I. Context

The United States grants patents to “whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement,” in addition to meeting the disclosure, novelty, and non-obviousness requirements. Generally speaking, biotechnology patents are different from other patents because they require highly specific facts to meet these statutory requirements. To successfully and efficiently patent emerging biotechnological inventions (see Table I), the general strategies of (1) carefully balancing patent prosecution considerations and (2) speeding up the process of patent prosecution should be employed. Furthermore, specific patenting challenges unique to stem cell-related patents, as well as ethical and public policy issues, should be taken into account.

II. General Patent Strategies

A. Patent Prosecution Considerations

(i). Assessment and Analysis of a Company’s Intellectual Property Inventory and its Business Objective.

The starting point in intellectual property for new companies is an evaluation of the current state of the intellectual property owned or licensed by the company. Is the purpose of this intellectual property to expand new products or protect existing ones? Which technologies form the core of the product line? Which inventions provide value more in the short-term than the long-term? Who are important competitors and which technologies will they need to continue to compete? Through answering these and related questions, patent applications may be categorized as “will utilize,” “likely not to utilize,” or “will not utilize.” Based on these classifications, a sensible business plan for these technologies may be developed.

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Table I: Some Protectable Applications in Biotechnology.

<table>
<thead>
<tr>
<th>Tools</th>
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<td>- Software</td>
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<td>- Devices and Methods</td>
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<td>Health Care Products</td>
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<td>- Nucleic acid sequence</td>
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<td>- Protein and small molecules</td>
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* J.D. Candidate 2006, Santa Clara School of Law; Ph.D. Pharmacology, 2001, Georgetown University; B.A. Molecular and Cell Biology, 1997, University of California at Berkeley. The authors would like to thank Dr. Mircea Achiriloaie for his helpful comments on this paper.

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4 Id.
(ii). Building a Patent Portfolio Quickly — by Acquiring or Licensing patents or Applications from Universities or Defunct companies

Many biotechnology companies build or strengthen their patent portfolios by negotiating with universities for exclusive or non-exclusive licenses of their inventions or by acquiring patents from defunct companies. Until the Bayh-Dole Act in 1980, “the federal government sponsored basic research and encouraged its widespread publication in the public domain without regard for potential commercial applications.” After this legislation was enacted, universities were able to transfer their patented technology to businesses in the industry. Universities benefit from the revenue generated from the licensed technology, e.g. Cohen-Boyer’s recombinant DNA patent. The business benefit is similarly clear. Many small or start-up biotechnology firms rely on exclusive licensing rights to ensure access to high-risk capital and to promote investment in downstream development.

A license does not grant a company the right to make, use or sell the invention any more than a patent does; it is an agreement by the licensor not to sue the licensee for patent infringement. The licensing agreement terms play a critical role for both the licensees and the licensor. While companies aim for profits and so emphasize protection of their patent rights, the primary focus in research universities may be on innovative research and the free exchange of ideas rather than merely extracting profits from their inventions, though often these profits may be employed in pursuit of research goals. Still, researchers may wish for licensing agreements to be drafted in such a way as to avoid stifling innovation, particularly when technologies may be fundamental to future, and critical to present, medical applications.

(iii). Due Diligence on Patent Applications and Extensive Search for Potential Infringement

Conducting due diligence on patent applications and extensively searching for potential infringement on issued patents are always important in serious patent prosecution. Diligent organization of a patent portfolio and vigilant surveillance of competitors’ activity or other third parties’ potential patent infringement not only provides protection to an invention, but may also be used to soften the hazard of litigation. Conducting an extensive search for potential infringement on issued patents could help patent applicants decide whether to pursue patents for their inventions, or to alter their invention to avoid infringement. A biotechnology-related patent is time-consuming and expensive. It requires an average of three years to complete and costs upwards of $15,000. Thus, prior to committing resources to developing a new product, potential infringement should be thoroughly investigated.

7 U.S. Patent No. 4237224
8 Behfar Bastani, Evelyn Mintarno and Dennis Fernandez, Technology Transfer: From the Lab to the Shelf, Stanford BioMedicine Quarterly, Fall 2003 at 23.
10 See Bastani, supra note 9, at 23.
11 Id.
13 Id.
Record-keeping of all invention records should also be strictly followed. It is generally recommended to maintain an inventor notebook with conception dates and concept diagrams that are signed by two witnesses. Further, all inventor notebooks, invention disclosure forms (IDF), patent proposals, and literature should disclose inventions as confidential. Information about all inventors should also be properly maintained. For example, in the case of Ethicon v. US Surgical, the plaintiff Ethicon failed to obtain consent from an omitted inventor to join its patent infringement lawsuit. This resulted in the dismissal of the case.

(iv). Blocking Strategy
In addition to the defensive strategy of protecting a company’s pre-existing core technology, offensive strategy may be useful. An intelligent offensive patent strategy may be used to block future competition, secure emerging standards, increase the company’s valuation, and collect licensing royalties by determining the emerging standard or trend and patenting it or purchasing patent rights. A recent attempt at this strategy involved Microsoft’s patenting of the interface used in Apple’s iPod; if the patent turned out to be valid and the iPod were determined to infringe upon it, Microsoft would gain some iPod revenue simply for “inventing” the interface despite having nothing to do with the manufacture or development of the product. Similarly, a company developing stem-cell related therapies for a specific purpose, such as cancer treatment, might notice a difficulty in keeping stem cell lines fresh and usable, and while not a stem cell growing company or even able to improve directly on existing technology, might predict a certain method to be necessary for success. This company might be able to successfully prosecute this patent and, should the prediction turn out to be true, generate revenue in the future despite some ignorance of the manufacturing process or the other contributing causes of the problem.

(v). Deriving and Maximizing Value from Non-utilized and Utilized Patents
A patentee may intelligently elect not to license patented core-technological inventions to preserve its exclusive position in the market. However, to maximize the values of a portfolio of patents, patentees may consider: (1) licensing out patents that are unlikely to be utilized or will not be utilized because the patents do not meet the company’s business objective; (2) infringement litigation against competitors to obtain monetary damages and exclusive positions in the marketplace; or (3) cross-licensing with competitors for necessary technology to gain market access. In the particular case of stem cell patent portfolios, most companies will have no choice but to look for cross-licensing agreements if they are to compete, simply because so many patents have already been issued. As of August 31st, 2005, 4822 of the patents available for download at the USPTO website made some mention of stem cells, many tangentially but virtually all in earnest and unrelated to plant matter. Already 108 issued patents include the term in the title, and 97 of these are listed as assigned to a company. Amgen is listed as the assignee on 16, dwarfing any other single player in this particular category, but the area still appears divided in terms of ownership; opportunities to form alliances in the event of significant

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14 Id.
17 See Isacson, supra note 4, at 566.
commercialization of stem cells abound. As of the same date, 10,157 of the not-yet-issued patent applications on that site mentioned stem cells. Nearly all of these will not be relevant to a particular patent application, but it is critical that they be considered carefully. Certainly some will be cited in a first office action response to any stem cell patent application, but that alone does very little to mitigate litigation risk or ensure access to crucial technologies.

B. Speeding Up the Process of Patent Prosecution

(i). Submitting a Petition to Make Special
An excellent strategy to increase patent protection speed is to claim high priority within the U.S. Patent and Trademark Office (USPTO). An application may be made to advance out of turn for examination or for further action if it is made special on the grounds of prospective manufacture, actual infringement, applicant's health and age, environmental quality, recombinant DNA-related invention, certain new applications, HIV/AIDS and cancer-related inventions, counter terrorism-related inventions, and applications relating to biotechnology filed by applicants who are small entities. Earlier examination of a patent application sometimes results in earlier granting of a patent. Some of these categories legitimately apply to nearly all stem cell-related innovations, so petitions to make special should correspondingly be filed often on patents related to this technology.

(ii). Making Narrow Claims Only
The USPTO requires a limited claim scope for biotechnological patents and usually restricts support for claims to working examples in the specification. As a result, broad patent claims are likely to be rejected if insufficient working examples are provided. The Federal Circuit Court in Amgen v. Chugai held that § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. Thus, claiming all possible genetic sequences that have a particular protein-like activity by merely making a protein’s generic DNA sequence is insufficient and invalid. The court in University of California v. Eli Lilly further ruled that a description of rat insulin cDNA is not a description of the broad classes of vertebrate or mammalian insulin cDNA. A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition of the claimed subject matter sufficient to distinguish it from other materials. Accordingly, narrow and specific claims are more likely to increase the speed of patent issuance. If desired though not at the expense of speed, broader claims may then be sought in a continuing application.

20 Amgen v. Chugai, 927 F.2d 1200, (Fed Cir. 1991).
21 University of California v. Eli Lilly, 119 F.3d 1559, 1568 (Fed. Cir. 1997).
III. Specific Patent Prosecution Challenges in Unique Areas of Biotechnology

A. Bioinformatics-related Software Patent Prosecution

Bioinformatics is the use of computational tools and databases in relation to genomic, proteomic medical and health data. Given the advantages stem cell therapies possess over other therapies depend on complex interactions between cells, the environment they are in which influences their differentiation, and expression of different subsets of the genome at different times, it is exceedingly likely that those prosecuting stem cell patents will need a good understanding of the concerns unique to bioinformatics-related patents at one point or another.

The USPTO has created a special examination unit, Art Unit 1631, in December 1999, to review bioinformatics-related patent application. By November 2001, 1776 patents had already been issued by the USPTO for bioinformatics-related invention.

The majority of bioinformatics inventions involve applications of computer-implemented protocols or software in collecting, storing, processing, or analyzing biological data. The patentability and protectability of software inventions have been an intensely debated topic for decades. According to the U.S. Court of Appeals for the Federal Circuit (CAFC) in In re Warmerdam and In re Lowry, claims to data structures per se do not constitute patentable subject matter pursuant to 35 U.S.C. § 101. However, a machine (such as computer) or a computer-readable medium (such as a CD-ROM or floppy disk) encoded with a data structure is patentable. These rulings are consistent with the USPTO’s guideline for patentable subject matter in computer-related inventions: “when functional descriptive material is recorded on some computer-readable medium it becomes structurally and functionally interrelated to the medium and will be statutory in most cases since use of technology permits the function of the descriptive material to be realized.” Thus, a machine or manufacture, such as software, having a practical application in the technological arts is patentable. Technical application could be identification of a drug target or prediction of a protein structure. For example, Affymetrix developed a software with special technical application that enables researchers to perform gene expression, single nucleotide polymorphism (SNP) mapping and resequencing analysis with integrated data management, and scalable client-server configuration.

Patent prosecution in bioinformatics presents a certain degree of difficulty. First, value is based on the value of the therapeutic products, instead of the tools (software) used to identify these products. Many bioinformatics companies employed the tactic of “reaching through” claims by establishing mechanisms to claim profitable bioinformatics-derived therapeutic products rather than the tool used for their identification. However, because these patents are mostly related to screening methods that are upstream from the

23 Id.
24 In re Warmerdam, 33 F. 3d 1354, 1360-1361 (Fed. Cir. 1994).
25 In re Lowry, 32 F.3d 1579, 1583-84 (Fed. Cir. 1994).
26 See Hultquist, supra note 21, at 743.
28 Id. (citing In re Alappat, 33 F. 3d. 1526, at 1544 (Fed. Cir. 1994); State Street Bank & Trust Co. v. Signature Financial Group, Inc., 149 F.3d 1368, 1373 (Fed. Cir. 1998)).
therapeutic product, drafting the claims purely based on the tools may be insufficient. One solution is to limit the scope of the claim. Alternatively, if it can be shown that the claims are enabling to one of ordinary skill in the art, rejection for insufficiency of this type of claim may be overcome.

Another problem is the variety of business models being used in the industry. Some bioinformatics market participants may license access to databases, while others may sell software, systems, or testing equipment or perform tests for clients. Since effective patent claims cover what is sold, patent prosecutors should anticipate such diverse business models and aim to block future competitors when drafting claims.

The interdisciplinary nature of bioinformatics-related patents also presents challenges both to the USPTO and patent prosecutors. The scarcity of judicial precedents and the difficulty of finding a patent drafter or examiner who is well versed in information technology, biology, and patent law increases the difficulty and effort of obtaining a bioinformatics patent. Furthermore, since the bioinformatics field develops quickly, the success of drafting patent applications should be based on a vision of the future progress of bioinformatics, in addition to knowledge of patent law and business.

B. Genomics Patent Prosecution

Certain challenges exist for prosecuting genomics-related inventions to meet the utility requirement. These challenges apply equally to a subset of stem cell-related patent applications. According to the USPTO's new utility guidelines, inventions must have well-established utility, such that a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention, and the utility is credible, substantial, and specific. For genomics-related patents, the utility of a specific DNA sequence is often unclear until further characterization of a particular DNA sequence's function and activity. Merely claiming a sequence of DNA fragment without any indication of a function or specific asserted utility is not patentable.

For example, Incyte and similar genomics companies filed thousands of provisional patent applications with the USPTO for ESTs (Expressed Sequence Tags), which have unknown function at the present. Opponents of this tactic argue that patent rights should be reserved for uncovering the true biological function of a gene, not merely sequences of the gene fragments. Similarly, discoveries about stem cells may not be obviously useful; the potential uses seem countless but a potential use is not necessarily utility. Still, the concern may be less than that in genomics simply due to common perception of therapeutic utility for anything to do with stem cells.

Another tactic to meet the utility requirement is to conduct several functional assays. The inventor can submit a declaration on sequence behavior asserting that the invention is more likely than not to have some function. The invention is still protected even if a new usage is discovered for the original claims. For example, Viagra was originally patented as a heart remedy. This possibility may be particularly significant to stem cells, since the possible applications seem manifold and poorly-defined.

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30 See Wilson, supra note 24.
31 See Fernandez, supra note 3, 33-34.
33 See Restaino, supra note 13, at 11.
35 Id.
Some genomics-related claims are too general to meet the written description requirements. Under the guidelines for the written description, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art could reasonably conclude that the inventor had possession of the claimed invention. The federal district court in University of California v. Eli Lilly held that merely naming a type of known material, without any knowledge as to what that material consists of, is not a description of that material. For example, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. A definition by function is not sufficient to define the genus because it is only an indication of what the gene does, rather than what it is. In the case of stem cells, this consideration translates well: one does not have to travel far to find someone claiming a great stem cell therapy if only they could overcome some mechanistic hurdle. Patenting a new application of stem cells may require not only claiming the utility but also sufficient elucidation of how the stem cells used would have to be adapted to the use, or a convincing explanation for why this no adaptation is necessary.

IV. Ethical Issues and Public Policy

Recently, the patentability of new biotechnological inventions, related to topics including human embryonic stem cells, human cloning and human/non-human chimeras, have raised not only technical challenges to patent prosecution, but also moral and ethical concerns. The USPTO determines patentable subject matter under 35 U.S.C. § 101 on a case-by-case basis following tests set forth in Chakrabarty. For example, one such test says that an artificial manufacture or composition of matter is patentable.

On one hand, the USPTO considers purified and isolated stem cells and human cloning-related inventions patentable subject matter and rarely rejects applications based on public policy and morality grounds, as long as they meet the criteria of novelty, utility and nonobviousness. For example, the USPTO has issued several patents on cloning methods specifically related to non-human animals, such as patents granted to Geron-Biomed and the University of Massachusetts at Amherst. On the other hand, the USPTO did not grant a patent on the claimed human/non-human chimera based on the argument that granting patents on people would violate the 13th Amendment to the Constitution abolishing slavery, claiming that neither the USPTO nor Congress has never defined "human." Further, in a media advisory issue in 1998, relying on the decision from Tol-O-Matic, Inc. v. Proma Produkt-und Marketing Gesellschaft, the USPTO stated that the utility requirement of § 101 excludes inventions deemed to be "injurious to the well being, good policy, or good morals of society."

37 University of California v. Eli Lilly, 119 F.3d at 568.
38 Id. at 568 (citing Fiers v. Revel, 984 F.2d., 1164, 1169-71 (Fed. Cir. 1993)).
41 Audrey R. Chapman, Mark S. Frankel and Michele S. Garfinkel, Stem Cell Research and Applications Monitoring the Froniters of Biomedical Research, American Association for the Advancement of Science, Nov. 1999, at 26.
These conflicting decisions from the USPTO raise the question of whether the United States patent laws are to be used as a means of regulation. The patent system lacks the expertise and resources to engage in regulating outside the USPTO’s expertise, and the USPTO is not really authorized to make regulatory changes due to societal concerns for all of its applications. Also, a refusal to grant a patent for such controversial biotechnological inventions does not prevent the application. The patent right is a right to exclude others from making, using, and selling the invention, not a right to do something. Thus, by not granting a patent, the PTO may instead enable anyone to practice the disrupted technology. Patent law only enables the USPTO to either grant or not grant a patent. The USPTO does not have a wide range of regulation options. That is, even though the USPTO may grant or reject a controversial biotechnological invention, it does not get to regulate all of industry through patents.

However, the legislature of the US, state legislatures, and foreign governments all have some measure of power over industrial applications, and indeed many have exercised this power on the subject of stem cells already, even before a major health application has been deployed. Legislative risk is likely the most significant risk to ventures dependent on stem cell therapies for revenue. Stem cell technologists were set back by a freeze on federal funding for new stem cell lines, and California stem cell technologists have been granted a new lease on life by a voter initiative. Various interest groups throughout the globe have strong feelings about technologies pertaining to embryonic stem cells, and these feelings have already and will certainly continue to find expression in law. Mitigating these risks involves a careful combination of campaign contributions (something more than familiar to big pharmaceutical companies and any other large industry), public awareness campaigns touting the benefits of stem cell therapies, and vigorous lobbying efforts. Certainly each of these is already underway at some level; however, it is clear from recent political developments that the issue may not yet be decided at the federal level in the US.

V. Conclusions

Patenting new biotechnological inventions provides a constant challenge. In addition to its fast growth and increasingly interdisciplinary nature, both patent prosecutors and the USPTO face the ethical and public policy issues of patenting human cell-related inventions. Even though patents are only a part of an intellectual property strategy, effective and efficient patent strategies are essential to provide incentives to advance biotechnology research and growth of the industry.

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44 See Nash, supra note 45, 299-300.
45 Id.
46 See Chambers, supra note 46, at 231.
47 See Nash, supra note 45, 299-300.