

RUNNING TITLE: PRINCIPLES AND PRACTICE OF CLINICAL RESEARCH

CHAPTER TITLE: Technology Transfer

AUTHOR: Jack Spiegel, Ph.D.¹

AFFILIATION: Senior Advisor for Technology Transfer Operations
Office of Technology Transfer
National Institutes of Health
6011 Executive Blvd., Suite 325
Rockville, MD. 20852, USA
Telephone: 301-435-5587
Facsimile: 301-402-0220
E-mail: spiegelj@od.nih.gov

Abstract

This Chapter focuses on basic concepts of commercial technology transfer as practiced at NIH. It develops the theme that patent protection is a necessary prerequisite for effective transfer of inventions requiring further research and development. Inventors need to be engaged and interactive when patents are prepared and prosecuted. The jargon and concepts of patents are foreign to many basic research scientists. Therefore, effort is extended to explain the major patentability laws, and relate them to the *quid pro quo* philosophical cornerstone of our patent system. Finally, the licensing policy and practices of NIH are introduced as the vehicle employed to transfer our patents effectively and appropriately into the hands of commercial partners. The flexibility of the licensing process is emphasized as a key to modifying and tailoring exclusionary patent rights to better fit our research philosophy and public health mission.

I. What is Technology Transfer?

Technology transfer does not have a universally accepted definition. In its broadest aspects, it relates to a process of sharing knowledge. As with many broad concepts, technology transfer takes different forms according to one's motivations and desired outcomes. Government agencies, academic institutions, and private industry invoke the term to elicit remarkably disparate intents. This polymorphism extends to variants within each group. Technology transfer may have a very different look and flavor at the National Institutes of Health (NIH) compared to NASA or a Department of Defense agency. Likewise, small biotech companies and big pharmaceuticals may reveal strikingly different colors when technology transfer light travels through their respective prisms of commercial interest.

We need to refine this broad concept as a starting point in our understanding of technology transfer at NIH. Consider technology transfer as the exchange of information, materials, or intellectual property rights between and among government, academic, or industry laboratories to facilitate further research and commercialization. Much of this definition is familiar to scientists in a research environment. NIH scientists are experienced and comfortable exchanging information and materials with colleagues in varied institutions, including industry. They engage in such exchange in furtherance of research on a regular basis through publication, meetings and symposia, material transfer agreements, informal material sharing, formal and informal collaborations, as well as myriad collegial communications.

The exchange of intellectual property rights to facilitate further commercialization is the element of the definition that may appear foreign to many NIH scientists. At first

blush, such endeavor may appear both alien and offensive to investigator's instincts to share basic science. Yet, this aspect of technology transfer may be as critical to the mission of advancing public health as more traditional modes of sharing knowledge. Indeed, obtaining intellectual property rights to further commercialization may well be the defining step that transforms good science to a public health benefit. A goal of this chapter is to support this proposition.

Toward this end, this chapter will explore the esoteric world of patents. It will provide insight into the purpose of patents in our commercial society. It will lead us to a realization that patents are a tool, and like many other powerful tools, can be used for noble or lesser purposes. This chapter aims to educate and hopefully reassure NIH researchers in the use of this tool to advance this organization's goals and mission. Finally, the chapter will introduce the many faceted ways patents are used in NIH technology transfer, and what to expect when patents are employed to advance your scientific discoveries.

II. Patents as Intellectual Property

Patents, trademarks, copyrights, and trade secrets are the four types of intellectual property protection that may be applied to inventions. Each of these protects different aspects of intellectual property, and each is obtained and enforced under distinct sets of laws. Patents and copyrights are controlled solely by Federal law, whereas trademarks are governed by both Federal and State law. Trade secrets are the antithetical alternative to patents, and are controlled by State law.

Patents will be developed in this chapter as the intellectual property tool used for technology transfer at NIH. Copyright protection is not available to cover the work developed by federal employees at NIH. Trade secrets are not compatible with the operation of federal facilities, nor with the open scientific philosophy and mission of NIH. Trademarks do make a small contribution to technology transfer at NIH. Trademarks, however, have very limited applicability to promote commercial transfer of our early stage inventions toward the goal of developing products for the public health.

Patents are a tool used to protect and exploit certain categories of new and useful inventions. That protection and exploitation takes form as an enforceable legal right to exclude others from making, using, selling, or importing the patented invention. Similar to real property, a patent right may be assigned, licensed, sold, bought, and willed. There is no natural right to patents in the way that there is a natural right to life, liberty, and the pursuit of happiness. Rather, patent rights are derived from and issued by national governments according to their national laws. Most countries issue and enforce patents, including all industrialized nations. The U.S. Patent and Trademark Office (USPTO) in Alexandria, Virginia issues patents in this country. The USPTO is part of the Department of Commerce. Patent rights are not enforceable outside a country's national borders. Efforts are under way, however, to lessen this territorial nature and harmonize different national patent laws. For example, European countries are striving to establish a single European patent enforceable in all countries belonging to the European Patent Community.

It is important to remember that patents confer an exclusionary intellectual property right. Patents do not give inventors a *per se* right to make, use, or sell their

inventions. There are circumstances that can preclude a patent owner from working a patent. One example is very common in the biomedical arena. A drug requiring FDA regulatory approval cannot be used merely because it is patented. A second common example of this principle occurs when the practice of one invention is restricted by a patent to another inventor. The patent laws prohibit two patents to the same invention, but it is possible to have patents of different scope that overlap one another. The rationale permitting such overlapping patents will be discussed later as part of the rules governing patentability.

Another important characteristic of patents is that the exclusionary right only lasts for a definite and limited period of time. The length of patent protection varies according to national patent laws. In a few countries, patent term is calculated from the time the patent issues. This was the case in the United States for patent applications filed prior to June 8, 1995. Such patents expire seventeen years from the date they issue. U.S. law was changed as part of the General Agreement on Tariffs and Trade (GATT) to harmonize certain aspects of our patent laws with the rest of the industrialized world. Thus, as in most industrialized countries, patents issued on U.S. patent applications filed after June 8, 1995 now expire twenty years from their filing date. The twenty year term of US patents is subject to limited adjustments and extensions of time based upon certain delays at the Patent Office and in seeking regulatory approval from the FDA. When the patent term expires, the invention enters the public domain and the patent owner's exclusionary rights end.

Scientists who are uncomfortable associating NIH research with patents will not be assuaged by this thumbnail characterization of patent rights. It is reasonable to ask

why NIH should embrace a tool designed to exclude others from making or using the science from our laboratories, and why our Government should issue a tool to promote monopolies in the marketplace.

III. Rationale for Using Patents

A. Different Research Outcomes

Apprehension about linking our science and institutional philosophy to a system of exclusionary rights is not misplaced. Patents should have nothing to do with the vast majority of good science coming from NIH laboratories. Most of our scientists' work product comprises scientific knowledge elucidating fundamental mechanisms and pathways of disease. This knowledge is often an incremental advance in the existing knowledge base and, occasionally, is a breakthrough and enabling discovery.

Additionally, a multitude of biological materials come from our labs. Most of these materials are tools useful in advancing research. Both these tools and knowledge need to be distributed and shared with colleagues as quickly as possible. Traditional avenues of technology transfer such as publication, material transfer, and other modes of open disclosure are well suited for this purpose. Notably, patents do not add value to this type technology transfer and may, not only slow the transfer process, but also stifle it.

Another genre of work product occasionally comes from basic research efforts. These technologies still contribute legitimately to the knowledge base when transferred via traditional means. However, their maximum value in advancing health outcomes requires further research and development. Such technologies typically take the form of potential vaccines, therapeutics, diagnostics, and devices. These technologies impact

health dramatically when they are successfully developed into publicly available products. In many regards, these products are the pinnacle achievements of our research goals. They are the outcomes that much of our more routine research seeks to stimulate and support. Nonetheless, despite their potential importance, these technologies remain early stage and are many years away from their final form and from wide distribution to the general patient population. The further work to develop these technologies into final form suitable for public distribution will not be done in the laboratory where it originated. In all likelihood, that development is not appropriately done anywhere at NIH.

B. Product Development in Private Industry

Indeed, history informs us this special category of technology has little to no chance of being developed further into publicly available health products if disclosed to the scientific community by traditional publication alone. Private biotechnology, diagnostic, and pharmaceutical industries are the province for bringing research and development of such early-stage technologies toward publicly available products. Furthermore, most of these products require some level of regulatory review and approval at the FDA. The probability of any candidate making it to a final product in the marketplace is very small, and the cost associated with bringing such products to market can easily run in the hundreds of millions of dollars.

Technology transfer of these special technologies is not about dissemination of information and research results to inform the scientific community. The object is to transfer these technologies into the hands of private companies willing, able and committed to moving them forward into the marketplace. Many biotechnology companies advance products part way down the development road before passing them

on to larger pharmaceutical companies. Therefore, the pathway toward product launch may involve the subsequent transfer of the technology from one company to another.

The basic research community embraces incremental advancement built on prior research from colleagues. Such incremental advances are adequately rewarded through publication and career advancement. By contrast, pharmaceutical or vaccine developers seek rewards from sales of their developed products. Those sales must underwrite the enormous research and development costs to launch the products, including obtaining any necessary FDA or other regulatory approval. It is critical to sell the developed products in sufficient volume and at the high enough price to support those costs and return a fair profit. Competition in the marketplace reduces market share, and drives down the price of products. It is not surprising that the preferred business model is a monopoly market for each product.

1. Eliminate Competition

Success in a market attracts competitors. This is particularly true if a competitor can enter a market more cheaply than the pioneer. Generic drugs enter a market significantly faster and cheaper than the first-to-market pioneer drug because the copycat generic does not have to reproduce all the development work of the pioneer (e.g., clinical trials necessary to obtain regulatory approval). In other words, the generic piggybacks on the development paid for by the pioneer. Having reached the market at reduced cost compared to the pioneer, the generic can undercut the pioneer's product price.

Eliminating competition in this market scenario is a two fold proposition. The first goal is to establish a dominant position in a market. This can be accomplished by being the first to market. The second goal is to maintain a monopoly position by

restricting subsequent entry of competitors into the market. A simple and effective way to accomplish both goals is through patent protection. A patent on the product provides a clear path to be first to market and prevents immediate entry of competitors. Until a patent expires, it creates the perfect market monopoly. Rather than relying on slow and costly market dynamics to eliminate competition and recoup developmental costs, a patent owner need only obtain an injunctive court order against infringers enforcing the exclusionary right.

2. The Drug Development Model

Industries such as pharmaceuticals are built upon the strength of their patent protection. There are many more new drug candidates than resources to pursue their development. In an environment of drug candidate excess, companies only pursue those drugs having strong patent protection. The necessity for an exclusive patent position is non-negotiable in the drug development industry. This paradigm is not altered by the intercession of intermediate players such as biotech companies. Such intermediate participants also must satisfy their financial sources (e.g., venture capitalist) and the future development partner. None of these players are willing to accept the risk inherent in non-existent or weak patent protection.

The pharmaceutical drug development model is extraordinary in our economy. It exemplifies a disciplined rigorous use of patent laws to drive progress in an industry characterized by extreme financial, regulatory, and social pressures. The drug development industry flourishes in high risk ventures by exploiting patent monopolies on their products.

The severest critic of patent regimes should now appreciate the necessity of NIH seeking patent protection on those inventions requiring significant corporate research and development to bring important health products to the public. Comfort follows from confidence that such patent filings neither undermine nor jeopardize our commitment to basic research and its unencumbered dissemination to the scientific biomedical community. Inventors of technologies chosen for patent filings can take pride not only in the scientific merit of their inventions, but also in the public health benefits that may arise from their commercial transfer to private industry.

C. Inventor Interaction and Communication

Successful commercial technology transfer at NIH requires ongoing interaction and communication between inventors and the Office of Technology Transfer (OTT) at NIH. It is critical that the attorney drafting the patent application tap our scientists' insight into the science, diagnostic, and therapeutic potentials surrounding the inventions. Obtaining a patent is not a simple bureaucratic registration. Patent applications undergo rigorous examination at the USPTO and foreign patent offices; often taking several years to complete. Deciding that an invention is patentable and determining the appropriate scope of patent protection involves iterative communications with a Patent Examiner. These communications are formal documents relating the invention to various patent law requirements. Each legal requirement must be satisfied before a patent can issue and more often than not involves an assessment of the invention and its relation to the state of the science of the invention, e.g., the work of others in the scientific literature and patents. Inventors are copied on these communications, and scientific input from

inventors can be critical to an NIH patent attorney and the Patent Examiner agreeing upon the proper application of the patent laws to the invention.

Inventor input may also be critically important when OTT seeks commercial partners and negotiates licenses related to the patent rights on behalf of NIH and its inventors. That input helps OTT assess the commercial value of the technology, appropriate companies in the marketplace, appropriate benchmarks and milestones for the development of the technology, and the scientific merits of statements from license applicants about their capabilities and technology development plans.

The rest of this chapter is a primer designed to familiarize NIH inventors with basic concepts of patent law, USPTO patent examining procedure, NIH patenting and licensing policies, and basic OTT patenting and licensing processes. The purpose is two fold. Firstly, better appreciation of the technology transfer process should increase the likelihood scientists will seek OTT's opinion regarding the potential commercial value of their research outcomes. Secondly, this information should improve inventors' communications and interactions with our patent attorneys during preparation and prosecution of their patent applications.

IV. Historical Beginnings of Patents

Patent systems exist in all industrial countries. The philosophical foundation of our patent system extends back centuries with the first formal patent statute enacted in Venice in 1474. Concepts of intellectual property were important to the rise of industrialization in Europe. Intellectual property concepts spread to the American Colonies based largely on British practice.

The importance of developing intellectual property systems was realized by our Founding Fathers. Article 1, Section 8, of the Constitution provides Congress authority to enact laws embodying patents and copyrights. In a single sentence, the Constitution sets out the fundamental principle underpinning these two intellectual property modalities. Congress shall have power---“to promote the progress of science and useful arts by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries”. The terms science, authors, and writings refer to what evolved to be copyrights, whereas useful arts, inventors, and discoveries refer to what evolved to be patents. It is interesting that two centuries ago the domains of literature, music, and art were associated with the term “science” and what we think of today as science was referred to as “useful arts”. The concept of securing to inventors an exclusive right to their discoveries for a limited time is the fundamental property right the Government bestows with a patent. The first phrase of the sentence establishes another extremely important concept about patents. The exclusive right to a discovery for a limited time is granted in return for something. The exclusive patent grant must promote the progress of the useful arts. In other words, there is a *quid pro quo* between the patent owner and society. Unless society receives its benefit, there is no basis to grant the inventor a limited exclusionary property right. The Constitution struck a bargain between the inventor and society. While the Constitution distinctly defined the benefit granted to the inventor, it left to Congress the responsibility to define what the inventor must do to obtain that benefit.

Over the years, Congress has promulgated patent laws in satisfaction of the above Constitutional charge. The patent laws are codified in Title 35 of the United States Code

(35 U.S.C.), and the implementing administrative regulations are found in Title 37 of the Code of Federal Regulations. Since Federal law establishes and controls patents, these laws are interpreted and adjudicated by various federal courts, including the Court of Appeals for the Federal Circuit, and the U.S. Supreme Court.

An important set of patent laws establish the requirements for patentability. Three sections of these patentability requirement laws (Sections 101, 102, and 103) establish that a patent must be new, useful, and unobvious. Section 101 in Title 35 of the U.S. Code addresses the concepts of “useful” or utility and one aspect of being “new”. Another aspect of being “new”, known in patent terminology as “novelty”, is found in 35 U.S.C. Section 102. 35 U.S.C. Section 103 introduces the concept of obviousness.

V. 35 U.S.C. 101: Concepts of New and Useful

Section 101 states: “Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.” Patent law thus sets forth statutory categories of invention eligible for patent protection. The “process” category includes both methods of making and methods of using. Manufacture refers to things made in industry; i.e., the proverbial widget. Compositions of matter usually involve chemical compositions. The law states that inventions within these categories must be new and useful. This concept of “new” excludes that which naturally and always exists. Thus, products of nature, natural phenomena, and scientific principles are part of the public domain and cannot be patented. For example, Newton and Einstein were the first to identify and describe

scientific principles always existing in nature; they didn't invent them. Our patent system does not confer an exclusive monopoly on the first person to identify, understand or describe a law of nature. However, while a scientific principle itself may not be patented, new and useful processes applying that principle are eligible for patent protection.

Advancements in the scientific landscape and evolution in judicial interpretation influence when certain discoveries qualify as patentable subject matter under Section 101. There have been dramatic shifts in this area over the last quarter century. The advent of recombinant DNA technology raised the question of whether genetically modified organisms are not patentable as products of nature. The landmark Charkabarty Supreme Court decision in 1980 [1] declared that such inventions are patentable. The Court viewed recombinant organisms as not previously existing in nature. The new organism arose through the industry of the inventor and, therefore, did not remove from the public domain that which was always there. That Court decision established the principle that "new" under Section 101 encompasses "anything under the sun made by the hand of man." Simple extension of this principle has led to patenting naturally occurring genes and gene sequences by claiming them in a form not normally found in nature (i.e., in an isolated or purified form). This interpretation of Section 101 has had profound impact on the development and growth of the biotechnology industry.

The Charkabarty principle has had important ramifications in the patent and commercial world. It has been extrapolated through more recent judicial decisions to other categories of invention historically thought not to be patentable. The application of algorithms to software and the inclusion of methods of doing business into the ranks of patentable subject matter are recent examples causing concern in a number of industries.

While patents are territorial, industries are global. The patent laws of the major industrial nations vary, but they tend to revolve around similar basic concepts. Seismic eruptions in the fundamental patent laws of a major economic player cause shockwaves throughout the international patent and business communities. Anxieties and rhetoric rise in various commercial, financial, political, legal, and academic venues as national courts interpret patent laws and national legislatures adjust their patent laws and philosophies.

The second prong of Section 101 requires that patentable inventions must be useful. As usual, the meaning of this statutory term has been interpreted by the courts through numerous litigations. That case law deems a utility must be credible, substantial, and specific in order to satisfy the usefulness requirement of Section 101.

A. Credible Utility

Credible utility historically has been a low threshold requirement employed to weed out inoperative inventions. The USPTO does not have laboratory facilities to test inventions. Consequently, Patent Examiners accept the scientific and utility statements of applicants unless there is a compelling reason to question them. For engineering inventions, this usually involves challenging inventions that disobey the laws of physics, such as perpetual motion machines. Patent Examiners resolve this problem by having applicants provide evidence or a working model demonstrating that the invention is operable.

Interpretations vary in certain technology areas as to what constitutes a proper threshold requirement for credible utility. Such was the case in the pharmaceutical and gene therapy fields. For a period of time in the 1980s through the mid-90s, many Patent Examiners consistently rejected the utility of therapeutic inventions in areas such as

cancer and gene therapy as incredible under Section 101. Citing publications critiquing the available *in vitro* and *in vivo* animal models of cancer, as well as conflicting court decisions about unpredictability in this area, these Patent Examiners resolved that evidence for therapeutic utility short of positive Phase II / Phase III clinical trials was not credible. Applicants argued against those criticisms and availed themselves of administrative procedures, keeping related applications pending for years. The prosecution histories of these cases are marked by endless rounds of “no it isn’t”; “yes, it is” repartee. Demonstrating choreographic precision putting Balanchine to shame, applicants ended this “Dance of the Intransigent Examiner” by submitting clinical trial evidence in anticipation of their NDA filings at the FDA. The patent soon issued, providing applicants seventeen years of market exclusivity coordinated around the same time they gained FDA approval to market the drug.

Section II. of this chapter described a patent law change in 1995 whereby patent term changed from 17 years from issue of the patent to 20 years from filing of the application (or its earliest parent application) from which the patent issued. As the GATT implementation rambled toward reality, it became evident that the next ballet season needed a new dance program. The USPTO solicited input from the patent bar and interested parties, held hearings, and published a new set of Utility Guidelines. Those new guidelines supported a low threshold - minimum barrier approach to the Section 101 credibility requirement of utility for therapeutic inventions. Patent Examiners were reminded that the Patent Office is not the FDA. Appreciative pharmaceutical and biotechnology communities rose for a rousing standing ovation. The USPTO reveled in the glorious curtain call.

B. Substantial Utility

The substantial utility requirement provides that the proposed use of the invention be a “real world” utility. This requirement is designed to avoid two problems.

Occasionally, applicants seek a patent on an invention they believe may be or may lead to something important, but they don’t really know what their invention actually does or where it might lead when they file the patent application. Since Section 101 requires them to identify some utility, applicants proffer an insignificant “throw-away” possibility that isn’t incredible on its face (i.e., it obeys the laws of physics), but it is not very specific, meaningful or relevant. For example, the inventor might make a knockout mouse, but not know yet how the genetic deficiency impacts the animal. The inventor wants a patent on the mouse; not how to use it. Applicant tries to avoid the issue by declaring the mouse is useful as snake food. Nice try, but no patent! Snake food would not be considered a substantial real-world use for a genetically engineered knockout mouse. Were the scenario changed such that the knockout caused the mouse to be digestible to a species of snake incapable of digesting normal mice, then a proffered utility as food for that species of snake would be acceptable. There is now a real world relationship between the nature of the invention and the proposed utility.

The other situation where the issue of substantial utility arises is the case of “research utility”. For example, an inventor isolates and purifies a cell surface receptor from embryonic brain tissue that is not expressed in the adult. Analysis of the domain structure of the protein leaves no doubt that it must function as a trans-membrane receptor. Unfortunately, the inventor does not know what the receptor binds to. Its differential expression implies it may be important to brain development. The patent

application proffers the receptor is useful for screening embryonic brain tissue for morphogenetic factors in development. This would be deemed an unsubstantial research utility under Section 101, because the object of the utility is do research on the invention to determine its real function.

The concept of a “research utility” must be distinguished from a utility for research. As above, a research utility performs research on the invention itself. In contrast, a utility for research involves a tool useful for doing research on something else. Sephadex® is a tool useful for separating molecules based on molecular size. It is known that Sephadex® functions by molecular exclusion. It has a legitimate patentable utility even though you may not know the identity of the molecules being separated. Many research tools are patentable inventions. The receptor example above would have been better served to pass as a research tool were it known that it bound serotonin. The utility for research could be to screen for serotonin agonists in developing brain.

C. Specific Utility

The third requirement for utility is that it be specific. Problems arise when the utility of an invention is described only by generalized characteristics of a large heterogeneous group to which it belongs. The key is that applicant is not able to identify any utility that specifically applies to and defines the specific invention as opposed to the generic group to which it is thought to belong. Take, for example, the case of a particular expressed sequence tag (EST) sequence where the identity of the associated gene is unknown. Applicant enumerates a laundry list of generalized utilities traditionally associated with ESTs, such as probes for full-length genes, chromosome markers, forensic probes, etc. None of these generalized utilities, which are common to all ESTs,

distinguishes the special and specific function of applicant's invention, the particular EST. At least one specific activity associated with that EST must be identified. Where the EST is used as a gene probe, one must know to what gene or larger sequence it specifically binds or hybridizes. Even if its utility is as broad as a chromosome marker, one must at least know which chromosome it can specifically distinguish from all the chromosomes in the cell. When an invention is defined merely by generalized function, it ultimately reduces to being a research utility as described previously. When one uses an EST as a generic gene probe, you are actually conducting research on the EST to identify its real specificity. This contrasts to applying the specificity of the EST to probe for the known corresponding gene in a diagnostic assay for the gene.

Both the specific and substantial requirements for utility advance the premise that at least one legitimate patentable utility must exist in a currently available form. This requirement does not preclude learning new uses for the invention at a later time. Those new uses may be distinct separately patentable inventions. The patent monopoly is granted for successfully providing a useful new deliverable to the American people. Paraphrasing the Supreme Court in *Brenner v. Manson* [2], a patent is granted for the prize; not for the hunt.

VI. 35 U.S.C 102: Concept of Novelty

The law does not permit patents for that already in the public domain. To do otherwise, would remove something from the public for a period of time. It matters not whether the subject matter became part of the public domain as a gift of nature or through human industry. Section 102 extends the concept of "new" introduced in Section 101

beyond things already in the public domain by the grace of nature. Section 102 establishes the concept of “novelty” to exclude from patent protection things introduced into the public domain by others or through certain prohibited actions by the inventor.

Section 102 is divided into seven subsections (a) through (g) defining different circumstances or events resulting in a loss of novelty and forfeiture of the right to patent protection. Novelty may be lost when an invention is disclosed to the public or exploited, e.g., sold, by the inventor before engaging the patenting process. Engaging the patenting process is defined in different subsections of 35 U.S.C 102 with respect to when the subject matter is invented or when the application for patent is filed. This distinguishes US patent law from the rest of the world which defines novelty solely in relation to the date an application is filed.

A. 35 U.S.C. 102(b)

Four subsections, 102(b), 102(c), 102(d), and 102(f), set forth activities that absolutely bar an inventor from seeking a patent. Section 102(b) denies a patent if “the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States”. This complex subsection identifies a number of issues, but they all relate to events occurring more than one year before the patent application is filed in the United States. The first issue is that the invention cannot be described in another issued patent or published in the literature anywhere in the world. If so patented or published, the invention is considered to be in the public domain and not patentable. Inventors’ own publications are included in this prohibition. With the advent of other publication media, printed publication is interpreted to include any indexed form

of information storage reasonably available to an interested party. Patents and literature relating to inventions are referred to in patent terminology as “prior art”. If the invention is described in the prior art anywhere in the world less than a year before filing the patent application in the United States, the issues are controlled under the provisions of Section 102(a).

Section 102(b) also identifies certain public and commercial activities that cannot be conducted in the United States. The public use or sale of the invention may take place outside the United States as long it does not involve a patent or publication, as indicated above. Public use in the United States does not have to be for commercial purposes. It merely needs to take place in such a way that the public is aware of the completed invention operating for its intended purpose. Under appropriate circumstances, public use before a single person can initiate the 102(b) bar to a patent. The “on sale” provision of this subsection does not require a consummated sale or signed contract. Certain offers for sale can initiate the bar as well. The public policy and court interpretations are very clear; do not publicly use or try to commercialize your invention in this country more than a year before you file for a patent.

B. 35 U.S.C 102(c)

Section 102(c) is a rarely invoked provision indicating a patent is barred if the inventor abandons the invention. The public policy behind this provision requires inventors to be diligent in seeking patent protection once they make an invention. Inventors, of course, are free to maintain an invention as a trade secret. If an inventor takes that route and later decides to file for a patent, the resulting patent is in jeopardy of being unenforceable due to this subsection of 35 U.S.C. 102. Evidence of the inventor’s

abandonment of the invention comes in the discovery process of interference or litigation proceedings by another who independently invents the same invention and diligently seeks a patent, or by an infringer seeking to invalidate the patent rather than being excluded by it, respectively.

C. 35 U.S.C. 102(d)

Our patent laws set out circumstances and rules whereby inventors can file for patents in foreign countries, and subsequently file for the same invention in the United States. Section 102(d) is a provision of the novelty laws designed to impress diligence on inventors who first file patent applications abroad. For example, it provides that a patent will be barred if an application for the invention is filed in the United States by the same inventor more than a year after it issues as a patent anywhere else in the world. This circumstance rarely arises.

D. 35 U.S.C. 102(f)

Section 102(f) denies issuance of a patent if applicant did not himself invent the subject matter sought to be patented. This arises when an inventor derives the invention from someone else. While it is rare for scientists to seek patents on inventions stolen from others, rejections based on this section appear at times when a Patent Examiner cites publications from the inventor's laboratory. These references include authors who are not inventors on the application. Such rejections are unfortunate, because different authorship does not imply or provide evidence that the inventor derived the invention from the other authors. Indeed, there are more appropriate ways for the Patent Examiner to resolve such publications. Regardless, the issue is resolved in a technical manner that does not imply fraudulent behavior by the inventor.

The four subsections of the 35 U.S.C 102 novelty law described above constitute bars against the issuance of patent. If the Patent Examiner accurately applies the facts to these subsections of Section 102, the bar is not arguable. It may be possible to avoid a 102(b) bar based on prior art by amending the invention so the cited reference no longer applies.

E. Date of Invention/Reduction to Practice

The remaining three subsections of the novelty law, 102(a), 102(e), and 102(g), relate to the date of the invention. The date of invention is the date the invention is completed or reduced to practice. There are two ways to reduce an invention to practice under U.S. patent law. As a matter of patent law, an invention is constructively reduced to practice when an application for it is filed in the U.S. Patent Office. Therefore, the filing date is also its constructive reduction to practice date. Prior to the constructive reduction to practice, an invention may be actually reduced to practice by physically making or practicing the completed invention.

F. 35 U.S.C. 102(a)

Section 102(a) states that a person shall be entitled to a patent unless “the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent”. The prior art portion of this section applies if the patent issued or the reference published before the date of invention. When applying Section 102(a), the Patent Examiner takes the date of invention to be the filing date of the application (its constructive reduction to practice date). However, applicant can overcome 102(a) prior art by showing evidence of an earlier actual reduction to practice to be the date of the

invention. This can be done by submitting a particular form of declaration to the Patent Examiner providing evidence of the earlier actual reduction to practice. This evidence may be excerpts from laboratory notebooks.

Another significant element of Section 102(a) is the “by others” concept. An earlier discussion under Section 102(f) described a type of prior art reference from the inventor’s laboratory having additional authors. Such a reference is legitimate prior art under Section 102(a) because, on its face, it represents invention by others. Section 102(a) prior art can be overcome by providing evidence that it is not the work of “others”. Evidence of this kind again is submitted via a special type of declaration to the Patent Office which has the effect, for patentability purposes, of removing the “others” from the prior art, e.g., coauthors from a publication. Viewed now as only the work of the inventors, the reference is no longer appropriate prior art under this section of 35 U.S.C 102.

A very important and distinctive feature of U.S. patent law derives from analyzing the relationship between Section 102(a) and 102(b). Any prior art published more than a year before the filing date (the 102(b) date) is a statutory bar under Section 102(b). Prior art published between this critical 102(b) date and the filing date of the application is prior art under 102(a). We just saw that a reference authored only by the inventors, published during this 102(a) period, is not considered the work of others and cannot be used to deny a patent under Section 102(a). Consequently, inventors have a one year grace period from the time they publish or disclose their invention before they must file an application on their invention in the United States to avoid a 102(b) bar. This is because during that year grace period their own publication/disclosure is not prior art

against them under 102(a). This is a significant benefit provided by the U.S. patent system. The value of this benefit must be balanced against the fact that other countries do not have similar grace periods. Most of the industrialized world operates under an absolute novelty system where any disclosure prior to filing is a bar to getting a patent. Therefore, an applicant taking advantage of this grace period in the U.S. forfeits patent rights around the rest of the world.

G. 35 U.S.C. 102(e)

The next subsection of the novelty law relating to the date of invention is Section 102(e). The prior art effect of patents under Sections 102(a) and 102(b) is determined against the date those patents issue. Subsection 102(e) of 35 U.S.C. 102 bestows a preferred prior art status to U.S. patents. Section 102(e) bases the prior art effect of U.S. patents upon the filing date of the patent application. This is analogous to viewing a literature reference as prior art as of the date the manuscript was received by a single special publisher, rather than by its publication date. Consequently, an invention is not novel under 35 U.S.C. 102(e) if a U.S. patent describing the same invention had a filing date prior to the date of invention sought by the patent applicant. In a manner similar to 102(a), this conflict can be overcome by showing evidence of an actual reduction to practice predating the filing date of the prior art patent.

The same U.S. patent may constitute prior art against an invention both under 102(a), based on its issue date, and under 102(e), based on its filing date. Both attacks on the novelty of the invention are defeated by the same evidentiary showing of an earlier reduction to practice. The 102(e) prior art effect, however, is markedly more difficult to overcome. This follows from the fact that the filing date of a patent may be years earlier

than its issue date. This makes U.S. patents potentially powerful prior art tools, and illustrates the advantage/preference provided by U.S. patent law to U.S. patents compared to foreign patents. This advantage is exploited sometimes by using early filed U.S. patents, containing voluminous disclosures of numerous potential applications and embodiments of the invention (including prophetic ones), as a defensive publication against future competitor patents.

Recent changes in U.S. patent law permit U.S. patent applications to be published eighteen months after filing. Once a patent application publishes, it becomes eligible as prior art under Section 102(e) against other patent applications. Again, the prior art effect of the published application is measured against its filing date.

H. Sections 102(a) and 102(e) Relate to Disclosure Not to Claims

The novelty defeating property of patents under 35 U.S.C 102 (a) and 102(e) depends upon their disclosures describing the same invention. Patent applications contain a specification portion that provides a detailed description of the invention, as well as background information about the subject area. The patent culminates with a claim, or set of claims, that set out the boundaries of the invention protected by the patent. Patent rights relate to the embodiments defined in the claims of an invention. The description and teachings in the specification often are broader than patent rights defined in the claims. If the claims of a prior art patent define the same invention claimed in the patent application seeking a patent, then resolution of the conflict requires additional consideration. It is not permissible to overcome a Section 102 (a) or 102(e) prior art patent claiming the same invention by showing evidence of an earlier actual reduction to practice. Otherwise, two patents would exist claiming the same invention.

This is not permitted. The application will be denied a patent if the filing date is more than 6 to 12 months (depending on the complexity of the technology area) later than the 102(a) or 102(e) prior art patent claiming the same invention. If the two filing dates are within this range, the PTO resorts to 35 U.S.C. 102(g), the final subsection of the novelty law, to resolve the conflict.

I. 35 U.S.C. 102(g) and Interference Proceedings

Section 102(g) instructs that applicant is entitled to a patent unless: “before the applicant’s invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other”. This very complex subsection of the novelty law introduces a new consideration, i.e., conception.

Conception relates to the formation in the mind of the inventor of a definite and permanent idea of the complete and operative invention as it is thereafter to be applied in practice. Conception is established when the invention is made sufficiently clear to enable one skilled in the art to reduce it to practice without the exercise of extensive experimentation or the exercise of inventive skill. Since conception is a mental process, there must be some documented record or evidence of the idea that took place in the mind of the inventor, some type of corroboration of the idea. For example, an inventor A

might have conceived of a compound A and asked another person to synthesize compound A after drawing him the chemical structure of compound A.

Documentation is critically important to resolution of Section 102(g) issues. Up to now, all communications at the PTO were between the applicant and the Patent Examiner. This is referred to as *ex parte* prosecution. Under *ex parte* rules, evidence of actual reduction to practice, etc. is submitted under oath, and the Examiner accepts its authenticity accordingly. The resolution of issues under 102(g), however, involves comparing evidence between two different parties using much more stringent rules of proof. To accomplish this, the USPTO sets up a special *inter partes* proceeding known as an “Interference” to determine the earliest date of invention (i.e., who invented the invention first) under Section 102(g). Interferences are handled by a panel of three Administrative Patent Judges at the USPTO’s Board of Patent Appeals and Interferences. Simple submissions of evidence under oath are not sufficient in an *inter partes* environment. Interference evidence must comply with the Federal Rules of Evidence used in Federal litigations. Indeed, Interferences resemble small scale litigations.

Interference rules require evidence related to conception, diligence, and actual reduction to practice of the invention be corroborated and authenticated. This places severe requirements on laboratory notebooks to be of probative evidence. Generally, this involves paper lab notebooks being hardbound, consecutively numbered/dated pages, and the entries witnessed by a non-inventor capable of appreciating the data. Records kept in a haphazard fashion and “lack of diligence”, i.e., unexplained and unreasonable gaps in time in preparing the invention for patenting, can also present problems. Interferences are difficult and expensive propositions (1 to 2 years and about a million dollars) that

NIH avoids when possible. Important inventions, however, tend to be pursued competitively at the Patent Office, as well as in the laboratory and marketplace. Furthermore, NIH often is involved with corporate partners who rely upon our effective cooperation and participation in such interfering cases. It is not unreasonable to expect that important inventions arising in active competitive fields may become involved occasionally in Interference. Inventors working in areas of this nature that may lead to commercially important inventions should consider contacting OTT or their IC Technology Development Coordinator regarding guidance in this regard sooner rather than later.

Among the U.S. patent laws, 35 U.S.C. 102(g) and Interference practice epitomize the concepts of date of invention, rewarding the first to invent, and diligence in bringing inventions to the Patent Office. The Interference process also reveals a recurrent theme in our patent laws giving preference to U.S. inventions and inventors. The requirement that “the invention was made in this country” severely limits foreign inventions in the Interference process. They generally are limited to their constructive reduction to practice date (filing date) as the best date of invention in this country, because evidence of conception, actual reduction to practice, and diligence are performed outside this country.

VII. 35 USC 103: Concept of Obviousness

Development through the courts of the concept of novelty relative to the prior art led to an important realization. In order to defeat an invention under Section 102, a prior art reference must anticipate every element of the claimed invention. Any element of an

invention not recited in or inherent in (e.g., if a reference describes mixing NaOH and HCl, it inherently describes producing NaCl) the prior art reference renders the invention, viewed in its entirety, novel relative to that prior art. Patent attorneys are a clever species capable of tweaking claim language subtly to avoid prior art without unduly limiting the invention. Additionally, every element of the claimed invention must be found within the teaching of a single reference. The teachings of two individually deficient prior art teachings cannot be combined into a hypothetical “super reference” that anticipates every element of the invention.

What if there was a difference between what a prior art reference described and the claimed invention, but that difference was minor or insignificant? The patent system struggled for a long time with various concepts of obviousness, and how to cope with obvious differences between claimed inventions and the prior art.

In 1952, the patent laws were amended to introduce 35 U.S.C. 103 to state: “A patent may not be obtained though the invention is not identically disclosed or described as forth in Section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art to which said subject matter pertains”. The landmark *Graham v. John Deere Company* Supreme Court decision [3] in 1966 established the following factual inquiries for determining obviousness: (1) determine the scope and content of the prior art; (2) ascertain the differences between the prior art and the claims in issue; (3) resolve the level of ordinary skill in the pertinent art; and (4) evaluate evidence of secondary considerations of nonobviousness.

Other court decisions refined these inquiries and helped focus the basic considerations of this obviousness concept and the frequent pitfalls encountered applying them. A common problem in obviousness determinations is a tendency to fragment claimed inventions into isolated parts and apply art against the various parts of the invention instead of the complete invention. The courts have consistently cautioned that the invention must be considered as a whole when applying prior art. It is important that references be viewed without benefit of impermissible hindsight vision afforded by knowledge of the claimed invention. Many excellent inventions seem obvious once we are taught about them, and we integrate the invention into our knowledge base. The challenge is to analyze prior art based on what they teach, not what we want them to mean to defeat the invention. References may be combined for their respective teachings in making a single obviousness argument. When references are combined, however, there must be a motivation for making the combination. That motivation to combine must be suggested by the teachings of the references themselves, and cannot arise from knowledge of the invention gained from reading the application. Obviousness is meant to be viewed through the eyes of a hypothetical person of ordinary skill in the art. That mythical figure has been variously described as one who knows all (is aware of all relevant prior art), but has no imagination (cannot extend the teachings of the prior art beyond what it says). The courts have cautioned that there can be additional factors that militate against an invention being considered obvious. These are referred to as secondary considerations of nonobviousness, and include unexpected results, commercial success, long-felt need, failure of others to solve the problem, copying by others, and skepticism of experts that the invention would not solve the problem. It is interesting that

some secondary considerations relate to events and information obtained after the invention is made and filed. For example, evidence of commercial success of an invention in the marketplace undoubtedly comes after the invention is made and usually after the patent application is filed.

The concept of secondary considerations helps explain how patents may encompass overlapping inventions. Section II of this chapter discussed the possibility of two patents having claims of overlapping scope. This can happen even though two patents cannot issue to the same invention. An example of overlapping claims arises when a patent issues to a species of invention after a prior patent claiming the generic invention. The generic patent is said to dominate the species, and may exclude the species patent holder from working the species invention. Likewise, the species patent holder may exclude the generic patent from working the species within the scope the generic invention. The generic patent holder, however, is free to exercise exclusionary rights regarding all other species within the scope of the claims. The question may arise as to how a later discovered species can issue in view of a prior generic disclosure of the invention. Shouldn't the species be obvious in view of the generic disclosure? In many cases species are deemed obvious when they appear to possess all the distinguishing characteristics of the genus. If an otherwise obvious species demonstrates unexpected results (i.e., secondary considerations of nonobviousness) compared to other members of the genus, however, it may be a basis to issue a patent to that now nonobvious species within the scope of the genus. This provides an important concept in patent law that distinguishes the patentability of invention (satisfying all the patentability statutes to

obtain a patent) from phenomena such as dominance that prevents a patent right from being enforced.

On the other hand, a generic invention is anticipated and not novel in the face of a prior art species. Such prior art species force an applicant for a generic invention to limit the scope of the genus so as to exclude or avoid the previously known species.

Obviousness is a conclusion of law reached after a determination of relevant facts (e.g., the *Graham v. Deere* factual inquiries). It is remarkable that two patent attorneys viewing the same facts seldom reach the same legal conclusion regarding obviousness (unless they work for the same client). Obviousness determinations involve much subjective argument that inundates patent prosecution histories and litigations. This certainly is the situation in biotechnology areas such as obviousness issues related to DNA sequences. Current case law attempts to treat DNA sequences in a manner similar to theories developed for chemical patent practice. It will be interesting to see how the legal system evolves obviousness to deal with the informational nature of DNA, as well as issues of homology and polymorphism.

VIII. More is Needed to Establish the *Quid Pro Quo*

The *quid pro quo* scorecard arguably still seems to favor the patent owner. The utility requirement is a nice positive start, but Section 101 issues provide only a minimal threshold entry barrier to patentability. Was it ever a serious concern that entrepreneurs would abuse the patent system by flooding it with useless patents? Only a small percentage of exclusionary patent rights are actually enforced in commerce. The vast majority of the patents that issue have little value in the marketplace. It could be argued

that the landscape of enforced patents would look fairly similar today if the utility requirement didn't exist.

The “new” requirement of Section 101, the elaborate “novelty” law of Section 102, and the “obviousness” of Section 103 serve as public guardians of the system. They help keep applicants from receiving inappropriate patents on things already in the public domain. Fortunately, there is another set of patentability requirements that may help balance out the deal.

IX. 35 U.S.C. 112 and the Need to Know

There are a group of requirements set forth in Section 112 of Title 35 of the U.S. Code, defining the sufficiency of an invention disclosure, i.e., defining what an applicant must satisfy before a patent can issue. The public policy is that society deserves to be informed about the invention. It is important that society knows how to make and use the invention so it can effectively exploit it once the patent expires, and the invention enters the public domain. While the patent monopoly is in force, it is important for society to know exactly what the patent excludes. This enables society to get out of the way of the protected area (i.e., not infringe the patent claims), and to be able to exploit and develop the technological field from the boundary of that protected area outward. Thus, knowledge of how to make and use the invention is necessary to engineer around the invention, and to make improvements upon it even during the enforceable life of the patent. Remember, improvements are a statutory category of invention. Improvements are eligible for further patents, and may displace the original invention in the marketplace. Both these activities advance the field by introducing new approaches and better mouse traps. The *quid pro quo* then becomes a limited time monopoly in return for

an enabling disclosure allowing society to fully understand the new and useful invention. This enabling knowledge is an incentive to innovate on and around the patented invention, and it enables society to fully exploit it when the patent expires.

A. The First Paragraph of Section 112

35 U.S.C. 112 has a number of parts organized in separate paragraphs of text. This Chapter will discuss only the first and second paragraphs of this section of the patent law. The first paragraph of Section 112 states: “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”. This first paragraph of Section 112 makes three separate requirements. These are referred to as the written description, enablement, and best mode requirements.

1. The Written Description Requirement

The written description requirement assures that the applicant provides a full description of the invention. The requirement instructs applicant that the description must be clear, concise and in exact terms. It is directed toward skilled artisans in the field of the invention. This is a clear instruction not to wordsmith an obfuscated exposition that keeps the real invention secret or unclear. The courts have interpreted this requirement as providing evidence the applicant invented the claimed invention and was in possession of the invention at the time of filing.

The written description requirement has taken on heightened significance in gene patenting. A number of court decisions over the past fifteen years developed the principle that a gene is a chemical composition defined by its structural and physical properties. Patent case law regarding chemical compositions indicates that a composition must be described by its physical properties, not by its function alone. Knowledge of at least one function associated with the composition is necessary to establish patentable utility, but functional knowledge must correlate to a physical structure. One cannot claim to be in possession of a chemical composition merely by describing its function. Genes can be defined by a distinguishing combination of physical properties (e.g., size, restriction patterns, melting temperature, etc). Nucleotide sequence is the typical way the structure of a gene is defined. Possession of a gene composition similarly demands evidence of being in possession of its physical structure. Therefore, written description is not satisfied absent disclosure of the nucleotide sequence or some other set of physical properties that distinguish the structure of the gene. Importantly, the written description requirement is not satisfied merely by describing a gene by its function.

2. The Enablement Requirement

Section 112 places another legally distinct requirement on the description of the invention. The disclosure must be sufficient to enable those working in the field of the invention (skilled in the art) to make and use the invention. This is referred to as the enablement requirement. While the written description requirement aims at assuring the inventor was in possession of the invention at the time of filing, the enablement requirement aims at assuring that society is in possession of the invention when the patent issues. As indicated previously, that possession, in the form of knowledge about the

invention, may be an incentive for others to invent around and improve upon the excluded invention during the term of the patent. Ultimately, that enabling knowledge should be sufficient to assure possession of the invention within the public domain once the patent term expires.

An important question is how to judge whether any particular disclosure is sufficient to establish enablement. The courts have interpreted this requirement to mean that the skilled artisan should not have to engage in undue experimentation in order to make and use the claimed invention based on the description in the application. To aid in determining what constitutes undue experimentation, the Federal court and the USPTO have provided a set of eight illustrative factors to be considered.[4] These factors include: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in that art; (4) the amount of additional experimentation required; (5) the amount of direction and guidance provided by the application; (6) the presence or absence of working examples in the application; (7) the degree of unpredictability in the art; and (8) the breadth of the claims.

Analyzing the interplay of these factors provides guidance in establishing the proper balance between the sufficiency of the enabling disclosure and the scope of the claims (patent rights). The more unpredictable the art associated with the invention, the more direction, guidance, and working examples are required to support any particular breadth of claim scope. Ultimately, the scope of claims seeking patent protection should be commensurate with the enabling disclosure teaching how to make and use that breadth of invention. An important factor in determining the scope of claims is the nature of the prior art. Broader claims increase the chance that the invention will impinge the prior art

under Sections 102 or 103. Crowded mature technology fields tend to force new patents to have narrower claim scope. This is independent of whether the disclosure teaches how to make and use a broad scope of invention. Pioneering patents in new technology areas tend to have broad claims as their scope is dependent only on the sufficiency of the enabling disclosure.

3. The Best Mode Requirement

The third requirement of the first paragraph of Section 112 is for applicant to disclose the best mode of the invention. The policy behind this requirement is that applicant should not disclose a less preferred way of making and using the invention to gain market exclusivity while reserving the best mode as a secret. In return for the patent monopoly, society deserves knowledge of the best way of making and using the invention known by the inventor when the application was filed.

B. The Second Paragraph of Section 112

The second paragraph of Section 112 states: “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”. The second paragraph of Section 112 requires the patent application delineate at least one claim separate from the specification of the application which is defined and controlled by the written description, enablement, and best mode requirements of the first paragraph of this section. The claims are the portion of the patent that defines the property lines of the invention receiving the patent right. Claims set out the boundaries or metes and bounds of the invention. Claims must employ clear and distinct language to accomplish this goal as compared to real property that can rely on land surveys and fences to define property

boundaries. The language of the claims must be sufficiently clear to determine if the scope of the claimed invention is commensurate with the enabling written description in the specification. The language of the claims also must be sufficiently clear to permit those working in the field of the invention to know if they are infringing or “trespassing” on the claimed invention.

X. Procedures for Prosecuting a Patent Application at the USPTO

The statutes described in this Chapter represent the main patentability requirements. There are many additional statutes, regulations, and guidance that control formal requirements of the patent application and the examination procedures of the Patent Office. These can be viewed at the USPTO website, www.uspto.gov, with special attention to the Manual of Patent Examining Procedure (MPEP). As indicated previously, inventors are copied on all major actions and responses involving the Patent Office. Inventors may be requested to comment and provide scientific assistance toward responding to such actions. A brief description of the major administrative action-response chains are provided below to place communications from and to the USPTO in context.

Soon after receiving the application, the Patent Office will notify applicant of receipt and any formalities regarding the filing that may be deficient. Once the formal matters have been satisfied, the application eventually is taken up by a Patent Examiner. The Examiner may issue a Restriction Requirement action which indicates the application claims more than one invention capable of supporting a patent. For example, claims to a composition, a method of making, and various methods of using the

composition may each support a separate patent. Examiners are not required to examine more than one patentable invention in a single application. The Restriction Requirement forces applicant to choose or elect claims corresponding to one of the indicated patentably distinct inventions for examination in that application. The claims to non-elected inventions are said to be restricted, and they are withdrawn from consideration in that application. Applicant is free to file one or more additional applications, called Divisions, seeking examination on the withdrawn claims. Division applications cannot change the written description of the invention in the specification. While each Division is a separate application with its own Serial Number and filing date, Divisions receive benefit of the filing date of the original application for purposes of applying prior art under Sections 102 and 103 (and for purposes of calculating patent term).

After analyzing (examining) the elected invention, the Patent Examiner sends a first Office Action on the Merits discussing the invention relative to each section of the patentability laws. If any of these statutes is not satisfied, the Examiner rejects the claims. The Office Action sets a six month statutory deadline to respond. Failure to respond to the Office Action within this time period results in abandonment of the application. In the response to the Office Action, applicant may amend the claims and specification to satisfy and overcome the criticisms and rejections. Changes to the specification must be formal (e.g., correct a spelling error), and cannot add new matter in support of or that changes the nature of the invention. In addition to, or in place of amendments, the response can argue why a rejection is improper based on the facts of the case, or the Patent Examiner's interpretation of the law.

The Patent Examiner again examines the application in view of applicant's response. If all the rejections and criticisms are overcome, and no new ones are proffered, the Patent Examiner mails a Notice of Allowance. Again applicant has a statutory period to pay an issue fee and satisfy any outstanding formal matters to have the patent issue. More likely, however, the Patent Examiner maintains some or all of the previous rejections, and will send out another Office Action. If the new Office Action contains any new ground of rejection not necessitated by applicant's amended response, this second Office Action is sent out under the same ground rules as the First Office Action on the Merits. On the other hand, if the new Office Action maintains the same rejections of claims and/or adds new rejections necessitated by applicant's amendment, the new Office Action is made Final. A Final Rejection closes examination of the application. The Final Rejection has a six month statutory period for response during which time applicant may again submit amendments and arguments in an After Final Response to overcome the rejections. Since examination is closed by the Final Rejection, there is no requirement on the Patent Examiner to enter into the record any amendment or argument that raises new examination considerations or that does not satisfy all the outstanding rejections so as to place the entire application into condition for allowance. If the After Final Response is not entered into the record or does not place the case in condition for allowance, the Patent Examiner notifies applicant via an Advisory Action. The Advisory Action indicates the disposition of the After Final Response and any claims remaining under rejection. It also advises that the statutory time period set in the Final Rejection continues to operate. In other words, After Final Responses that do not place

all claims in condition for allowance do not stop the statutory clock of the Final Rejection.

Applicant, at this point, has several options. Applicant can allow the application to go abandoned by not responding before end of the Final Rejection statutory deadline. Applicant can submit another After Final Response. This follows the same rules and time issues as the previous After Final Response. Namely, it has no right of entry, and the statutory clock on the Final Rejection continues to run. Another option is to file a Request for Continuing Examination (RCE). This request, together with a fee equivalent to a new filing fee, stops the Final Rejection clock, reopens examination, and requires the Patent Examiner to enter into the record any previously non-entered After Final Responses. The Patent Examiner once again examines the claims in view of all the responses now on the record, and issues a new Office Action. The cycle of amended response, Final Rejection, and After Final practice may be repeated.

A final option for responding to a Final Rejection or Advisory Actions is to submit a Notice of Appeal. This notice stops the Final Rejection statutory clock, and begins a new statutory deadline to file an Appeal Brief. This Appeal Brief and a corresponding Examiner's Answer are transmitted to the USPTO Board of Patent Appeals and Interferences. The appeal is reviewed and ruled on by a panel of three Administrative Patent Judges. Decisions of this Board of Appeals affirming the Patent Examiner's rejections can be appealed further to the Court of Appeals for the Federal Circuit. Appeal from this Federal appellant court is to the United States Supreme Court. Appeals to the Federal courts are handled for NIH by the Department of Justice.

XI. Obtaining Foreign Patents

Commercial partners, requiring U.S. patent rights as an incentive to invest in product development of NIH technologies, often desire foreign patent protection as well. Products may have commercial value worldwide, and many of the market forces described earlier exist in all major industrial countries. Foreign patent rights, therefore, can enhance the value of NIH technologies to our commercial partners. Foreign patent laws are complex and vary by nation. Even a superficial survey of them is beyond the scope of this Chapter. Filing and prosecution of these cases are handled by foreign associates of the NIH contract law firms responsible for handling the corresponding U.S. applications. Since patent issues in the various countries often track U.S. prosecution, our inventors seldom are burdened with foreign prosecution events. However, there are some basic foreign filing concepts that are useful for our inventors to understand in order to follow the commercialization of their technologies.

Two important considerations about foreign filing have been mentioned previously. Patents are territorial so each country issues its own patents, and national patent rights have no effect outside individual country borders. We have also already seen that nearly all foreign countries award patents to the first to file; rather than the first to invent. As a result, these countries operate under an absolute novelty system that does not permit a grace period on disclosure before a patent must be filed. Despite this decentralization and first to file requirement, there are two mechanisms of cooperation between all industrialized countries to lessen the burden of worldwide filings.

A. The Paris Convention

The first of these mechanisms is the Paris Convention of 1883. This is a treaty administered by the World Intellectual Property Organization (WIPO). WIPO is an agency of the United Nations. All industrialized countries that have joined this treaty recognize filings made in other member countries. The nature of this recognition extends a one year priority benefit to patent applications earlier filed in any other member country. For prior art purposes, this treaty treats the filing date in the later-filed country as if it were the first-filed country. Thus, prior art published in the intervening period between filing in the first country and the subsequent filing in the second country is shielded. This allows an applicant to first file in his home country, and then wait up to a year to file elsewhere without jeopardizing any rights in the foreign countries.

B. The Patent Cooperation Treaty (PCT)

The second mechanism to facilitate foreign filing is the Patent Cooperation Treaty (PCT), which is administered also through WIPO. The PCT took the benefits accorded by the Paris Convention, and significantly extended and advanced them. Again, all industrialized countries have joined this treaty. The PCT permits a single international patent application to be filed by member countries. This PCT application can be filed at the end of the Paris Convention year, and extends the Paris Convention benefit up to an additional eighteen months. Consequently, it is possible to file in your home country, and not have to file individual national applications elsewhere in the world for thirty months. The PCT application establishes an international filing date used to determine patent term in later-filed national patents. If a country's patents expire twenty years from filing, then applications entering that country via PCT expire twenty years from their PCT international filing date.

PCT applications are searched for prior art and optionally examined by Patent Examiners in the U.S., Japanese, or European Patent Offices. However, no patent issues from the PCT process. The PCT application is published, and the results of the search and examination are provided to any national patent offices entered via PCT.

C. The European Patent Convention

The European community has organized a European Patent Convention (EPC) with a European Patent Office (EPO) that advances the spirit of the Paris Convention and the PCT by developing a regional European Patent. The EPO grants a European Patent that can be converted into national patents throughout most of Europe without the time, expense, and effort of further search and examination in each country. The European Patent, however, has no enforcement rights in the EPC countries. The EPO is a designated country in the PCT. Therefore, it is possible to enter the EPO at thirty months after first filing, and have the invention examined in English. The benefits afforded by the Paris Convention, PCT, and EPO permits NIH to preserve foreign patent rights in much of the industrial world economically and almost effortlessly for a significant period of time. This time permits NIH to realize better the commercial value of the technology and to seek commercialization partners to develop the technology into products.

XII. The NIH Path to Filing Patent Applications

The patent filing path typically pursued by NIH involves initial filing of a Provisional patent application in the USPTO. Provisional applications are not examined, but serve as placeholder applications for a year. Provisional applications automatically expire at the end of a year. They are placeholders in the sense that they provide priority

benefit for prior art purposes similar to the Paris Convention, but they do not count against the twenty year term of any eventual U.S. patent. On the anniversary of the Provisional application filing, it is converted into another patent filing. There are then two options. In the event there are no foreign patent rights available (i.e., there was a disclosure prior to filing the Provisional application destroying the absolute novelty requirement of foreign countries), the Provisional application is converted to a regular U.S. Patent application. This application is examined as described previously. In the more typical situation where potential foreign rights still exist, the Provisional application is converted into a PCT application. The PCT application is filed back into the U.S. as a national filing at the end of the eighteen month PCT process. This provides thirty months from the initial Provisional application filing date to evaluate the technology and seek commercial partners before having to prosecute the application in the USPTO. When NIH desires to preserve and pursue foreign rights worldwide, EPO and other selected national patent applications are filed also at the end of the eighteen month PCT process.

The path OTT takes in deciding to file for patent protection is guided by the NIH Patent Policy. The policy is applied to inventions reported in Employee Invention Reports (EIR) coming to OTT from the laboratories via Technology Development Coordinators (TDC) or offices in each Institute/Center (IC). OTT cooperates with IC technology transfer personnel to evaluate inventions relative to potential prior art, commercial potential, and NIH patent policy. Prior art and commercial potential issues vary with each technology. The patent policy is consistent and clear. The foundation of that policy is that NIH seeks patents where further investment is needed to develop a product. The corollary of this proposition is that NIH does not seek patent protection for

inventions that clearly are research tools. Our policy appreciates the purpose of the patent system to stimulate innovation in return for public disclosure. However, that *quid pro quo* is not what drives our decision process toward filing patents. NIH scientists do not require the incentive of exclusive patent rights to encourage their ingenuity and industry. Neither NIH scientists, nor their intended audiences, rely on patents to obtain their knowledge about NIH science outcomes. That knowledge will be communicated in an enabling fashion to the public much more rapidly and effectively through traditional publication than through the patent process.

NIH files for patent protection when patents will be a necessary incentive for commercial partners to invest in the technologies and develop them into products to improve the public health. Markets such as therapeutics, vaccines, and some diagnostics operate in environments of extreme risk. Players in these markets require strong patent protection before they will consider investing in developing a product. It is necessary for NIH to seek patent protection on such inventions so they may reach their fullest potential for advancing public health. The NIH patent policy and invention review processes reflect these realities.

All entrepreneurs manage risks in their respective businesses. Most entrepreneurs desire monopoly status in their markets, and will employ all legal tools and business practices to attain it. It is not surprising then that most companies seeking NIH technologies prefer exclusive patent rights to maximize their advantage over competitors. Market forces, vagaries, and expediencies in our economy, however, cause the contribution, significance, and need for intellectual property in diverse business sectors to diffract across a broad spectrum. Part of our challenge in transferring NIH technology to

the commercial world is determining the best wavelength along that spectrum to encourage competition without stifling the incentive to develop our product.

Rarely must a single enterprise operate simultaneously near both ends of this spectrum. Such is the fate of technology transfer at NIH. Much of our research outcomes benefit from free and open dissemination unencumbered by intellectual property issues. Some of our research outcomes rely on rigorous patent protection and its exclusivity to realize its maximum potential for advancing our mission. It is relatively easy to discriminate candidates belonging solely at one dipole or the other. Prudence dictates that NIH deals with each end of this dipole appropriately. We must not disadvantage, prejudice, or compromise one mode of technology transfer because it coexists alongside the other.

The challenge is what to do with research outcomes that do not neatly sort into one of these distinct technology transfer modes. Many NIH inventions are early stage discoveries with multifaceted components and potentials. Some of those components and potentials may be diagnostic or therapeutic in nature, and would require various amounts of additional research and development to realize their benefit. Some components may be characterized as research tools useful in aiding or stimulating further basic or applied research. The markets related to these diagnostic, therapeutic, or applied research tool inventions may range from niche to expansive. Some inventions are so early stage that markets and market players are not evident. It is seldom easy, and sometimes impossible, to predict which potential will pan out scientifically or will resonate in the marketplace.

A preferred course of action would allow the technologies to mature, and then take appropriate intellectual property action as the uncertain potentials crystallize and

reveal themselves. As we have learned in this Chapter, patent systems do not encourage such a deliberate and measured approach to seeking intellectual property protection. The patent system forces an early commitment if meaningful patent protection is contemplated. This translates into making now or never patent filing decisions. Consequently, our technology transfer process must make rapid decisions on pursuing patent protection for early stage inventions. Our general policy is to err on the side of caution, and file for patents in these gray areas. Once filed, we rigorously seek the broadest possible patent protection. There is a mechanism to introduce incremental improvements to an earlier invention via a special application called a Continuation-in-Part (CIP). What is needed is a mechanism to enforce the ensuing exclusionary patent rights in ways that are complementary to the spectrum of NIH research and commercialization goals in technology transfer. Much effort is directed toward assuring the emerging intellectual property is transferred in the most advantageous way to the private sector.

XIII. The NIH Licensing Process

The tool employed to transfer NIH patent rights to our commercial partners is the license. A license is a legal agreement that grants permission to engage in an activity that is otherwise prohibited. As we have learned, patents create the right to exclude others from making, using, selling, or importing inventions described by the patent claims. NIH licenses are legal agreements by which NIH agrees not to exercise its patent right to exclude the licensed party (licensee) from making, using, and selling the invention.

A. Flexibility Provided by Licenses

There is significant flexibility in negotiating the terms of licenses. The patent owner (licensor) may license the patent right exclusively to a single party. This contractually binds the licensor not to license the patent right to anyone else. Even though an exclusive licensee does not own the patent, they contractually are the only party that can operate free of its exclusionary rights. This effectively transfers the ability to establish a monopoly position in the marketplace to an exclusive licensee. Provisions of the exclusive license permit the licensee to enforce the patent right against competitors. The size and nature of a market sometimes are such that two parties are willing to invest in developing an invention, and then compete in the marketplace. This permits the licensor to co-exclusively license to the two parties.

The licensor may forgo exclusive licensing, and choose to license its patent rights nonexclusively to many parties. Nonexclusive licenses grant licensees freedom to operate in the marketplace, but they have to compete with any number of other licensees of the invention. The licensor retains the right to exclude others who do not take a nonexclusive license.

Licensors may exercise additional flexibilities in the licensing process. Different parts of patent rights, for example, can be parsed in the license. In this way, the license may be limited to certain fields of use. If a company does not desire, or is not able, to develop all potential fields of use, agreement may be reached to limit the scope of the license. Patent rights to a cancer drug, for example, may be exclusively licensed to one party for treating breast cancer, and licensed to another party for prostate cancer. This permits both health problems to be addressed. Otherwise, products directed to only one may be developed.

When there are foreign patents, those territorial rights may be bundled into a single license or licensed independently. This may facilitate NIH strategies for transferring technologies for neglected diseases to companies interesting in making products available in developing country markets. Finally, the licensor may parse a license to distinguish the right to make and use an invention from the right to sell. This permits NIH to give out licenses for research purposes or internal use, but deny the right to commercialize or sell the invention. Alternatively, NIH as licensor can grant an exclusive commercial license that reserves the right to grant other licenses for research purposes. Patent rights to a monoclonal antibody, for example, potentially could be licensed exclusively for therapeutic uses, co-exclusively for *in vivo* diagnostic uses, nonexclusively for *in vitro* diagnostic uses, and nonexclusively for research purposes only.

License agreements permit licensors to include benchmark provisions to ensure diligent development of the invention. If a benchmark requirement is not satisfied in an exclusive license, it can be a basis to terminate the license. This would free-up the patent rights, and make the technology available to another party better able to develop the commercial product.

B. NIH Licensing Policy

NIH has developed an official licensing policy aimed at exploiting the flexibilities of the licensing process to adapt our patent portfolio to coincide with our institutional philosophy and goals relative to our technologies. Application of this licensing policy becomes the mechanism to reconcile and compensate miscalculations precipitated by the need to rush to patent filing. This licensing policy becomes the mechanism to calibrate

and fine tune the best practice of our patent rights as the technologies and markets mature. The application of this licensing policy is the tool that transforms a one-dimensional right to exclude into a multidimensional means to advance our public health mission.

The NIH licensing policy instructs to license nonexclusively where possible and exclusively when necessary. When engaging in exclusive licensing, provisions should be included and care taken to ensure appropriate scope in the fields of use and territory, and to ensure expeditious development of the invention. The licensing policy takes special notice of our responsibility not to encumber the research process, and to ensure the continuing availability of our research tools and materials.

OTT is responsible for commercial technology transfer at NIH. OTT has developed a number of license models and procedures to advance the NIH licensing policy. In addition to models for commercial exclusive and commercial nonexclusive licenses, there are other models to meet particular goals of the licensing program. A Commercial Evaluation License (CEL) model allows companies to test out the invention to see if it serves their commercial purposes. This nonexclusive license grants the right to make and use the invention for a limited period of time. This license prohibits sale or further distribution of the invention. At the end of the evaluation period, the company can apply for a commercialization license or another special license for internal use. Similar to the CEL, an Internal Commercial Use license permits licensee to make and use, but not to sell the invention. Unlike the CEL, however, the Internal Commercial Use License is not time limited. It is designed to permit the company to use the invention as

an internal tool within their research and development programs to produce other products.

NIH scientists collaborate occasionally with colleagues at academic institutions in making inventions. Patent rights to inventions arising from such collaborations are co-owned by NIH and the academic institution. Each co-owner of a patent right has an undivided right to the invention in the entirety. This means the co-owners each can license the invention independently. It is wasteful and potentially embarrassing for each party to file separate patent applications for the same invention, or for one party to exclusively license its rights while the other nonexclusively licenses its rights. It is advantageous, therefore, that one party take the lead in patenting and licensing such co-owned inventions. NIH has developed a series of model licenses to establish and govern such inter-institutional relationships. The reader is invited to visit the OTT website at www.ott.nih.gov to view copies of these models, as well as ones for Cooperative Research and Development Agreements (CRADAs), Material Transfer Agreements (MTA), and Biological Material License Agreements (BMLAs).

XIV. Other OTT Functions

Evaluating and transferring NIH technologies to the private sector is a complex enterprise.[5] In order to maximize the licensing program, effective strategies have been developed to market early stage NIH inventions.[6] The OTT is responsible for developing policy for both intramural and extramural technology transfer. OTT has developed and advanced significant policy positions regarding sponsored research agreements, research tool guidelines, and best practices for licensing of genomic

inventions.[7] [8] The OTT has initiated a program in International Technology Transfer to transfer relevant technologies and enhance capacity building in developing countries.[9] This program has had marked success in transferring NIH technologies associated with malaria, dengue, pertussis, AIDS, rotavirus, typhoid fever, and meningitis to public and private institutions in India, Mexico, Brazil, Korea, Argentina, Egypt, China, and South Africa. Monitoring our licensees to ensure they are diligent in development of the technologies and their financial responsibilities is an important and expanding program at OTT.[10] The reader is directed to the OTT website and the cited references of this section for additional information about OTT, the patenting and licensing processes, and these other aspects of NIH technology transfer.

XV. Conclusion: The Measure of NIH Technology Transfer is Its Success

OTT is proud of our success in advancing technology transfer during our brief lifetime in this endeavor. Our website elaborates statistics regarding various aspects of OTT patenting and licensing activity since 1995. Reflective of our level of activity are figures from fiscal year 2005 when OTT received 388 invention disclosures (EIRs), executed 307 licenses, and received 98.2 million dollars in royalty income from our licensees. In accordance with our Royalty Policy, 8.9 million dollars of that income was shared with 916 inventors in recognition of their inventive contributions. The remainder was distributed to the ICs to underwrite their technology transfer operations and support new scientific research. We are proudest of the roster of FDA-approved products to which NIH inventions contributed, and were licensed to product developers. These include: Synagis®, Videx®, Velcade®, Taxol®, Kepivance™, Taxus Express 2™,

Hivid®, Fludara®, RotaShield®, Havrix®, Twinrix®, Zevalin®, Zenapax®, Sporanox®, NeuTrexin®, Certiva™, Vitravene®, Thyrogen®, LYMErix™, AcuTect®, and NeoTect®. The arrays of NIH technologies currently in clinical trials make us confident that the next decade's roster of FDA-approved products will eclipse this decade's list. These past and future products never would exist to benefit large numbers of patients were it not for the inventiveness of our scientists, and the application of our commercial technology transfer process to the outcomes of that research endeavor.

The compendium of FDA-approved products improving patients' lives underscores the importance of the technology transfer process to the NIH mission. Scientists comfortable with patents appreciate now how the NIH technology transfer process helps transform their rough diamonds into polished jewels. Scientists who are still uncomfortable embracing patents, hopefully now appreciate the NIH licensing process is a way of turning lemons into lemonade.

References

1. Diamond v. Charkabarty, 447 U.S. 303 (S.Ct. 1980)
2. Brenner v. Manson, 383 U.S. 519 (S.Ct. 1966)
3. Graham v. John Deere Co., 383 U.S. 1 (S.Ct. 1966)
4. In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed Cir. 1989)
5. Ferguson, S.M. (2002). Products, Partners & Public Health: Transfer of Biomedical Technologies from the U.S. Government. *The Journal of BioLaw & Business* **5(2)**, 35-39.
6. Ramakrishnan, V., Chen, J, and Balakrishnan, K. (2005). Effective Strategies for Marketing Biomedical Inventions: Lessons Learnt from NIH License Leads. *Journal of Medical Marketing* **5**, 342-352.
7. Ferguson, S.M. and Kim, J.P. (2002). Distribution and Licensing of Drug Discovery Tools – NIH Perspectives. *Drug Discovery Today* **7(21)**, 1102-1106
8. Gupta, R., Kim, J., Spiegel, J., and Ferguson, S. (2004). Developing Products for Personalized Medicine: NIH Research Tools Policy Applications. *Personalized Medicine* **1(1)**, 1-9.
9. Salicrup L, A., and Fedorkova, L. (2006). Challenges and Opportunities for Enhancing Biotechnology and Technology Transfer in Developing Countries. *Biotechnology Advances* **24**, 69-79.
10. Keller, G.H., Ferguson, S.M., and Pan, P. (2003). Monitoring of Biomedical License Agreements: A Practical Guide. *Pharm. Dev. Regul.* **1(3)**, 191-203.

Footnote

1. The opinions expressed are those of the author and do not necessarily represent the views of OTT, NIH, or HHS. The author wishes to express gratitude to my wife, Carol, for editing the manuscript and thwarting my assault upon the English language.