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BioInsights

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Biotechnology Disputes with Investigators over Publication of Clinical Trial Data

Below are just two examples of the ongoing conflict between the research community's need to publish and the pharmaceutical/ biotechnology industry's need to maintain the confidentiality of the studies it sponsors during drug development.

Immune Response Corporation's HIV Drug Remune

Immune Response Corporation ("IR") recently entered into arbitration in a dispute with the University of California at San Francisco and a member of its faculty, Dr. James Kahn, requesting that the arbitrators order UCSF to pay up to $10 million in damages for violation of its confidentiality obligations. The dispute centers on Dr. Kahn's publication of clinical data from a clinical trial of IR's HIV drug, Remune, over IR's objections. At issue is whether a 250 patient sub-analysis should have been included in the results of the 2,527 patient study. IR believes that failure to include the additional analysis was scientific misconduct, while Dr. Kahn believes that the additional analysis was misleading. After several months of IR refusing to provide all the study data to Kahn and the other researchers, and Kahn refusing to include the sub-analysis, IR filed a request to have the dispute settled by a panel of arbitrators, as provided in the agreement between the parties.

Despite IR's attempts to prevent the study's publication, the researchers submitted the results to the Journal of the American Medical Association, which published them on November 1. Following publication, IR saw a 25% one day drop in its stock's value. IR is now looking to a panel of arbitrators to order the University and Kahn to pay up to $10 million in damages and prohibit Kahn from using the data in the future.

While the arbitration's outcome is uncertain, it is apparent that despite an agreement to the contrary, Immune Response was unable to prevent publication of its study results.

Boots Pharmaceuticals, Inc.'s Synthroid Bioequivalence Study

Several years before the Remune dispute, the University of California at San Francisco was involved in a strikingly similar dispute. In 1987, UCSF researcher Dr. Betty Dong entered into a collaboration with Boots Pharmaceuticals, Inc. to study whether rival thyroid replacement drugs were bioequivalent to Boots's market leading Synthroid. Based on the results of the study, Dr. Dong concluded that the rival products were bioequivalent to Synthroid. In 1995, Boots prevented Dr. Dong from publishing her results and conclusion based on the standard contract Dr. Dong had signed that prevented her from publishing without Boots's consent. When Boots and Dr. Dong were unable to reach agreement on data interpretation, UCSF, faced with the likelihood of a breach of contract action and the possibility of significant damages, urged Dr. Dong to comply with the publishing rights clause, or litigate with Boots without the support of UCSF. Dr. Dong withdrew her article from publication in the Journal of the American Medical Association. Boots later published a repudiation of Dr. Dong's unpublished work, citing numerous flaws in the study methodology that made bioequivalence conclusions impossible. Under pressure from the FDA, Boots eventually entered into negotiations with UCSF to allow publication of Dr. Dong's article, despite Boots's continued stance that the conclusions from the study were not supported by the data.

PUBLICATION PROVISIONS IN RESEARCH AGREEMENTS

While the ethical and legal debate over investigator's interpretation and publication of clinical study data is likely to continue for some time, as suggested by the Immune Response dispute and the ensuing public interest in the dispute, it is imperative that pharmaceutical and biotechnology companies that engage universities and institutions to perform research and clinical studies take appropriate measures to best protect their confidential information and trade secrets. Since publication of confidential information may serve as a statutory bar to patent protection and result in loss of trade secret protection, particular focus must be paid to the publication clause of all research agreements.

Publication clauses should always provide the sponsor with the prior opportunity to review and comment on any public disclosure (including any publication, poster session, abstract, manuscript and grant application) related to the research or study to: (1) afford the sponsor with an adequate opportunity to file patents on any patentable material that may be contained in the proposed publication, and (2) ensure compliance with the agreement's confidentiality provisions by permitting removal of sponsor's trade secrets from the proposed publication.

Protecting Patentable Inventions

Under the United States' patent laws, an inventor will be denied a patent if, more than twelve months before filing the patent application, the inventor disclosed the invention in a printed publication in the United States or a foreign country. Other countries do not grant the inventor a grace period following disclosure for filing the patent application.

The sponsor's rights to review publications must extend to presentations because the delivery of a speech at an academic conference may constitute or result in a printed publication. In addition, the sponsor should have the right to review any manuscripts, abstracts, poster sessions and hand-outs for teaching purposes that relate to the research study, and any other dissemination of the invention that may be accessible to the public, including information that may be accessible to the public through the Freedom of Information Act, such as grant proposals. Since dedication of an invention to the public is the basis for the publication bar of the Patent Act, disclosure of the knowledge of an invention to another without securing a commitment of confidentiality may be considered dissemination of the invention to the public because the inventor no longer controls the knowledge of the invention.

The sponsor should request a copy of the patent and publication policies of the university or institution and thoroughly consider the impact such policies may have on the agreement's confidentiality and publication provisions; particularly if the agreement is "subject to" such policies. Reasonable patent policies generally provide for a short delay in the publication of research results for patenting purposes and sponsor's review of confidential information, but the university will be reluctant to agree to any provision that permits suppression of the publication or the sponsor's right to impose substantive changes in the publication.

Protecting Trade Secrets

Finally, the sponsor should take all appropriate measures to limit public disclosure of its trade secrets and proprietary information, including clinical data, by: (a) limiting access to only those investigator's who have a need to know; (b) discussing confidentiality at the outset with each clinical investigator; (c) requiring that each investigator sign a confidentiality agreement or ensuring that each investigator have a written agreement with the university or institution; (d) prohibiting the photocopying of proprietary documents, including, except to the extent necessary to conduct the study, study data; (e) monitoring access by maintaining logs of the nature and scope of disclosure; (f) limiting the scope of proprietary information to only that information that is necessary for the individual investigator or researcher to perform the contract services; and (g) marking documents as "proprietary" or "confidential".

A well-drafted publication clause will strike a fair balance between the sponsor's interest in protecting its patentable information and trade secrets and the university's general commitment to openness in research and publication of results.

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Clients in the News

CAS Medical Systems, Inc. (Branford, CT) a medical device company listed on NASDAQ, acquired Mallinkrodt, Inc.'s sleep apnea monitor product line.

Epigenix, Inc., a New Haven based start-up focusing on transgenic animal models, recently closed a $1 million seed financing from a European investor.

Pharmacia Corporation (Peapack, NJ) announced that it will spin off its Swedish metabolic disease research activities and plasma products business to a new company named Biovitrum AB. Biovitrum's expected value will rank among the top 5 in European biotech companies.

Karo Bio AB (Stockholm) announced a two year extension of its collaboration with Merck & Co., Inc. for the discovery, development and commercialization of ligands to estrogen receptors. The collaboration has been successful in design and synthesis of selective compounds that in pre-clinical studies have led to prioritization of clinical indications for further development.

Karo Bio AB (Stockholm) announced that its subsidiary, Karo Bio USA, Inc. entered into a strategic alliance in infectious disease with Aventis Pharma, Aventis S.A.'s global prescription drug business. Through the alliance, which was valued at more than $32 million, Karo Bio agreed to provide Aventis with access to the company's proprietary BioKey drug discovery technology for targets identified through Aventis' genomics programs.