Expert Opinion

The carbon nanotube patent landscape in nanomedicine: an Expert opinion

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Carbon nanotubes (CNTs) have extraordinary properties that make them promising candidates for a wide variety of potential biomedical applications, including new therapeutics, drug delivery systems and diagnostics. Because of their enormous commercial potential across industries, a classic patent landgrab is underway as competitors are busy locking up broad patents on CNTs. This is creating a chaotic, tangled patent thicket, where the validity and enforceability of numerous patents is unclear. In this article, the authors summarize the CNT patent landscape for nanomedicine, identifying key building block patents while raising legal questions regarding their validity.

Keywords: carbon nanotubes, drug delivery, multi-walled carbon nanotubes, nanomedicine, nanotechnology, patent thickets, patents, single-walled carbon nanotubes, US Patent & Trademark Office

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1. Introduction

1.1 Nanotechnology and nanomedicine

The global nanotechnology phenomenon is in full swing. There is enormous excitement and expectation regarding nanotechnology's potential impact on every aspect of society. Although early forecasts for commercialization efforts are encouraging, there are bottlenecks as well. Some formidable challenges include legal, environmental, safety, ethical and regulatory questions, as well as emerging thickets of overlapping patent claims (see Section 3) [1]. In fact, patent systems are under great scrutiny and strain with patent offices around the world struggling to evaluate the swarm of nanotech-related patent applications. Governments are impressed by nanotechnology's potential and are staking their claims by investing billions of dollars in research and commercialization [2].

Lux Research, Inc. predicts that by 2014, US$2.6 trillion in global manufactured goods may incorporate nanotechnology (~ 15% of total output) [3]. It has been reported that governments, corporations and venture capitalists in 2006 spent US$12.4 billion on nanotechnology research and development, up 13% from 2005 [4]. In fact, in the past few years, international spending on nanotech products has far surpassed that spent on nanotechnology research and development. For example, in 2006, governments spent US$6.4 billion, up 19% from 2005. One widely cited market report noted that in 2005, nanotechnology was incorporated into > US$30 billion worth of manufactured goods [5]. A recent study claims that presently there are ~ 500 nanotech-based consumer products in the marketplace [201].

While nanotechnology promises to transform most industries, it will have a particularly profound impact on healthcare and medicine. Clearly, nanotechnology is greatly impacting biology, biotechnology and medicine. This arena of nanotechnology is generally referred to as nanomedicine and sometimes broadly

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called bionanotechnology [6,7]. The future impact of nanomedicine on society could be huge. Specifically, nanomedicine will drastically improve the patient's quality of life, reduce societal and economic costs associated with healthcare, offer early detection of pathologic conditions, reduce the severity of therapy and result in improved clinical outcome for the patient. There are a few nano-medicine-related products on the market. The FDA has approved around a dozen nanotech-related products, both drugs (sirolimus, doxorubicin HCl, estrodiol topical emulsion, fenofibrate, paclitaxel and megestrol acetate) and medical devices (NanOss, Vitoss, TiMesh). Other potential applications are under consideration and development [6-8]. While it may be difficult to predict whether nanomedicine deliver only incremental improvements of existing technologies or whether it will act as a broader catalyst for a vast technological and healthcare revolution, one thing is clear: in the coming years, novel products will appear in the marketplace [9].

In this perspective article, we emphasize one such area of nanomedicine with respect to carbon nanotubes (CNTs) that is already producing significant results – drug delivery [10]. Drug delivery accounts for 78% of global sales in nanomedicine and 58% of patent filings worldwide [11]. Drug companies now recognize that drug delivery systems (DDS) need to be an integral part of their research and development operations at an early stage. According to one market report, nanotech-enabled drug delivery systems will generate > US$1.7 billion in 2009 and > US$4.8 billion in 2012 [202]. This report also projects that the total global drug delivery products and services market will surpass US$67 billion in 2009. Another report places the nanotechnology-enabled drug delivery market for 2005 at about US$1.25 billion, growing to US$5.25 billion by 2010 and US$14 billion by 2015 [12].

1.2 Big pharma and nanomedicine

The pharmaceutical industry depends upon innovation, both for profitability and for developing superior therapies. In today's global economy, the industry faces enormous pressure to deliver high-quality products to the consumer while maintaining profitability. Companies must constantly reassess how to improve the success rate of new chemical entities (NCEs) while reducing research and development costs as well as cycle time for producing new drugs, especially new blockbusters. The industry is presently facing a crisis and its business model is clearly broken [1]. Its challenges include a weakened product pipeline, generic and international competition, withdrawal of several drugs and patent expiration on blockbusters [1]. Nanotechnology not only offers the potential to address some of these issues, but it can also provide significant value to pharma portfolios. Nanotechnology can enhance the drug discovery process via miniaturization, automation, speed and the reliability of assays. This would result in reducing the cost of drug discovery, design and development, allowing faster introduction of new cost-effective products to the market. For example, nanotechnology can be applied to existing microarray technologies, exponentially increasing the hit rate for promising compounds that can be screened for each target in the pipeline. Inexpensive and higher throughput DNA sequencers based on nanotechnology would reduce the time for both drug discovery and diagnostics. It is clear that nanotechnology-related advances represent a great opportunity for the drug industry as a whole.

The nano-pharma market is expected to significantly grow in the coming years. Analysts project that by 2014, the market for pharmaceutical applications of nanotechnology will be ~ $18 billion per year [203]. According to a 2007 report, the US demand for nanotechnology-related medical products (nanomedicines, nanodiagnostics, nanodevices and nanotech-based medical supplies) will increase > 17% per year to US$53 billion in 2011 and US$110 billion in 2016 [13]. This report predicts that the greatest short-term impact of nanomedicine will be in therapies and diagnostics for cancer and CNS disorders. In fact, the National Cancer Institute (NCI) is funding a multi-million dollar cancer initiative to create centers of cancer nanotechnology. Several nanomedicine-based treatments for cancer are either approved or are pending approval by the FDA [14,15].

1.3 What are carbon nanotubes?

CNTs are tubular structures made of 'rolled-up' layers of interconnected carbon atoms having diameters ranging from about one nanometer to tens of nanometers with lengths up to centimeters. They are essentially graphitic sheets rolled into seamless tubes, exclusively composed of carbon atoms. In fact, CNTs are a third allotropic form of carbon along with diamond and graphite. CNTs are typically classified as either 'multi-walled or MWNTs' (with concentric hollow cylinders of carbon atoms nested inside one another) or 'single-walled or SWNTs' (a single layer of carbon atoms and a hollow core).

NEC researcher Iijima is widely, but incorrectly, credited with discovering CNTs in 1991 [16,17]. CNTs were discovered by Bacon in the late 1950s, although they were not fully appreciated at that time [18]. Furthermore, they were reinvestigated in the 1970s by Endo and co-workers [19].

CNTs are usually synthesized by carbon-arc discharge, laser ablation of carbon or chemical vapor deposition [20]. After nanotubes are synthesized, often a variety of processing steps are necessary to prepare them for a specific product application. Because many synthesis processes also create amorphous carbons and metal catalyst impurities, the product materials generally need to be purified via microwave heating and a solution wash. Many applications require solubilizing nanotubes in water and other solvents [21]. The development of nanotube-polymer composites, for example, requires interlacing polymers with individual nanotubes [22]. Nanotubes can be functionalized to have certain properties or recognize particular target molecules (see also Section 2).

CNTs aggregate as a result of van der Waals interactions between individual tubes. SWNTs (~ 1 nm diameter and 20 – 1000 nm in length) generally aggregate more readily than their MWNTs (~ 1.4 – 100 nm diameter and 1 – 50 µM in length) due to their greater surface area. Both types of nanotubes are narrow and long and exhibit unique chemical, electrical, biologic, optical, mechanical and thermal properties. For example, nanotubes can be lighter than aluminum and stronger than steel. Nanotubes have different electrical properties ranging from semiconducting to metallic (depending on their chiral twist) and have a current carrying capacity of one billion amps per square centimeter – while copper wires burn out at one million amps per square centimeter [23]. It is estimated that nanotubes can transmit nearly twice as much heat as pure diamond and they are likely to remain stable at higher temperatures than metal wires [24-26]. Therefore, they have been proposed as a replacement for copper wires. In fact, due to such extraordinary properties, CNTs are being considered for a wide range of products and applications across several industry sectors of nanotechnology, including nanomedicine [6,24-26]. Because CNTs are amenable to functionalization, they provide for a broad range of applications in biomedicine. Specifically, CNTs are now being tested for applications in drug delivery, diagnostics and imaging, medical devices and gene therapy [27].

Ultrapure samples of SWNTs cost ~ $750/gram, while samples containing impurities cost ~ $60/gram [204]. In recent years, there has been a substantial increase in the number of companies (Nanocyl, Nanothinx, Nanocarblab etc.) or university spin-offs (Carbolex, recently acquired Carbon Nanotechnologies, Inc. etc.) producing commercial quantities of nanotubes as well as an increase in the informed speculation regarding their enormous potential.

1.4 The carbon nanotube patent landscape – a tangled mess?

According to a recent market report, the global market for CNTs in 2006 generated revenues of ~ US$51 million; they will reach > US$800 million by 2011 [28]. Such commercial promise has created a frenzy to establish broad patent protection on CNT inventions. Therefore, biomedical firms seeking to develop CNT-based applications now face a dense thicket of patent claims held by various entities – universities, start-ups, government laboratories and corporations. This fragmented patent landscape is likely to create substantial legal uncertainty and risk for all these players if and when they seek to bring CNT-based inventions to the marketplace [1,25,29,30]. If this trend continues (and it is happening in the US and abroad), it could stifle competition, limit access to some inventions or even cause commercialization efforts to simply grind to a halt.

This emerging thicket of CNT patent claims has resulted from wider trends of patent proliferation, but also exists because of the continued issuance of surprisingly broad nanotechnology patents by the US Patent and Trademark Office (USPTO) [1,29-31,204]. For the past decade or so, there has been a dramatic increase in the number of new nanotechnology patent applications filed and patents granted at the USPTO. This is partly the result of court decisions in the past two decades that have made it easier to secure broad patents. During this period, laws have also tilted the table in favor of patent holders, no matter how broad or tenuous their claims. Consequently, the USPTO faces an uphill task as it attempts to handle the enormous backlog of applications filed. This information overload (due to increased patent and non-patent literature) has also created challenges for the USPTO, an agency that traditionally struggles with this issue. Furthermore, this overburdened agency has yet to implement a solid plan to handle the enormous growth in nanotechnology patent applications filed [1]. The problems range from poor patent quality and questionable examination practices to inadequate search capabilities, rising attrition, poor employee morale and a skyrocketing patent application backlog [1,32]. This has resulted in added wait time to review patent applications (i.e., an increase in patent pendency) and concerns about the validity and enforceability of numerous issued patents (reflecting a decrease in patent quality) [1,204]. A recent report puts the average nanotechnology patent pendency at 4 years [5], a period that is simply too long for certain nanotechnologies that peak and are then obsolete in a few years. This excessive delay has serious business consequences, particularly for smaller companies and start-ups because these entities rely heavily on venture funds for their success.

Therefore, reforms are urgently needed at the USPTO in order to restore the delicate balance between innovation and competition. Although efforts are underway at the USPTO to improve the quality and efficiency of the patent examination process, shortcomings continue to beset patent examination [1]. Government and non-government entities, such as the National Academy of Sciences, National Academy of Government Administration, Government Accountability Office and others, have recently become more vocal in their criticism of the USPTO. They have produced authoritative reports with detailed recommendations regarding overhauling the USPTO and the US patent system [33-35]. Even Congress has gotten involved and has been holding patent reform hearings in an effort to eliminate questionable patents as well as to provide adequate safeguards against abuses to the patent system. All players involved in technology agree that a robust patent system is essential for stimulating the development of commercially viable products.

Without reforms, the somewhat cursory patent examination that is presently in place will result in the issuance of too many invalid and unenforceable nanomedicine patents. This is likely to produce a crowded, entangled patent landscape with few open-space opportunities for commercialization. Navigating this minefield may prove to be the major bottleneck to viable commercialization [29,30], negatively impacting the entire nanomedicine revolution.

Two recent reports from the nanotube industry may possibly alleviate some of this uncertainty. First, two US companies with large CNT patent portfolios, Carbon Nanotechnologies, Inc. (a Texas-based manufacturer of CNTs) and Unidym (a developer of nanotube-based electronics in Silicon Valley) merged on 23 April 2007 [36]. This merger may herald further consolidation in the nanotube industry to allow easier package licensing of necessary patents for nanotube product development. Second, more attention is being paid to research from the 1970s and 1980s on tiny carbon fibers that may serve to invalidate prior art for some basic building block CNT patents (see also Section 1.3) [37,38].

This perspective article surveys the biomedical applications of CNTs and outlines the CNT patent landscape. It provides an expert opinion by identifying some examples of broad CNT patents and summarizes select legal arguments that may be used to challenge these patents.

2. Biomedical applications of carbon nanotubes

Recently, CNTs have attracted great interest for medical and biotechnologic applications [6,7,24,27,28,39]. Due to their nanoscale size, CNTs have the ability to interact at the cellular level. They have an affinity to be absorbed by cells or biomolecules. CNTs can also be functionalized to target certain types of normal or diseased cells.

As CNTs are not easily suspended in organic solvents, it is often necessary to modify them chemically to exploit them for certain applications. In fact, this is the major limitation in the utilization of CNTs in biomedical applications. In this regard, both covalent and non-covalent modification of CNTs have been done [21]. Both approaches produce conjugated CNTs where one component is the CNT, while the other is a biopolymer or biomolecule (e.g., peptide, protein, gene, DNA etc.). The recent focus on toxicity of CNTs [40,41] is in part related to their insolubility and presence of catalysts. Hence, functionalization should alleviate some of these safety concerns as well. In fact, a recent study demonstrated that functionalized CNTs are rapidly cleared from blood without being retained in organs [42]. Many of the sensor and therapeutic applications of nanotubes also require functionalizing the nanotubes to target certain types of molecules [43]. Clearly, functionalized CNTs are emerging as new tools in the field of nanomedicine because they can be modified via encapsulation with biopolymers or by covalent linking of functional chemical moieties to their external walls and tips.

Within the different potential nanomedicine applications of CNTs (biosensors, composite materials, molecular electronics etc.), a particularly promising area is the use of functionalized CNTs as novel carrier systems for the delivery of therapeutics. In fact, the delivery of therapeutics via novel delivery systems is significant enough to be considered as 1 of the top 10 biotechnologies for improving global health, especially in developing countries [44]. In this regard, functionalized CNTs offer enormous potential for drug, gene, antigen or vaccine delivery. Several research groups have published data demonstrating that CNTs can be intrinsically used as drugs or for site-specific drug delivery to targeted cells [45]. It has also been shown that functionalized SWNTs can be transported across both the cellular and nuclear membranes to deliver a therapeutic peptide [46]. Alternatively, double functionalization of SWNTs has been shown to deliver multiple therapeutics [47]. Functionalized CNTs have been used for plasmid DNA gene delivery [48,49] while SWNTs have served as carriers for RNA delivery for the purpose of RNA interference [50]. Gene delivery via 'nanotube spearing' (magnetic transfection) is yet another way to deliver plasmid DNA-modified CNTs into host cells [51]. Functionalized CNTs hold enormous promise as carriers for the delivery of vaccine antigens. For example, peptide–CNT conjugates have been shown to be useful in eliciting protective antibodies [52].

In the future, endohedral CNTs (non-covalent complexes in which the internal cavity of the CNT is filled with molecules) may be exploited for drug or gene delivery. The cavity of the CNT may be used to transport agents from one end to the other (e.g., neurotransmitter translocation). As water readily transverses this hydrophobic cavity, CNTs have applications as molecular channels [53]. Strangely, contrasting applications of CNTs in cell physiology have been reported – CNTs can act both as channel blockers [54] and as ion-flow channels [55].

Hyperthermia therapy via SWNTs is a unique way of destroying cancer cells. In this procedure, chemically modified SWNTs are allowed to bind to cancer receptor sites prior to irradiation via infrared irradiation, producing heat to destroy the tumor site [56].

CNTs can also be used for imaging purposes. CNTs possess intrinsic fluorescent properties so they can be fluorescently labeled to emit in the visible spectral range. There is ongoing research where CNTs have been conjugated with quantum dots and used as intracellular probes [57]. Nanotubes can also be used as miniature biosensors (electronic [58] and optical [59]) for drug discovery and diagnosis. Researchers have shown that nanotubes can detect small amounts of molecules through electrical, optical or mechanical means. Such detectors might form the basis for pharmaceutical research tools that provide specific information about targets for therapeutics [60]. They also open the door to point-of-care diagnostics, where patients can obtain real time information on their health by placing a drop of a body fluid on a chip.

Some researchers are using nanotubes as the scaffold material for engineering certain tissues [61], while others are seeking to leverage the mechanical properties of nanotubes to develop lighter and stronger bone implants [62].

3. The carbon nanotube patent landscape

3.1 The uncertain landscape

Since the discovery of CNTs, substantial research dollars have poured into nanotube research at academic institutions, government labs, corporate research groups and start-ups around the world. A recent report showed that 446 CNT patents have already been issued in the US [206]. This report highlighted that out of 8557 claims in these patents, 420 claims were directed to building block type of claims. A more recent report tracked the number US CNT patents issued during 1994 – 2006, noting that after a slow initial growth, there was a noticeable spurt in patenting activity starting in 2001, and that at the end of 2006 there were still > 4400 US patent applications pending [28]. More recently, a May 2007 patent search on the Derwent World Patent Index by the authors found > 27,000 references to CNTs in US patents and published US patent applications; > 1200 of these incorporated CNTs or their equivalents in their title.

With any newly emerging technology, the USPTO has the difficult task of judging the claims of the initial patent applications. The earliest patents are often awarded claims that broadly encompass downstream products resulting from future development of the technologies. However, the USPTO has arguably been more generous to early CNT patentees than patentees of other emerging technologies for two reasons.

First, unlike other emerging technologies, CNT research is interdisciplinary. Some nanotube patent applications can be characterized as 'chemicals and materials engineering' inventions, while others can be characterized as 'semiconductor, electrical' inventions or 'biotech, organic chemistry' inventions. As a result, until recently, nanotube patent applications were often directed to different centers for review at the USPTO and different examiners were reviewing similar applications against different prior art and, arguably, in light of somewhat disparate patent case law criteria. Examiners are USPTO employees who review patent applications and grant patents. The phrase 'prior art' refers to various sources of information that the USPTO uses to reject a patent application. In other words, it is the 'knowledge' that exists at the time of the claimed invention that is used to establish whether or not it is novel. It can include documentary material, such as publications, patents, websites or other disclosures that suggest that the invention is not new. It can also include evidence of actual uses or sales of the technology within the US.

Second, in many cases, different terminology has been used by patentees to describe similar nanotube inventions. For example, nanofibers, fibrils and nanotubes have been used to describe multi-walled nanotubes [101], while single shell nanocylinders, buckytubes, nanowires and nanotubes have been used to describe single-walled nanotubes [102,103]. In other cases, patentees use similar terminology to describe different inventions. A patent claim might refer generally to CNTs without explicitly differentiating between single-walled or multi-walled nanotubes, significantly enlarging the scope of the patent.

As a result of the many broad and often overlapping CNT-related patents issued by the USPTO, firms in every industry seeking to commercialize CNTs face considerable uncertainty, risk and costs in navigating the patent landscape [1,30,31]. Clearly, the specter of patent infringement litigation looms large, particularly in the biotechnology and pharmaceutical industries where patent disputes are more frequently litigated rather than resolved through cross-licensing [63]. However, biomedical firms commercializing nanotubes may be faced both with intra-industry patent disputes as well and inter-industry disputes. Many of the key building block patents regarding CNTs are held by firms in other industries, particularly in the electronics and materials industries. Firms in completely different industries may be less likely to resolve patent disputes with each other through cross-licensing. Thus, identifying key building block CNT patents and assessing the risk of patent infringement across industries is crucial.

3.2 Identifying key 'building block' carbon nanotube patents

Patent claims are commonly divided into device, method and composition of matter claims. To use CNTs in a biomedical device without fear of patent infringement, a company may need licenses not only for the patent on the specific nanotube device, but also the methods of fabrication, purification and functionalization, as well as the basic composition of matter of the CNT itself. There are multiple composition of matter patents covering the basic CNT structure. NEC's US5747161 [104] patent claims: '*A graphite filament having a tubular structure and an outer diameter of 30 nm or less, said tubular structure comprising a helical structure of carbon hexagons*.' IBM researchers are credited with later fabricating a single-walled nanotube and IBM's US5424054 [105] patent claims: '*A hollow carbon fiber having a wall consisting essentially of a single layer of carbon atoms*.'

However, several other broad composition of matter patents arguably overlap these two patents. For example, patent US6683783 [106] from Carbon Nanotechnologies, Inc. claims: '*A composition of matter comprising at least about 99% by weight of single-wall carbon molecules*.' Other composition of matter patents using terms like 'carbon fibril' may also be overlapping. Hyperion's earlier US4663230 [107] patent claims: '*An essentially cylindrical discrete carbon fibril characterized by a substantially constant diameter between 3.5 and about 70 nanometers*.'

Such multiple broad and overlapping composition of matter patents underscore the uncertainty in navigating the CNT patent landscape. In fact, there may also be substantial overlap among the many patents on methods of fabricating, purifying and functionalizing nanotubes. There are three primary routes to synthesizing nanotubes: arc-discharge, laser

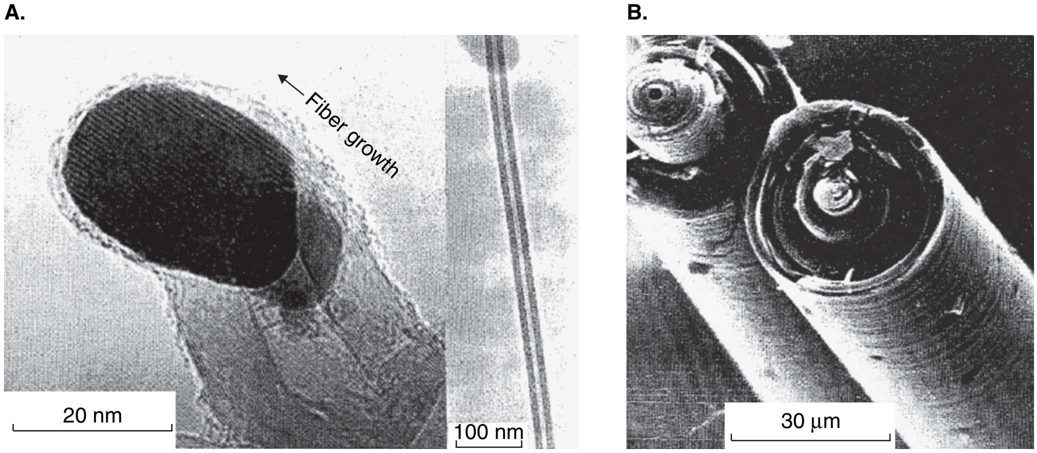

Figure 1. Images of 'vapor phase grown carbon fibers' dated 1988.
Reprinted with permission from ENDO M: Grow carbon fibers in the vapor phase: what you can make out of these strong materials and how to make them. *Chemtech* (1988) **18**(9):568-578. © Copyright (2007) American Chemical Society.

ablation and chemical vapor deposition (CVD). Arc discharge relies on application of a charge between two graphite electrodes in the presence of an inert gas. Laser ablation techniques are based on vaporizing a graphite composite target in an inert atmosphere. CVD involves the flowing of a carbon-containing gas over transition metal particles to produce nanotubes. Of the three techniques, CVD is perhaps the most preferred method because it enables higher atomic quality and percent yield, and provides manufacturers with control over nanotube orientation, diameter, length and other parameters. Different variations of CVD include conventional CVD, plasma enhanced CVD and high pressure carbon monoxide CVD. Universities and firms are filing a variety of improvement patents claiming CVD using different temperatures, pressures, substrate materials, hydrocarbon gases and catalysts. For example, Unidym's US6129901 patent [108] claims: '*A process for synthesis of carbon nanotubes, comprising: anodizing an aluminum substrate in an effective bath to produce an alumina template with a plurality of pores each having a pore diameter; depositing an effective catalyst into the pores; and exposing said alumina template with the catalyst containing pores to an effective hydrocarbon gas at an effective temperature to grow carbon nanotubes in said pores*.'

Finally, many types of end nanotube products have already been patented. Broad device patents may pre-empt certain industries. For example, Stanford University's US6528020 patent [109] on nanotube sensors broadly claims: '*A molecular sensor comprising: i) a nanotube device comprising at least one carbon nanotube, wherein a first end of said nanotube is in electrical contact with a first conducting element and a second end of said nanotube is in electrical contact with a second conducting element; and ii) a coating of one or more sensing agents deposited on said nanotube; wherein said sensing agents are so chosen such that the agents-coated nanotube responds to a particular molecular species*.' C-Sixty's US7070810 patent [110] broadly claims the use of CNTs for drug delivery.

3.3 Uncertainty regarding validity of carbon nanotube patents

In light of the large number of potentially overlapping nanotube building block patents, licensing disputes and eventual patent infringement litigation are certain. In fact, patent litigation has already erupted between pharmaceutical companies on nanoparticle-based therapeutics. The Irish company Elan Pharma International sued US-based Abraxis, alleging that its Abraxane® drug (a nanoparticle formulation of paclitaxel for treatment of metastatic breast cancer) violated Elan's US5399363 and US5834025 patents [64,111,112]. Abraxis has responded by challenging the validity of Elan's patents.

Litigants in CNT-related patent lawsuits will face several legal attacks on the validity of CNT patents. Under US patent law, key validity questions affecting some of these patents include: i) whether CNTs are patentable subject matter under 35 U.S.C. § 101; ii) whether the rich prior art of carbon fiber research anticipates the patent under 35 U.S.C. § 102; and iii) whether the patent adequately discloses and enables the invention under 35 U.S.C. § 112.

Under US law, natural phenomena are generally not patentable [1]. As the Supreme Court explained in the seminal *Diamond vs. Chakrabarty* case: '*[A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that* $E = mc^2$*; nor could Newton have patented the law of* *gravity. Such discoveries are "manifestations of nature, free to all men and reserved exclusively to none."* [65] Thus, a likely initial challenge to the validity of patents claiming nanotube compositions of matter is that the CNT structure is a natural phenomena, akin to a new mineral discovered in the earth and, thus, not patentable subject matter. After all, scientists have found that CNTs occur naturally in coal and even charcoal [66-68].

However, holders of nanotube composition of matter patents will likely counter such invalidity arguments by citing the cases upholding gene patents as not involving natural phenomena because the inventors had isolated or purified the gene fragment from the human genome [69]. Similarly, patent holders would likely argue they had isolated and characterized the CNT structure and, thus, are entitled to patent it. Notably, however, another composition of carbon, the buckminsterfullerene (also known as carbon-60), was isolated and characterized in 1985 but was not patented. Some commentators have suggested that it may have been unpatentable as a naturally occurring product of nature [70].

CNT composition of matter patents may also be attacked as having already been anticipated by prior research in the 1970s and 1980s on carbon fibrils. Carbon fibers have a rich history of research dating back to 1890 [71] and, since at least the 1970s, scientists have explored properties of tiny carbon fibrils. For example, a 1976 paper titled 'Filamentous Growth of Carbon through Benzene Decomposition' described the creation of hollow tubes of carbon fibers [19]. These tubes were made of '*concentric sheets of carbon, set around the fiber axis, as the annual rings of a tree*'. The researchers describe the tube as '*running parallel to the axis. The diameter of which widely varies from about 20 Å to more than 500 Å*' [19].

Endo, who was one of the 1976 article's authors, also published a subsequent article in 1988 titled 'Grow Carbon Fibers in the Vapor Phase: What You Can Make out of These Strong Materials and How to Make Them.' [72] In this article, Endo described the creation and properties of fibers made up of concentric layers of carbon, with a hollow tube in the center ~ 10 nm or less in diameter (**Figure 1**). In a later interview, Endo characterizes this hollow tube as a CNT [207]. Endo has been called 'one of the fathers of the carbon nanotube,' and was recently awarded *Small Times* Lifetime Achievement award for his work on MWNTs [73].

Finally, US law also requires that a patent '*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*' [74]. Applying this 'enablement' requirement to nanotechnology inventions raises several new questions for courts to address.

Many CNT patents contain notably broad claims, which might not be fully enabled by the written description in those patents. For example, many CNT patents simply use the term 'nanotube' in the claims, without distinguishing between MWNTs and SWNTs. SWNTs are more difficult to produce and to manipulate postproduction; thus, a patent claiming 'nanotubes' that only enabled MWNTs may be limited by lack of enablement.

However, considerable uncertainty exists as to what level of scrutiny the USPTO and the courts will use in evaluating the enablement of nanotechnology patents. Courts have imposed different levels of scrutiny for different high tech fields. The threshold for showing enablement has traditionally been low in the semiconductor field, while being very high in the biotechnology field [75]. Consequently, many biotechnology patent claims have been invalidated on enablement grounds [74]. CNTs have applications in both the semiconductor and biotechnology fields and it remains to be seen how CNT patents not specifically related to those fields will be treated.

3.4. Consolidation in the carbon nanotube patent landscape

In light of the many broad, overlapping nanotube patents, some have suggested that a patent pool on building block nanotube patents would be necessary to commercialize CNT inventions. Patent pools are defined as legally permissible cooperative agreements whereby the members of the pool have access to the patents of the entire pool in exchange for a set price [1]. However, successful patent pooling is likely to be difficult. Patent pools have historically been successful when they involve similarly sized patent holders in the same industry with mutually infringing patents. With CNTs, the key patents are held by different universities, government labs, large companies and start-ups scattered throughout different industries. Furthermore, there are no industry-established standards related to CNTS and CNT-based products, and efforts to establish patent pools where no clear standards exist would likely trigger hostile scrutiny from antitrust authorities.

Nonetheless, there is some evidence of consolidation within the CNT industry and the development of CNT patent license packages. As mentioned earlier (see Section 1), two prominent US companies holding CNT patents, Carbon Nanotechnologies, Inc. and Unidym, have recently merged. This new entity, named Unidym, now commands a broad nanotube patent portfolio, including patents on nanotube structures, methods of fabrication and refinement and certain biomedical applications. By offering a nanotube license package, Unidym seeks to simplify the patent landscape for companies seeking to commercialize nanotubes. However, uncertainty is likely to remain as several other broad patents may arguably be infringed by any CNT-based product.

4. Conclusion

While CNTs have several unique properties that are being developed into new therapeutics, the uncertain CNT patent landscape is likely to create substantial risk for firms bringing them to market. Notably, these patent minefields are also becoming common among other types of nanomaterials. Firms attempting to navigate the CNT minefield would do well to seek licensing packages applicable within their industry and to closely follow legal arguments regarding nanomaterials patent validity of nanomaterials.

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