IS INFORMED CONSENT NEEDED TO USE CLINICAL TRIAL DATA IN PATENT APPLICATIONS?

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I. INTRODUCTION

Pharmaceutical companies are discovering new and more effective pharmacologic products for diagnosing, preventing and treating disease on an almost a daily basis. The Food and Drug Administration (FDA) requires manufacturers to demonstrate the safety and efficacy of these products through, among other things, the conduct of clinical trials that test the new product in human subjects.[1] These clinical trials establishing safety and efficacy of the new product are generally large, lengthy and conducted at multiple sites, because a single site cannot recruit patients in sufficient numbers to show a statistically significant difference between the new product and placebo for efficacy.[2] The conduct of clinical trials has now grown into a multi-billion dollar per year industry.

Most of the clinical trials that bring new drugs from bench to bedside are designed and financed by pharmaceutical companies (sometimes referred to as Sponsors) and conducted at academic research centers or commercially oriented networks of contract-research organizations (CROs) and site-management organizations (SMOs).[3] Some trials have four layers of involved organizations (pharmaceutical company, CRO, SMO and physician-investigator). Furthermore, separate academic medical centers are joining together to form clinical research network joint ventures.[4] These relationships between the Sponsors and academic institutions, CROs and SMO are generally governed by clinical trial agreements having strict intellectual property and confidentiality provisions in favor of the Sponsor.

The data that results from a clinical trial is generally stored centrally by the pharmaceutical company or CRO. Individual investigators may receive only portions of the data, or no data at all. Trial subjects are rarely, if ever, informed of whether they received the test product or a placebo during their participation in the trial. Pharmaceutical companies prefer to retain control over the analysis of all the data in large trial.[5]

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[1] See generally Chow S-C, Liu J-P, Design and Analysis of Clinical Trials John Wiley New York 1998 and Spilker B.A. The Drug Development and Approval Process (http://www.phrma.org).
[2] Bodenheimer, Thomas; "Uneasy - - Clinical Investigators and the Pharmaceutical Industry", The New England Journal of Medicine, Vol. 342, No. 20, pages 1539-1544.
[3] Bodenheimer, page 1540
[4] Bodenheimer, page 1541
[5] Bodenheimer, page 1541

Before a prospective subject is enrolled in a clinical trial, he or she must voluntarily consent to participate in the trial by signing an Informed Consent form in accordance with the provisions of FDA regulations set forth at 21 C.F.R Part 50. The Informed Consent forms generally do not place confidentiality obligations on the trial's subjects, but do place confidentiality obligations on the investigator and the Sponsor, as further described below.

II. USE OF CLINICAL TRIAL DATA IN PATENT APPLICATIONS

Patent applications, particularly in the chemical and biotechnology areas, have traditionally included working examples how the inventive materials are made and used or how the inventive processes are carried out. Such examples generally show the preparation of such compounds and then their specific use or uses. Clinical trial data is one way of showing such uses. It should be noted, however, that the clinical trial data necessary to demonstrate efficacy and safety for drug approval purposes for the FDA are considerably higher than the standard necessary to demonstrate patentable utility under 35 U.S.C. § 101.

Clinical trial data as used in patent applications can show dosing schedules and administration routes that otherwise would require extensive experimentation to determine. Thus, clinical trial data can, besides showing the inventive compound would be patentable utility, show enablement of how to use that compound.

Working examples that employ clinical trial data generally either refer to individual trial subjects anonymously (e.g. Patient A, etc.) or statistical compilations of many subjects' data. The data published in patent applications may be both measured effects and visibly observed effects. The data may compare before and after measurements or observations or comparison of the test compound to placebo.

III. INFORMED CONSENT IS NOT REQUIRED BY PATENT LAWS OR INTERNATIONAL PATENT TREATIES

The U.S. Patent Laws have certain requirements that must be met to obtain a U.S. Patent. These include patentable subject matters (35 U.S.C. §100); utility (35 U.S.C. §101); novelty (35 U.S.C. §102); unobviousness (35 U.S.C. §103); and certain formality requirements such as written description, enablement, best made and definiteness (35 U.S.C. §112). Informed consent of trial subjects whose personal data is included in the patent application is not a requirement of the U.S. Patent Laws.

Likewise, international patent treaties such as the Paris Convention and TRIPS do not have any requirement for obtaining informed consent of clinical trial subjects so as to use their personal data in patent applications.

IV. U.S. LEGAL REQUIREMENTS FOR INFORMED CONSENT IN NON-PATENT AREAS

A. The Common Rule

Under the "Common Rule" applicable to seventeen federal agencies whose responsibilities cover areas involving human subject research, including the FDA, "adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data must be made."[6] FDA institutes this mandate by requiring that Informed Consent forms include a statement describing the extent to which the confidentiality of records identifying the subject will be maintained.[7] Furthermore, Institutional Review Boards (IRBs), the independent boards charged with ensuring that appropriate safeguards exist to protect the rights and welfare of research subjects, must consider the protection of each subject's privacy among these safeguards. [8] Accordingly, Informed Consent forms generally contain a provision which describes (1) who will have access to the subject's data, (2) how the data will be used, and (3) the extent to which the data could be disseminated. A typical provision follows:

> All the personal information that you provide during the course of the study will remain confidential. Information from this study will be submitted to Sponsor. Medical records which identify you and the consent form signed by you may be inspected and/or copied by the U.S. Food and Drug Administration, the Sponsor and its representatives and the IRB. The results of this research study may be presented at meetings or in publications. Your identity will never be revealed in those presentations. You should understand that Sponsor has an economic interest in using the information and results from you and other study participants for the development of commercial products that may help others by improving the diagnosis and treatment of various medical problems. Sponsor may patent products or sell discoveries based on this research. By signing this consent form you authorize access to this confidential information and state that you understand that you and your heirs will not be compensated in any way for Sponsor's use of this information in the future.

B. HIPAA

New federal regulations promulgated under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) will affect the research institutions that conduct clinical trials on Sponsor's behalf. HIPAA prohibits covered entities (as defined by HIPAA) from disclosing specific identifiable health information (PHI) without satisfying HIPAA's requirements designed to protect patient confidentiality. While, in general,

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[6] 45 C.F.R. 46.111(a)(7).
[7] 21 C.F.R. 50.25 (5)
[8] 21 C.F.R. 56.107(a) and 56.111

research institutions will be "covered entities" and Sponsors will not, HIPAA will affect the research institution's ability to disclose research subjects' PHI to the Sponsor.

Under HIPAA, in addition to the Informed Consent form described above, in clinical trials that involve treatment the research institution must obtain from each subject an authorization that permits the disclosure of the subject's PHI to the Sponsor and the Sponsor's use of the PHI (Authorization).[9] Furthermore, the Authorization must (1) describe the extent to which the PHI will be used or disclosed for treatment, payment or healthcare operations, (2) describe any additional restrictions on the use or disclosure of the PHI to be adhered to by the research institution beyond that required by HIPAA, (3) refer to any applicable consent and/or privacy notice given to the subject and clearly state that the Authorization is binding, and (4) disclose, if applicable, if any financial benefit was given to the research institution by the Sponsor in exchange for disclosure of the PHI to the Sponsor.

One exception to the requirement to obtain the Authorization is for information that has been "de-identified." HIPAA lists eighteen specific identifiers, including birth date, hospital admission and discharge dates and social security numbers, that must be removed from the health information to be considered de-identified. Accordingly, if the Sponsor is not collecting this information, it is not necessary for the research institution to obtain an Authorization. However, most of the information listed above is critical in making valid conclusions about the safety or efficacy of the product in the trial or for, in the case of social security numbers, uncovering fraud on the part of the investigator. Accordingly, in most instances, an Authorization will be necessary.

Subjects may revoke their Authorization at any time. Although research institutions may condition its providing research related treatment on continuing authorization, once the subject is no longer receiving treatment, the subject may withdraw authorization. Potentially, the subject could prevent the research institution from releasing any additional PHI to the Sponsor after the subject has completed treatment, which could have serious implications for clinical trials that assess the long-term effects of an experimental treatment. While this issue remains controversial, it may be subject to further revision prior to the HIPAA implementation date in April 2003.

V. PRACTICE TIPS

A. Patent Use Clauses in Informed Consent Forms

The Sponsor and patent drafter should confirm that all of the trial subjects (whose data is to be used in the patent application) have signed appropriate Informed Consent forms (and Authorizations, if needed) that include a release to use that data in patent applications. The release provision should be the same or similar to that provided above. The patent drafter should be aware of the possibility that test subjects can revoke their

[9] 45 C.F.R. 164.508

Authorization at any time; however, since the Authorization permits the Covered Entity (i.e. the physician-investigator) to disclose PHI, PHI that has been disclosed to the Sponsor prior to the revocation cannot be retrieved.

B. Use of U.S. Clinical Trial Data in Patent Applications

The drafter of the patent application should obtain a summary of clinical trial results from the Sponsor that maintains the confidentiality of the research subjects. Furthermore, the patent drafter, after completing the patent application, should reconfirm that the clinical trial data that is in the patent application does not disclose the identity of any of the trial subjects.

C. Use of Non-U.S. Clinical Trial Data in Patent Applications

If the patent application is to include data from clinical trials outside the U.S., the patent drafter should confirm that the data received and to be used in the application was acceptable under the laws relating to collection and dissemination of personal data in that country or countries. The European Union has provided the benchmark in this area through its Data Protection Directive.

In summary, the Sponsor and the drafter of a U.S. patent application should ensure the trial investigator has taken all of the proper steps to release the data to them and that the Sponsor and drafter of the patent application are free to use the data given them in any manner to obtain patent protection as long as the trial subjects' identity is not disclosed.