of nanotechnology, the USPTO has implemented a nanotechnology classification in a laudable effort to foster consistent categorization in the review of patent applications and maintain an organized storehouse of issued patents that involve nanotechnology. Developed in 2004, this classification spans 263 subclasses pertaining to inventions

related to research and technology development at the atomic, molecular or macromolecular levels, in the length of scale of approximately 1–100 nanometer range in at least one dimension, and that provide a fundamental understanding of phenomena and materials at the nano-scale and to create and use structures, devices and systems that have novel properties and functions because of their size.⁴

As of May 31, 2011, the USPTO reports over 6,930 issued patents and over 8,725 pending patent applications classified as nanotechnology-related inventions.⁵

¶5 While undoubtedly helpful for internal purposes, the USPTO's nanotechnology classification system merely groups patents together to ease prior art searches undertaken by patent examiners. The classification fails to assess relationships among and between these patents; identify potentially overlapping and infringing claims; and communicate information to critical stakeholders, including industry, consumers, and other regulatory agencies. It also leaves discretion to individual patent examiners to reassess and reclassify previously issued patents (before 2004) to determine if they are appropriate for the recently implemented nanotechnology classification. Problems of overlapping claims and complicated scientific aspects that arise will largely be left to courts to sort out—a clumsy forum for determination of complex patent law issues that arise based on scale, size, and interactions at the nanoscale that transcend previously envisioned physical and chemical boundaries.

¶6 Specifically, the USPTO and courts will increasingly face three core problems involving nanotechnology: (1) limitations of and inconsistencies among current definitions of nanotechnology; (2) uncertainty and lack of uniformity in measurement capabilities regarding critical aspects of size, properties, and characteristics at the

³ See discussion *infra* Part III-B.

⁴ *Class 977 Nanotechnology Cross-Reference Art Collection*, U.S. PAT. & TRADEMARK OFF., <http://www.uspto.gov/web/patents/biochempharm/crossref.htm> (last updated Mar. 18, 2010).

⁵ *USPTO Patent Full-Text and Image Database*, U.S. PAT. & TRADEMARK OFF., <http://patft.uspto.gov/netahtml/PTO/search-adv.htm> (search “Query” for “ccl/977/\$”) (search last conducted May 31, 2011); *Patent Application Full Text and Image Database*, U.S. PAT. & TRADEMARK OFF., <http://appft1.uspto.gov/netahtml/PTO/search-adv.html> (search “Query” for “ccl/977/\$”) (search last conducted May 31, 2011).

nanoscale; and (3) the role of patent claims to accurately and consistently encapsulate and distinguish the scope of nanotechnology inventions. Although pressing, the first two problems apply across all scientific disciplines and federal regulatory agencies confronted with emerging applications of nanotechnology. This Article touches on these first two problems in a broad context, but it focuses on the third problem as positioned against the function and activities of the USPTO. Given the recent interest of the Supreme Court in questions of patentability and appropriate claim scope of genetic inventions,⁶ the time is ripe for the USPTO to extract lessons for nanotechnology. Honing in on U.S. patent law, policy, and the current practice of the USPTO, as well as the effect of judicial review in shaping case law in scientific and technical areas, this Article extracts general lessons and extrapolates those lessons to the emerging realm of nanopharmaceuticals. While courts have yet to confront these issues on a regular basis, one particular case is useful in examining how nanotechnology patents may play out in courts.

¶7 This Article utilizes the recent district court case *Elan Pharma International, Ltd. v. Abraxis Bioscience*,⁷ which involved a blockbuster nanotechnology cancer treatment, to illustrate inherent problems with the USPTO nanotechnology patent classification system and patent claim scope. Part II discusses the patent system and the USPTO, highlighting statutory provisions relevant to nanotechnology and identifying informative cases that apply and interpret those provisions. Part III examines the USPTO response to nanotechnology, tracing the development of the 977 patent classification system and identifying where clarification is needed from the USPTO and courts as nanopatenting progresses. Part IV discusses *Elan Pharma*, tying it to the three problems identified above and to the scientific and technical aspects of nanotechnology in the pharmaceutical realm. Part IV also analyzes both the *Elan Pharma* patent involved in the case and the subsequent patent awarded to Abraxis Bioscience following the case and attempts to reconcile the two. Part V suggests a research agenda to assist the USPTO in fulfilling its mission to foster and reward innovation, while also assisting in broader efforts to gather nanotechnology information. These suggestions include improving the existing nanotechnology classification process, increasing feedback and collaboration with other federal agencies relevant to nanotechnology inventions, instituting independent educational programs for patent examiners, and utilizing new pilot peer review pathways for nanotechnology applications to encourage broader dialogue on the scope of patent claims and relationships to already issued patents. Part VI concludes.

II. THE USPTO AND PATENT RIGHTS FOR INVENTIONS

¶8 Article I, Section 8, Clause 8 of the Constitution grants Congress the power “[t]o promote the Progress of Science . . . by securing for limited Times to . . . Inventors the exclusive Right to their . . . Discoveries.”⁸ The USPTO, first established as a governmental bureau in 1802, is now within the Department of Commerce. Congress vested authority in the USPTO to review and award patents within the confines of the U.S. Patent Code⁹ and USPTO regulations¹⁰ and to disseminate patent-related

⁶ See discussion *infra* Part II-A-1.

⁷ No. 06-438 GMS, 2007 WL 6382930 (D. Del. Dec. 17, 2007).

⁸ U.S. CONST. art. 1, § 8, cl. 8.

⁹ 35 U.S.C. §§ 1–376 (2006).

information to the public.¹¹ This Part describes the traditional role of the USPTO in granting patent protections for inventions, highlights general patent requirements, and discusses legal precedent focusing on advancements in genetics that may pose future challenges for emerging nanopharmaceutical developments. It also examines the characteristics of pharmaceutical patents given the statutory schemes for generic drug development and approval by the Food and Drug Administration (FDA).

A. Patent Requirements and Case Law

¶9 Patent law sets forth four general areas of invention: processes, machines, manufactures, and compositions of matter.¹² In return for the public disclosure of an invention,¹³ the applicant is rewarded with exclusive rights to the invention for twenty years from the date that the application was filed with the USPTO.¹⁴ The patent then gives the patent holder “the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States.”¹⁵

¶10 Patent law is not technology specific. The federal patent statute,¹⁶ USPTO regulations,¹⁷ and internal USPTO policies and procedures¹⁸ all apply to nanotechnology-related inventions as they do to inventions in any other technological field. Absent direction from the USPTO or courts, examiners must review nanotechnology patents by applying the substantive requirements for patentability set out in 35 U.S.C. § 101 (utility), § 102 (novelty), § 103 (nonobviousness), and § 112 (specification) and must assure all other patent requirements in Title 35 are fulfilled. Due to the evolving nature of the understanding of the science and technologies involved, questions remain about the application by the USPTO and courts of the substantive requirements to nanotechnology, as well as the foundational issue of patentable subject matter. This Part examines these concerns as linked to specific provisions in the patent law¹⁹ and addresses recent case law that may impact nanotechnology in the future.

¹⁰ *Id.* § 2(b)(2).

¹¹ *Id.* § 2(a)(1), (2).

¹² *Id.* § 101. The USPTO defines process as a “process, act or method, and primarily includes industrial or technical processes”; machine as “need[ing] no explanation”; manufacture as “articles that are made, and includes all manufactured articles”; and compositions of matter as “relat[ing] to chemical compositions and may include mixtures of ingredients as well as new chemical compounds.” U.S. PATENT & TRADEMARK OFFICE, GENERAL INFORMATION CONCERNING PATENTS 2–3 (2011), *available at* http://www.uspto.gov/patents/resources/general_info_concerning_patents.pdf. These four categories “taken together include practically everything that is made by man and the processes for making the products.” *Id.*

¹³ 35 U.S.C. § 112.

¹⁴ *Id.* § 154(a)(2). Where a patent application was submitted prior to June 8, 1996, the term of exclusive rights extends seventeen years from the application filing date. MPEP § 2701 (8th ed. Rev. 2, May 2004).

¹⁵ 35 U.S.C. § 154(a)(1).

¹⁶ *Id.* §§ 1–376.

¹⁷ 37 C.F.R. §§ 1–150 (2010).

¹⁸ *See, e.g.*, MPEP (8th ed. Rev. 8, July 2010).

¹⁹ This examination of patent law is admittedly only a cursory snapshot of the core provisions and case law in the interest of length.

1. Patentable Subject Matter

¶11 As the Supreme Court has identified through case law spanning over a century, the threshold question for determining patentability is whether the invention claims “laws of nature, physical phenomena, and abstract ideas.”²⁰ If the claimed invention falls into one of these three broad categories, it is outside the scope of patentable subject matter as a foundational determination before even reaching issues of utility, novelty, nonobviousness, and specification. Anything falling within these three categories is “part of the storehouse of knowledge of all men . . . free to all men and reserved exclusively to none.”²¹ Supreme Court case law tracing back to 1874 instructs that merely removing natural sources from a naturally occurring material does not make it a new composition of matter or article of manufacture worthy of patent protection because the primary characteristics and functioning of the product do not significantly differ from what already exists in nature.²² Case law involving abstract ideas teaches that the USPTO cannot issue patents for principles in the abstract, which are akin to fundamental truths.²³ There must be some tangible process tied to the formula or idea that moves it into the realm of patentability.²⁴

¶12 Two recent high profile Supreme Court decisions tackling these boundaries of patentability:²⁵ the Federal Circuit’s highly anticipated July 29, 2011 decision regarding

²⁰ *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980).

²¹ *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).

²² *Am. Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. (23 Wall.) 566, 584 (1874). Subsequent cases exploring similar questions of physical phenomenon and products of nature relating to claimed inventions for compositions of matter or articles of manufacture include *Funk Brothers Seed Co.*, 333 U.S. 127 (combinations and mixtures of root nodule bacteria were not patentable where they served as packaging function and bacteria still performed in their natural way); *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884) (synthetic version of alizarine, a dye already existing in nature, imbued with a brighter hue was not patentable subject matter because it was a known product of nature); *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156 (4th Cir. 1958); *General Electric Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d Cir. 1928) (ductility and high tensile strength of purified tungsten making it pliable at room temperature were characteristics given by nature, not the inventor, and thus not patentable); *In re Merz*, 97 F.2d 599 (C.C.P.A. 1938) (purified ultramarine dye unpatentable even though produced with new process creating brighter hue); *In re Marden (Marden II)*, 47 F.2d 958, 959 (C.C.P.A. 1931) (patent for purified vanadium exhibiting increased ductility and malleability denied because it was a product of nature and “nothing more or less than vanadium freed from all of its impurities”); *In re Marden (Marden I)*, 47 F.2d 957 (C.C.P.A. 1931) (purified uranium with increased ductility not patentable because it was a purified form of a product of nature; the court found the process, but not the composition, patentable); and *Ex parte Latimer*, 1889 Dec. Comm’r Pat. 123 (holding that purified pine needle fiber derived from *Pinus australis* was not patentable as a new article of manufacture for use in textiles).

²³ *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972) (citing *Le Roy v. Tatham*, 55 U.S. (14 How.) 156, 175 (1852)).

²⁴ The chronological trilogy of cases on this point are *Gottschalk*, 409 U.S. 63 (algorithm to convert binary-coded decimal numerals into pure binary code not patentable because not a process but an abstract idea); *Parker v. Flook*, 437 U.S. 584, 590 (1978) (claiming process for monitoring conditions during catalytic conversion process in petrochemical and oil-refining industries not a patentable process because “post-solution activity” does not alone transform an unpatentable principle into a patentable process); and *Diamond v. Diehr*, 450 U.S. 175 (1981) (claims to previously unknown method for molding raw, uncured, synthetic rubber into cured precision products using a mathematical formula to complete some of the steps with a computer is patentable, as it patents an industrial process rather than the mathematical formula).

²⁵ These two cases are *Bilski v. Kappos*, 130 S. Ct. 3218 (2010), and *Laboratory Corp. of America Holdings v. Metabolite Laboratories*, 548 U.S. 124 (2006) (per curiam). *Bilski* involved patent claims

the patentability of genetic sequences²⁶ and the recent grant of certiorari to examine whether diagnostic tests that correlate results and patient health are phenomena of nature²⁷ pose questions for nanotechnology patents. Although outside the scope of this Article, this collection of cases signals past and present struggles by courts and the USPTO to apply bright-line rules to determine whether a claimed invention is not patent eligible as a law of nature, physical phenomenon, or abstract idea. This is surely informative for nanotechnology as patenting trends continue; aside from litigation involving allegations of patent infringement for a nanotechnology patent, there may also be challenges to USPTO (and Patent Board of Appeals) determinations of ineligibility that make their way to the Federal Circuit and Supreme Court. To be sure, nanotechnology products and inventions will inevitably cross all scientific and technical areas that have thus far raised questions in terms of patentable subject matter and laws of nature, physical phenomenon, and abstract ideas.

2. Utility

¶13 In addition to enumerating the four technological categories of patentable subject matter, § 101 also requires that an inventor show that the claimed invention is “useful.” As discussed in the context of patentable subject matter, “[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement” may obtain a patent, subject to the conditions of the application

related to the interaction of commodities buyers and sellers and methods of hedging against the risk of price fluctuations using a mathematical formula. *Bilski*, 130 S. Ct. at 3223. The Federal Circuit had previously applied the machine-or-transformation test and found the invention is not patentable subject matter. *In re Bilski*, 545 F.3d 943, 964 (Fed. Cir. 2008). The court held that “[a] claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.” *Id.* at 954. In *Metabolite*, the majority ultimately dismissed the writ of certiorari as improvidently granted following oral arguments. *Metabolite Labs.*, 548 U.S. at 125. The patent claim covered not only the action of assaying body fluid samples to measure homocysteine levels, but also the action of correlating the assay result to a vitamin deficiency. *Id.* at 129 (Breyer, J., dissenting). However, the strong dissent by Justice Breyer foreshadows future attention from the Court. Examining precedent and the scope of the patent claim, Breyer concluded that the patent was invalid as an unpatentable natural phenomenon. *Id.* at 137 (citing *Flook*, 437 U.S. at 588 n.9).

²⁶ *Ass’n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329 (Fed. Cir. 2011). The panel reversed the district court’s decision that the composition claims to “isolated” DNA molecules claiming *BRCA1* and *BRCA2* genes cover patent-ineligible products of nature under 35 U.S.C. § 101 because the molecules as claimed do not exist in nature. *Id.* at 1334, 1342. It reversed the decision that the method claim to screening potential cancer therapeutics via changes in cell growth rates is directed to a patent-ineligible scientific principle and affirmed the decision that method claims directed to “comparing” or “analyzing” DNA sequences are patent ineligible, reasoning that they include no transformative steps and cover abstract mental steps and are thus patent ineligible. *Id.* at 1334.

²⁷ The Supreme Court granted certiorari on June 20, 2011. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347 (Fed. Cir. 2010), *cert. granted*, 131 S. Ct. 3027 (2011). The patents at issue in *Prometheus* claim blood level measurement and assessment methods coupled with correlation of patient blood levels, patient health, and proper dosage of thiopurine drugs for treatment of “gastrointestinal and non-gastrointestinal autoimmune diseases.” *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1339 (Fed. Cir. 2009). The Federal Circuit originally held the claims patentable and valid in 2009 based on the machine-or-transformation test. *Id.* The Federal Circuit upheld that decision in December 2010. *Prometheus Labs.*, 628 F.3d at 1347.

requirements.²⁸ An inventor must show that the invention has a specific, substantial, and credible utility where credibility is measured from the perspective of one skilled in the art.²⁹ This inquiry also ties into the § 112 specification assessment, discussed below, which requires a description of how to make and use the invention. Given the fact that the USPTO rarely invokes the utility requirement as grounds for denying a patent (and accused infringers rarely hinge a legal defense on it),³⁰ it is similarly unlikely to be a hurdle for nanotechnology patents. By its very nature, nanotechnology introduces characteristics and functions not observed at the macro scale or micro scale that lead to new uses based on those characteristics and functions. Both the National Nanotechnology Initiative (NNI) definition and the USPTO definition instruct that the size is not the only aspect to be considered; the novel features that result, as well as the ability to control and manipulate at that size, are also critical.³¹

3. Novelty

¶14 Novelty is generally described as what it does not include. An invention is not novel if it was: (1) known or used by others, patented, or described in a printed publication prior to the invention by the patent applicant;³² (2) in public use or on sale for over a year prior to the date of the application;³³ (3) abandoned by the inventor;³⁴ (4) patented for more than a year prior to the U.S. application in a foreign country;³⁵ (5) described in another patent;³⁶ (6) not invented by the applicant (as in the case of theft);³⁷ or (7) made by a person other than the applicant or assignee.³⁸ Case law offers that “there can be no hard and fast rule” to determine novelty and each case must be examined on a case-by-case basis;³⁹ but, essentially, an invention must accomplish something new to satisfy the substantive novelty requirements.

¶15 Claims based on the novel properties of nanotechnology inventions often distinguish new claims from prior art due to the different features, characteristics, and properties at the nanoscale that did not exist at the macro scale. Nanotechnology inventions often exhibit unexpected, size-dependent properties that result in the very novelty of the invention. For example, gold nanoparticles (approximately 13 nm in diameter) have fluorescent properties not present at a larger scale, and their ability to bind to DNA make them excellent sensors to detect and image life-threatening viruses and bacteria.⁴⁰ One such detection system reports ten times the sensitivity and 100,000 times

²⁸ 35 U.S.C. § 101 (2006).

²⁹ Utility Examination Guidelines, 66 Fed. Reg. 1092, 1097 (Jan. 5, 2001).

³⁰ MARTIN J. ADELMAN ET AL., CASES AND MATERIALS ON PATENT LAW 181 (1st ed. 1998).

³¹ See discussion *infra* Part III.

³² 35 U.S.C. § 102(a).

³³ *Id.* § 102(b).

³⁴ *Id.* § 102(c).

³⁵ *Id.* § 102(d).

³⁶ *Id.* § 102(e)(2).

³⁷ *Id.* § 102(f).

³⁸ *Id.* § 102(g)(2).

³⁹ Union Carbide Co. v. Am. Carbide Co., 181 F. 104, 106 (2d Cir. 1910).

⁴⁰ KEWAL K. JAIN, THE HANDBOOK OF NANOMEDICINE 69–70 (2008).

the specificity of genomic detection systems currently in use.⁴¹ Because the nanotechnology definition implemented by the USPTO requires size-dependent properties to be included in the 977 Class,⁴² patent applicants must include some indicia of inclusion into that size range that results in a novel property exhibited by the claimed invention.

¶16 Two century-old cases demonstrate courts' long-standing view regarding novelty and are relevant to nanotechnology. Both cases involve a new form of an already known man-made substance that gave the invention an increased commercial or therapeutic value. In one, the inventor laid claim to a man-made substance, calcium carbide, in crystalline form when it was previously only available in a man-made amorphous form.⁴³ The Second Circuit held that a "[m]ere change of form in and of itself does not disclose novelty"⁴⁴ but could be based on superior efficiency, durability, purity, or other comparative aspects that gave the invention commercial benefit.⁴⁵ Similarly, the Seventh Circuit held that aspirin—a purified, crystallized version of acetyl salicylic acid (a man-made substance)—was patentable because, although it is chemically the same, after it is heated with acetic anhydride to produce a crystallized form, it holds a tight bond while passing through the acidic fluids of the stomach and releases effectively in the intestines. This increases the therapeutic effect.⁴⁶ The court noted that "a chemical formula is simply the symbolical expression of the composition or constitution of a substance That is to say, two substances, having the same chemical formula, may differ widely, as to impurities, upon qualitative analysis."⁴⁷ Subsequent cases have echoed this view.⁴⁸

4. Nonobviousness

¶17 Logically tied to concepts of novelty, patent applications can also be rejected by patent examiners on grounds of obviousness, where patent examiners conduct a comparison of the invention to what is already in the public domain, termed the prior art. If the patent examiner determines that the differences between the scope and content of subject matter in the application and the prior art renders the subject matter as a whole obvious at the time of invention to a "person having ordinary skill in the art," it will be deemed obvious and unable to acquire patent protection.⁴⁹

¶18 In a recent trend, the USPTO and the Federal Circuit have construed obviousness by applying the "teaching, suggestion, or motivation" (TSM) test. Under this test, an invention is obvious if the "the prior art, the problem's nature, or the knowledge of a person having ordinary skill in the art reveals some motivation or suggestion to combine

⁴¹ So-Jung Park et al., *Array-Based Electrical Detection of DNA with Nanoparticle Probes*, 295 SCIENCE 1503 (2002).

⁴² See discussion *infra* Part III.

⁴³ *Union Carbide*, 181 F. at 105.

⁴⁴ *Id.* at 106.

⁴⁵ *Id.* at 106–07.

⁴⁶ *Kuehmsted v. Farbenfabriken of Elberfeld Co.*, 179 F. 701 (7th Cir. 1910).

⁴⁷ *Id.* at 703–04.

⁴⁸ See, e.g., Lori Andrews & Jordan Paradise, *Genetic Sequence Patents: Historical Justification and Current Impacts*, in MAX PLANCK INST. FOR THE HISTORY OF SCI., *LIVING PROPERTIES: MAKING KNOWLEDGE AND CONTROLLING OWNERSHIP IN THE HISTORY OF BIOLOGY* 137, 151–52 (Jean-Paul Gaudillière et al. eds., 2009) (discussing cases addressing the issue of gene patenting).

⁴⁹ 35 U.S.C. § 103(a) (2006).

the prior art teachings.”⁵⁰ The Supreme Court clarified the scope of the TSM test in *KSR v. Teleflex*, holding that the narrow, rigid manner of evaluating obviousness under the TSM test is inconsistent both with § 103 and with the Court’s precedent.⁵¹ Referencing the 1966 case *Graham v. John Deere Co. of Kansas City*,⁵² the Court reiterated the need for an expansive and flexible approach in which the inquiry is not limited to the TSM test, but considers whether the improvement to the prior art is more than “the predictable use of prior art elements according to their established functions.”⁵³ Although the Court stated that the TSM test “captured a helpful insight” that a patent is nonobvious merely because each element of the patent was independently known in the prior art, it should not become a rigid and mandatory formula.⁵⁴ The USPTO, the Board of Patent Appeals and Interferences, and the Federal Circuit will be attempting to apply this expansive view of the obviousness inquiry to all areas of invention in the coming years.⁵⁵

¶19 The USPTO appears to maintain the position that claim limitations related to size or scale are insufficient to overcome prior art.⁵⁶ The USPTO relies on the 1955 U.S. Court of Customs and Patent Appeals case of *In re Rose*⁵⁷ to support its position that the nonobviousness requirement is not fulfilled by the mere nanoscale “miniaturization” of already-patented products.⁵⁸ *In re Rose* involved claims to an apparatus and methods of packaging, handling, and storing lumber where the claimed invention related merely to a difference in size from that in the prior art.⁵⁹ Analogizing to this case, merely scaling down to the nanoscale would conflict with *In re Rose*.

¶20 However, where a patent application also provides a novel use and utility (and fulfills all other patentability requirements) in addition to identifying and claiming a difference in scale, it would be eligible for patent protection. Of course, this also depends

⁵⁰ *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 399 (2007).

⁵¹ *Id.* at 400.

⁵² 383 U.S. 1 (1966).

⁵³ *KSR*, 550 U.S. at 417. The Court stated:

Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, this analysis should be made explicit. As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.

Id. at 418 (citations omitted).

⁵⁴ *Id.* at 418, 419.

⁵⁵ For a discussion of the case’s relevance to nanotechnology, see Matthew J. Dowd et al., *KSR International Co. v. Teleflex Inc.: Another Small Issue for Nanotechnology?*, 4 NANOTECHNOLOGY L. & BUS. 293 (2007).

⁵⁶ *In re Rose*, 220 F.2d 459 (C.C.P.A. 1955).

⁵⁷ *Id.*

⁵⁸ R. Scott Roe, Note, *Nanotechnology: When Making Something Smaller is Nonobvious*, 12 B.U. J. SCI. & TECH. L. 127, 130 (2006) (citing Vivek Koppikar et al., *Current Trends in Nanotech Patents: A View from Inside the Patent Office*, 1 NANOTECH. L. & BUS. 24, 28 (2004)).

⁵⁹ *In re Rose*, 220 F.2d at 463 (“Appellant argues that this claim recites that the package is of appreciable size and weight so as to require handling by a lift truck whereas [the prior art references’] packages can be lifted by hand. We do not feel that this limitation is patentably significant since it at most relates to the size of the article under consideration which is not ordinarily a matter of invention.”).

on the scope of the claims present in prior art patents and whether a size range that covered the nanoscale was specifically claimed in the prior art patent that covered the nanotechnology invention for which a patent is sought.⁶⁰ The USPTO has indicated that patent applicants would be more likely to avoid rejection on obviousness grounds if they affirmatively provide both a statement that the prior art did not recognize that the reduction of the disclosed invention to nanoparticle size would have specific benefits and recite a standard deviation from average particle size.⁶¹

¶21 Case law also establishes that a product claim is not obvious unless the process for making that product is also obvious.⁶² This relates to the level of ordinary skill in the art, as measured from the date of the invention. Courts have examined this in the context of crystalline drug forms.⁶³ For nanotechnology, inventors should explicitly set forth that the methods for making the nano-sized invention were not obvious because the methods to scale it either top-down or bottom-up did not exist at the time of the prior art.⁶⁴

¶22 Anticipation is another facet of obviousness that has been discussed in the context of nanotechnology. A patent claim is deemed “anticipated” by the prior art “if each and every limitation is found either expressly or inherently in a single prior art reference.”⁶⁵ Despite a finding of novelty based on the newfound properties grounded in changes in size, patent claims may face “inherency” rejections where the claimed invention focuses on the inherent properties at the nanoscale.⁶⁶ The doctrine of inherency allows the examiner to locate similar art and argue that the claimed property is inherently or necessarily possessed in that prior art because it “necessarily flows from the teachings of the applied prior art.”⁶⁷ This strong reliance on nanoscale properties may complicate the patent examination process, as searching prior art for size and property limitations is not an easy task where inventions span numerous scientific fields. As a result, many examiners are inclined to reject the application for inherency.⁶⁸ For example, a substantially identical structure or composition may establish a prima facie case of obviousness, even if the claimed nanotechnology characteristic is not disclosed or claimed in the prior art.⁶⁹ However, as discussed in Part III, the USPTO nanotechnology classification aims to ameliorate some of these problems.

⁶⁰ Part II-B, *infra*, discusses this in terms of literal infringement and the reverse doctrine of equivalents.

⁶¹ *USPTO Holds Second Nanotechnology Customer Partnership Meeting*, USPTO CONNECTION (Moazzam Latimer LLP, McLean, Va.), May 2004, at 3, <http://www.moazzamlaw.com/dev/Vol1-Issue1.pdf> [hereinafter *Second Nanotechnology Meeting*].

⁶² Jeremy M. Stipkala, *Overcoming Obviousness When Patenting Nanotechnology Inventions*, 23 NATURE BIOTECHNOLOGY 677, 677 (2005).

⁶³ *Id.* (citing *In re Irani*, 427 F.2d 806 (C.C.P.A. 1970)).

⁶⁴ *Id.* at 678.

⁶⁵ *Celeritas Techs., Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1361 (Fed. Cir. 1998).

⁶⁶ Nikolas J. Uhlir, Note, *Throwing a Wrench in the System: Size-Dependent Properties, Inherency, and Nanotech Patent Applications*, 16 FED. CIR. B.J. 327, 342 (2007).

⁶⁷ *Id.* at 343–44.

⁶⁸ *Id.* at 339–41.

⁶⁹ *Id.*

5. Specification

¶23 In addition to showing the utility, novelty, and nonobviousness of the claimed invention, the applicant must also include a specification.⁷⁰ This specification must include a written description that provides the manner and process of making and using the invention in such concise, exact terms as to “enable any person skilled in the art” to make and use it.⁷¹ Pursuant to this section, the applicant also must set forth the best mode of carrying out the invention and must sufficiently disclose the invention.⁷² As the second paragraph of § 112 mandates, the specification section must conclude with “one or more claims particularly pointing out and distinctly claiming the subject matter” of the invention.⁷³ This two-paragraph section offers the public the general knowledge included in the patent in return for the exclusive patent rights to the invention being awarded to the inventor.⁷⁴ Patent examiners use the specification to interpret the scope of the claims and relationship to the prior art.

¶24 The Federal Circuit recently visited the scope of the written description requirement in *Ariad Pharmaceuticals, Inc., v. Eli Lilly & Co.*⁷⁵ Ariad and its research partners discovered the activation mechanisms of the NF-kB protein in human cells in response to certain diseases such as AIDS and various cancers, and they identified how the protein subsequently binds to other cells in the human body and causes the cells to produce proteins that fight infections.⁷⁶ The proteins produced by NF-kB are harmful when produced in such excess.⁷⁷ Ariad filed a patent for methods to reduce binding of NF-kB to limit the negative impacts of excess protein production.⁷⁸ However, when it submitted its patent application, Ariad had not finalized the listed techniques it claimed could effectively reduce NF-kB binding. On review, the Federal Circuit examined the state of jurisprudence regarding written description.

¶25 The court addressed two primary issues in *Ariad*: (1) whether § 112 contains a written description requirement separate from the enablement requirement; and (2) if so, the scope of that written description requirement.⁷⁹ The court provided a lengthy analysis

⁷⁰ 35 U.S.C. § 112 (2006) (“The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention. The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.”).

⁷¹ *Id.*

⁷² *Id.* The best mode requirement pertains to the best mode as contemplated by the inventor at the time of invention.

⁷³ *Id.*

⁷⁴ See Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1022 (1989).

⁷⁵ 598 F.3d 1336 (Fed. Cir. 2010). For a thoughtful analysis of the case, see Joseph Jakas, Comment, *Encouraging Further Innovation: Ariad v. Eli Lilly and the Written Description Requirement*, SETON HALL L. REV. (forthcoming 2012).

⁷⁶ *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 560 F.3d 1366, 1369–70 (Fed. Cir. 2009).

⁷⁷ *Ariad Pharm.*, 598 F.3d at 1340.

⁷⁸ *Id.* at 1355. These techniques included manipulating NF-kB inhibitors, using an NF-kB molecule that did not have the ability to produce the harmful proteins, or using decoy molecules to bind to NF-kB binding sites. *Id.* at 1356.

⁷⁹ *Id.* at 1342.

of the history and interpretation of § 112, looking to the statute and relevant court precedent. The Federal Circuit determined that the two requirements were, indeed, separate and that the written description requirement should be applied to original claims.⁸⁰ The court further held that an inventor must specifically show “possession [of the claimed invention] as shown in the disclosure” upon filing of the patent application.⁸¹ Thus, an inventor would not satisfy the requirement by describing a broad method and listing a few ways to accomplish that method. Without a more detailed description, the inventor fails to possess the full scope of the claimed invention.

¶26

Although how lower courts will interpret and apply this decision remains unclear and somewhat controversial, the Federal Circuit’s decision in *Ariad* may have an impact on nanotechnology patents that claim a broad range of sizes. After *Ariad*, an inventor must show in the disclosure of the invention that she was able to produce the size within the range being claimed. To accomplish this, the inventor should disclose separate species within the claimed range rather than general description of a broad category. The inventor should also be specific about the effects of the invention, linking the disclosed structure and size to the desired function of the claimed invention. The core failure of the *Ariad* patent is that it merely predicted how certain claimed techniques would have the desired effects of reducing binding before actually achieving those effects as a result of the research. Nanotechnology inventions could have similar issues with the possession requirement if they disclose unfinished (yet informative) research findings to claim an invention not yet completed.

B. Critiques of Nanotechnology Patenting

¶27

Academics⁸² and practitioners⁸³ alike have written on the topic of nanopatenting, focusing much of their discussion on the scope of claims and the approach to claim

⁸⁰ The court parsed out the statute as: the specification must contain (1) a written description of the invention and (2) a written description “of the manner and process of making and using [the invention] in such full, clear, concise, and exact terms as to enable any person skilled in the art . . . to make and use the same.” *Id.* at 1344.

⁸¹ *Id.* at 1351 (internal quotation marks omitted).

⁸² See, e.g., Indrani Barpujari, *The Patent Regime and Nanotechnology: Issues and Challenges*, 15 J. INTELL. PROP. RTS. 206 (2010); Diana M. Bowman & Graeme A. Hodge, *A Small Matter of Regulation: An International Review of Nanotechnology Regulation*, 8 COLUM. SCI. & TECH. L. REV. 1 (2007); K. Eric Drexler & Jason Wejnert, *Nanotechnology and Policy*, 45 JURIMETRICS J. 1 (2004); Frederick A. Fiedler & Glenn H. Reynolds, *Legal Problems of Nanotechnology: An Overview*, 3 S. CAL. INTERDISC. L.J. 593 (1994); Ernest J. Getto et al., *Nanotechnology: Will Tiny Particles Create Large Legal Issues?*, SCITECH LAW., Summer 2009, at 6, 6; Dennis S. Karjala, *Protecting Innovation in Computer Software, Biotechnology, and Nanotechnology*, 16 VA. J.L. & TECH. 42 (2011); Mark A. Lemley, *Patenting Nanotechnology*, 58 STAN. L. REV. 601 (2005); Thomas M. Mackey, *Nanobiotechnology, Synthetic Biology, and RNAi: Patent Portfolios for Maximal Near-Term Commercialization and Commons for Maximal Long-Term Medical Gain*, 13 MARQ. INTELL. PROP. L. REV. 123 (2009); Glenn Harlan Reynolds, *Nanotechnology and Regulatory Policy: Three Futures*, 17 HARV. J.L. & TECH. 179 (2003); Douglas J. Sylvester & Diana M. Bowman, *Navigating the Patent Landscape for Nanotechnology: English Garden or Tangled Grounds?*, in BIOMEDICAL NANOTECHNOLOGY: METHODS AND PROTOCOLS 359 (Sarah J. Hurst ed., 2011); Georgios I. Zekos, *Patenting Abstract Ideas in Nanotechnology*, 9 J. WORLD INTELL. PROP. 113 (2006).

⁸³ See, e.g., Laurie A. Axford, *Patent Drafting Considerations for Nanotechnology Inventions*, 3 NANOTECHNOLOGY L. & BUS. 305 (2006); Raj Bawa, *Nanotechnology Patenting in the US*, 1

drafting.⁸⁴ The claims are critical during review by examiners to determine scope and whether an invention has an adequate written description. Similar to arguments raised regarding the emergence of biotechnology and genetic technologies at the end of the last century and the beginning of the twenty-first century,⁸⁵ some contend that the proliferation of nanotechnology patents may create a patent thicket due to overlapping claims.⁸⁶

¶28

Due to the nature of broad claim drafting, nanotechnology-related patents are likely to literally infringe traditional product patents with broad claims and no reference to scale. However, many scholars posit that the reverse doctrine of equivalents may preclude a finding of literal infringement where the claimed invention is sufficiently different from the previously patented product, despite the fact that the accused claimed invention literally infringes the accuser's patent claims.⁸⁷ The reverse doctrine of equivalents was espoused by the Supreme Court in *Graver Tank & Manufacturing Co. v. Linde Air Products Co.*:

[W]here a device is so far changed in principle from a patented article that it performs the same or a similar function in a substantially different way, but nevertheless falls within the literal words of the claim, the doctrine of equivalents may be used to restrict the claim and defeat the patentee's action for infringement.⁸⁸

Two requirements must be satisfied for the reverse doctrine of equivalents to apply: the accused product must literally infringe the accuser's patent claims while also being "sufficiently different" from the patented product.⁸⁹

¶29

Both Congress and the Federal Circuit have supported the basic principles of the reverse doctrine of equivalents set out by the Supreme Court. In enacting § 112 in 1952,

NANOTECHNOLOGY L. & BUS. 31 (2004); Dowd et al., *supra* note 55; Drew Harris et al., *Strategies for Resolving Patent Disputes Over Nanoparticle Drug Delivery Systems*, 1 NANOTECHNOLOGY L. & BUS. 372 (2004); Koppikar et al., *supra* note 58; John Josef Molenda, *The Importance of Defining Novel Terms in Patenting Nanotechnology Inventions*, 1 NANOTECHNOLOGY L. & BUS. 174 (2004); Sean O'Neill et al., *Broad Claiming in Nanotechnology Patents: Is Litigation Inevitable?*, 4 NANOTECHNOLOGY L. & BUS. 29 (2007).

⁸⁴ See *Nanotechnology Gold Rush Yields Crowded, Entangled Patents*, PRNEWswire (Apr. 21, 2005), <http://www.prnewswire.com/news-releases/nanotechnology-gold-rush-yields-crowded-entangled-patents-54373177.html>. For example, Stephen B. Maebius, chair of the Nanotechnology Industry Team at Foley & Lardner LLP, advised companies filing nanotech patents to draft claims of intermediate scope rather than broad claims in response to court determinations in a number of biotechnology patents that held such broad claims invalid. *Id.*

⁸⁵ See Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698 (1998) (citing Garrett Hardin, *The Tragedy of the Commons*, 162 SCIENCE 1243 (1968)).

⁸⁶ See, e.g., Lemley, *supra* note 82; Sylvester & Bowman, *supra* note 82.

⁸⁷ See, e.g., Lemley, *supra* note 82; Terry K. Tullis, *Application of the Government License Defense to Federally Funded Nanotechnology Research: The Case for a Limited Patent Compulsory Licensing Regime*, 53 UCLA L. REV. 279 (2005); Andrew Wasson, *Protecting the Next Small Thing: Nanotechnology and the Reverse Doctrine of Equivalents*, 2004 DUKE L. & TECH. REV. 0010, available at <http://www.law.duke.edu/journals/dltr/articles/2004dltr0010>.

⁸⁸ *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608–09 (1950).

⁸⁹ *Texas Instruments, Inc. v. U.S. Int'l Trade Comm'n*, 846 F.2d 1369, 1371 (Fed. Cir. 1988).

Congress imposed “requirements for the written description, enablement, definiteness, and means-plus-function claims that are co-extensive with the broadest possible reach of the reverse doctrine of equivalents.”⁹⁰ The Federal Circuit said that the reverse doctrine of equivalents and § 112 “spring from the same roots and very often take account of the same factors and considerations”⁹¹ and the Supreme Court said that § 112 is “an application of the doctrine of equivalents in a restrictive role.”⁹² Given this view that the 1952 amendments codified the reverse doctrine of equivalents, the Federal Circuit has never relied upon the reverse doctrine of equivalents to affirm a decision of noninfringement independently of a § 112 analysis.⁹³ Some predict that, although the reverse doctrine of equivalents has existed only in theory for the last sixty years, it may be a successful defense for nanotechnology patent holders against claims of literal infringement.⁹⁴ Unique properties at the nanoscale may perform a similar function as chemicals, materials, or processes at the micro scale or macro scale, but operate in a substantially different manner. For example, nanocrystals diffuse at different rates given extremely small changes in size. Recent breast cancer research reports that the time for a 100 nm nanocrystal particle to reach tumor cells was two and a half times that of 20 nm particles (389 minutes as compared to 158 minutes).⁹⁵ One can assume that much larger particles, in the range of traditional pharmaceuticals, take much longer to reach a target site because of biological interactions. This has enormous implications for pharmaceutical development and pharmacokinetics, in that the purpose (i.e., drug delivery) remains the same, yet the rate of diffusion and biological and pharmacological interactions may differ dramatically.

¶30

Many of these projections remain untested because patent litigation targeted to nanotechnology has been limited thus far. However, future cases are likely to attack issues of patentability under § 101 in the context of genetic sequence patents, as well as the specific application of the core substantive requirements. The USPTO, the agency actively reviewing and issuing nanotechnology patents, is presently tackling many of these questions. If genetics are a litmus test for emerging medical technologies, then developments and inventions in nanotechnology (and nanopharmaceuticals specifically) will soon be appearing in court dockets. Part III provides an overview of the USPTO’s efforts to gather information and classify inventions that utilize nanotechnology.

⁹⁰ *Tate Access Floors, Inc. v. Interface Architectural Res., Inc.*, 279 F.3d 1357, 1368 (Fed. Cir. 2002). However, their application differs as to the timing of the inquiry. Whereas a § 112 analysis is made during examination of the patent application or during a court’s determination of patentability, the reverse doctrine of equivalents serves as a defense to a claim of literal infringement where a court’s inquiry is focused on the alleged infringing product’s characteristics.

⁹¹ *Texas Instruments*, 846 F.2d at 1372 (Davis, J., concurring in part).

⁹² *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 28 (1997).

⁹³ *Tate Access Floors*, 279 F.3d at 1368.

⁹⁴ See, e.g., M. Veronica Mullally & David R. Winn, *Patenting Nanotechnology: A Unique Challenge to IP Bar*, N.Y. L.J., July 6, 2004, at t2.

⁹⁵ Masaaki Kawai et al., *Dynamics of Different-Sized Solid-State Nanocrystals as Tracers for a Drug-Delivery System in the Interstitium of a Human Tumor Xenograft*, 11 BREAST CANCER RES. R43 (2009), <http://www.biomedcentral.com/content/pdf/bcr2330.pdf>.

III. THE USPTO NANOCCLASSIFICATION

¶31 The term nanotechnology encompasses an array of technologies at the nanoscale, where “nanoscale” refers to measurements less than 100 nm (i.e., 10^{-9} m; one billionth of a meter). The NNI’s definition of nanotechnology involves three inter-related (and inseparable) aspects:

[(1)] Research and technology development at the atomic, molecular or macromolecular levels, in the length scale of approximately 1–100 nanometers,

[(2)] Creation and use of structures, devices and systems that have novel properties and functions because of their small and/or intermediate sizes, and

[(3)] Ability to be controlled or manipulated on the atomic scale.⁹⁶

To earn the term nanotechnology, a particle or material must possess unique physical, chemical, or biological properties at the nanoscale that make that particle or material function in a manner that can be harnessed and controlled to utilize those unique properties. As discussed above, the USPTO has adopted a variation of the NNI definition for nanotechnology, keying in on the 1 to 100 nm range.⁹⁷ Nanobiotechnology merges nanotechnology and biotechnology and is described as “a field that applies the nanoscale principles and techniques to understand and transform biosystems . . . and which uses biological principles and materials to create new devices and systems integrated from the nanoscale.”⁹⁸ Nanomedicine is an important facet of research and development, which, according to the National Institutes of Health, “refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve.”⁹⁹ There is widespread research activity in biomolecule and biomimetic devices, biosensors, molecular motors, biomolecular fabrics, engineered enzymes and proteins, and drug discovery and delivery.¹⁰⁰ The pharmaceutical and medical device industries, two of the most patent-motivated industries, are at the forefront of nanotechnology research and development.

¶32 One source reports that the USPTO began issuing nanotechnology-related patents as early as 1976.¹⁰¹ However, it was not until the infusion of federal research funding for nanotechnology research and development that the unifying term nanotechnology made

⁹⁶ ENVTL. PROT. AGENCY, NANOTECHNOLOGY: AN EPA RESEARCH PERSPECTIVE, FACTSHEET 1 (2007), available at <http://epa.gov/ncer/nano/factsheet/nanofactsheetjune07.pdf>.

⁹⁷ See *supra* pp. 3–4.

⁹⁸ Mihail C. Roco, *Nanotechnology: Convergence with Modern Biology and Medicine*, 14 CURRENT OPINION IN BIOTECHNOLOGY 337, 337 (2003).

⁹⁹ *Nanomedicine Overview*, NAT’L INST. OF HEALTH COMMON FUND, <http://commonfund.nih.gov/nanomedicine/overview.aspx> (last updated Jan. 1, 2011).

¹⁰⁰ Alan L. Porter et al., *Refining Search Terms for Nanotechnology*, 10 J. NANOPARTICLE RES. 715, 718 (2008).

¹⁰¹ Tyson Winarski, Esq. & Elizabeth Stoker-Townsend, *Nanotechnology Thriving on Patents*, INTELL. PROP. TODAY, Apr. 2005, at 26 (citing the National Science Foundation). However, the first patent within the USPTO patent classification system was filed in September 1975 and issued in August 1978. *Injectable Compositions, Nanoparticles Useful Therein, & Process of Mfg. Same*, U.S. Patent No. 4,107,288 (filed Sept. 9, 1975).

its way into the scientific and technical literature and into patent applications for inventions. In response to a surge of nanotechnology inventions, the USPTO embarked on a multi-phase project to systematically identify nanotechnology-related patents, patent applications, and research publications to ultimately develop a method of classification to capture the breadth of nanotechnology.¹⁰² The USPTO's goals in developing a nanotechnology classification system were to construct a uniform framework to standardize the terminology, create an effective system for disclosure and cross-referencing, assist inventors and examiners in identifying and reviewing relevant prior art, and decrease inadvertent patent infringement.

A. Development of the "977" Class

¶33 The USPTO initiated the 977 classification project in November 2001, recognizing that patent examiners assessing nanotechnology patent applications were increasingly confronted with challenges relating to their level and type of training and the multidisciplinary features of nanotechnology. These challenges included a lack of familiarity with the underlying science and technologies, the utilization of complex and often new terminology, and the expanse of the scientific literature. These difficulties increased the risk that examiners were not equipped to assess the scope of the invention and previous inventions and increased the risk that relevant publications would be overlooked during examination.¹⁰³ The USPTO recognized that the broad range of technological specialty areas and prior art reflected in the applications increased the likelihood that separate patent examiners would contemporaneously issue overlapping or even conflicting patents.¹⁰⁴

¶34 Cognizant of these challenges facing examiners, the USPTO initiated the nanotechnology classification project. This multi-phase project proceeded incrementally in three core phases. The first was defining and setting the scope of nanotechnology for USPTO purposes; the second was creation of a cross-reference digest; and the third was the development of the 977 classification system. To develop a classification of nanotechnology patents and to cross-reference the patents and supporting documents, the USPTO established a definition for purposes of "searching for, identifying, and classifying documents" related to nanotechnology.¹⁰⁵ The USPTO arrived at a definition of nanostructure "to mean an atomic, molecular, or macromolecular structure that: (a) [h]as at least one physical dimension of approximately 1–100 nanometers; and (b) [p]ossesses a special property, provides a special function, or produces a special effect

¹⁰² 35 U.S.C. § 8 provides authority to the USPTO to classify patents. It reads: "The Director may revise and maintain the classification by subject matter of United States letters patent, and such other patents and printed publications as may be necessary or practicable, for the purpose of determining with readiness and accuracy the novelty of inventions for which applications for patents are filed." *Id.*

¹⁰³ See Barnaby J. Feder, *Tiny Ideas Coming of Age*, N.Y. TIMES, Oct. 24, 2004, at WK12.

¹⁰⁴ See, e.g., EROSION, TECH., & CONCENTRATION GRP., NANOTECH'S "SECOND NATURE" PATENTS: IMPLICATIONS FOR THE GLOBAL SOUTH 8 (2005), <http://etcgroup.org/upload/publication/54/02/com8788specialpnanomar-jun05eng.pdf> [hereinafter NANOTECH'S "SECOND NATURE" PATENTS].

¹⁰⁵ Vance McCarthy, *USPTO Poised to Ring in a New Era of Simplified Search and Better Visibility for Nano Patents*, NANO SCI. & TECH. INST. (Dec. 20, 2005), <http://www.nsti.org/news/item.html?id=35>.

that is uniquely attributable to the structure's nanoscale physical size."¹⁰⁶ The USPTO then established five categories of inventions involving nanotechnology: (1) nanostructures and chemical compositions; (2) devices that include at least one nanostructure; (3) mathematical algorithms; (4) methods or apparatuses for making, detecting, analyzing or treating nanostructure; and (5) specified uses of nanostructures.¹⁰⁷

¶35 The agency next organized a task force consisting of twenty-five internal patent professionals from USPTO technology centers and the classification office to develop a list of nanotechnology-related terms used by inventors that would assist in the identification of nanotechnology publications within the existing patent database. The task force developed 150 search terms to be employed to sketch out trends and concepts emerging from the patented inventions relating to nanotechnology. To garner input from the larger community of consumers of nanoproducts, the USPTO also invited the public to a series of Nanotech Partnership Meetings¹⁰⁸ through a Nanotechnology Customer Partnership initiative. The initiative was envisioned by the USPTO as "a forum to share ideas, experiences, and insights between individual users and the USPTO."¹⁰⁹ To further inform the process, the USPTO also initiated a trilateral discussion on the topic of effective and consistent international review of nanotechnology applications and development of classes and subclasses for nanotechnology inventions with the European Patent Office and Japanese Patent Office.¹¹⁰

¶36 As a result of these efforts, the USPTO in August of 2004 established a nanotechnology cross-reference digest—designated Class 977, Digest 1. This cross-reference digest operated by gathering all nanotechnology publications in a single place, replacing the inefficient keyword searches of prior art in multiple scientific fields by examiners.¹¹¹ The Office of the Commissioner of Patents provided that the new 977 cross-reference digest would (1) "[f]acilitate the searching of prior art related to Nanotechnology"; (2) "[f]unction as a collection of issued U.S. patents and published pre-grant patent applications relating to Nanotechnology across the technology centers"; and (3) "[a]ssist in the development of an expanded, more comprehensive, nanotechnology cross-reference art collection classification schedule."¹¹²

¶37 The important efficiency outcome of the cross-reference digest was to weed out prior art that was not actually developed by nanotechnology or did not actually contain nano-sized materials. For a variety of reasons, including the massive federal funding initiative supporting nanotechnology research and development as well as misunderstandings about nanotechnology, many inventors, scientists, and companies (often inaccurately) describe their research, inventions, or resulting products as involving

¹⁰⁶ U.S. PATENT & TRADEMARK OFFICE, CLASSIFICATION DEFINITIONS: CLASS 977, NANOTECHNOLOGY 1 (2010) [hereinafter CLASS 977 DEFINITIONS], available at <http://www.uspto.gov/web/patents/classification/uspc977/defs977.pdf>.

¹⁰⁷ *Id.*

¹⁰⁸ McCarthy, *supra* note 105.

¹⁰⁹ *Nanotechnology Customer Partnership Meeting*, U.S. PAT. & TRADEMARK OFF., http://www.uspto.gov/patents/init_events/nanotech.jsp (last updated July 4, 2009).

¹¹⁰ *Second Nanotechnology Meeting*, *supra* note 61.

¹¹¹ NANOTECH'S "SECOND NATURE" PATENTS, *supra* note 104, at 8; McCarthy, *supra* note 105.

¹¹² Memorandum from the Office of the Comm'r for Patents to Patent Prof'l Emps., *Nanotechnology Digest and Forthcoming Nanotechnology Cross-Reference Art Collection (XRAC)—Class 977* (Aug. 25, 2004), <http://www.uspto.gov/web/offices/pac/dapp/opla/documents/nanotechdig.pdf>.

or containing nanotechnology. For example, a keyword search of the prefix nano in the USPTO patent database returns tens of thousands of results where the majority of these patents are not technically nanotechnology as defined and classified by Class 977, Digest 1. Creating a nano-specific definition and class requirements has aided the USPTO in identifying and assessing prior art by eliminating irrelevant prior art from the start. However, the classification is also constrained by the USPTO's definition of nanotechnology.¹¹³

¶38 The USPTO next converted the single digest to a nanotechnology classification schedule with 263 cross-reference art collection subclasses,¹¹⁴ facilitating the routing of patent applications to examiners with particular expertise. The USPTO based these classes on international patent classes available, as well as prior experience. In November 2005, the USPTO Classification Order 1850 officially abolished Class 977, Digest 1 and established the Class 977 and the cross-reference art collection Subclasses 700 through 963.¹¹⁵ Each contained subclass definitions and a search note.¹¹⁶

¶39 While there is no centralized nanotechnology art unit within the USPTO centers, the 977 Class assists in locating applications and distributing among art units.¹¹⁷ The lack of a nanotechnology art unit means that, to date, the USPTO has not assigned a group of “nano” examiners because of the diversity of nanotechnology inventions. When an application is submitted to the USPTO, it is distributed to one or more of the existing art units and linked subclasses such as “chemistry: molecular biology and microbiology” (Class 435) or “drug, bio-affecting and body treating compositions” (Class 424) based on the patent claims, and then filtered to the 977 classification as a cross-reference tool. In tandem with creation of the 977 classification, the USPTO has partnered with outside professionals and experts to train and educate patent examiners on nanotechnology terminology and concepts.¹¹⁸

B. Nanopharmaceutical Subclassifications

¶40 The 977 classification is comprised of 263 subclassifications: 700 through 963. Subclassifications 700 to 838 encompass various forms of a “nanostructure.”¹¹⁹ Subclassification 839 is reserved for mathematical algorithms “specifically adapted for

¹¹³ See discussion *supra* notes 106–107 and accompanying text.

¹¹⁴ Charles R. Eloschway, *Nanotechnology-Related Issues at the United States Patent and Trademark Office*, COMMUNITY RES. & DEV. INFO. SERVICE 5 (Dec. 2006), ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/iprworkshop_eloschway_en.pdf.

¹¹⁵ David J. Robeson, *Nanotechnology and the USPTO*, NAT'L ASS'N PAT. PRAC. 3 (2006), http://www.napp.org/disclosure/linked_files/Nanotechnology%20and%20the%20USPTO_05.01.2006.pdf.

¹¹⁶ CLASS 977 DEFINITIONS, *supra* note 106.

¹¹⁷ *Where Science and Law Meet: Nanotechnology and Intellectual Property Issues*, NAT'L CANCER INST. 3 (Oct. 2006), http://nano.cancer.gov/action/news/featurestories/monthly_feature_2006_oct.pdf [hereinafter *Where Science and Law Meet*].

¹¹⁸ Feder, *supra* note 103; *Patent Office Struggles to Stay Ahead of Nanotech Industry*, ELECTRO IQ (Apr. 20, 2004), <http://www.electroiq.com/index/display/nanotech-article-display/269406/articles/small-times/legal/2004/04/patent-office-struggles-to-stay-ahead-of-nanotech-industry.html>.

¹¹⁹ U.S. PATENT & TRADEMARK OFFICE, CROSS-REFERENCE ART COLLECTIONS: CLASS 977 NANOTECHNOLOGY 1–3 (2010), available at <http://www.uspto.gov/web/patents/classification/uspc977/sched977.pdf> [hereinafter CLASS 977 SCHEDULE].

modeling configurations or properties of [a] nanostructure”;¹²⁰ subclassifications 840 to 901 encompass “manufacture, treatment, or detection of [a] nanostructure”;¹²¹ subclassifications 902 to 962 encompass “specified use of [a] nanostructure”;¹²² and subclassification 963 is reserved for miscellaneous.¹²³

¶41 The subclassifications within the 977 class most relevant to nanomedicine and pharmaceutical development are those that fall into subclassifications 904 through 926. These are specified uses of nanostructure for “medical, immunological, body treatment or diagnosis,” divided into areas such as “drug delivery” (977/906), “mechanical repair performed/surgical” (977/908), “therapeutic or pharmaceutical composition” (977/915), “vaccine” (977/917), and “topical chemical” (977/926).¹²⁴ A particular patent will first list its primary classifications and subclassifications and then list the 977 cross-reference classifications and subclassifications. As of May 31, 2011, the 977/904 through 977/926 classifications consist of a total of 896 patents, many of which are listed in multiple subclassifications based on the substance of their claims.¹²⁵

¹²⁰ *Id.* at 3.

¹²¹ *Id.* at 4.

¹²² *Id.*

¹²³ *Id.* at 5.

¹²⁴ *See infra* Figure 1.

¹²⁵ This count was retrieved using a specific methodology to eliminate duplicate patents listed in multiple sub-classifications. *USPTO Patent Full-Text and Image Database*, *supra* note 5 (search “Query” for “ccl/977/904 or ccl/977/905 or ccl/977/906 or ccl/977/907 or ccl/977/908 or ccl/977/909 or ccl/977/915 or ccl/977/917 or ccl/977/920 or ccl/977/921 or ccl/977/922 or ccl/977/923 or ccl/977/924 or ccl/977/925 or ccl/977/926”).

FIGURE 1. USPTO NANOTECHNOLOGY SUBCLASSIFICATIONS 977/902 THROUGH 977/926¹²⁶

<p>977/902: Specified Use of Nanostructure 977/903: For conversion, containment, or destruction of hazardous material 977/904: For medical, immunological, body treatment, or diagnosis 977/905: Specifically adapted for travel through blood circulatory system 977/906: Drug delivery 977/907: Liposome 977/908: Mechanical repair performed/surgical 977/909: Obstruction removal 977/910: Strengthening cell or tissue 977/911: Cancer cell destruction 977/912: Cancer cell repair 977/913: Stem cell therapy implantation 977/914: Protein engineering 977/915: Therapeutic or pharmaceutical composition 977/916: Gene therapy 977/917: Vaccine 977/918: Immunological 977/919: Dental 977/920: Detection of biochemical 977/921: Of toxic chemical 977/922: Of explosive material 977/923: Cell culture 977/924: Using nanostructure as support of DNA analysis 977/925: Bioelectrical 977/926: Topical chemical (e.g., cosmetic or sunscreen, etc.)</p>

¶42

Patents for various FDA-approved and marketed pharmaceutical products have been classified in the 977 cross-reference system. For example, within the *Orange Book*¹²⁷ listing for Depocyt, an FDA-approved nanoparticle formulation of cytarabine for treatment of lymphomatous meningitis, the patent and exclusivity references include U.S. Patent No. 5,455,044 (method for treating neurological disorders).¹²⁸ In the patent itself, the primary classification is 424/450 (drug, bio-affecting, and body-treating compositions; preparations characterized by physical form; liposomes), followed by 977/907 (nanotechnology; specified use of nanostructure for medical, immunological, body treatment or diagnosis; specifically adapted for travel through blood circulatory system; liposome), 977/911 (nanotechnology; specified use of nanostructure for medical, immunological, body treatment or diagnosis; mechanical repair performed; surgical; cancer cell destruction), and 977/915 (nanotechnology; specified use of nanostructure for medical, immunological body treatment, or diagnosis; therapeutic or pharmaceutical composition). Similarly, the *Orange Book* listing for Estrasorb, an FDA-approved micellar nanoparticle estrogen delivery system for topical treatment of menopausal hot flashes, lists U.S. Patent No. 5,629,021 (micellar nanoparticles) within the patent and

¹²⁶ CLASS 977 SCHEDULE, *supra* note 119.

¹²⁷ The *Orange Book* is a publication of the Food and Drug Administration that lists patent and exclusivity information for pioneer and generic drugs. The searchable electronic version is available at *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG ADMIN., <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm> (last updated Oct. 28, 2011).

¹²⁸ Method for Treating Neurological Disorders, U.S. Patent No. 5,455,044 (filed May 14, 1993).

exclusivity references.¹²⁹ This patent's primary classification is 424/489 (drug, bio-affecting and body treating compositions; preparations characterized by physical form; particulate form), followed by 977/915 (nanotechnology; specified use of nanostructure for medical, immunological, body treatment or diagnosis; therapeutic or pharmaceutical composition) and 977/926 (nanotechnology; specified use of nanostructure for medical, immunological body treatment or diagnosis; topical chemical).

¶43 However, the underlying patents for many pharmaceutical products utilizing nanotechnology that have been approved by the FDA and are currently on the market have not been classified by the USPTO as nanotechnology.¹³⁰ As discussed below, there may be a variety of reasons for this, including the particular claim drafting, date of patent application, or other special circumstances relating to product development and commercialization. For example, many of the FDA-approved drugs utilizing nanotechnology were approved well before the USPTO implemented the 977 classification system.¹³¹

¶44 As the Appendix illuminates, the development of such a nanotechnology classification system, while proactive on the part of the USPTO, suffers from a number of limitations. The first major limitation is the USPTO's cut-off at 100 nm or less particle size. As described below, the first litigation involving an FDA-approved nanodrug was based on a preexisting patent that had not been classified by the USPTO in their nanotechnology classification because the claims regarding particle size exceeded the 100 nm ceiling (and the patent application was filed well before 2004). In fact, Abraxane, one of the first marketed nanodrugs and the subsequent product at issue in the litigation described in Part IV, has a 130 nm mean particle size;¹³² the claim drafting moved that into the 977 classification based on the use of the phrase "less than about 200 nm" coupled with examples provided within the patent specification within the 50–220 nm range, which begins below 100 nm.¹³³ Because of broad claiming, many patents that have been awarded may be inaccurately excluded from the nanotechnology classification. In reality, nanomedicine products resulting from such patents could be deemed nano for FDA purposes (the Center for Drug Evaluation and Research within the FDA defines

¹²⁹ Micellar Nanoparticles, U.S. Patent No. 5,629,021 (filed Jan. 31, 1995).

¹³⁰ These products were identified using a two-pronged search methodology: a search of the relevant scientific literature reporting on research and development in nanopharmaceuticals and the FDA's website providing information on FDA-approved drugs, *Drugs@FDA Database*, U.S. FOOD & DRUG ADMIN., <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm> (last visited Dec. 20, 2011). Where a product was identified in the scientific literature as a nanopharmaceutical, the FDA database was used to retrieve that product's approval information. Searches were conducted from January 2011 through May 2011. The Appendix references all scientific sources.

¹³¹ The Appendix provides information both from the scientific literature and the FDA on FDA-approved nanotechnology pharmaceutical products. Of the twenty-six products identified in the Appendix, only three of them have patents listed in the *Orange Book* that have been classified by the USPTO as qualifying for the 977 nanotechnology classification (i.e., Abraxane, DepoCyt, and Estrasorb).

¹³² See ABRAXIS BIOSCIENCE, ONCOLOGIC DRUGS ADVISORY COMMITTEE MEETING BRIEFING PACKAGE: ABRAXANE (Aug. 4, 2006), <http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4235B2-01-AbraxisBioscience-background.pdf>.

¹³³ Compositions & Methods of Delivery of Pharmacological Agents, U.S. Patent No. 7,820,788 B2 col. 38 l. 22 (filed Oct. 26, 2006).

nanoscale material as having a particle size of less than 1,000 nm)¹³⁴ and not for USPTO purposes (defining nano as having a particle size of 100 nm or less). Other drug products may deviate from the 100 nm ceiling depending on the size of the actual nanodrug product compared to the total size of the particle containing the drug product and any encapsulating material or adjuvant.

¶45 The second limitation is that the USPTO began the classification project in 2004, without installing a uniform mechanism to retroactively reclassify existing patents into the new 977 classification system. Retroactively classifying already-issued patents into the new classification system was encouraged, though not required: “While every effort has been made to make the subclasses as complete as possible, the agency encourages patent examiners to classify newly issuing patents as well as previously published patent documents into the Class 977 cross-reference art collection subclasses”¹³⁵ An individual examiner may take the initiative to reclassify an already issued patent, but time constraints and meager salaries counsel otherwise. This may cause problems down the road in litigation, as Part IV illustrates.

¶46 The third limitation is that the information, once the patent is placed in the class and given a subclassification for cross-referencing, is not tracked or otherwise effectively utilized to identify patterns that may be playing out in the resulting marketed products or relationships to other issued patents. The USPTO’s efforts serve as an example for other federal agencies in terms of gathering information relevant to nanotechnology and categorizing nano-specific features that could be useful in the future as more becomes known about the potential products, uses, and risks of nanotechnology. This information would be particularly useful to regulatory agencies overseeing the resulting products, such as the FDA. For example, as the Appendix reflects, there is often a disconnect between scientific research findings, information provided to the FDA for approval purposes, and what is actually presented to the public about the nanotechnology involved in commercial products. Utilization and effective linking of this information among agencies could serve as a mechanism to fill in the information gaps currently confronting other relevant agencies.

¶47 Despite the nascent state of patent litigation involving the scale or characteristics of nanotechnology, the scholarly literature has identified several concerns that will emerge as patenting continues that tie into the three limitations described above. The first major concern is that overlapping claims will result from broad claiming of scale in early patents coupled with more precise scale claims linked to particular properties and functions in later patents. For example, early patent claims may conflate the macro, micro, and nanoscale in a manner that is problematic for later inventions that identify and harness something present at a range in the nanoscale but not at the micro or macro scale. Another concern is the convergence of technologies at the nanoscale, in that overlapping patents and claims may cross multiple technologies, with many issued before nano was a widespread word. Many of these concerns will abate given the USPTO’s classification

¹³⁴ OFFICE OF PHARM. SCI., CTR. FOR DRUG EVALUATION & RESEARCH, MANUAL OF POLICIES AND PROCEDURES, § 5015.9 REPORTING FORMAT FOR NANOTECHNOLOGY-RELATED INFORMATION IN CMC REVIEW 3 (2010), *available at* <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/UCM214304.pdf> [hereinafter NANOTECHNOLOGY MAPP].

¹³⁵ *Class 977 Nanotechnology Cross-Reference Art Collection*, *supra* note 4.

system as patenting moves forward, although questions will arise with regard to inventions submitted and patents issued prior to the development of the classification system. In performing the cross-listing classifications, the USPTO is merely putting issued patents into those 263 subclasses and not making determinations on claim scope and potential infringement from one patent to the next, except as part of the evaluation of prior art.

¶48 Part IV explores how the limitations in the USPTO's classification system play out in the courtroom by describing litigation involving a blockbuster nanotechnology-enabled treatment for cancer. This litigation highlights the problems posed by nanotechnology: the limitations of current definitions of nanotechnology; the critical aspects of size, properties, and characteristics at the nanoscale; and the importance of specificity in the scope of claim drafting. While this case is the first of its kind, the influx of nanotechnology patent applications into the USPTO over the last decade (as well as the thousands of issued patents classified as nanotechnology by reviewers for prior art purposes) suggests that similar litigation targeting the scope of nanotechnology claims will be forthcoming.

IV. "NANOTECHNOLOGY" IN COURT: *ELAN PHARMA V. ABRAXIS BIOSCIENCE*

¶49 Nanotechnology-specific issues have yet to loom large in the context of patent litigation. A targeted search of legal cases identifies very few patent disputes resulting in litigation that relate to the nano-size or characteristics of the invention at the nanoscale.¹³⁶ Most cases that include a reference to nano consist of non-patent allegations, including breach of contract, licensing issues, or trademark or copyright issues regarding a company name or product.¹³⁷ However, one high profile case in the realm of nanobiotechnology, *Elan Pharma v. Abraxis Bioscience*,¹³⁸ is particularly on point and instructive. The case exemplifies problems regarding scale range and lack of uniformity in patent claim drafting, the relationship between earlier non-nanotechnology classified patents and later nanotechnology classified patents, and the struggle in the courtroom by judges and juries to provide resolution to thorny scientific and technical issues. The case and the relevant patents are described below.

A. *The Patent Litigation*

¶50 *Elan Pharma v. Abraxis Bioscience* involved Abraxane, the Abraxis Bioscience blockbuster drug for treatment of breast cancer, approved by the FDA in 2005 for treatment of metastatic breast cancer and marketed widely. Sales generated \$314.5 million in 2009.¹³⁹ Abraxane, the alleged infringing product, is the albumin formulation of paclitaxel, a cancer-fighting agent that has been used in FDA-approved drugs, such as

¹³⁶ A search of Westlaw state and federal cases retrieved forty-four cases. Search conducted June 2011.

¹³⁷ However, cases involving nanotechnology that do not utilize the term nanotechnology will not be identified by a search of case law resources, nor will litigation that has not progressed to the stage of reporting in an official reporter.

¹³⁸ *Elan Pharma Int'l Ltd. v. Abraxis Bioscience Inc.*, No. 06-438 GMS, 2007 WL 6382930 (D. Del. Dec. 17, 2007).

¹³⁹ Jessica Merrill, *Celgene Moves into Solid Tumors with \$2.9 Billion Abraxis Acquisition*, PINK SHEET: PRESCRIPTION PHARMACEUTICALS & BIOTECHNOLOGY, July 5, 2010, at 11.

Taxol, for years.¹⁴⁰ In addition to allowing the faster administration of the drug (thirty minutes as opposed to three hours for the previous formulation, Taxol), the albumin-bound formulation “eliminates the need for a solvent that can be toxic and also means greater doses of paclitaxel can be given before side effects become intolerable.”¹⁴¹

¶51 The jury determined that Abraxane infringed on several of Elan’s patent claims in U.S. Patent No. 5,399,363 (’363 Patent),¹⁴² issued by the USPTO in 1995. The Elan ’363 Patent claimed anticancer compositions in the form of “surface modified nanoparticles” in “crystalline” form that “exhibit reduced toxicity and/or enhanced efficacy.”¹⁴³ The Elan Patent specifically claimed:

Particles consisting essentially of 99.9% by weight of a crystalline medicament useful in treating cancer susceptible to treatment with said medicament, said medicament having a solubility in water of less than 10 mg/ml, and having a non-crosslinked surface modifier adsorbed on the surface thereof in an amount of 0.1–90% by weight and sufficient to maintain an average effective particle size of less than 1000 nm¹⁴⁴

The court determined that the scope of the nanoparticles as claimed required that “90% of the particles have a number average particle size of less than 1000 nanometers.”¹⁴⁵ Other key terms construed by the court were “surface modifier,” defined as “a substance that modifies the surface properties of the crystalline medicament,”¹⁴⁶ and “non-crosslinked,” defined as “the individually adsorbed molecules of the surface modifier are essentially free of intermolecular crosslinkages.”¹⁴⁷

¶52 While it was not identical to the Elan Patent, Elan argued that Abraxane infringed because “more than one particle” out of over 61 trillion nanoparticles in the product were “entirely crystalline” and “non-crosslinked surface modifiers.”¹⁴⁸ Abraxis argued that Abraxane’s eight percent crystalline form did not require that any specific particle be entirely crystalline,¹⁴⁹ but did acknowledge that the human serum albumin, which is captured by the ’363 Patent’s definition of “surface modifier,” is adsorbed on the surface

¹⁴⁰ The drug ingredient is named paclitaxel; one brand name drug product is called Taxol. *See Paclitaxel*, DRUGS.COM, <http://www.drugs.com/international/paclitaxel.html> (last visited Dec. 19, 2011).

¹⁴¹ Merrill, *supra* note 139, at 12.

¹⁴² Verdict Form at 1, *Elan Pharma*, No. 06-438 GMS, 2008 WL 2556294. The jury, however, did not find willful infringement of the ’363 Patent. *Id.* at 5. The jury also found Elan’s patent 5,834,025 and the ’363 patent not invalid for lack of enablement, failure of written description, or inequitable conduct. *Id.* at 2–4.

¹⁴³ Surface Modified Anticancer Nanoparticles, U.S. Patent No. 5,399,363 (filed July 1, 1992) col. 1 l. 45–50. The listed patent assignee is the Eastman Kodak Company, who licensed the technology to Elan Pharma for development.

¹⁴⁴ *Id.* at col. 14 l. 7–14. The abstract reads: “Dispersible particles consisting essentially of a crystalline anticancer agent having a surface modifier adsorbed on the surface thereof in an amount sufficient to maintain an effective average particle size of less than about 1000 nm.” *Id.* at [57].

¹⁴⁵ Order Construing the Terms of U.S. Patent Nos. 5,399,363 and 5,834,025 at 3, *Elan Pharma*, 06-438 GMS, 2007 WL 6137001 (internal quotation mark omitted).

¹⁴⁶ *Id.* at 2 (internal quotation marks omitted).

¹⁴⁷ *Id.* (internal quotation marks omitted).

¹⁴⁸ Defendant Abraxis Bioscience, Inc.’s Opening Brief in Support of Its Motion for Judgment as a Matter of Law of Noninfringement, Invalidity, Inequitable Conduct, and Its Motion for New Trial at 5–6, 12, *Elan Pharma*, No. 06-438-GMS, 2008 WL 2856297 (internal quotation marks omitted).

¹⁴⁹ *Id.* at 2.

of Abraxane to prevent crosslinking.¹⁵⁰ The jury found a sufficient number of the Abraxane medicament particles were entirely crystalline and thus infringed the '363 Patent.

¶153 The outcome of the 2008 Delaware district court case was a jury verdict of \$55.2 million to Elan Pharma for Abraxis' infringement of the '363 Patent issued in 1995.¹⁵¹ The monetary damages amount reflects a six percent royalty on the sales of Abraxane during the infringement period of January 7, 2005 to June 13, 2008.¹⁵² In June 2010, Celgene acquired Abraxis Bioscience for approximately \$2.9 billion in cash and stocks,¹⁵³ the acquisition was finalized in October 2010.¹⁵⁴ Celgene also agreed to pay Elan a one-time licensing fee of \$78 million when it acquired Abraxis under terms that Elan will not "receive any additional payments for sales of [Abraxane], or any other [nab]-Paclitaxel product."¹⁵⁵ It is not clear what terms were negotiated among the parties regarding the relationship between the '363 Patent and the pending patent applications at the USPTO covering the Abraxane product and technology. Part IV-B discusses the two key patents in more detail.

¶154 Subsequent to the litigation, the USPTO granted Abraxis two patents for its nanoparticle technology on October 26, 2010¹⁵⁶ and April 12, 2011.¹⁵⁷ Celgene plans to initiate a marketing campaign aimed at increasing Abraxane drug sales to \$1 billion by the year 2015.¹⁵⁸ Celgene anticipates that Abraxane will retain patent protection and large profits until 2023,¹⁵⁹ likely based on calculations involving the licensing deal from Elan, which resulted from this litigation, coupled with the recently issued patent for certain aspects of the technology. Five other drugs are currently in development based on the nanoparticle technology in Abraxane, including drugs in Phase III clinical trials for treatment of first-line non-small cell lung cancer and pancreatic cancer.¹⁶⁰

¶155 Notably, this case illustrates the limitation inherent in the definition of nanotechnology as under 100 nm. The USPTO has not classified the Elan Patent in the 977 cross-reference nanotechnology classification, likely because the patent broadly claims nanoparticles "under 1000 nm" which, while including particle size under 100 nm, also includes the 101–999 nm range as well.

¹⁵⁰ Plaintiff Pharma International Ltd.'s Opening Claim Construction Brief at 5–6, *Elan Pharma*, No. 06-438-GMS, 2008 WL 2856297.

¹⁵¹ William F. Prendergast & Heather N. Schafer, *Nanocrystalline Pharmaceutical Patent Litigation: The First Case*, 5 NANOTECHNOLOGY L. & BUS. 157, 157 (2008).

¹⁵² Verdict Form, *supra* note 142, at 5.

¹⁵³ Andrew Pollack, *Prominent Drug Chief to Sell Abraxis BioScience to Celgene for \$2.9 Billion*, N.Y. TIMES, July 1, 2010, at B3; Press Release, Celgene Corp., Celgene to Acquire Abraxis BioScience Inc. (June 30, 2010), <http://ir.celgene.com/phoenix.zhtml?c=111960&p=irol-newsArticle&ID=1442901>.

¹⁵⁴ Press Release, Celgene Corp., Celgene Completes Acquisition of Abraxis (Oct. 15, 2010), <http://ir.celgene.com/phoenix.zhtml?c=111960&p=irol-newsArticle&ID=1483257>.

¹⁵⁵ *Elan and Celgene Enter into Settlement and License Agreement Related to ABRAXANE*, BUSINESS WIRE, Feb. 24, 2011, available at <http://www.businesswire.com/news/home/20110224007229/en/Elan-Celgene-Enter-Settlement-License-Agreement-Related>.

¹⁵⁶ '788 Patent.

¹⁵⁷ Compositions & Methods of Delivery of Pharmacological Agents, U.S. Patent No. 7,923,536 B2 (filed Apr. 12, 2010).

¹⁵⁸ Merrill, *supra* note 139, at 11.

¹⁵⁹ *Id.* at 12.

¹⁶⁰ *Id.* Other investigations include refractory invasive bladder cancer and malignant melanoma.

B. The Patents

¶56 The 1995 Elan Patent and the subsequently issued Abraxis Biosciences patents illustrate what is sure to be an increasingly problematic aspect of nanotechnology patenting—claim scope and drafting. Both patents claim characteristics and interactions of serum albumin and Taxol, an anti-cancer agent. The relationship between the two patents warrants a brief primer.

¶57 Taxol (paclitaxel) is a molecule that contains many non-polar (hydrophobic) carbon rings that share electrons equally, causing the solubility of Taxol in water to be significantly reduced and inhibiting its effectiveness as a cancer therapy.¹⁶¹ The protein serum albumin, a molecule having both hydrophobic and hydrophilic properties, can be used as a surface modifier to enhance the solubility of Taxol. Non-polar domains interact with Taxol, and the polar (hydrophilic) domains interact with water.¹⁶² Due to its dual nature, albumin will self-assemble on a Taxol particle and create a shell of albumin, coating the Taxol particle, whereby hydrophobic Taxol is insulated from water and other Taxol particles.¹⁶³ The albumin thus prevents the aggregation of multiple Taxol particles and enhances the solubility in water.¹⁶⁴ Both the Elan Patent and the Abraxane Patents rely on the Taxol and serum albumin interaction at the nanoscale.

1. The Elan '363 Patent

¶58 The Elan '363 Patent is drafted extremely broadly. Claim 1 covers any particles that have an average size of less than 1,000 nm and are composed of one of the named poorly water-soluble anti-cancer medications and any adsorbed surface coating.¹⁶⁵ Claim 1 gives specific examples of the types of medication and includes Taxol in this list.¹⁶⁶ The use of Taxol for the specific purpose of an anti-cancer agent is stated in Claim 5.¹⁶⁷ Beginning with Claim 12 of the '363 Patent, the different types of surface modifiers are listed.¹⁶⁸ Claim 12 is especially broad because it covers any surface modifier that is “a surfactant.”¹⁶⁹ Surfactants are an entire class of small molecules that have both hydrophobic and hydrophilic properties. Claim 15 goes on to state other specific surface modifiers including bovine serum albumin,¹⁷⁰ which contains hydrophobic and hydrophilic domains.

¶59 This patent is not classified by the USPTO as within the 977 nanotechnology cross-reference system, due to both procedural and substantive reasons mentioned in Part III. On the procedural side, there is no retroactive classification of issued patents into the 977

¹⁶¹ For a primer on hydrophobic and hydrophilic interactions, see BRUCE ALBERTS ET AL., *MOLECULAR BIOLOGY OF THE CELL* 57–58 (4th ed. 2002).

¹⁶² Toru Takagishi, *Amphiphilic Polymers (Binding Properties for Small Molecules)*, in 1 *POLYMERIC MATERIALS ENCYCLOPEDIA* 228, 228 (Joseph C. Salamone ed., 1996).

¹⁶³ A.G. Garro et al., *Reversible Exposure of Hydrophobic Residues on Albumin as a Novel Strategy for Formulation of Nanodelivery Vehicles for Taxanes*, 6 *INT'L J. NANOMEDICINE* 1193, 1193 (2011).

¹⁶⁴ *Id.*

¹⁶⁵ *See* '363 Patent col. 14 l. 7.

¹⁶⁶ *Id.*

¹⁶⁷ *Id.* at col. 14 l. 35.

¹⁶⁸ *Id.* at col. 14–15.

¹⁶⁹ *Id.* at col. 14 l. 68.

¹⁷⁰ *Id.* at col. 15 l. 5.

cross-reference system. Individual patent examiners may initiate reclassification. Coupled with examiner discretion, the Elan Patent was filed back in 1992 and issued in 1995.¹⁷¹ Its expiration is quickly approaching, likely making it an unpopular candidate for reclassification energy.

¶60 On the substantive side, the USPTO's definition of nanostructure may limit inclusion of certain patents including the Elan Patent. Based on physical dimension requirements alone, the Elan particles could simply be too large. The '363 Patent claims surface modified particles in crystalline form in the range of less than 1,000 nm,¹⁷² less than 400 nm,¹⁷³ and less than 300 nm.¹⁷⁴ While each of the three claimed particle sizes may be within the 1–100 nm range, they might not be. Examples in the patent that illustrate the invention identify the smallest final particle size to be 240 nm.¹⁷⁵

2. The Abraxis '788 Patent

¶61 Unlike the Elan Patent, the Abraxis Patent has been classified as a nanotechnology patent by the USPTO. The patent's primary classification is denoted as 530/350 and the nanotechnology subclassification is 977/779 (nanotechnology; nanostructure; within specified host or matrix material; possessing nano-sized particles, powders, flakes, or clusters other than simpler atomic impurity doping); 977/906 (nanotechnology; specified use of nanostructure; drug delivery); and 977/911 (nanotechnology; specified use of nanostructure; for medical, immunological, body treatment, or diagnosis; mechanical repair performed; surgical; cancer cell).¹⁷⁶

¶62 The scope of the '788 Patent is much narrower, but it appears that there is some overlap with the '363 Patent regarding the nanoparticle composition. Claim 1 of the Abraxis Patent claims

A pharmaceutical composition for injection comprising paclitaxel and a pharmaceutically acceptable carrier, wherein the pharmaceutically acceptable carrier comprises albumin, wherein the albumin and the paclitaxel in the composition are formulated as particles, wherein the particles have a particle size of less than about 200 nm, and wherein the weight ratio of albumin to paclitaxel in the composition is about 1:1 to about 9:1.¹⁷⁷

There are eleven subsequent claims.

¶63 In '788, the only anti-cancer compound claimed is paclitaxel,¹⁷⁸ the only surface modifier is human serum albumin,¹⁷⁹ and the average particle size is limited to less than 200 nm.¹⁸⁰ As compared to the Elan '363 Patent, there are arguably areas of overlap.

¹⁷¹ *Id.* at [22], [45].

¹⁷² *Id.* at col. 14 l. 14.

¹⁷³ *Id.* at col. 14 l. 29.

¹⁷⁴ *Id.* at col. 14 l. 31.

¹⁷⁵ *Id.* at col. 8 l. 28, col. 9 l. 63.

¹⁷⁶ '788 Patent. This Part analyzes the earlier issued patent, as the later patent ('536 Patent) is subject to a terminal disclaimer.

¹⁷⁷ *Id.* at col. 38 l. 17–24.

¹⁷⁸ *Id.* at col. 38 l. 18.

¹⁷⁹ *Id.* at col. 38 l. 25.

¹⁸⁰ *Id.* at col. 38 l. 22.

Taxol (paclitaxel) was specifically mentioned as a possible anti-cancer compound in the '363 Patent. The average particle size of less than 200 nm in the '788 Patent would fall within the average particle size of less than 1,000 nm (and less than 400 and 300 nm) in the '363 Patent, and bovine serum albumin was specifically mentioned as a surface modifier in the '363 Patent.¹⁸¹

FIGURE 2. COMPARISON OF KEY CLAIMS IN THE '363 AND '788 PATENTS

Patent Claims	'363 Patent ¹⁸²	'788 Patent ¹⁸³
Particle Size & Ranges	“Average effective particle size” of < 1,000 nm; < 400 nm; < 300 nm	“particle size [of paclitaxel and albumin] of less than about 200 nm”
Agents	“anti-cancer agents”; claims taxol among others	paclitaxel
Surface modifiers	Any surface modifier that is a “surfactant”; claims bovine serum albumin among others	human serum albumin
Indications	“anticancer agent”	Cancer, arthritis, restenosis
Route of Administration	“administer[ed] to a mammal”	Various, including intravenous, orally, etc.

C. Reconciling the '363 and '788 Patents

¶164 A comparison of the two patents described in Parts IV-A and IV-B illustrate the problems that courts, the USPTO, and industry will face as nanotechnology development pushes forward. This Part raises a number of comparative points in order to frame Part V; this is not intended to be an exhaustive analysis of the patents, and the author acknowledges that this is a cursory look rather an in-depth examination.

¶165 The particle range of the claims is significant to the discussion of the novel properties that emerge at the nanoscale. In the '363 Patent, all examples provided within the patent exceed 240 nm; in the '788 Patent, all examples provided in the patents are within the range of 50 to 220 nm, a range starting squarely under the 100 nm outer bounds range set forth by the USPTO. Another critical aspect that came to light in the litigation is the surface modifier form; the '363 Patent claims non-crosslinked surface modifiers that include those in “crystalline form.” This was at the heart of the litigation regarding Abraxane’s mechanism of action and drug form. The patents seemingly overlap in a number of regards: both claim in the size range greater than 200 nm, both claim either the agent Taxol or paclitaxel, and both claim a form of serum albumin as an agent, though the '536 Patent claims are limited to cancer, arthritis, and restenosis.¹⁸⁴

¶166 In contrast to the Elan Patent, the Abraxis Patent claims average particles sizes less than 200 nm¹⁸⁵ and example preparations provide an average range for the particle rather than a final particle size as presented in the Elan Patent. For instance, Example 12 of the Abraxis Patent describes preparation of particles “in the range 50–220 nm.”¹⁸⁶ While it is

¹⁸¹ Cf. *infra* Figure 2.

¹⁸² '363 Patent col. 14–15.

¹⁸³ '788 Patent col. 38.

¹⁸⁴ '536 Patent col. 37.

¹⁸⁵ See *supra* Figure 2.

¹⁸⁶ '788 Patent col. 19 l. 20.

unclear, perhaps the claim is drafted so that the nanoparticle size is sufficiently small to impart special diffusion properties not present at the scale offered in the Elan Patent.

¶167 Additionally, the distinction between bovine serum albumin and human serum albumin may or may not be significant. Claim 2 of the '788 Patent covers *human* serum albumin¹⁸⁷ (HSA) as the surface modifier, rather than the *bovine* serum albumen (BSA) claimed in the '363 Patent.¹⁸⁸ HSA and BSA share seventy-six percent identical amino acids and approximately eighty-seven percent of the amino acids are either identical or have similar chemical properties.¹⁸⁹ This degree of sequence homology suggests that HSA and BSA are interchangeable for constitution of soluble nanoparticles that do not aggregate, though it is unclear if this is the case when utilized in a human.

¶168 Parts III and IV argue that the USPTO nanotechnology classification, while a laudable effort, is not performing as well as it could to quell the impending problems that will confront the patent system. Part V details a research agenda of possible steps that could improve outcomes for nanotechnology patenting.

V. A RESEARCH AGENDA

¶169 This Article presents three core challenges facing the USPTO and reviewing courts as nanotechnology develops and litigation emerges: (1) limitations of and inconsistencies among current definitions of nanotechnology; (2) uncertainty and lack of uniformity in measurement capabilities regarding critical aspects of size, properties, and characteristics at the nanoscale; and (3) the role of patent claims in accurately and consistently encapsulating and distinguishing the scope of nanotechnology inventions. Keying in on the third problem, this Part suggests mechanisms to more effectively utilize the 977 classification system, learning from experience and case law in other scientific and technological areas, scholarly criticisms of the patent system as applied to nanotechnology, and the Abraxane litigation and related patents.

A. Improve the Internal 977 Process

¶170 The lowest-hanging fruit is, of course, to recommend that the USPTO reassess the 977 classification system and develop improvements to the system. These improvements can come in two forms: substantive and procedural. One major substantive improvement

¹⁸⁷ *Id.* at col. 38 l. 25.

¹⁸⁸ *See* '363 Patent col. 16 l. 8.

¹⁸⁹ These results were reached utilizing both the European Bioinformatics Institute EMBOSS Needle online tool and the protein sequence database on the National Center for Biotechnology Information's website. EMBOSS is a bioinformatics tool that can be used to create an optimal alignment between two proteins that have similar, but not identical, amino acid sequences. The program uses the Needleman-Wunsch algorithm and a pre-determined scoring matrix to create the alignment; the resulting optimal alignment is displayed graphically along with the percentage of identical and chemically similar amino acids between the two proteins. *See EMBOSS Needle: Pairwise Sequence Alignment*, EUR. BIOINFORMATICS INST., http://www.ebi.ac.uk/Tools/psa/emboss_needle/ (last visited Dec. 19, 2011). First, users should obtain the protein sequences for HSA and BSA. *E.g.*, *Protein Database*, NAT'L CTR. FOR BIOTECHNOLOGY INFO., <http://www.ncbi.nlm.nih.gov/protein/> (last visited Dec. 19, 2011) (accessed by searching for "178344" and "3336842," the unique identifiers for HSA and BSA, respectively, and clicking "FASTA"). Users should then paste the resulting sequences into EMBOSS (one in "first protein sequence" and the other in "second protein sequence") to compare the two sequences. *EMBOSS Needle: Pairwise Sequence Alignment, supra.*

would be to revisit the definition and qualifications for inclusion into the 977 classification. As evidenced in the pharmaceutical realm, many products utilizing nanotechnology may exceed the rigid 100 nm ceiling and are, in fact, legitimately nanotechnology as a scientific and technical matter. This is the stance recently taken by the FDA's Center for Drug Evaluation and Research and the Research Office of Pharmaceutical Science (CDER). In May 2010, CDER jointly issued an internal Manual of Policies and Procedures (MaPP) instructing drug reviewers to capture relevant information pertaining to "nanomaterial-containing drugs" and to organize data into a nanotechnology database.¹⁹⁰ This MaPP describes the terms nanomaterial and nanoscale material as involving "[a]ny materials with at least one dimension smaller than 1,000 nm."¹⁹¹ The 1 to 1,000 nm range included in CDER's conception of nanoscale as compared to both the NNI and USPTO definitions extending from 1 nm to 100 nm implies that the FDA has determined, as many scientists have argued for years, that nanotechnology is not necessarily capped at 100 nm, as the size-dependent novel properties vary with the material, environment, and interactions.¹⁹²

¶71 On the procedural side, a second improvement would be to tackle retroactive classification of patents applications submitted before 2004. The USPTO should establish an internal task force to discuss such an action, particularly identifying priority sub-classifications and proper scope and application of the retroactivity. For example, patents that have expired would be less of a priority as challenges to those patents would not be forthcoming. The task force should also consider prioritizing scientific and technical areas with the most active patent litigation.

B. Collaborate with Other Agencies

¶72 Inextricably tied to the first suggestion regarding internal improvements, the USPTO should also strive to improve not only the internal functioning of the 977 classification system, but also its interoperability with other relevant regulatory agencies. Although useful within the USPTO, this system of classification and wealth of nanotechnology-specific information could be more broadly shared and utilized by other relevant administrative agencies as they tackle the inherent challenges of nanotechnology and nanomedicine specifically. The USPTO should develop mechanisms to collaborate with other agencies, specifically the FDA, to extend the utility of their information-gathering and classification efforts. For purposes of this Article, the FDA is a prime example of a regulatory agency that would benefit from improvements in the USPTO process and joint collaboration efforts. Given the close relationship between patents and pharmaceutical development, enhanced feedback mechanisms between the FDA and USPTO would assist in a variety of ways.

¶73 Perhaps most helpful would be active collaboration between the USPTO and FDA regarding patent disclosures for purposes of listings in the *Orange Book*. As a key resource for generic drug companies in developing bioequivalent versions of pioneer

¹⁹⁰ NANOTECHNOLOGY MAPP, *supra* note 134, at 1.

¹⁹¹ *Id.* at 3.

¹⁹² See Paradise, *Reassessing 'Safety' for Nanotechnology*, *supra* note 2.

drugs,¹⁹³ the *Orange Book* provides all relevant patents that the generic sponsor must consider when developing the generic drug and filing for FDA approval. The Appendix reveals that very few nanodrugs disclose patents that have been classified by the USPTO as nanotechnology, suggesting an apparent disconnect between the information presented to the FDA and information presented to the USPTO or, as discussed earlier, a difference in defining nanotechnology. As a means to more effectively track nano-specific features and outcomes of nanodrugs, some type of feedback mechanism or cross-reference system between the two agencies would bolster transparency and foster uniformity in the drug industry with regard to information disclosure in the patent application process and eventual FDA application for market approval.

¶74 The USPTO should also build on the actions of other agencies in providing guidance to industry on nanotechnology issues. The FDA would be an ideal ally for the USPTO in this respect, as the FDA has possibly been the most proactive agency in terms of identifying regulatory challenges to the existing oversight system.¹⁹⁴ The FDA has thus far formed a multi-center task force,¹⁹⁵ instituted a drug specific internal policy,¹⁹⁶ published draft guidance for industry,¹⁹⁷ solicited public comments through public meetings,¹⁹⁸ and partnered with research institutions to examine particular aspects of nanotechnology.¹⁹⁹ In particular, development by the USPTO of a document similar to the FDA's draft guidance to industry may be especially helpful to patent applicants when contemplating whether to specifically describe their inventions in the nanoscale range. A "how to" for applicants would assist in more uniformity at the inventor and claim level.

C. Provide Training and Resources for Examiners

¶75 Any critique of the USPTO necessarily entails some treatment of patent examiner expertise, credentials, and performance. As nanotechnology is a confluence of

¹⁹³ The requirements and framework of the generic drug approval process is found in 21 U.S.C. § 355(j) (2006). A showing of bioequivalence requires "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study." 21 C.F.R. § 320.1(e) (2010).

¹⁹⁴ See Paradise, *Reassessing 'Safety' for Nanotechnology*, *supra* note 2.

¹⁹⁵ U.S. FOOD & DRUG ADMIN., NANOTECHNOLOGY TASK FORCE, NANOTECHNOLOGY: A REPORT OF THE U.S. FOOD AND DRUG ADMINISTRATION NANOTECHNOLOGY TASK FORCE 20–21 (2007), *available at* <http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/Nanotechnology/ucm110856.pdf>.

¹⁹⁶ NANOTECHNOLOGY MAPP, *supra* note 134.

¹⁹⁷ Draft Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology, 76 Fed. Reg. 34,715 (June 14, 2011); *see also* *FDA Draft Guidance Questions and Answers*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/ucm258391.htm> (last updated June 9, 2011); News Release, U.S. Food & Drug Admin., FDA Takes 'First Step' Toward Greater Regulatory Certainty Around Nanotechnology (June 9, 2011), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm258377.htm>.

¹⁹⁸ Consideration of FDA-Regulated Products that May Contain Nanoscale Materials, 73 Fed. Reg. 46,022 (Aug. 7, 2008).

¹⁹⁹ *Nanotechnology Partnerships at FDA*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/ucm208110.htm> (last updated July 22, 2010).

disciplines, very few patent examiners have advanced degrees in nanotechnology.²⁰⁰ Acknowledging the high turnover of patent examiners, less than ideal wages, and heavy workloads, the USPTO can take certain actions to address issues with delivery of information to patent examiners. First, the USPTO should contract with disinterested outside parties to train and educate patent examiners on nanotechnology and nanotechnology patent drafting. In November 2004, the USPTO established a working group consisting of outside lawyers and scientists to provide guidance to key figures as the USPTO began training examiners in nanotechnology concepts and terminology.²⁰¹ It is unclear how this working group has been utilized to date. Other sources report that some select law firms that supply counsel to the nanotechnology industry are hosting educational sessions for patent examiners. For example, Burns, Doane, Swecker & Mathis, LLP began a monthly forum to provide nanotechnology education to examiners.²⁰² Such arrangements raise potential conflicts of interest and should possibly be avoided by the USPTO.

¶76 The USPTO should pursue partnerships with the NNI, which is the federal vehicle for nanotechnology funding and development. Placed within the National Science and Technology Council as a national coordinating entity for nanotechnology research, development, and education, the NNI is made up of twenty-five federal agencies.²⁰³ The NNI serves as coordinating entity for agencies dealing with nanotechnology and fosters collaborative efforts in research and education among the agencies.²⁰⁴ A direct partnership between NNI and the USPTO in training and resources would help feed cutting-edge research findings and processes into patent examiners for consideration when reviewing patent applications and classifying them.

D. Utilize the Patent Peer Review Pilot Program

¶77 The USPTO implemented a pilot program to gather information on peer-reviewed publications and research in the public domain to locate “prior art that might not otherwise be located by the USPTO during the typical patent examination process.”²⁰⁵ The original pilot program began in 2007 and lasted two years,²⁰⁶ returning evidence that the public is “capable of contributing to the location of prior art of value to the examiner during the examination process.”²⁰⁷ The scope of the initial pilot program was limited to patent applications in computer-related arts.²⁰⁸ The project was then expanded to include patent applications in Class 705, “Data Processing: Financial Business Practice,

²⁰⁰ See, e.g., *Where Science and Law Meet*, *supra* note 117, at 3.

²⁰¹ Feder, *supra* note 103.

²⁰² *Patent Office Struggles to Stay Ahead of Nanotech Industry*, *supra* note 118.

²⁰³ NAT'L SCI. & TECH. COUNCIL, SUBCOMM. ON NANOSCALE SCI., ENG'G, & TECH., NATIONAL NANOTECHNOLOGY INITIATIVE STRATEGIC PLAN 1 (2011), *available at* <http://www.nano.gov/nnistrategicplan211.pdf>.

²⁰⁴ See, e.g., *id.* at 35.

²⁰⁵ *Peer Review Pilot FY2011*, U.S. PAT. & TRADEMARK OFF., http://www.uspto.gov/patents/init_events/peerpriorartpilotindex.jsp (last updated May 31, 2011).

²⁰⁶ *Id.*

²⁰⁷ *Id.*

²⁰⁸ *Id.*

Management, or Cost/Price Determination.”²⁰⁹ Out of the total 189 applications accepted into the program, thirty applications had at least one claim rejected based on prior art contributed by the public.²¹⁰ In fifteen of those thirty applications, the patent examiner did not find the prior art used to ultimately reject the claim.²¹¹

¶78 The USPTO expanded the program again in October 2010, which will continue through September 2011.²¹² As described by the USPTO:

In addition to statistical data on participation rates and the number of prior art references found and utilized by the USPTO, this pilot will be evaluating the effectiveness of the process more closely as it relates to patent examination efficiency and quality and peer participation behaviors. This pilot will test whether a peer review process is a viable addition to the normal processes of the USPTO and as an option for applicants to choose among the other products offered by the USPTO.²¹³

Although the additional pilot program expansion includes several patents areas, including several primary drug classifications, the 977 classification is not included. Several of the drug classifications, however, may implicate an overlap with nanotechnology, such as 424/514 (Drug, Bioaffecting and Body treating compositions).²¹⁴ As previously discussed, many drugs utilizing nanotechnology are currently on the market or in research and development stages.

¶79 The USPTO should consider using the peer review pilot as a mechanism to gather nanotechnology-specific information and prior art from stakeholders outside the USPTO. Particularly cueing in on nanopharmaceuticals, the USPTO should select a set of nanotechnology subclassifications to present as the next phase of the pilot program.

VI. CONCLUSION

¶80 Nanotechnology is no longer a forecast. It has arrived in basic consumer products, environmental remediation, electronics, mechanics, energy, optics, computing and information technology, industrial manufacturing, and health care and medicine. The resulting innovations and inventions are beginning to inundate the USPTO, an agency still trying to grapple with the patent ramifications of genetics over a decade after the completion of the Human Genome Project. The USPTO’s newly created 977 nanotechnology classification aims to organize nanotechnology patents into relevant subclassifications for ease in prior art searches and uniformity in cross-referencing. The USPTO system installs a collection of patents and patent applications that share the

²⁰⁹ John Doll, *Extension and Expansion of Pilot Concerning Public Submission of Peer Reviewed Prior Art*, 1333 OFF. GAZ. PAT. & TRADEMARK OFF. 103 (2008),

<http://www.uspto.gov/web/offices/com/sol/og/2008/week33/TOC.htm#ref13>

²¹⁰ David J. Kappos, *A New Pilot Program Concerning Public Submission of Peer Reviewed Prior Art*, 1361 OFF. GAZ. PAT. & TRADEMARK OFF. 230, 230 (2010),

<http://www.uspto.gov/web/offices/com/sol/og/2010/week52/TOC.htm#ref15>.

²¹¹ *Id.*

²¹² *Peer Review Pilot FY2011*, *supra* note 205.

²¹³ Kappos, *supra* note 210, at 235.

²¹⁴ *Eligible Classes and Subclasses for the Peer Review Pilot 2011*, U.S. PAT. & TRADEMARK OFF., http://www.uspto.gov/patents/init_events/class_subclasses_FY2011pilot.jsp (last updated Jan. 4, 2011).

common feature of falling within the nanotechnology penumbra—inventions at the nanoscale that exhibit unique features because of their 1–100 nm size. Despite the laudable effort, the classification system suffers from serious shortcomings.

¶81 This Article argues that as nanotechnology development and patenting progresses, three core problems will continue to raise challenges for the USPTO and courts: (1) limitations of and inconsistencies among current definitions of nanotechnology; (2) uncertainty and lack of uniformity in measurement capabilities regarding critical aspects of size, properties, and characteristics at the nanoscale; and (3) the role of patent claims to accurately and consistently encapsulate and distinguish the scope of nanotechnology inventions. Careful examination of *Elan Pharma v. Abraxis Bioscience*²¹⁵ helps to illustrate these three inherent problems and the related shortcomings of the USPTO nanotechnology patent classification system. Tying this case to U.S. patent law and policy, case precedent, and practice of the USPTO, we can extract lessons to apply to the emerging realm of nanopharmaceuticals.

¶82 Drawing from this analysis, a variety of adjustments would serve to assist the USPTO in fulfilling its mission to foster and award innovation while also facilitating effective information gathering to feed into regulation of the resulting products and inform any ensuing patent infringement litigation. These include improvements to the existing nanotechnology classification process, increasing feedback and collaboration with other federal agencies relevant to nanotechnology inventions, instituting independent educational programs for patent examiners, and utilizing the pilot peer review system for nanotechnology applications to encourage broader dialogue on the scope of patent claims and relationships to already issued patents.

²¹⁵ No. 06-438 GMS, 2007 WL 6382930 (D. Del. Dec. 17, 2007).

Appendix: FDA-Approved Drugs Utilizing Nanoscale Properties or Materials

Product	Indications ⁱ	Company ⁱⁱ	Formulation Description	Original NDA Approval ⁱⁱⁱ	U.S. Patent No. ^{iv}	977 Nano subclass
Zoladex	Anti-cancer drug ^v	AstraZeneca	Polymer rods used as nanocarrier ^{vi}	12/29/89*	7,118,552; 7,220,247; 7,500,964	None
Adagen	Immunodeficiency disease ^{vii}	Sigma Tau	PEG-adenosine deaminase ^{viii}	3/21/90*	None	None
Tricor (discontinued)	Lipid regulation ^{ix}	Abbott	Nanocrystalline fenofibrate ^x	12/31/93 ^{xi}	5,145,684; 6,277,405; 6,375,986 ⁱ ; 6,652,881; 7,037,529; 7,041,319; 7,276,249; 7,320,802	ⁱ 773; 896
Doxil	Anti-cancer drug for metastatic ovarian and breast cancers, and HIV-related Kaposi's sarcoma ^{xii}	OrthoBiotech Products, LP	Liposomal doxorubicin ^{xiii}	11/17/95*	None	None
Abelcet	Fungal infections ^{xiv}	Sigma Tau	Amphotericin B/lipid complex ^{xv}	11/20/95*	5,616,334; 6,406,713	None
DaunoXome	HIV-related Kaposi's sarcoma ^{xvi}	Gilead	Nano-sized drug for treatment of solid tumor ^{xvii}	4/8/96*	None	None
Feridex	<i>In vivo</i> imaging of liver tumors ^{xviii}	AMAG Pharms Inc.	Iron nanoparticles ^{xix}	8/30/96*	5,248,492	None
Amphotec	Fungal infections ^{xx}	Aldopharma USA	Amphotericin B/lipid colloidal dispersion ^{xxi}	11/22/96*	None	None
Gastromark	Used for improved imaging of abdominal structures ^{xxii}	AMAG Pharms Inc.	Nano-sized contrast agent ^{xxiii}	12/6/96*	None	None
Ambisome	Fungal infections ^{xxiv}	Astellas	Liposomal Amphotericin B ^{xxv}	8/11/97	5,874,104; 5,965,156	None

Product	Indications ⁱ	Company ⁱⁱ	Formulation Description	Original NDA Approval ⁱⁱⁱ	U.S. Patent No. ^{iv}	977 Nano subclass
Renagel	Chronic kidney disease ^{xxvi}	Genzyme	Crosslinked poly(allylamine) resin ^{xxvii}	10/30/98	5,496,545; 5,667,775; 6,509,013; 6,733,780; 7,014,846; 7,459,151	None
Depocyt	Treatment of lymphomatous meningitis	Pacira	Liposomal cytarabine ^{xxviii}	4/1/99 (accelerated approval)	5,455,044 ⁱ ; 5,723,147	ⁱ 907; 911; 915
Rapamune	Immunosuppressant for prevention of organ rejection	Wyeth	Nanocrystalline sirolimus ^{xxix}	9/15/99	5,100,899; 5,145,684; 5,212,155; 5,403,833; 5,989,591	None
Visudyne	Age-related macular degeneration ^{xxx}	QLT	Liposomal verteporfin ^{xxxi}	4/12/00	5,095,030; 5,707,608; 5,756,541; 5,770,619; 5,798,349; 6,074,666	None
Copaxone	Multiple sclerosis ^{xxxii}	TEVA	Copolymer of alanine, lysine, glutamic acid, and tyrosine ^{xxxiii}	2/12/02*	5,981,589; 6,054,430; 6,342,476; 6,362,161; 6,620,847; 6,939,539; 7,199,098	None
Somavert	Acromegaly ^{xxxiv}	Pharmacia & Upjohn	PEG-HGH ^{xxxv}	3/25/03	5,350,836; 5,681,809; 5,849,535; 5,958,879; 6,057,292; 6,583,115	None
Emend (Aprepitant)	Prevents nausea and vomiting induced by chemotherapy	Merck & Co. [¥]	Nanocrystalline aprepitant ^{xxxvi}	3/26/03	5,145,684; 5,538,982; 5,719,147; 6,048,859; 6,096,742; 6,235,735; 7,214,692	None

Product	Indications ⁱ	Company ⁱⁱ	Formulation Description	Original NDA Approval ⁱⁱⁱ	U.S. Patent No. ^{iv}	977 Nano subclass
Estrasorb	Menopausal therapy ^{xxxvii}	Graceway	Estradiol in micellar nanoparticles ^{xxxviii}	10/9/03	5,629,021	773; 915; 926
Abraxane	Anti-cancer drug for treatment of metastatic breast cancer ^{xxxix}	Abraxis Bioscience	Albumin-bound paclitaxel ^{xl}	1/7/05	5,439,686; 5,498,421; 6,096,331; 6,506,405; 6,537,579 ⁱ ; 6,749,868; 6,753,006; 7,820,788 ⁱⁱ ; 7,923,536 ⁱⁱⁱ ; ; RE41,884 ^{iv}	ⁱ 729; 773; 775; 896; 906; 915 ⁱⁱ 779; 906 ⁱⁱⁱ 779; 906; 911 ^{iv} 700; 904
Triglide	Lipid regulation ^{xli}	SkyePharma	Nanocrystalline fenofibrate ^{xlii}	5/7/05	6,696,084	None
MegaceES	Eating disorders ^{xliii}	Par Pharm	Nanocrystalline megestrol acetate ^{xliv}	7/5/05	5,145,684; 6,592,903; 7,101,576	None
Emend (fospipitant dimeglumine)	Prevents nausea and vomiting induced by chemotherapy	Merck & Co. ^{xl}	Nano-sized drug molecules	1/25/08	5,512,570; 5,538,982; 5,691,336; 5,716,942; 7,214,692	None

Special thanks to Research Assistant Ethan Fitzpatrick, Ph.D., a Seton Hall University School of Law second year law student, for constructing this Appendix. These products were identified by a two-pronged search methodology: a search of the relevant scientific literature reporting on research and development in nanopharmaceuticals and the FDA's website providing information on FDA-approved drugs. See *Drugs@FDA Database*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/InformationOnDrugs/ucm135821.htm> (last updated June 18, 2009). Where a product was identified in the scientific literature as a nanopharmaceutical, the FDA database was used to retrieve that product's approval information. Searches were conducted January 2011 through May 2011. The references below provide all scientific sources identified in the search.

Roman numerals indicate a direct link between a specific patent (in the "U.S. Patent No." column) and the USPTO classifications within that patent (in the "Classification" column).

*Approval letters not available.

¥ Uses Elan Corporation's NanoCrystal Technology.

ⁱ Drug indications were identified utilizing the approval letters posted at the FDA's drug search database. *Search by Drug Name, Active Ingredient, or Application Number*, U.S. FOOD & DRUG ADMIN., <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm> (last visited Dec. 19, 2011). Where the original approval letters were not available at the drug search database, the table notes this with an asterisk in the "Original NDA Approval" column and secondary sources for indications are identified in that drug's informational row.

ⁱⁱ Company information was accessed using the FDA's drug search database. *Id.*

ⁱⁱⁱ New Drug Applications (NDAs) are submitted to and approved by the FDA.

^{iv} Patent information was accessed using the FDA's electronic listings of the *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG ADMIN., <http://www.accessdata.fda.gov/scripts/cder/ob/docs/querytn.cfm> (last visited Dec. 19, 2011).

^v K.K. Jain, *Advances in the Field of Nanooncology*, BMC MED., Dec. 13, 2010, at 1, 4 tbl.1, available at <http://www.biomedcentral.com/1741-7015/8/83>.

^{vi} *Id.*

^{vii} Volker Wagner et al., *The Emerging Nanomedicine Landscape*, 24 NATURE BIOTECHNOLOGY 1211, 1214 tbl.2 (2006).

^{viii} *Id.*

^{ix} *Id.* at 1215 tbl.2.

^x *Id.*

^{xi} Original NDA was approved December 31, 1993. Subsequent NDAs have been approved and the drug formulation based on the original NDA was discontinued. Patent information reflects currently active formulation and NDA for Tricor.

^{xii} Rakesh K. Jain & Triantafyllos Stylianopoulos, *Delivering Nanomedicine to Solid Tumors*, 7 NATURE REV. CLINICAL ONCOLOGY 653, 654 tbl.1 (2010).

^{xiii} *Id.*

^{xiv} Wagner et al., *supra* note vii, at 1214 tbl.2.

^{xv} *Id.*

^{xvi} Jain & Stylianopoulos, *supra* note 11, at 654 tbl.1.

^{xvii} *Id.*

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- xviii Wagner et al., *supra* note vii, at 1215 tbl.2.
- xix *Id.*
- xx *Id.* at 1214 tbl.2.
- xxi *Id.*
- xxii Pilar Rivera Gil et al., *Nanopharmacy: Inorganic Nanoscale Devices as Vectors and Active Compounds*, 62 PHARMACOLOGICAL RES. 115, 118 (2010).
- xxiii *Id.*
- xxiv Wagner et al., *supra* note vii, at 1214 tbl.2.
- xxv *Id.*
- xxvi *Id.* at 1215 tbl.2.
- xxvii *Id.*
- xxviii *Id.* at 1214 tbl.2.
- xxix *Id.* at 1215 tbl.2.
- xxx *Id.* at 1214 tbl.2.
- xxxi *Id.*
- xxxii *Id.*
- xxxiii *Id.*
- xxxiv *Id.*
- xxxv *Id.*
- xxxvi *Id.* at 1215 tbl.2.
- xxxvii *Id.* at 1214 tbl.2.
- xxxviii *Id.*
- xxxix Jain & Sylianopoulos, *supra* note xii, at 654 tbl.1.
- xl *Id.*
- xli Wagner et al., *supra* note vii, at 1215 tbl.2.
- xlii *Id.*
- xliii *Id.*
- xliv *Id.*

