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CLINICAL TRIALS: A NEW FORM OF INTELLECTUAL PROPERTY?

Introduction

Clinical trials are not adequately protected by current forms of intellectual property and should be recognized as a new form of intellectual property. (For purposes of this paper, I call the new right a “CT” so as not to confuse it with the underlying clinical trial.) The average cost of developing a new drug has reached \$802 million in 2000 dollars up from \$231 million in 1987.^[1] While some of this increase is related to inflation, the increases were particularly acute in clinical trials.^[2] Clinical costs increased 5 times faster than pre-clinical costs.^[3]

Like other forms of intellectual property, creating a CT encourages investment into the creation, maintenance, development, disclosure, and efficient use of clinical trials and thereby affording the public a benefit. Moreover, the recognition of the CT, like other forms of intellectual property, allows for the CT to be treated as a commodity and thus sold, licensed, and transferred. Additionally, in an increasingly global society the recognition of the CT allows for easier international harmonization.

Current forms of intellectual property do not adequately protect clinical trials mainly because: (1) a sponsor does not necessarily have clearly defined rights in the clinical trial, (2) public access to clinical trials is limited; and (3) incentives are frequently commensurate with other types of benefits and do not stand on their own.

My proposal for a new form of intellectual property recognizes increased public disclosure and access as a quid pro quo for a sponsor’s clear and delineated rights to clinical trials and compulsory licensing fees.

Part One explains what a clinical trial is and how it fits into the drug approval process. Part Two identifies and explains the four types of intellectual property (patents, copyrights, trademarks, and trade secrets) and to what extent clinical trials are protected by these various regimes. Finally, Part Three explains the scope of the new form of intellectual property, the CT.

Part I: The Clinical Trial and FDA Approval Process

A. What is a Clinical Trial?

A clinical trial is any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects.^[4] Clinical trials may be classified by the desired goal, audience, or phase. Clinical trials defined by goals include: safety studies, efficacy studies, pharmacokinetic studies, and pharmacology studies. Safety studies focus on evaluating whether and to what extent a drug is suitable for human consumption. Safety studies may include testing for dose tolerance, dose frequency, and duration of exposure to medicine.^[5] Efficacy studies are studies designed to see whether the desired result of the drug is being produced. Pharmacokinetic studies, including bioequivalence studies, are studies that focus on one or more of the basic pharmacological concepts: absorption, distribution, metabolism, and excretion.^[6] Bioequivalency studies are designed to show that as between different formulations, different dosage forms, products manufactured at different sites, or products made using different manufacturing methods that (1) the rate and extent of absorption are extremely similar; (2) the amount of each preparation reaching the bloodstream does not significantly differ; and (3) the preparations are chemically equivalent.^[7] To be bioequivalent for an ANDA approval (see Section I.B. below), the applicant must show that either the rate and extent of absorption of the drug does not show a significant difference from the rate and extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses or the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.^[8] Pharmacology studies focus on new dosage formulations, new routes of administration, new dosing regimens, or other

characteristics of a drug's pharmacologic profile.^[9] Clinical trials that are classified by audience typically involve special populations, such as the elderly, children, or pregnant women.

Generally, the pharmaceutical industry identifies four phases of clinical studies, appropriately called Phase I, Phase II, Phase III, and Phase IV. Phase I clinical studies are generally small, closely monitored studies done on healthy subjects to evaluate the safety of the drug.^[10] Phase I studies are designed to gain information about metabolism, side effects and pharmacokinetic and pharmacological effects.^[11] Phase I studies also may provide key information into the development of Phase II studies.^[12] Phase II clinical studies are early studies done on a small number of patients further investigating the safety of the drug as well as preliminary efficacy results.^[13] Phase III clinical studies are expanded to involve a larger patient population and further test the efficacy of the drug.^[14] Phase IV clinical studies are generally post-marketing studies that are not part of the NDA process prior to approval.

B. Who is involved in a clinical trial?

The various players in a clinical trial include: sponsors, subjects, investigators, staff of the investigators, contract research organizations (“CROs”), Institutional Review Boards (“IRBs”), and regulatory agencies, like the Food and Drug Administration (“FDA”). Sponsors are those individuals, pharmaceutical companies, governmental agencies, academic institutions, private organizations or other organizations who take responsibility for and initiate a clinical trial.^[15] Subjects include both healthy humans and patients with a disease who participate in a clinical trial, either as a recipient of the new drug or as a control.^[16] Investigators are those individuals who actually conduct and lead the administration of a clinical trial.^[17] The staff of the investigator includes other physicians, nurses, and assistants that aide the investigator in carrying out the clinical trial. CROs are persons that assume some of the obligations of the sponsor as an independent contractor.^[18] CROs provide an array of services ranging from finding investigator sites to developing protocols to analyzing data. Various types of CROs include independent companies that conduct clinical trials themselves, academic departments or government agencies that conduct clinical trials, medical practices that solicit sponsors to

contract with them to conduct a clinical trial, and companies that place clinical trials primarily in a network of medical clinics that they have created.^[19] IRBs are the boards that govern the investigating site that must approve and review the clinical trial protocol, including informed consent forms. The U.S. regulatory agency governing the drug approval process is the FDA. Other countries have analogous agencies.

An investigator is motivated to conduct clinical trials because he may be able to reward in one of the following ways: by gaining prestige in his career, by obtaining medical benefits for his patients (i.e. access to investigational new medicines or treatments), by obtaining new medical or scientific equipment provided by the sponsor, by obtaining more staff, by obtaining financial rewards, and by being able to publish articles related to the clinical trial.^[20]

Sponsors selection of CROs and investigators usually takes into consideration the client population needed for the study, the reputation of the CRO or investigator (academic institutions or those affiliated with an academic institution tend to have a better reputation), cost, rights to publish, and ownership of intellectual property related to or derived from the clinical trial. CROs and investigators that are academic institutions will rarely agree to a sponsor contract that does not give them the right to publish study results. Moreover, these academic institutions often will fight vigorously for intellectual property rights.

C. *How does a Clinical Trial fit into the Drug Approval Process?*

The Center for Drug Evaluation and Research (“CDER”), a division of the FDA, is in charge of approving drugs that are marketed for human use. Prior to a new drug being approved for the general public, an estimated eight-and-a-half years is needed to study and test the drug.^[21] The ultimate desired result achieved through interactions with the FDA is an approval of either a New Drug Application (“NDA”)^[22] or an Abbreviated New Drug Application (“ANDA”).^[23] This approval allows a sponsor to market their drug to the public.

The New Drug Development Process begins with identification of a compound or chemical entity for potential human use followed by pre-clinical research. Pre-clinical research

may include: synthesis studies, including manufacturing scale-up capabilities; purification; and animal testing, usually performed in both rodents and non-rodents.

Although some studies in the pre-clinical phase may be ongoing, the sponsor will want to begin the clinical phase next. During the clinical phase clinical trials are developed, implemented and the resulting data is analyzed. Once the sponsor decides initiate a clinical trial, the sponsor (or a CRO designated by the sponsor) must: (1) develop a clinical trial protocol which usually requires assessing: the goals of the trial; the appropriate population(s) the trials should be done on; the appropriate forms for data collection; the appropriate mechanisms for distribution and collection of drugs, data, etc.; and the methods of analyzing data.; (2) choose and contract with the appropriate CROs and investigators; (3) obtain IRB approval from the investigator site; (4) oversee the administration of the clinical trial; (5) collect clinical trial data; (6) analyze clinical trial data; (7) report clinical trial results to the FDA; (8) and in some circumstances, report clinical trial results in a publication, such as the American Medical Association Journal or the New England Journal of Medicine.

Prior to clinical studies being initiated, the FDA requires sponsor's to submit data in the form of an investigational new drug application ("IND") indicating that the drug is reasonably safe for use in initial, small-scale clinical studies.^[24] The IND technically allows for drugs to be shipped in interstate commerce for purposes of conducting clinical trials.^[25] (Where a sponsor desires to manufacture and administer clinical trials within a single state, the sponsor need not file an IND.) A sponsor may submit three main types of data that provide the necessary support in their IND: (1) nonclinical data from in vitro laboratory or animal studies of the drug; (2) compiled data from previous clinical testing or marketing of the drug in the U.S. or another country whose population is relevant to the U.S. population; or (3) new pre-clinical studies. Compared to the number of IND submissions, approximately seventy percent will complete Phase I studies, thirty-three percent will complete Phase II studies, and twenty-five to thirty percent will complete Phase III studies.^[26]

Results of the clinical trials are used to support an NDA or ANDA. Usually, the FDA does not approve a drug for marketing prior to the completion of clinical trials. However, the FDA can grant NDA approval that is conditional upon the sponsor engaging in Phase IV studies.

In analyzing whether to approve a drug, the FDA will review the following: (1) whether the drug is safe and effective for the proposed uses, and whether the benefits outweigh the risks; (2) whether the drug's proposed labeling is appropriate; and (3) whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.^[27] Throughout the approval process, the sponsor and FDA frequently meet to discuss courses of action for the drug for which approval is sought. The sponsor is supplying the FDA with nonclinical as well as clinical data. In addition to the staff of CDER, CDER uses an advisory committee to obtain non-binding, outside advice and opinions to advise the agency on certain decisions.^[28]

D. NDAs and ANDAs

An NDA is made pursuant to the requirements of § 505 (b) of the Federal Food, Drug, and Cosmetic Act ("FFDCA"). The sponsor can submit an application under § 505 (b)(1) or § 505 (b)(2). Under § 505 (b)(1), a sponsor must submit the following to support his NDA: (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (F) specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.

Under a § 505 (b)(2) application, the applicant submits all information required under § 505(b)(1) except it need not supply those studies required under section A (full reports of

investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use). Thus, the applicant is allowed to submit an NDA where certain clinical trials relied on in the application are not conducted by or for the applicant and for which the applicant has not obtained a right of reference from the original sponsor of the clinical trial.

An ANDA is made pursuant to the requirements of § 505 (j) of the FDCA. An ANDA must contain information to show that the conditions of use prescribed, recommended, or suggested in the labeling have been previously approved (“listed drug”), information to show that the route of administration, the dosage form and the strength of the new drug are the same as those of a listed drug, information to show that the new drug is bioequivalent to the listed drug, information to show that the labeling is the same as the listed drug.

In both 505(b)(2) and 505(j) applications the applicant must file a certification that indicates how another’s patents relate to the drug that they investigated.^[29] This certification must claim that: (i) the patent information has not been filed; (ii) that the patent is expired; (iii) that there is a patent and the date that the patent will expire; or (iv) that the patents are invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted (“Paragraph IV certification”).^[30] Where a paragraph IV certification is made, the applicant must provide notice to the patentee who then has 45 days to bring an infringement suit.^[31] If an infringement action is initiated, then a stay on the approval is granted for a suggested 30-months, which can be shortened or lengthened, to account for the actual time of litigation.^[32]

In deciding whether to file an NDA or an ANDA, the applicant must first determine whether the active ingredient has been previously approved. If not, the applicant must file an NDA pursuant to 505(b)(1). If the active ingredient has been tested previously, the applicant may have the choice of filing an NDA or ANDA. In deciding which to file, the applicant will try to balance the costs of engaging in clinical trials, the costs of the application, and the costs of potential litigation when a paragraph IV certification is made with the possible benefits of

approval, including any periods of exclusivity (see Section E below) that may be acquired and the market for the drug. An ANDA applicant is benefited by having a lower cost of applying for approval. This lower cost reflects the FDA's ability to charge less because the review of the application is less labor-intensive as there is no need for the FDA to review previous safety and efficacy studies.

E. Exclusivity

An approved drug may be protected by patent exclusivity and non-patent exclusivity, including pediatric exclusivity and orphan drug exclusivity. Patent exclusivity exists for the life of the patent and allows only the patentee (and its licensees) to market the patented drug. Non-patent exclusivity exists regardless of whether there is patent exclusivity. Non-patent exclusivity can be granted for 7 years, 5 years, 3 years, 180 days, or 6 months. A 7-year period of exclusivity is granted for rare diseases^[33]. A 5 year period of exclusivity is granted where a new active ingredient (including esters and salts) is approved.^[34] During this 5 years no application may be submitted that relies on the original's trials except that those applications with a Paragraph IV Certification may be filed at the beginning of the fourth year of exclusivity to seek approval which will not be granted until the end of the 5-year period.^[35] A 3-year period of exclusivity is granted where a product is approved that is based on a previously approved active ingredient and contains new clinical trials (other than bioavailability studies) that are essential to approval.^[36] The 3-year period of exclusivity does not contain a provision similar to the 5-year period that allows for early filing of an application if accompanied by a Paragraph IV certification. A 180-day period of exclusivity is granted to the first ANDA applicant that files a Paragraph IV certification.^[37] The 180-day period begins at the earlier of the date of first commercial marketing or the court decision that the patent that was subject to certification was invalid or not infringed.^[38] Pediatric exclusivity can not be granted independently and only extends 7-year, 5-year or 3-year exclusivity by six months for pediatric studies.

Offering a sponsor the exclusive rights to market drugs is a powerful incentive. Non-patent exclusivity is important regardless of whether a patent is in place. If the patent is held invalid or unenforceable during the period of non-patent exclusivity, the patentee is still allowed to maintain the exclusivity on the remaining time left in the non-patent exclusivity. Moreover, non-patent exclusivity delays the time for which others can file an application relying on those studies. Finally, by only allowing pediatric exclusivity to attach to other forms of non-patent

exclusivity, there is no exclusivity incentive for a sponsor to engage in pediatric clinical trials if they have no other exclusivity related to the drug.

Part II : Current Forms of Intellectual Property

A. Patents

The patent laws are enacted by Congress pursuant to its power under Article I, section 8, clause 8 of the Constitution. The patent statute, Chapter 35 of the U.S. Code, further defines patent rights.

1. Subject Matter

Patents are granted to whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof.^[39] Additionally, the invention must be novel^[40] and non-obvious.^[41] The novelty and non-obvious requirements prevent patents from being granted on trivial advances. The utility requirement prevents patents for being granted where there is no use for the invention. Utility issues most frequently arise in the chemical arts where a compound is discovered but the potential uses of the compound are unknown.

2. Rights

A patent gives the owner the right to exclude others from making, using, selling, offering for sale or importing the claimed invention in the United States.^[42] The grant of a patent, however, does not give the inventor the right to practice the invention. In fact, the inventor may have to comply with other laws and regulations, such as those promulgated by the FDA. A patentee can lose his rights to enforce his patent if it is held invalid or unenforceable. A patent will be unenforceable where the patent was obtained through fraud. In some situations, a finding of unenforceability may be cured.

3. Application and Registration

Unlike other forms of intellectual property, a patent can only be recognized through a formal application process. In order to receive a patent, the applicant must apply to the U.S. Patent and Trademark Office which analyzes the patent to determine whether it meets the

rigorous patent standards. Throughout the application process, the patent application is kept confidential.^[43] If the patent application is abandoned, the information remains confidential. Once the patent issues, the patent, as well as the history of the application becomes public. In efforts to comply with international patent law, patents are now automatically published 18-months after filing unless designated otherwise. If the applicant desires not to have the application published after 18-months, the applicant must file a non-publication request and is precluded from filing internationally.^[44] The Patent Office maintains an easily searchable database of all patents that may be accessed via the Internet.^[45]

4. Duration

A patent lasts for 20 years from the date of filing.^[46] After a patent expires, the patent is dedicated to the public.

5. Ownership and Transferability

An inventor(s) that creates a patentable invention is the first owner of the patent. Patents are freely assignable and may be assigned in whole or in part.^[47] Frequently, patents are assigned from an employee to his employer through his employment contract. Additionally patents may be licensed only with the permission of the owner.^[48]

6. Underlying Policy

Obtaining this right to exclude for 20 years, or as some would define it a limited monopoly, is a strong and powerful right, but it is not without its costs. In return for this right, the inventor must disclose his invention, including the manner and process of making and using it, so that one of ordinary skill in the art would be able to make and use the invention.^[49] In addition, the inventor must set forth the best mode of carrying out the invention.^[50]

In determining the duration and scope of patent rights, Congress has determined that the benefits of the scope and duration of the patent rights afforded to the owner provide enough incentive to encourage disclosure of the information to the public and are commensurate with the detriment to the public of not being able to practice the invention without a license for the duration of the patent.

7. How are clinical trials currently protected by patents?

Assuming that all of the statutory requirements are met, patent law could protect new chemical entities and new drugs, new formulations of drugs, methods of manufacturing chemicals or drugs, and methods of using the chemicals or drugs. Thus, patents may be obtained from clinical trial results that indicate a new use or method of using a drug. However, the underlying studies are not generally protected by patent law. In fact, the patent law makes an exception that allows others to engage in clinical research without violating a patent.^[51] In an effort to balance this exception, Congress provided that the filing of a Paragraph IV certification for either ANDAs or NDAs is an act of infringement.^[52]

The patent laws also recognize that the time to get a drug approved by the FDA can be considerable and can decrease the value of the patent because by the time the drug is approved there is considerably less time to enforce the patent. To further encourage disclosure of inventions, a patent term extension may be granted for those compositions or processes that are subject to regulatory review by the FDA pursuant to the FDCA.^[53] The term of the patent may be extended if it has been subject to a regulatory review period before commercial marketing or use.^[54] The patent is thereby extended by the amount of time equal to the regulatory review period that occurs after the patent issues, less periods of time where the applicant was not acting diligently in the review process.^[55] However, the grant of such extension shall not exceed 14 years.^[56]

B. Trademarks^[57]

Trademark law, unlike patent and copyright law, has both federal and state laws that dictate its scope, rights, and enforcement. The Federal trademark law, the Lanham Act,^[58] describes the scope of federal protection afforded to trademarks. Congress enacted the Lanham Act under its power to regulate interstate commerce. States also have their own statutes and/or common law doctrine that govern trademarks.

1. Subject Matter

A trademark is used to identify goods or services with a source. A trademark may take the form of a word, logo, design, color, scent, or sound. The trademark must be inherently distinctive or become distinctive due to acquired meaning. Trademarks come into existence when they are used in commerce to identify the source or quality of goods or services.^[59]

2. Rights

A trademark gives the owner the right to exclude others from using the mark or a colorable variation thereof in connection with the sale, offering for sale, distribution or advertising of goods or services that is likely to cause confusion, mistake or deception^[60] or dilutes the trademark.^[61] A trademark owner can lose its rights if the mark becomes generic, if the rights have been abandoned, or if the trademark was obtained through fraud.^[62]

3. Application and Registration

Although a federal trademark registration is not necessary to recognize trademark rights, registration does afford the owner benefits, including the right to sue under the Lanham Act.^[63] Federal trademarks may only be registered if there is use in interstate commerce.^[64] Federal registration will not be permitted in a variety of circumstances, including if the trademark so resembles another registered trademark that it is likely to cause confusion, mistake, or deception, if the trademark is merely descriptive or as whole is functional.^[65] Registered trademarks are published in the Official Gazette and are easily searchable in the trademark database that now may be accessed via the Internet.

4. Duration

Trademarks can exist for an infinite length of time. A trademark ceases to exist if the mark becomes generic, if the rights have been abandoned, or if the trademark was obtained through fraud.^[66]

5. Ownership and Transferability

Trademark rights are owned by the entity that creates the association between the mark and the good or service. Trademark rights are assignable^[67] and licensable. Licensing can be limited in scope to either a particular market (either geographic, type of store (i.e. supermarkets,

pharmacies, etc.)), duration, or type of good or service. When licensing a trademark, the owner must take great care to insure that quality control standards and control remain with the owner. Failure to take these precautions may result in loss of trademark rights.

6. Underlying Policy

Trademarks are generally justified as providing a benefit to the public and providing incentive to owner to maintain consistent quality in his product. The public is benefited by being able to quickly and efficiently identify and distinguish products. Additionally, consumers benefit by receiving goods or services that have a consistent quality.

7. How are clinical trials currently protected by trademarks?

There is very little in the clinical trial process that would be protected by trademark law. The only possible areas where trademark protection would be available would be for the trademarked name of the drug and in some rare instances, services that would be provided with a drug that was offered (i.e. if for example a mark were attached to a way of administering chemotherapy that was in a specific simulated environment). However, the brand name of a drug is usually not used in the actual clinical trial. In fact the technical name of the drug is frequently not revealed to the subject^[68] or not revealed to either the subject or the investigator.^[69] Once the drug is on the market, however, the trademark protection of a drug is valuable.

C. Copyrights

The copyright laws are enacted by Congress pursuant to its power under Article I, section 8, clause 8 of the Constitution. In turn, Congress has enacted the Copyright Statute.^[70]

1. Subject Matter

Copyrights protect the original works of authorship that are fixed in any tangible medium of expression regardless of whether it has been published.^[71] A copyright protects expression, and not the underlying facts or ideas, procedures, processes, systems, methods of operation, concepts, principles, or discoveries.^[72]

2. Rights

Copyright protection consists of a bundle of rights including the right to distribute copies and the right to create derivative works.^[73] Copyrights protect the owners from unauthorized use of the copyrighted work. Copyrights do not protect uses which are considered fair uses.^[74] Copyrights do not protect the owner if another individual develops the exact same work or a substantially similar work provided that the new work was developed independently.

3. Application and Registration

Similar to trademarks, copyrights need not be registered. However, a copyright owner may not receive statutory damages and attorney's fees without this registration.^[75] To register a copyright, the applicant must deposit a sample with the Copyright Office.^[76] The Copyright Office checks to make sure that the application contains copyrightable subject matter prior to registering the copyright.^[77] The Copyright Office maintains a depository and keeps records of the copyrights that are available to the public.^[78]

4. Duration

A copyright will last for the life of the author plus 70 years and for those works that are works made for hire, the copyright will last for 95 years from the shorter of the date of first publication 120 years from creation.^[79]

5. Ownership and Transferability

The copyright is owned by the initial author(s) of the work^[80] The author is either the creator or the entity that contracted for a work made for hire.^[81] Works made for hire generally come in two flavors: those made by employees within the scope of employment and those specially ordered or commissioned. Copyrights may be assigned or licensed.^[82] A copyright license need not give the licensee all the rights that are conferred on the copyright owner. Thus, the rights that attach to a copyright are divisible. The Copyright Act provides for compulsory licensing in certain contexts, such as with sound recordings. The royalty rates are set by Congress.

6. Underlying Policy

The policy reasons generally given to justify granting copyrights include: (1) protections and benefits afforded to the author; (2) public benefits; and (3) other economic benefits. Those protections and benefits afforded to the author include the incentive to create the work, the right to control one's creation, prestige, and leverage for negotiations. The public benefits by having more access to both more obscure works and the "blockbuster" works. Finally other economic

benefits include encouraging publisher investment and allowing for transactions and bargaining occurring between authors and publishing companies.

7. How are clinical trials currently protected by copyrights

The copyright laws protect various aspects of the clinical trial process. Copyright law protects any reports or publications of clinical results, to the extent that they are expression.. Moreover, to the extent that any forms are designed for administration of the clinical trial process, those forms may be copyrightable. A copyright may exist in the labeling of the drug.

Copyrights in the clinical trial arena are problematic because (1) copyrights will not protect the underlying data; (2) ownership and control of publication is difficult and (3) copyright protection may be unenforceable. First, to the extent that copyright protection is granted, it does not protect the underlying data. Second, conflict over ownership and control of copyrights will be greatest with respect to trial protocols, study reports and forms created for clinical trial data collection. The sponsor may only retain ownership and control of these works if (1) the sponsor's employees create or co-create these works; (2) the sponsor's contract with the CRO and/or investigator contains a works made for hire provision; or (3) the sponsor subsequently purchases the copyright. Some CROs and investigators, especially those that are affiliated with academic institutions, refuse to allow an employee of the sponsor to work with them as a co-author and will not agree to sign a work-made-for hire agreement. Moreover, they frequently have explicit clauses retaining publication rights to the study they are performing. A sponsor that wants to maintain ownership and control is therefore forced to go to a site, often those not affiliated with academic institutions, to perform their trial. Being forced to use a CRO or investigator that is not affiliated with an academic institution is most problematic where the trial must be done a special population that is only accessible through these particular institutions. Moreover, the sponsor is forced to choose between a prestigious institution and retaining copyright ownership.

Enforcement of copyrights may also be difficult. Although copyrights on labels for drugs may exist, an ANDA applicant will not be held liable for copyright infringement because the FDA requires that the labels are the same as the labels of the approved drug.^[83] Similarly, incorporating another's study by reference into a 505(b)(2) or 505(j) application is unlikely to be a source of copyright infringement because there is no copyright in the underlying data that is referred to and to the extent that any copyright protection exists in the submitted clinical trial, the 505(b)(2) or 505(j) applicant is not copying the work as it is incorporated by reference.

D. Trade Secrets

Trade secrets are protected by state law. The Uniform Trade Secrets Act has either been enacted in original or modified form in most states. Owners of trade secrets are protected from misappropriation of their trade secrets.

1. Subject Matter

Trade secrets are “information, including formulas, patterns, compilations, programs, devices, methods, techniques or processes, that derives independent economic value, actual or potential, from not being generally known to and not being readily ascertainable by proper means by others who can obtain economic value from its disclosure or use and is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.”^[84] A trade secret can exist only to the extent that the owner maintains its secrecy. Trade secret law does not protect against the independent creation or development of the same trade secret.

2. Rights

Once the trade secret has been identified or asserted, trade secret law protects against misappropriation. Misappropriation occurs when trade secrets are acquired by improper means or are disclosed or used when the original acquisition was improper.^[85] Trade secret law does not protect against acquisition of trade secrets by proper means, including reverse engineering and independent development.

3. Application and Registration

Trade secrets do not require any application or registration.

4. Duration

A trade secret can exist indefinitely. However, the life of a trade secret can be shortened if the trade secret is disclosed to the public, becomes generally known to the public or the owner fails to take reasonable steps to maintain its secrecy.

5. Ownership and Transferability

Trade secrets are owned by the entity (corporation, partnership, inventor, etc.) that creates the trade secret and maintains its secrecy. In addition, trade secrets may be transferred and licensed. When licensing trade secrets, the owner can divide its rights by limiting use of the trade secrets to either particular markets, geographic locations, or particular uses (e.g. for research use only).

6. Underlying Policy

Trade secret protection is frequently justified based on commercial morality and the impropriety of stealing another's property. By protecting a trade secret, the scope of protection is much more limited than those of the patent laws as it does not protect against those who independently create or develop the trade secret. The public benefits from the existence of trade secret law because it provides incentive to develop trade secrets that indirectly benefit the public (i.e. a special mixture of gasoline which cannot be readily ascertained from the final product can be beneficial to the public).

7. How are clinical trials currently protected by trade secrets?

Trade secret law does not adequately protect clinical trials because the trade secret law is not uniform throughout the U.S., the competing interests of numerous players within the clinical trial process make reasonable efforts to maintain secrecy difficult, the value of a study may be questionable, maintaining the clinical trial as a secret necessarily does not promote public disclosure and there may be takings issues with respect to 505(b)(2) applications.

First, since trade secret law varies from state-to-state and the drug approval process is federal in nature, there may not be uniformity in the various state's trade secret statutes or the judicial interpretation thereof. Thus, the sponsor may be in a position where he is able to

successfully assert that the information in a clinical trial is a trade secret in some states while not being a trade secret in other states. The Texas Appellate Court refused to find that collateral estoppel applied to bar Upjohn from claiming that a trade secret existed in the clinical trial data.^[86] A previous decision by the district court in Utah, prior to dismissal of the case, had found that Upjohn could not claim trade secrets with respect to information in case report forms and technical and statistical reports not authored by Upjohn.^[87] Moreover, unlike patents that establish rights of the owners as compared to the world, trade secret law is often interpreted to reflect the nature of the property as between the two parties involved.^[88] Courts have readily recognized clinical trials as trade secrets where there were improper acts by a competitor.^[89] When a competitor offered to establish honorariums in return for access to a competitor's clinical trial data, the Massachusetts Superior Court was willing to issue a preliminary injunction requiring destruction of clinical trial information that the competitor has obtained, cessation of any communication with the investigators that were performing the clinical trials, and no disclosure of clinical trial information without permission of the sponsor or the court.^[90]

Second, since some CROs and investigators, particularly those that are affiliated with academic institutions, maintain rights to publish information, a court decision could decide that giving this right away is not considered reasonable efforts to maintain secrecy, thus destroying the existence of a trade secret. Clinical protocols were not considered to be trade secrets where published and described extensively in medical literature.^[91] The court then went on to find that two out of three of the investigation drug brochures at issue that revealed clinical trial results were not trade secrets as they were already generally known.^[92] The court went on to note that efforts to maintain secrecy were not reasonable where there was no written agreement between the sponsor and the investigator (even though it was alleged that this was industry custom), the documents were not marked confidential, the material was disseminated to approximately 19 centers, no policy of document retrieval, and there were no letters contesting the investigator's publication of clinical trial information.^[93] The sheer number of people involved that have

access to the clinical trial information – the investigators, CROs, IRBs, and patients - make maintaining secrecy a difficult task.

Third, a trade secret requires showing value. For failed studies, the value of the study is questionable. A sponsor would claim that there is value in maintaining that information as a secret as other competitors could waste money on the same futile research. Even so, failing to recognize the failed trial as a trade secret does not encourage its disclosure. For successful trials that are used as the basis for an FDA application much of the information is available under the Freedom of Information Act^[94]. A government agency may withhold disclosure of information if it falls into one of the exceptions, including a trade secrets exception. Data from a clinical trial that is provided to the FDA may be claimed as a trade secret or confidential information where the release would result in an unwarranted invasion of personal privacy.^[95] However, the value of the clinical trial may be determined based on the ability to rely on the study in FDA approval. The court refused to grant motion for summary judgment where there was a genuine issue of material fact – more specifically, the sponsor as well as the FDA claimed that dissemination of the information would cause harm to its competitive position while the defendant claimed that there would be no substantial economic harm as the information in the tables used was analyzed to determine the efficacy and safety of Oralet [a narcotic lollipop] and could not be relied upon by a competitor for approval.^[96]

Fourth, by allowing trade secret protection of clinical trials, there is necessarily a desire to keep the information obtained in the secret. Thus, the owner of the trade secret is required to balance how much disclosure is necessary to lure potential licensees while maintaining secrecy. If some other form of intellectual property is recognized that encourages the dissemination of types of clinical trials engaged in licensing could be encouraged or even mandated. Moreover, encouraging secrecy of information whether clinical trial results or methodology, encourages a gap between public knowledge disseminated and actual knowledge. Pfizer tried to claim a trade secret by investing in excess of \$20 million and 10 years on developing the most efficient means of developing clinical trials, i.e., the types of patients to

use, the dosage sequence, the means for measuring individual reaction, etc., as well as the things to be avoided as not being beneficial to the testing program.^[97] The court refused to grant a preliminary injunction because that information likely did not rise to the level of trade secret status.^[98] Moreover, the court noted that allowing a trade secret in this information would be against public interest because it would promote inefficiency in clinical trials.^[99]

Finally, if clinical trials are considered to be property, then relying on someone else's studies may be considered an improper takings.^[100]

Part III: The Proposed New Form of Intellectual Property

Congress is conferred with the power “to promote the progress of science and the useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and disclosures.”^[101] Pursuant to this authority, Congress should enact legislation recognizing the CT as a new form of intellectual property.^[102]

Failure to meet any of the standards set forth below, including subject matter eligibility and registration, shall preclude CT protection. The clinical trial that is not protected by a CT may not be relied upon for any FDA approval, including an IND, NDA, or ANDA.^[103]

1. Subject Matter

CTs should only protect those clinical trials that meet eligibility requirements. Eligibility requirements should include standards of good clinical practice. Other considerations for eligibility requirements may include requiring certain credentials of investigators, informed consent of patients, etc. The recognition of a CT provides an easy mechanism for implementing standards of clinical practice or necessary features of clinical trials. This benefit will not only flow to domestic policy decisions but provides benefits in the international arena. As with other forms of intellectual property, there has been an international effort to harmonize standards for clinical trials. Harmonization efforts in other areas of intellectual property often involve setting minimum standards for international recognition. Thus, recognizing the CT as a form of intellectual property will allow international minimums to easily be integrated into the protected CT. For example, if international harmonization efforts require that Phase II clinical trials

engage at least 200 patients, then this could be treated as a baseline for acquiring a CT. Thus, those Phase II clinical trials that do not have at least 200 patients would not qualify and therefore would not be considered a CT.

2. Rights

Only CTs may be relied on for FDA approval and non-patent exclusivity. An applicant may rely on another's CT in their FDA applications, regardless of whether they would grant permission, provided that the sponsor is compensated through a compulsory licensing scheme. The compulsory licensing scheme would require the Commissioner^[104] of CTs or Congress to establish equations for determining such a rate so that there will be no need for negotiations between the parties where the sponsor is in a position to demand a high rate. The equation for determining the rate should account for the cost of the CT relied on (or some factor(s) that can act as a proxy for cost, such as cost per patient and number of patients) and the estimated size of the market. When establishing the equation to determine the rate, the royalty due by application of the equation must be cost effective so that the later applicant will rely on the CT instead of engaging in their own clinical trial.

Additionally, any CROs or investigators shall be given the right to publish results or data derived from a CT that they actively participated in, subject to any limitations needed to preserve the sponsor's ability to obtain a patent. However, any such publication or results, whether positive or negative, shall include a statement indicating the sponsor of the CT as well as the CT registration number. The right to publish may not be waived by the CRO or investigator.

Where a CT is fraudulently obtained, the CT sponsor shall lose his CT rights and shall be liable for any damages incurred by an applicant as a result of reliance on the sponsors CT.

3. Application and Registration

Prior to engaging in a clinical trial, a CT application must be filed with the Commissioner.^[105] Upon receipt of the application, the Commissioner will grant a CT number and must classify the trial into the appropriate category. The established categories should take into consideration the phase as well as the type of disease that is being researched in as much as

the type of disease implicates a need for a longer trial time frame. Each category of applications will be assigned a “drop-dead” date where the CT is published. If approval occurs prior to the drop-dead date, then the publication will occur sooner. (This would be similar to the 18-month publication rule with patent applications.)

In an FDA application, a statement would be required indicating the use of a CT. Similar to those certifications required under 505 (b)(2) and 505(j) that require the applicant to assert and provide notice to the patentee that there is no infringement or that patent is invalid under paragraph IV, when someone else’s CT is going to be used as the foundation for an application, the applicant should be required to provide some “certification” as well as notice upon the owner of the CT. Moreover, enforcement of the CT would be easy as the FDA would be aware when someone else’s studies are relied upon.

The Commissioner of CTs shall maintain a register of all CTs. By registering the CTs, both positive and negative trials will be readily available to the public. Access to the trials shall include access to the results of the trial as well as the protocols.

4. Duration

The CT should last for 15 years from the earlier of the date of approval or the drop dead date. After the expiration of the CT, the CT shall be dedicated to the public for use.

5. Ownership and Transferability

The CT shall be owned by the sponsor of the clinical trial. The sponsor is free to assign or transfer the CT. The CT as well as any periods of non-patent exclusivity that are based on that particular CT shall be fully transferable.

6. Underlying Policy

Recognizing the CT as a new form of IP provides benefits to sponsors of the clinical trials, competitors in the pharmaceutical industry, and the public.

A sponsor benefits from the creation of the CT by being rewarded for its investment in a clinical trial though periods of non-patent exclusivity based on a CT. Receiving compulsory licensing fees also helps the sponsor to recuperate investment in the clinical trials. Sponsors are

also benefited by having clearly established rights, regardless of publication by CROs and investigators. This eliminates CRO and investigator demands for publication rights as a factor in deciding which CRO or investigator to hire.

Competitors benefited from the creation of the CT. First, publication of failed clinical trials prevents competitors from investing in the same or similar futile studies. Second, by having access to the underlying methodology as well as any forms for data collection, competitors should be able to develop better clinical trials and standards and quality of clinical studies will increase. Additionally, the FDA could make a recommendation to an applicant that they should rely on a CT without raising any due process issues. This would not be considered a governmental takings as the applicant would need to compensate the sponsor of the study under the compulsory licensing scheme.

The public benefits by having greater access to clinical trial information. More importantly, however, the creation of the CT should result in cheaper, better, safer drugs in the marketplace as well as performance of better clinical trials.

Conclusion

The CT should be recognized as a new form of intellectual property because the CT will encourage sponsor investment in clinical trials, minimize duplicative studies, increase the flow of information to the public, and including competitors within the industry.

^[1] Pharmaceutical Industry Profile 2002, PhRMA report at 20
<<http://www.phrma.org/publications/publications/profile02/index.phtml>>.

^[2] *Id.* at 22.

^[3] *Id.* at 22.

^[4] 21 CFR 312.3.

^[5] Bert Spilker, *Guide to Clinical Trials* (1991) at 11.

^[6] *Id.*

^[7] *Id.* at 351 and 641.

^[8] Federal Food, Drug, and Cosmetic Act ,505(j)(8)(B).

^[9] *Guide to Clinical Trials*, at 11.

^[10] CDER Handbook, p. 8 <<http://www.fda.gov/cder/handbook/index.htm>>.

^[11] 21 CFR 312.21.

- [12] 21 CFR 312.21.
- [13] 21 CFR 312.21; CDER Handbook at 8.
- [14] 21 CFR 312.21; CDER Handbook at 8.
- [15] 21 C.F.R. § 312.3.
- [16] 21 C.F.R. § 312.3.
- [17] 21 C.F.R. § 312.3.
- [18] 21 C.F.R. § 312.3.
- [19] *Guide to Clinical Trials* at 403-404.
- [20] *Id.* at 391.
- [21] CDER Handbook at 5.
- [22] Those applications filed pursuant to FDCA §505(b).
- [23] Those applications filed pursuant to FDCA §505(j).
- [24] 21 CFR 312; CDER Handbook at 5..
- [25] 21 CFR 312.1.
- [26] From Test Tube to Patient: Improving Health through Human Drugs, a special report prepared by CDER, <<http://www.fda.gov/cder/about/whatwedo/testtube-3a.pdf>>.
- [27] CDER Handbook at 7.
- [28] CDER Handbook at 11.
- [29] FDCA § 505(b)(2)(A) and 505(j)(2)(A)(vii).
- [30] FDCA § 505(b)(3).
- [31] FDCA § 505(c)(3).
- [32] FDCA § 505(c)(3)(C).
- [33] FDCA § 527.
- [34] Applies only to drugs approved after September 24, 1984.
- [35] FDCA § 505(c)(3)(D)(ii).
- [36] FDCA § 505(c)(3)(D)(iii).
- [37] FDCA § 505(j)(5)(B)(iv).
- [38] FDCA §505(j)(5)(B)(iv).
- [39] 35 U.S.C. § 101.
- [40] 35 U.S.C. § 102.
- [41] 35 U.S.C. § 103.
- [42] 35 U.S.C. § 154.
- [43] 35 U.S.C. § 122.
- [44] 35 U.S.C. § 122(b)(2)(B)(i).
- [45] The Internet database does not contain the prosecution history of the patent. The prosecution history may be obtained via request to the patent office.
- [46] 35 U.S.C. § 154.
- [47] 35 U.S.C. § 261.
- [48] Technically, there are rare situations in which a compulsory license may be granted but the patentee must be compensated at a reasonable royalty rate.
- [49] 35 U.S.C. § 112.
- [50] 35 U.S.C. § 112.
- [51] 35 U.S.C. § 271(e)(1) exempts acts of making, using, selling, offering for sale or importing a patented invention solely for uses reasonably related to the development of the submission of information under Federal law that regulates drugs.
- [52] 35 U.S.C. § 271(e)(2)(A).
- [53] 35 U.S.C. §155.
- [54] 35 U.S.C. § 156 (a)(4).
- [55] 35 U.S.C. § 156(c).
- [56] 35 U.S.C. § 156(c)(3).
- [57] This paper uses the term trademarks to refer to trademarks and servicemarks collectively.
- [58] Title 15, U.S.C.
- [59] Recent amendments that allow intent to use applications do not provide for registration until there is a bona fide use in commerce.
- [60] 15 U.S.C. § 1114(1).
- [61] 15 U.S.C. § 1125.

- [62] 15 U.S.C. § 1064.
- [63] 15 U.S.C. § 1114.
- [64] See commerce definition as defined in 15 U.S.C. § 1126.
- [65] 15 U.S.C. § 1052
- [66] 15 U.S.C. § 1064.
- [67] 15 U.S.C. § 1060.
- [68] This is considered a single-blind study.
- [69] This is a double-blind study.
- [70] Title 17, U.S.C.
- [71] 17 U.S.C § 102(a).
- [72] 17 U.S.C. § 102(b).
- [73] 17 U.S.C. § 106.
- [74] 17 U.S.C. § 107. Fair use is usually applicable in news reporting and educational settings.
- [75] 17 U.S.C. § 412.
- [76] 17 U.S.C. § 407.
- [77] 17 U.S.C. § 410.
- [78] 17 U.S.C. § 705(d).
- [79] 17 U.S.C. § 302.
- [80] 17 U.S.C. § 201(a).
- [81] 17 U.S.C. § 201(b).
- [82] 17 U.S.C. § 201(d).
- [83] See *SmithKline Beecham Consumer Healthcare, L.P. v. Watson Pharms., Inc.*, 211 F.3d 21, 29 (2d Cir. 2000) (No copyright infringement where label for generic version of Nicorrete gum was same).
- [84] Uniform Trade Secrets Act § 1 (4) (1985).
- [85] *Id.* at (2).
- [86] *Upjohn Co. v. Freeman*, 906 S.W. 2d 92, 101 (1995 Tex. App.).
- [87] *Id.* at 102 citing *Grundberg v. Upjohn*, 137 F.R.D. 372, 394-395. (D. Utah 1991)).
- [88] See *International News Service v. Associated Press*, 248 U.S. 215 (1918) (where news is deemed to be property as between the two parties but not as against the world).
- [89] See *Transkaryotic Therapies, Inc. v. Bain & Co., Inc.*, 2002 Mass. Super. Lexis 73, (2002).
- [90] *Id.*
- [91] *Hoffman-LaRoche Inc. v. Yoder*, 950 F. Supp. 1348, 1359 (S.D. Ohio 1997).
- [92] *Id.* at 1360.
- [93] *Id.* at 1361-1365.
- [94] 5 U.S.C. § 552(b).
- [95] *Public Citizen Health Research Group v. Food and Drug Administration*, 953 F. Supp. 400, (D.D.C. 1996)
- [96] *Id.* at 402-403.
- [97] *Pfizer Inc. v. ICI Americas Inc.*, 1984 Del. Ch. LEXIS 566, 12.
- [98] *Id.* at 15-17.
- [99] *Id.* at 17-18.
- [100] See *Ruckelshaus v. Monsanto*, 467 U.S. 986 (1984) (regulatory takings found where submission of information under the Federal Insecticide, Fungicide, and Rodenticide Act were done confidentially and then subsequent applicants were allowed to rely on those studies); See also Citizen's Petition filed by Pfizer Inc. and Pharmacia Corp at <http://www.fda.gov/ohrms/dockets/dailys/01/Jul01/073001/cp00001.pdf> (reliance on another's clinical trials without permission for a 505(b)(2) application is an unconstitutional takings).
- [101] U.S. Const. art. I, § 8, cl. 8.
- [102] By deriving this right from Art. I, § 8., cl. 8, Congress can avoid any problems where there is no interstate commerce. More specifically, the situation where a sponsor seeks to engage in clinical trials in the same state where the drug is manufactured need not file an IND.
- [103] Merely preventing a sponsor from collecting any revenues from a compulsory license fails to encourage disclosure of negative trials effectively as it allows a sponsor to do a cost-benefit analysis to decide whether he is better off foregoing a license fee if there is a positive result or whether he is better off letting a competitor potentially waste the same money if there is a negative result
- [104] The term Commissioner used herein shall refer to the head of the agency in charge of overseeing CT rights.
- [105] Perhaps this application would replace an IND application.