

Keeping Up Intellectual Property Lifelines for Life Sciences Ventures

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Today's biotechnology intellectual property (IP) strategists find themselves in an unenviable position. Modern biological research brings about an avalanche not only of scientific data, but also of unprecedented ethical, policy, and philosophical questions. New laws will undoubtedly result, including new or modified IP laws. IP, and especially patents, are typically crucial to the viability of biotechnology companies. Thus, critical IP strategy necessarily stands on the quicksand of biotechnology IP law. Some of the concerns of biotechnology companies in developing their intellectual property arsenal are explored in this article.

Sequence patents: Utility and Description Requirements

DNA sequence patenting has been at the core of a vigorous debate for the past decade. Issues such as whether DNA should be patentable subject matter and the detrimental effect DNA patents might have on biomedical research have been strongly disputed (1). The controversy seems to be subsiding now in light of established legal precedent and guidelines applicable to DNA patents adopted by the United States Patent and Trademark Office. As the dust settles, prior patents and current strategies need to be evaluated for compatibility with the emerging legal landscape.

It is now recognized that nucleic acids and proteins are patentable in the US and under most foreign patent regimes. As discussed below, however, sequence data itself is insufficient and additional information is necessary. While the amount and type of additional information varies with particular sequences, it is fair to say that in general the strength of patent protection depends on the amount and quality of additional information. In fact, this additional information should ideally support sequence-independent creative claims because unquestionably valid sequence claims are usually quite narrow.

To be entitled to patent protection inventions have always been required to be useful. The United States Patent and Trademark Office has recently promulgated utility guidelines to clarify this requirement (2). While the guidelines are applicable to any invention, they are uniquely relevant to DNA patents. Accordingly, inventions must have credible, substantial, and specific utility. To be credible, an assertion of utility must be believable to a person of ordinary skill in the art. For example, a perpetual motion machine lacks credible utility. Substantial utility refers to "real world" uses of inventions. For example, treatments for unspecified diseases or compositions useful only for further research do not meet this requirement. Finally, inventions must have specific (rather than general) utility. It is this requirement of that prevents patenting of just any nucleic acid sequence. Because all nucleic acids can be used, for example, as chromosome markers or as gene probes, such uses are general, not specific. To clear the utility threshold, knowledge additional to the sequence itself must be presented. Such knowledge may come, for example, from simple homology studies in some cases, or functional studies in other cases. Consequently, it is not possible to claim numerous expressed sequence tags (ESTs) without any analysis to support an assertion of specific utility. Refer to Figure 1: Enabling Technologies in Gene Analysis

Additional constraints on DNA or amino acid sequence claims are imposed by the written description requirements (2, 3). In general, the requirement is that the patent specification must convey to those of skill in the art that the inventor was in possession of the claimed invention at the time the application was filed. This requirement is clearly met by any sequence listed in the Sequence Listing section of an application. Written description is not easily met for any "genus" of sequences, that includes the "species" in the Sequence Listing and other sequences with similar characteristics. To generically disclose sequences, as many features as are known should be described in the specification. Examples of such features include in the case of polypeptides catalytic activities, structural domains, secondary or tertiary structure, interaction with binding partners, effect of mutations, or in the case of genes, promoters,

introns, alternative splicing sites, expression patterns, known alleles, homologous or analogous genes, etc.. Disclosure of such features, which may be in hypothetical examples, allows some room for argument during prosecution that generic claims are supported by a written description. Even so, written description of generic sequence claims is all too likely a costly topic in litigation. Consequently, the written description requirement severely limits sequence claims.

As a result of the utility and written description requirements, clearly valid claims to sequences are necessarily narrow. This is problematic because devious infringers can easily design around narrow claims. Also, investors are not easily attracted by dubious patent protection. Nevertheless, in some cases it is worth filing an application for a sequence with little more than a sequence homology study. Broader patent protection, however, is achievable based on as much information regarding the claimed sequence as possible.

Commercialization and licensing

Commercialization and licensing strategies of biotechnologies might necessitate considerable rethinking in light of a current controversy that surrounds patent licensing to academic institutions. Traditionally, patent owners have rarely attempted to enforce their patents on academic institutions for a number of reasons. Such reasons included the belief that academic research might fall under the experimental use exception to infringement, that damages resulting from infringement by academic research would be minuscule, and that suing academic institutions doing basic research may result in unfavorable publicity. It has now become clear that research in public universities can infringe patent rights (4, 5). Moreover, public research centers presently earn about \$870 million per year from patent licenses, and so they truly have become significant market players. The tacit tolerance of infringement by academic laboratories may be about to change, with significant implications.

Some companies, such Genetic Technologies, are actively pursuing licenses from public institutions (6). Calls have been heard to enact legislation to exempt public research institutions and basic research laboratories from patent infringement claims (7), as patents increase costs and might stifle basic research. Such legislation might be enacted if the practice of seeking licenses from universities becomes widespread. Not surprisingly, some recommend voluntary compliance with licensing guidelines (8), so that licensing practices do not fuel a debate of the status of academic research in the patent arena. An exemption to academic institutions would be adverse to the interests of the biotechnology industry. If academic laboratories cannot directly infringe, companies may not in some cases secondarily infringe through sales to universities. Therefore, the value of many markets and biotechnology patents might greatly diminish. While at present this concern is only speculative, it would seem wise to claim biotechnology inventions so as not to read exclusively on the academic research market. In addition, the time is certainly right for companies with patents that might be infringed by basic research to decide their own policies and best interests regarding licensing their patents to academic institutions.

Bioinformatics: Software Protection

Bioinformatics is the intersection of life sciences and information technology. Current research in genomics, proteomics, clinical, high-throughput assays, etc. generates terabytes of data. Bioinformatics products are necessary to mine the data, and include software and hardware, data acquisition, data storage, data display, data analysis, pattern recognition, molecular modeling, or predictive tools (*see* Figure 2 and Figure 3). To be sure, the bioinformatics industry is currently suffering with the rest of the economy. However, bioinformatics products will certainly continue to be on demand for many years to come. For example, the recently released National Institutes of Health Roadmap for Medical Research (9) identifies bioinformatics and computational biology as areas that require considerable future efforts. While investments are certainly necessary to produce such tools, intellectual property protection of such investments is fairly elusive. Given the large number of different bioinformatics applications, a universally applicable blueprint of IP development does not exist. Consequently, players in the bioinformatics sector would be well advised to scrutinize each type of intellectual property for any benefits it might bring.

Perhaps the only generalization applicable to most bioinformatics tools is that some original software is involved. Therefore, lessons learned from intellectual property protection and commercialization of software should apply to software-containing bioinformatics tools. Thus, copyright protection is available but it is quite thin because it only protects unauthorized copying, modification, or

distribution, not independent development of software with identical capabilities (*see* Table). In addition, licensing agreements should be used to define the rights of users, and perhaps prevent reverse engineering, or acknowledge that trade secrets are embodied in the software. Depending on the precise undertaking, some bioinformatics companies should consider use of digital rights management in distributing copyrighted materials. Also, when bioinformatics software is developed by collaboration of different entities, the collaboration agreement should address the issue of ownership of any intellectual property rights resulting from the joint effort (10). Nevertheless, even for bioinformatics tools made up exclusively of software, bioinformatics companies should also seek some patent protection.

Patents may confer bioinformatics applications what copyright cannot: protection for the concepts or algorithms underlying software applications (*see* Table). Obtaining good patent protection in this field, however, is quite challenging. One problem is the variety of business models currently used in the industry (11). Thus, some bioinformatics market participants license access to databases, others license software, others sell systems that include hardware and software, others sell components of systems, others are application service providers, others sell testing equipment, others perform tests for clients, etc.. This variety of business methods is problematic because effective patent claims cover what is sold. Thus, the diversity of business models makes it difficult to draft claims to anticipate and prevent any form of competition. On the other hand, this diversity should prompt bioinformatics companies to explore the possibility of enhancing their intellectual property portfolio with business method patents.

Other challenges to obtaining strong patent protection in bioinformatics come from the broad range of applications, the novelty of the field, and its cross-technical nature. Due to the broad range of bioinformatics products, bioinformatics patents are hardly “typical” (12). With little guidance from the scarce judicial precedent, drafting effective patent applications takes an unusually large amount of analysis and effort. The emerging bioinformatics field develops quickly, and therefore much of today’s technology will soon be obsolete. Patent applications typically issue two to three years and are effective for twenty years after filing. Therefore, effective patent applications must be based on a vision of the future progress of bioinformatics, which may be rather elusive. In addition, it is often difficult to find a patent drafter able to comprehend both information technology and biology, in addition to patent law and business (11). The patent office has certainly had its share of difficulties in finding patent examiners competent to examine bioinformatics applications. Consequently, even though patent protection for bioinformatics tools is desirable, obtaining it is often difficult.

While intellectual property protection is essential to most biotechnology and bioinformatics companies, any strategy for developing an effective intellectual property portfolio necessitates some guesswork regarding future legal developments that might negatively impact IP assets. The potential impact of such future developments may be somewhat alleviated through extensive diversification of IP portfolios, which should be based on a comprehensive analysis of the benefits that may be derived from all possible avenues of IP protection. Even though diversifying IP portfolios does not automatically guarantee the desired scope of any IP asset, it does offer the best hope that the IP estate of a company will provide the desired competitive advantage.

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Figure 1: Enabling Technologies in Gene Analysis

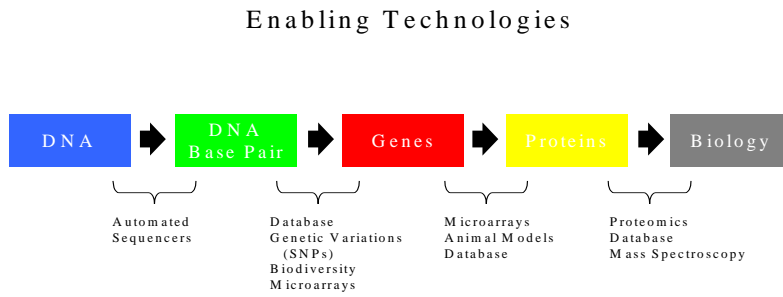


Figure 2 – The Bioinformatics Cycle

Databases of information are being collected from a variety of sources, including genomic and proteomic research, clinical trials, and high-throughput assays. Users and developers of bioinformatics tools often contribute to the development of databases. Database content is accessible over the internet to users, including agricultural researchers, pharmaceutical companies, academia, clinical laboratories, etc.. Aided by tools, users are able to gain new biological and medical insights. These insights are related to all levels of biological organization and their interconnections. Some of the insights contribute to the content and structure of databases.

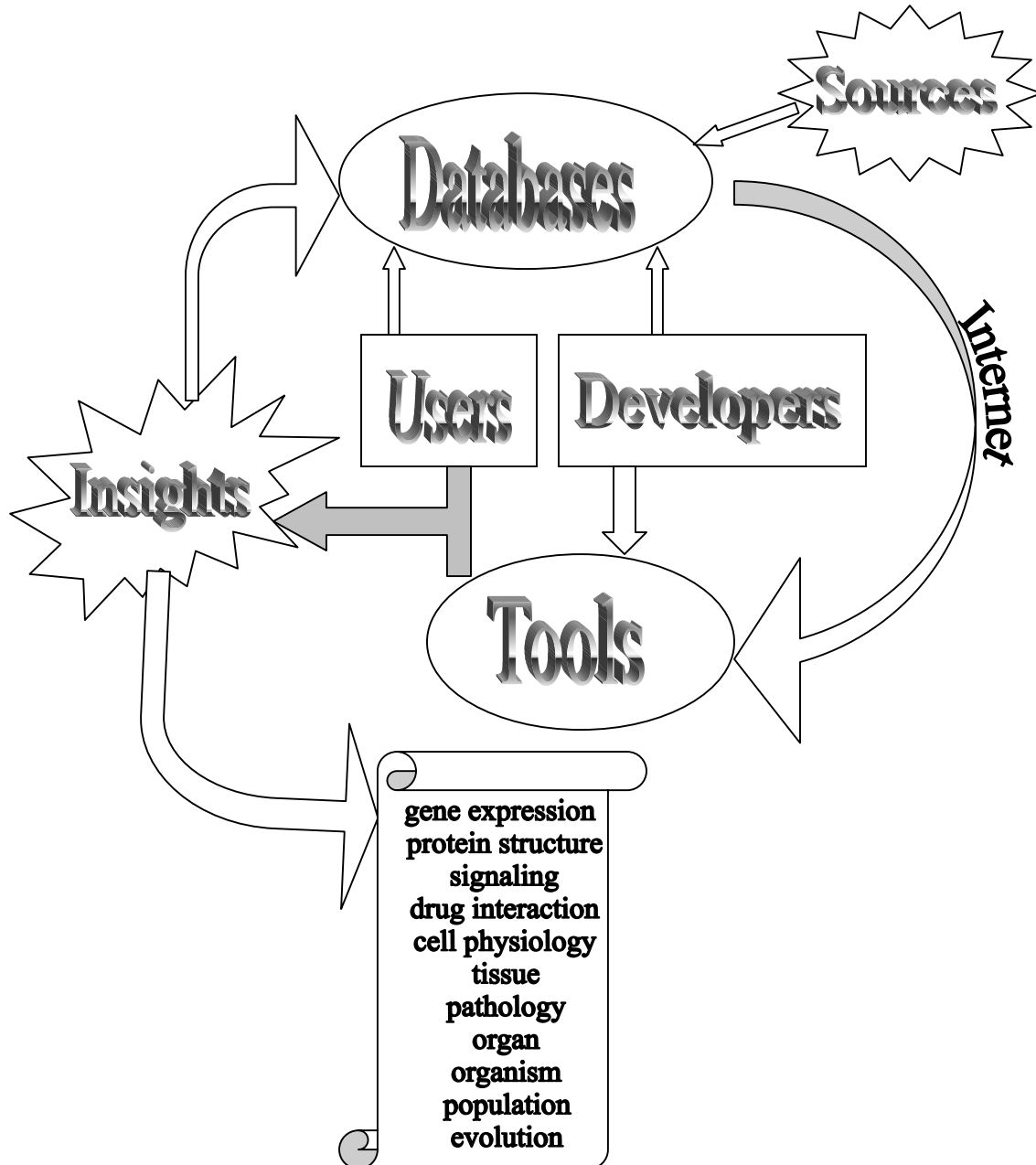


Figure 3: Bioinformatic Impact on Drug Discovery Process

Bioinformatics Companies' Impact on the Drug Discovery Process

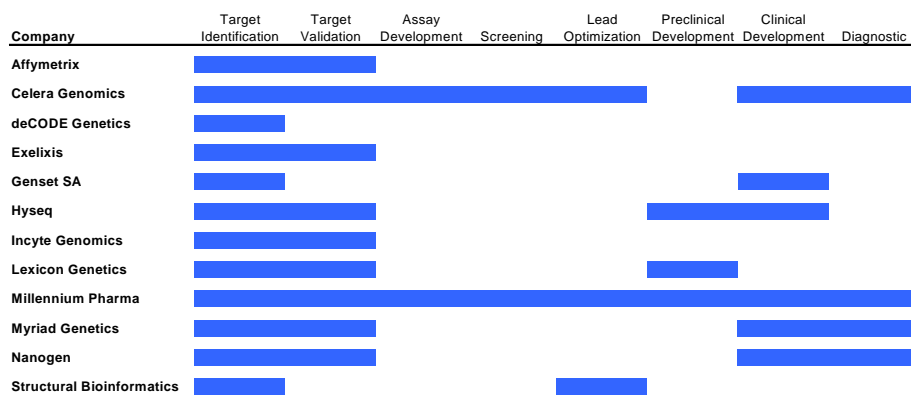


Table – Comparison of Copyright and Patent Rights

	Copyright	Patent
Subject matter	Original works of authorship fixed in a tangible medium of expression (e.g. software on hard drive or CD)	Inventions; must be useful, novel, and non-obvious
Establishment	Fixation in tangible medium of expression ¹	File and prosecute application with the United States Patent and Trademark Office and/or foreign patent offices
Duration	Generally, life of author plus 70 years ²	Generally, 20 years from filing of application
Infringing activities	Unauthorized use, copying, distribution or modification	Making, using, selling without permission; or aiding and abetting others engaged in such activities

¹ It is, however, advisable to mark materials with a copyright notice with the year of initial publication and the name of the copyright owner (e.g. © 2003 John Doe) to put potential infringers on notice of the copyright. In addition, registration with the United States Copyright Office may be a prerequisite to infringement lawsuits, makes copyright prima facie valid, and may result in award of statutory damages and attorney fees.

² In bioinformatics, copyrighted software is often created subject to assignment to an employer. Such “works made for hire” are entitled to a term of 95 years from initial publication or 120 years from creation, whichever comes first. Note that for such works the copyright notice referred to above should name the employer as the copyright owner.