disease result from the deficiency of hepatic-specific enzymes or proteins. Therefore, the introduction and expression of human genes in hepatic cells has become an active field of investigation. For these diseases, somatic gene therapy may be accomplished by the isolation and culture of hepatocytes obtained by partial hepatectomy, modification of these cells by introduction of the normal gene using retroviral vectors, and transfer of the corrected cells into the liver by transplantation or by direct injection. Thus, retroviral vectors have been used successfully for the *in vitro* transfer of recombinant genes into primary cultures of mouse, rat, and rabbit hepatocytes. Retroviral vectors also have been used to introduce genes, by stable means, into skin fibroblasts, keratinocytes, endothelial cells and muscle cells, thus demonstrating the feasiblity of accomplishing somatic gene therapy for a wide range of inherited metabolic disease.

Lastly, it should be noted that somatic gene therapy is no longer the "stuff of science fiction" , and the first human gene therapy protocols have recently been approved by the NIH and clinical trials have begun. The first approved trial for human gene transfer was not for the treatment of an inherited metabolic disease, but involved the use of a retrovirally transfered marker gene to determine the *in vivo* fate of tumor infiltrating lymphocytes (TILs) administered to patients with malignant melanoma. The first human trial of somatic gene replacement for an inherited metabolic disease also was approved in October of 1990 and was recently undertaken at the NIH. An adenosine deaminase (ADA) deficient 8-year old girl with Severe Combined Immune Deficiency is currently receiving infusions of T lymphocytes that have been modified by infection with a retroviral cosntruct expression human ADA. If these studies prove safe and effective, the next step will be transplantation of this patients genetically modified bone marrow stem cells. Suffice it to say, human gene therapy has begun, albeit by small first steps. It is likely that the feasibility of this approach to cure certain gene disorders will be demonstrated in the near future.

HIDDEN ISSUES

IN

PATENTING BIOTECHNOLOGY AT COLLEGES AND UNIVERSITIES

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[2] The section entitled "Trade Secret Protection at Colleges and Universities" was written by Steven McDaniel. During the writing of this article he served as a legal intern at Baylor College of Medicine while a student at the Bates College of Law of the University of Houston. He is currently a patent agent at the Houston law firm of Arnold, White and Durkee, and will join that firm as an associate upon graduation.

INTRODUCTION

This article addresses selected issues regarding the patenting of inventions made at colleges and universities. While these concerns are shared by patentees from other venues, they are of particular importance to university technology administrators and licensing officers and to patent lawyers who represent academic institutions with respect to intellectual property matters. Particular focus is directed to aspects of the patenting process which are often overlooked in an academic setting, and how the patenting process must be coordinated with so called "technology transfer" programs under which schools bring to the marketplace inventions made in their laboratories.

COLLABORATION AMONG SISTER INSTITUTIONS

Scientific advances, particularly those in the field of biotechnology, often involve the active collaboration of researchers at different institutions. Due to the confidential nature of the process by which inventions are patented and commercialized by colleges and universities, instances have arisen in which one institution has alone proceeded with patenting an invention unaware of the inventive contribution of scientists at a sister institution. It is even possible, without proper coordination, for two institutions, each of which receives the disclosure of the making of an invention from one of its scientists, to independently initiate the filing of a patent application on the identical invention or on separate components of one invention without knowing that the other institution is proceeding with the same exercise. This is particularly likely to occur in instances in which an institution's licensing officer or its patent counsel have not been told that a co-inventor either does not have a full time appointment at the client

institution or is affiliated with another school. This co-inventor may have assisted in the making of the invention in his laboratory at his own school with minimal contact with collaborators at the client institution or he may have conceived the essential elements of an invention while serving as a visiting professor at the client school at which the disclosure is made. Alternatively, the co-inventor may have conceived of the invention while on the faculty of one school and resigned his appointment, thereafter transferring to the client institution. In each of these instances, the co-inventor may have loyalties to two or more institutions, and these schools, in turn, may have claims to ownership of all or a portion of the co-inventor's work product. For these reasons, patent counsel should be ever sensitive to both multi-institutional appointments and actual collaboration among or between investigators at separate institutions. At a minimum, counsel should require all co-inventors to provide current resumes which detail all faculty affiliations for several years before the alleged date of the making of the invention.

At the first indication that researchers from different institutions may be involved in the making of an invention as co-inventors or that an inventor may have obligations to more than one institution, the patent attorney should promptly contact the technology administrators or licensing officials at each of the institutions to determine whether their schools have rights to the invention. Conflicts of interest which may arise as a result of common representation by a single attorney of two potentially divergent interests should be kept in mind. Barring such conflicts, the attorney should also review the patent and royalty policies of each institution to determine the respective rights of the institutions and their scientists to the subject invention. This investigation will inevitably lead to a consideration as to which attorney should handle the drafting and prosecution of the patent application and how the institutions will share the

substantial fees and expenses related to the patenting process. If the institutions have adopted progressive patent licensing policies, consideration may also be given to how the institutions and their scientists will share in any income realized from the commercialization of the invention. It may be advisable at this time as well to determine percentage of inventorship as to each individual inventor in order to anticipate future disagreements.

The question of institutional coordination is further complicated if state colleges, universities and research facilities are involved. Regarding the choice of patent counsel or the expenditure of monies for patenting an invention, many state institutions are subject to strict legislative or regulatory mandates which severely restrict or even prohibit the use of outside lawyers and other specialists for patenting and commercializing inventions which are made in state laboratories, by state employees or with the use of state owned equipment.

By addressing all of these issues at the first meeting with the inventors or the institution's technology administrator, the attorney will increase the likelihood of being able to contact the appropriate persons within each of the institutions involved and, thereby, promptly resolving any issues which may arise. This definitely should take place before the lawyer has committed time and effort to a project only to learn that another institution has primary responsibility for the project or, more importantly, that another lawyer, such as a member of a state university's legal staff, is required to prosecute the patent.

If two institutions own rights to an invention, it is essential that they coordinate every aspect of the patenting and commercialization effort. Following this section is a short form of cooperative agreement between sister schools governing the patenting and licensing of an invention which was made through the collaboration of inventors at two institutions. While

institutions and their administrators often find such abbreviated agreements more palatable than their lengthy counterparts, it may be advisable to augment such a basic form with clauses which address concerns which are unique to the schools involved. At a minimum, as with any collaborative effort of this nature, it is strongly suggested that one institution be given authority to oversee both the prosecution and licensing of the patent and related technology. Valuable time will be lost if both institutions each have to approve the filing of responses to office actions, the payment of fees or the terms of a license agreement. As experienced counsel and administrators know, it is often difficult and time-consuming to obtain approvals and checks for the payment of fees from academic institutions. This can be particularly vexing when the attorney is faced with a filing or other legal deadline.

Sample University Invention Cooperation Agreement

AGREEMENT

This Agreement, effective_____, 1999, by and between (INSTITUTION #1) (ADDRESS FOR INSTITUTION #1) and (INSTITUTION #2,) (ADDRESS FOR INSTITUTION #2) is made with reference to the following:

Employees of (INSTITUTION #1) and (INSTITUTION #2) have jointly made inventions and improvements entitled [INVENTION NAME], ("Proprietary Property"), and (INSTITUTION #1) and (INSTITUTION #2) desire to pool and jointly develop and commercialize their respective interest in the Proprietary Property for the purpose of providing for (i) unitary working, marketing, assigning, or licensing of the Proprietary Property, (ii) the allocation and payment of expenses incurred in obtaining and maintaining patent protection for the Proprietary Property and (iii) the receipt and division of royalties, fees, equity interests, revenues and other consideration received or derived from the licensing, sale or other commercialization of the Proprietary Property in proportion to their respective interests, all as hereinafter set forth.

Now, therefore, (INSTITUTION #1) and (INSTITUTION #2) agree as follows:

1. "Proprietary Property" shall mean and include the inventions disclosed and claimed in the applications for letters patent set forth on the attached Exhibit "A", and any divisional, continuation or continuation-in-part, renewal, extension, and reissue applications thereof and any patent or patents issuing therefrom.

2. The parties hereto agree that title to the Proprietary Property shall be assigned to and held by and in the name of (INSTITUTION #1). In view of time requirements in filing the aforementioned patent applications, employees or faculty members of (INSTITUTION #2) who are co-inventors of the Proprietary Property shall made direct assignments of such patent applications to (INSTITUTION #2). (INSTITUTION #2), however, recognizes that in order to properly commercialize the Proprietary Property, (INSTITUTION #1) should be vested with complete authority to apply for patents on the Proprietary Property and to take such other action as may be necessary or desirable to sell, assign, license or otherwise deal in the Proprietary Property.

3. (INSTITUTION #2) agrees to sell, assign and convey and hereby sells, assigns and conveys to (INSTITUTION #1) all of its right, title and interest throughout the world in and to the Proprietary Property and in and to the aforementioned application for a patent and any and all patents which may be granted therefore as well as any and all divisions, reissues, continuations, continuations-in-part and extensions thereof. (INSTITUTION #2) also agrees to sign and require all inventors who are employees or faculty members of (INSTITUTION #2) to sign all lawful papers, to execute all oaths and to do everything else possible to aid (INSTITUTION #1), its successors, assignees and nominees to obtain and enforce proper patent protection for the Proprietary Property.

4. (INSTITUTION #2) agrees that (INSTITUTION #1) shall have control of the working, selling, assigning, or licensing or otherwise dealing with the Proprietary Property; however, (INSTITUTION #1) shall consult with (INSTITUTION #2) and carefully consider any information or requests of (INSTITUTION #2) made to (INSTITUTION #1) concerning the same before proceeding with the working, selling, assigning or licensing thereof.

5. (INSTITUTION #1) and (INSTITUTION #2) agree that profits, royalties, or other revenues received from working, selling, assigning, licensing or otherwise dealing with the Proprietary Property shall be divided between the parties hereto in proportion to their respective interests, and that all legal fees and expenses and all other costs and expenses paid by (INSTITUTION#1) incident to obtaining and maintaining patent protection for the Proprietary Property shall be paid by the parties in proportion to their respective interests, which interests are as follows:

(INSTITUTION #1) - seventy-five percent (75%)
(INSTITUTION #2) - twenty-five percent (25%)

In the event that (INSTITUTION #1) enters into an agreement with an entity in which (INSTITUTION #1) together with its affiliates owns a controlling interest (fifty percent or more) for the licensing or other commercialization of the Proprietary Property, (INSTITUTION #1) agrees to re-negotiate the foregoing percentage interests of the parties in the Proprietary Property upon request by (INSTITUTION #2). (INSTITUTION #1) will remit to (INSTITUTION #2) its share of such profits, royalties or other revenues within thirty (30) days of receipt thereof.

6. (INSTITUTION #1) agrees to keep accurate records and books of accounting in accordance with good accounting practice with respect to the Proprietary Property, including an account of all (i) costs and expenses incurred in obtaining and maintaining patent protection for the Proprietary Property and (ii) all moneys or other consideration received by (INSTITUTION #1) during the calendar quarter for which it is accounting and all other information necessary for the accurate determination of charges and payments hereunder. (INSTITUTION #1) agrees to deliver to (INSTITUTION #2) within thirty (30) days following each calendar quarter a report setting forth such details as may be necessary for the accurate determination of charges and payments hereunder, and, in the case of payments, to accompany each such report with the payments shown to be due by it. (INSTITUTION #1) agrees to permit a representative of (INSTITUTION #2), during normal business hours, to inspect any all parts of the records kept by (INSTITUTION #1) which are relevant to a determination of the accuracy of any report required to be rendered to (INSTITUTION #2). (INSTITUTION #2) agrees to pay its share of all costs and expenses within thirty (30) days of receipt.

7. (INSTITUTION #1) and (INSTITUTION #2) agree that they will and will cause their employees and inventors to sign all lawful papers, execute all divisional, continuation, renewal, extension, and reissue applications, and make all rightful oaths and generally do everything proper to aid in obtaining and maintaining proper patent protection for said Proprietary Property. (INSTITUTION #1) and (INSTITUTION #2) also agree that they will properly discharge their responsibilities to their employees as set forth in their administrative policies governing the sharing of income or other considerations received in respect of the commercialization of inventions, patents or other manifestations of intellectual property.

8. (INSTITUTION #2) and (INSTITUTION #1) acknowledge that substantial additional research must be undertaken to explore further the potential of and to develop the Proprietary Property. In this respect both parties agree that they will use reasonable efforts to actively seek or cause their employees who invented the Proprietary Property to actively seek funding from potential sponsors of research, both private and public. Both (INSTITUTION #2) and (INSTITUTION #1), each further agree that in the event that they successfully secure research funding they will endeavor, to the degree permitted by the sponsor thereof, to subcontract to the other party certain aspects of such additional research which cannot be handled internally so as to enable the other party to actively participate in such continuing research.

9. For the purpose of accounting and other matters relating to the subject matter hereof, the addresses of the parties hereto are as follows:

(INSTITUTION #1)
ADDRESS
Attention: Oscar T. Shepler, Vice President for
Finance and Administration

(INSTITUTION #2)
ADDRESS
Attention: Christine K. Phillips
Office of Sponsored Programs

to such subsequent address as any party hereto may furnish the other party hereto in writing.

10. It is understood that this Agreement contains the entire agreement between the parties hereto. This Agreement shall be binding on and shall inure to the benefit of the parties hereto, their respective assigns and successors in interest.

(INSTITUTION)

BY_____

(INSTITUTION)

BY_____

INVENTORSHIP

Questions of inventorship for purposes of patent law can be challenging to patent attorneys. They are charged with the duty of drafting appropriate specifications and claims to properly protect the invention. In addition, they must identify, from among the many researchers who contributed their creative skills and labor to the project which resulted in the invention, those key persons whose contribution to the making of the invention is legally sufficient to qualify them to be listed as inventors on the patent application. While working with the principal inventor, the patent attorney is likely to learn that each researcher who was involved in an overall project may insist that the real value of his or her contribution be fully recognized, and these scientists may want both the professional satisfaction and economic benefits under a progressive technology transfer program that accrue to those whose names appear on the face of the patent.

The problem of defining inventorship can be particularly vexing in an academic setting where the basic principles of collaboration are an integral component of the philosophy of the institution, and where investigators commonly add as co-authors on papers many scientists whose contribution to an overall project may have been peripheral. Typically, a principal investigator will add as co-authors on a paper not only his direct collaborators, but also laboratory assistants, fellows and students in his laboratory. This collegial philosophy may result in extending credit and acknowledgment for contributing to scholarly achievement beyond the laboratory of the primary author or authors to include researchers in other laboratories at the school or other institutions. This spirit of properly sharing credit for the fruits of scholarly endeavors is brought home most vividly to the patent attorney who receives a written disclosure of the making of an

invention which lists as inventors not only the principal investigator on a long-term research project which was funded by external sources, but also key members of his research team. These members may include: (i) those persons who were actively engaged in the project, often over the life of a long-term grant; (ii) colleagues at sister institutions who may have provided technical assistance or biological materials used in the experiment and (iii) fellow scientists who made essential laboratory space or equipment available for the unfettered use of the researcher and his team. Finally, the researcher may have added the chair of his/her department as a co-inventor to acknowledge the significant technical and financial support he/she provided to the overall project.

In this atmosphere, it is essential that the patent attorney charged with the task of drafting a patent application for a university client address the question of inventorship promptly. First, memories fade with time. As with the veracity of the testimony of fact witnesses in a lawsuit, the fresher the recollection, the clearer the testimony. In the context of patenting an invention, the sooner after the making of the invention each researcher is asked about his role and the roles of each of his colleagues, the greater the likelihood the answers will be accurate. Second, academic researchers are a creative and restless breed. They travel widely and frequently to meet with colleagues, present papers, serve on study groups, and review projects with colleagues and sponsors of research, so they may be unavailable when they are most needed. More junior scientists also frequently transfer to other institutions on short notice to pursue other career opportunities or to expand their training or laboratory skills. Accordingly, their new job responsibilities may preclude their actively assisting the patent lawyer on matters related to their former institution. A scientist who is named as an inventor on a disclosure may have been a

visiting professor from abroad and he may be preparing to return home to a country which is blessed with a primitive telephone system. He also may speak very limited English and lose his effectiveness in addressing highly technical matters in the absence of his American colleagues. Finally, professional rivalries, both within and between academic institutions, may further cloud the inventorship issue and cause inventors to overlook the significant contribution of a former research associate or colleague. In any event, questions of inventorship are best addressed at the outset.

Attention should be focused not only on the researchers whose names appear on the form by which the invention is formally disclosed to the school and those who directly assist the patent lawyer with drafting the patent application, but also on other scientists from both within and without the client institution who may have played a significant role in the making of the invention. Particular attention should be paid to authors of the prior art within the client institution or those with whom the named inventors may have interacted on critical elements of the invention. The attorney should be particularly vigilant for laboratory techniques or cell lines, plasmids, compounds or other biological or chemical materials which were used in or are a part of the invention and which were supplied by colleagues in sister laboratories or by researchers at other institutions. Any of these scientists may have played a role in the project which led or contributed to the making of the invention.

All named inventors and members of the research team which led to the making of the invention must be educated about the importance of inventorship under patent law. They must be told that the improper designation of inventors on the patent could lead to a determination that the patent is invalid. They should be told that while the input of the inventors themselves is

essential to a determination of inventorship, inventorship is a difficult legal issue which cannot be allocated by the scientists themselves or resolved by the chair of the department or the administration of the institution. Inventorship must be determined by the patent attorney after all elements of the invention have been fully and accurately defined and the attorney has completed a full investigation of the relevant facts surrounding the making of each component of the invention. The scientists involved must be encouraged to come forward with all facts surrounding inventorship with the same candor and diligence with which they must examine the prior art, and they should be required to produce all documents--laboratory notebooks, articles, minutes of meetings--which may bear on defining the invention or help resolve the issue of inventorship.

The attorney should explain to the investigators that there are levels of contribution to an overall scientific effort and that not every member of a laboratory research team must automatically be designated as an inventor simply because he was part of the overall collaborative effort. The attorney must encourage all putative inventors to draw distinctions between (i) those who contribute to the original and non-obvious idea that results in the conception and, possibly, reduction to practice, of the invention as ultimately claimed in the patent application, (ii) those who perform or supervise standard laboratory tasks, (iii) those who manage the laboratory or provide equipment and services and (iv) those who contribute ideas and create suggestions to the overall project. The scientists must also be instructed to distinguish between when they followed the orders and advice of others or utilized a standard method for performing a particular laboratory procedure in the customary application. They must be encouraged to reveal not only with whom they worked directly, but to highlight instances in which they sought assistance from

colleagues or consulted the literature about an element of the invention. In short, they should provide a detailed, first-hand narrative of what they did and how they interacted with other members of the research team and other scientists. In particularly sensitive instances, such as those in which the principal investigator on a research grant disputes the contribution of a colleague and his status as an inventor, each inventor should be required to reduce to writing exactly what he did and what creative ideas he had.

The ultimate test for defining the inventorship issue is from the standpoint of the invention as strictly defined by the claims in the patent as filed, prosecuted and issued, not from the standpoint of who was most productive on the project which led to the invention or who contributed to the invention as it was initially disclosed to the school. Further, it will be easier to work with the inventors if each claim is explored in detail as to the contribution of each inventor on a claim-by-claim basis, rather than addressing the question more broadly in the vaguely defined context of "who was part of the team" which explored the many aspects of a project and ultimately produced a broadly defined invention. This focus on claims also makes it easier for an attorney to delete an inventor during the prosecution of a patent when claims must be deleted.

The question of inventorship must be continuously addressed throughout the patenting process as elements of the invention and claims are added or discarded. This can be in response to office actions, when claims are amended or deleted to avoid prior art uncovered by the Patent Office, or in response to a restriction requirement by which the claims of one inventor are made the subject of a separate application. This may also occur as a result of the discovery of prior art by the attorney or the inventors. In any event, any of these actions may require the deletion

of the inventor of the claim or claims which must be dropped or made the subject of a separate patent application. Particularly troublesome questions concerning inventorship should be brought to the attention of the examiner so that he may fully explore and possibly assist in the resolution of this issue. If inventorship has been changed or if possible co-inventors have been excluded as inventors during the prosecution of the patent, upon receipt of notice of issuance, the attorney should again encourage all listed inventors and other investigators to revisit the issue. Finally, it should be noted that inventorship can be changed during the prosecution of a patent or after issuance provided that there was no intent to deceive as to the identity of the true inventors.

FEDERAL GRANT APPLICATIONS - A WORD OF CAUTION

Biotechnology lawyers and scientists, particularly those active in genetics, have followed with great interest the case of E.I. DuPont De Nemours vs. Cetus Corporation which is currently pending in the United States District Court for the Northern District of California. This case concerns the validity of the patent on the process of polymerase chain reaction ("PCR") which teaches an experimental process of replicating genes. In December, 1991, Judge Marilyn Hall Patel, in an as-yet unpublished opinion, ruled on a motion for summary judgment by DuPont that a National Science Foundation grant proposal submitted concerning the contested process constitutes prior art and invalidates the patent under 35 U.S.S. §102(b). Cetus argued in opposition that the subject grant proposal was not properly indexed so as to be accessible to the public and to constitute a printed publication. In ruling, Judge Patel found as follows:

> The court finds that there is ample undisputed evidence of the accessibility of the NSF Grant Proposal to the relevantly skilled and interested public, and that the law does not require the strong showing of "highly likely discovery of the prior art" suggested by defendant during the pre-trial conference. The court concludes that no jury could

> reasonably find that the NSF Grant Proposal was not prior art within the meaning of section 102(b). In addition, on the basis of the same arguments and considerations, it concludes that no jury could reasonably find that the NIH Grant Application was not prior art within the meaning of section 102(b). Therefore, the only issue remaining for trial is whether this prior art anticipated the patents under section 102, or otherwise rendered them obvious under section 103.

Accordingly, Judge Patel then ruled that,

> For the above reasons, the court concludes that there are no underlying factual disputes and that, the Khorana NSF Grant Proposal and the Khorana NIH Grant Application were not accessible to the relevant public prior to March 28, 1984... as a matter of law... the two documents are prior art within the meaning of 35 U.S.C. §102(b). (1990 U.S. Distr. Lexis 18382).

If this ruling is allowed to stand on appeal, and if it is extended to apply to all grant applications and not just grant applications which were filed with the NSF at the time relevant to the application which allegedly disclosed the essential elements of the PCR process in this case, it will establish a troublesome precedent which must be addressed by Congress. In this context, it should be noted that the Khorana application may have been submitted during a period in which grant applications were not accorded the confidentiality which presently attaches to all grant applications. This holding may also severely hamper the ability of federal grantee institutions to obtain patents on inventions which are made under federally sponsored research projects. At a minimum, attorneys who prosecute patents on behalf of universities and other beneficiaries of federal grant support will have to include a detailed review of all grant submissions as an integral part of the study of the prior art.

In light of the uncertainty surrounding this issue, until this matter is finally resolved, investigators who intend to seek federal grant support for their laboratories for projects which may have commercial potential or may result in the making of patentable inventions are encouraged to seek the assistance of patent counsel. It may be advisable to file a patent

application on methods, compounds or other patentable aspects of the proposed research protocol before the filing of the grant application, or to write the grant application so that essential enabling elements of an invention are not fully disclosed, provided that this later alternative is practical without vitiating the effectiveness of the grant application. It may also be advisable from a legal standpoint to indicate in the cover letter which accompanies the grant application that it contains trade secrets and other proprietary information and that the grant application must be held in strictest confidence. This approach may, however, be offensive to academic researchers who would prefer that nothing which might be viewed as being unique or, more importantly, inappropriate for an academic institution, accompany their grant submissions.

REPORTING REQUIREMENTS - Invention Supported in Whole or in Part by Federal Funds

Attorneys prosecuting biotechnology patents on behalf of their institutional clients, whether they be colleges and universities, medical research foundations or charities, should be particularly vigilant for the presence of federal funding of all or a portion of a research project which produces a patentable invention. Accordingly, the attorney should conduct a thorough investigation of the funding underlying the project under which an invention was made.

If federal funds have been used in the making of an invention and if the institution wishes to acquire title to the invention, it must comply with the Public Law 96-517 and Public Law 98-620 which are implemented in 37 Code of Federal Regulations 401 et seq. (see also the Federal Register of March 19, 1987 at pages 8552-8563). Briefly, these regulations require a grantee institution which wishes to retain title to a sponsored invention to do the following: (i) within two (2) months of the disclosure of the invention by the inventor to the institution's licensing

office, notify the National Inventions Office of the NIH of the making of the invention, (ii) within two (2) years of receipt of the disclosure, file a written election to retain title to the invention and patents, (iii) provide the NIH and the sponsoring agency with copies of all patent applications filed (and as subsequently granted), (iv) grant the sponsoring agency a royalty-free license to use the invention and (v) include on the face of the patent application a legend acknowledging federal sponsorship. All notices and required documents should be sent to the NIH at The National Inventions Office, Extramural Inventions Office, Building 31, Room 5B-33, Bethesda, MD 20892. The attorney should also remind the grantee institution and the principal investigator on the grant (who, incidentally, may not be an inventor for patent law purposes) of his independent, but equally important, obligation to report promptly the making of the invention to the grantor agency. It is also suggested that the principal investigator report the making of the invention in his annual progress report to the agency. The attorney should retain copies of these reports since they may contain information which will be helpful in the prosecution of the patent and have additional significance for historical purposes.

Finally, with respect to federally-funded inventions, the attorney should remind the inventors and the institution's administration that, under the statutes cited above, (i) the institution must give the federal government prior notice of the abandonment of a patent application so that the agency may assume responsibility for its prosecution, and (ii) if the invention is not made publicly available within a reasonable time, the granting agency can exercise its march-in rights and acquire title to the invention (see 35 USC §203).

DEPOSITORY REQUIREMENTS

Any discussion of current issues in biotechnology patent law as applied and practiced on behalf of colleges and universities would be incomplete without brief mention of possible problems complying with biological culture deposition requirements. Patent attorneys who handle an increasing volume of patent applications relating to biotechnology, genetically engineered organisms, products of recombinant DNA techniques, vaccines, hybridomas, mutants and other organisms on behalf of academic clients must advise inventors and university administrators of the regulations governing the deposit of biological cultures with a recognized international depository.

Briefly summarized, under the patent law of the United States, a deposit is required (i) for enablement purposes under 35 U.S.C. 112 in cases in which a written description of the invention is inadequate to enable one skilled in the art to practice the invention or (ii) when the essential biological material which is the subject of the patent or is necessary to practice the patent is not known or is not readily available to the public or may not remain available for the life of the patent. A deposit may also be required under the law of the United States to disclose the best mode of practicing the invention under 35 USC 112, although the primary focus of Patent Office rejections to date have been based upon the enablement requirement. Similarly, the laws of the European Patent Community and many other foreign jurisdictions may require the making of deposits for enablement or best mode purposes. Deposits for inventors in the United States are most frequently made with the American Type Culture Collection, Rockville, Maryland, although there are many other depositories which are acceptable to the U.S. Patent

and Trademark Office and acceptable for foreign patent purposes under the Budapest Treaty (see the Federal Register of August 22, 2989 at page 34876).

The problem is one of timing. Researchers in university laboratories, particularly in critical and active fields such as biotechnology, frequently disclose the making of the invention to their administration on the eve of the publication of the discovery in a leading professional journal. Often the researcher sends a courtesy copy of the manuscript of the article announcing the invention to the world to the university's licensing office as an afterthought. If the university elects to apply for a patent on the invention in the United States, as is most commonly the case, compliance is quite routine and can be easily incorporated into the busy schedule to the researcher. The rules of practice of the Patent and Trademark Office entitled Deposit of Biological Materials for Patent Purposes (37 CFR 1 et seq.; see also the Federal Register, Volume 54, No. 161, August 22, 1989 at pages 34864 through 34883) require that the biological materials be readily available during the prosecution of the patent and that a deposit of the essential materials be made prior to issuance of the patent. See also In re Lundak, 773 F. 2d 1216 (Fed. Cir 1985). Under such loose time constraints, the two or three weeks which may be required to replicate the required number of cells will usually be available for the attorney and researcher to coordinate the making of the deposit in the quantities required.

However, if the inventor and his institution desire to file for foreign patent protection for the invention, in every foreign jurisdiction of significance the required deposit must be made at or before the filing of the U. S. National Application, if it is to be used to establish the priority date. For example, under the procedures of the European Patent Community, as set forth in

Rule 28 of the European Patent Office require, in pertinent part, a deposit must be made as follows (emphasis added):

"(1) If an invention concerns a microbiological process or the product thereof and involves the use of a micro-organism which is not available to the public, the European patent application and the resulting European patent shall only be regarded as disclosing the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art if:

(a) a culture of the micro-organism has been deposited in a culture collection not later than the date of filing of the application;

(b) the application as filed gives such relevant information as is available to the applicant on the characteristics of the micro-organism;

(c) the culture collection, the date when the culture was deposited and the file number of the deposit are given in the application.

(2) The information referred to in paragraph 1(c) may be submitted within a period of two months after the filing of the application. The communication of this information shall be considered as constituting the unreserved and irrevocable consent of the applicant to the culture deposit being made available to the public in accordance with this Rule.

(3) The culture deposited shall be available to any person upon request from the date of publication of the application. The request shall be addressed to the culture collection and shall be deemed to have been made only if it contains:"

In the general excitement which surrounds the rush to publish a researcher and his laboratory may not have enough time or laboratory resources to produce the required quantities of cells or other biological materials in order to make the required deposit in a timely manner. This is particularly true if they are at the same time busy assisting the patent lawyer in drafting the patent application for filing prior to the publication of the article or the delivery of the speech disclosing the invention. Accordingly, when a patent attorney first receives notice of the making

of an invention which involves a biological material, he should advise the inventor and the university official responsible for patenting matters of this important requirement.

INVENTION DISCLOSURE FORMS

Detailed forms on which inventions are disclosed to a college or university patent or licensing office can be particularly helpful in focusing on questions of inventorship and other important issues at the outset of the patenting process. At a minimum, the form should require a disclosure of the names, departmental appointments and institutional affiliations of each scientist who was initially deemed to have made a significant contribution to the making of the invention. For purposes of allocating any income which may be payable to inventors under the schools' patent policy, the form should require each contributor to the making of the invention to list his percentage contribution to the overall effort. While the initial percentages listed may be subject to subsequent adjustment, there are many benefits to having all inventors set out their contributions when they are physically present at the school and while a spirit of success and camaraderie permeate the laboratory. Years later, when the invention is ultimately commercialized, the inventors may have far different recollections of their roles in the making of the invention, particularly if they have left the original institution to pursue their careers elsewhere or developed healthy professional rivalries with former close colleagues. In order to minimize the conflict attendant to determining which scientists qualify as inventors for patent law purposes, institutions should consider applying the sharing of royalties under the school's patent policy to all scientists who contributed to the overall research project which resulted in the making of an invention in appropriate circumstances, rather than on attempting to limit the

application of the sharing formula only to scientists who ultimately qualify as inventors for patent law purposes. If researchers understand that they will not be deprived of the right to royalties and other income under the university's patent policy, they will be more forthcoming in addressing the question of inventorship and more helpful in drafting the patent application.

The disclosure form should also include a space in which the inventors list all sources for financial or other support (equipment, laboratory space, personnel, unique biological materials, etc.) to the project which resulted in the making of the invention together with references to grant numbers, research contracts or material transfer agreements (under which suppliers of unique biological materials used in the invention may have reserved ownership or licensing rights to products produced using the same). This information is essential in making certain that the inventors and the institution comply with all reporting requirements imposed by governmental and private sponsors of research and it gives notice to the patent attorney that these entities may have ownership rights in the invention.

All inventors should be required to sign the disclosure form since this is the most effective means of binding them should any questions arise in the future. The chairs of the inventors departments should also be required to sign the form since they are often uniquely qualified to verify the accuracy and completeness of much of the disclosure--the description of the invention, the enumeration of the prior art, the listing of the inventors and the contributions which may have been made by scientists in other departments or at sister institutions. Finally, the signature of the chair will also assure broader institutional support for the patenting effort.

TRADE SECRET PROTECTION AT COLLEGES AND UNIVERSITIES

For many university researchers, there will undoubtedly be a time period when valuable research-derived innovation exists as a trade secret. It may be a fleeting period of time if the researcher chooses to immediately make public his finding through publication or oral presentation, in which case he will most probably lose the protection accorded trade secrets unless he first files a patent application on the intellectual property rights in his invention. If he wishes to be more discrete, however, the researcher may elect to maintain his work as a secret for a longer period of time. He may do so because he wants time to prepare and file a grant application to fund further research on his invention, he may wish to conduct additional laboratory tests or other procedures before making his invention public, or may simply need time to prepare and file a patent application on his invention. Such an investigator, should he wish to go beyond simple secrecy, must know how to maintain his invention as a legal trade secret.

Overriding the need to retain a discovery in secret is the concern of most academicians to contribute freely to the scientific common knowledge and the rights of academic freedom as enjoyed by all researchers. Legal scholars make excellent arguments regarding the interference of what is perceived by many to be "legal maneuvering" with the researcher's desire to participate in a free and open discussion of technological issues by a prompt and full disclosure of the breakthroughs in his laboratory and the sharing of the fruits of his efforts with his professional colleagues. Researchers themselves may wish to publish as soon after the discovery of an invention as possible for the time-honored reason of gaining priority for their findings. However, with the current economic value attributed to intellectual property rights in biotechnology, the current downturn in federal and state funding of basic biotechnology research

and the practice of biotechnology as it actually presently occurs, protecting advances as trade secrets or ultimately patenting such inventions may enhance rather than impede free professional exchange. Furthermore, when procedures for protecting trade secrets are properly practiced by biotechnologists, such practices should allow the academic researcher the protection he requires for his work product both from a rapid publication as well as from a legal standpoint. At the very least, trade secrecy is a part of the law surrounding biotechnology about which each university inventor should be counselled.

Trade secrecy is usually a creature of state common law and, therefore, varies somewhat from state to state. Still, the basic requirements are similar. State law generally limits the permissible subject matter of trade secret protection and further requires that the owner of a trade secret demonstrate some measure of actual secrecy, reasonable efforts to maintain that secrecy, and, with respect to the misappropriation of trade secrets, misconduct by a third party in acquiring, using, or disclosing the trade secret.

Several basic precautions which can be taken to protect the secrecy of a discovery are:

(1) Taking reasonable precautions against disclosure to unauthorized persons;

(2) Marking laboratory notebooks and research plans such as grant proposals "CONFIDENTIAL";

(3) Using "confidentiality" legends and warnings on correspondence and memoranda and using "confidentiality" agreements;

(4) Restricting access of unauthorized visitors to designated areas;

(5) Locking up or otherwise securing unique cell lines, plasmids, constructs, formulations and other biological or chemical materials; and

(6) Taking technical precautions.

Of course, no precautions will be of use if the secret information is made publicly accessible. This is a particular problem in an academic setting where freedom of exchange of materials and information is encouraged. Ways in which a trade secret may be lost by public disclosure include, but are not limited to:

(1) Loss of secrecy through publication in professional or other journals or presentation at professional meetings;

(2) Loss of secrecy through deposit of a biological material without restrictions in a cell depository;

(3) Loss of secrecy through the sharing with professional colleagues of proprietary biological materials or chemicals or laboratory data without the execution of a confidentiality agreement;

(4) Loss of secrecy through disclosure to governmental agencies without restriction;

(5) Loss of secrecy through inadvertent disclosure, such as loss of a most probable DNA sequence by disclosure of the protein sequence;

(6) Loss of secrecy after two years from the date of disclosure of the making of an invention and the delivery of a copy of the patent application on the invention to federal grantee agency or to the NIH pursuant to the regulations promulgated under 35 USC 200-212 (see 37 CFR 401, et seq.); and

(7) Loss of secrecy by issued patents or foreign published specifications or applications.

Universities and their researchers may wish to consider the range of steps which may be taken to posture themselves regarding trade secret protection in a legally defensible position. That range of techniques varies from practices normally carried out in most efficiently run laboratories (without regard to protecting trade secrets) to techniques which would be sufficient to protect even the most highly sought after industrial confidences.

Employees engaged in research at most universities have signed, upon employment, agreements to follow disclosure protocols established by the institution, or they are otherwise expressly made subject to the secrecy and other intellectual property policies of their institutions. Additionally, confidentiality provisions are ordinarily inserted into technology transfer or materials transfer agreements at the insistence of a sister institution or an outside business entity to protect their own strategies and know how. Fearing that these confidential matters might be communicated to university employees or observed by them at some point during the relationship, a commercial concern will most likely demand such a clause. Universities typically limit their liability to instances of "knowing and intentional" disclosure in such agreements.

Public universities must also consider the extent to which information, including the terms and conditions of agreements already in place, may be obtainable by third parties upon request under any applicable freedom of information statute. Review of such requests from outside parties should be considered carefully for any potential trade secrets which may legally be excluded from the requested materials.

Additionally, prepublication review of manuscripts which may disclose patentable subject matter is desirable from the viewpoint of all parties involved in potential disclosures of confidential data. From the patent standpoint, such a review can help avoid the unintentional

loss of patentability in foreign countries having absolute novelty requirements. Additionally, a commercial concern or other sponsor of research may request an opportunity to review future manuscripts relating to licensed technology to guard against the inadvertent disclosure of the business's own proprietary information.

From the perspective of the individual researcher, certain practices can be used to protect intellectual property developed in his laboratory in addition to the support he can expect from his employers. There is enough latitude in such procedures to allow the individual researcher to tailor his requirements for security to his own needs and particular situations. Of course, the individual researcher is in ultimate control of certain aspects of protection. In particular, he may enhance the levels of protection by simply marking laboratory notebooks and research plans such as grant proposals "CONFIDENTIAL". Use of "confidentiality" legends, warnings and agreements is another technique over which he has control. Where necessary, such researchers may find it best to lock up or otherwise secure particularly sensitive materials and writings.

To some extent, physical security may be facilitated by complying with mandated or recommended laboratory procedures, such as carrying out research under the Guidelines for Research Involving Recombinant DNA Molecules of the National Institutes of Health or the Prudent Practices for Handling and Disposal of Infectious Materials of the National Research Council. The higher physical containment practices for conduct of experiments on pathogenic microorganisms are preferred where highly confidential experiments are taking place. Records of containment practices, as per NIH guidelines, are especially important for trade secret purposes.

Identification of potentially proprietary biological materials is possible through genetic engineering. For instance, combinations of genetic markers in unusual patterns tend to prove that a given strain was derived from the proprietary strain. Of course, the more unusual the combinations, the better. Well-documented records are of paramount importance. Non-critical alterations in DNA, RNA and protein sequences may also be utilized to identify such strains. Use of strains weakened to protect against inadvertent release into the environment are useful in protecting against misappropriation.

Centralized review should take place for each request for potentially valuable materials or information from within the laboratory. Documentation which may be useful possibly includes an "Approval Request for Release of Biological Materials or Unpublished Information" for in-laboratory use as well as a "Release of Biological Materials As An Unrestricted Gift or Restricted Release" to be sent to the requesting party. In this manner, a "paper trail" is established for all materials exiting the laboratory. The same sort of process should take place for each such material to be received into the laboratory from non-commercial sources. This may take place by use of an "Authorization to Obtain Materials From Outside Sources" and, if approved, should accompany the letter of request. The letter of request should establish the status of any restrictions on the use of the materials. This is important since many outside university researchers may be unaware of restrictions placed upon them by institutional, federal, or corporate sponsorship of their research.

Whatever solutions are eventually developed for the biotechnology trade, pragmatically speaking, trade secrecy is a fact of life in every university laboratory to greater or lesser extent. It behooves the individual researcher and any counsellor who would advise such a researcher, therefore, to be well-schooled in the art and law of trade secrecy.

U.S. Patent and Trademark Office Mission Statement

submitted by Stephen C. Yurish

The Patent and Trademark Office administers the laws relating to patents and trademarks in order to promote industrial and technological progress in the United States and strengthen the national economy. This mission is accomplished by:

- Examining patent and trademark applications, issuing patents and registering trademarks.
- Disseminating patent and trademark information to the public.
- Encouraging a domestic and international climate in which intellectual property can flourish.

