Patent due diligence in biotechnology transactions

A due diligence review may be your most important tool in assessing and reducing the risks associated with a business transaction.

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Last month, we began our exposition of due diligence investigations involving technology-based intellectual property. We discussed the purposes of due diligence, as well as the importance of understanding the business transaction involved and of obtaining the information necessary for risk assessment. We then began to explore how this information can be used to analyze and resolve some of the important issues in IP due diligence, including ownership of the patent estate and duration of patent protection. This month, we continue with assessment of the scope and validity of the target's patents, the risk of infringement, and how the target's prior contractual obligations or disputes with third parties can affect the value of the transaction. We conclude with an outline of the IP due diligence report.

Breadth of patent claims

Due diligence should include a review of the claims of the patents (and patent applications) to ensure that they are broad enough to cover any commercial products or processes of interest. The scope of the patent claims is a function of the detail and breadth of the disclosure in the patent specification. Even if the claims are broadly drawn, if the disclosure is minimal, the claims may be construed narrowly, and may not survive a validity challenge in court.

The protection afforded by a patent can also be narrowed by changes made to the claims, or by legal arguments advanced, during prosecution of the patent. If, for example, in order to obtain a patent, the patent applicant limits the claim language or urges that the claims are restricted to a particular scope of coverage, the patentee is subsequently precluded from taking an inconsistent position regarding the scope of patent protection. The prosecution histories should therefore be examined as part of due diligence, at least for the key patents of the target.

If the patent claims are narrowly drawn, it may be easier for competitors to design around them, and to enter the field of the patent while avoiding infringement. The investor will therefore need to determine whether the claims are broad enough both to cover the commercial product and to keep competitors at bay. Such an assessment may require not only a legal analysis of claim scope, but also input from technical advisors with substantial knowledge in the field of the patent.

The due diligence team may be able to make recommendations for improving the scope of patent protection. In the United States, for example, a reissue procedure is available by which the claims of a recently issued patent can be broadened under certain circumstances[1]. Or, if a related application is still pending, it can be used to pursue claims broader than those of the issued patent.

Patent validity

For key patents and patent applications, it may also be important to assess their strength—that is, the likelihood that the patent will survive a challenge to its validity in court, or that a patent will be granted on a patent application. A patent may be found invalid and an application unpatentable on a variety of grounds. The due diligence investigation may involve examining patent prosecution histories, conducting a search of earlier patents and scientific literature, and analyzing whether the descriptive portion of a patent is legally sufficient to support the claims. Some of the grounds for finding invalidity of particular relevance to biotechnology are briefly discussed below.

Prior disclosure of the invention. Biotechnology is a field with close connections to the academic community, which has a tradition of public disclosure, publication, and unrestricted dissemination of information, biological materials, and other research tools. If a public or unrestricted disclosure of the invention has been made before the filing date of a patent, such activity can constitute "prior art," and can, therefore, potentially be used to invalidate its claims, or to restrict their scope. University-owned patents, especially patents submitted in the early days when the academic community was not fully aware of the detrimental effect of such disclosures, are particularly vulnerable to challenge based upon such prior art.

Where the importance of a patent warrants it, the due diligence investigation may therefore include a search of the patent and scientific literature. A well-structured search may not only yield valuable information about whether patented products or methods have been previously described, but may also uncover useful information relevant to other issues, such as inventorship, widespread availability of biological materials previously considered proprietary, or criticisms of the invention, which may be damaging to claim scope or even validity. Because some of the latter information may have become public subsequent to the filing date of the patent, it is often important to search literature published even after the filing date of a patent.

A word of caution for online searching strategies: an in-depth knowledge of both the historic development of a technical field and the jargon used by patent lawyers in drafting patent applications may prove useful in identifying obscure or obsolete search terms that will uncover pertinent references. For example, search terms for "antibody" should include not only the obvious "immunoglobulin" or "IgG," "IgM," "IgE," "IgA," and their variants, but also more arcane terms such as "binding partner" and "antigen-binding ligand."

The written description requirement. Under US law, a patent must describe the invention in words or drawings in sufficient detail to show to a person of ordinary skill in the technical field of the patent that the inventor was "in possession" of the entire scope of the claimed invention[2]. This prerequisite is referred to as "the written description requirement," and noncompliance is grounds for invalidity. Due diligence may therefore include a review of a patent specification in conjunction with the applicable case law to assess the likelihood that a court would find the description of the subject matter of the claims inadequate.

The written description requirement has been applied stringently to biotech patents, requiring specific disclosure of the compounds or sequences claimed in the patent, especially in recent case law. The landmark court decision on written description for biotech patents is *Regents of the University of*

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California v. Eli Lilly & Co[3]. In *Eli Lilly*, the court found claims respectively directed to "human," "mammalian," and "vertebrate" insulin complementary DNAs (cDNAs) to be invalid on the ground that the written description was inadequate. The court noted that "[i]n claims to genetic material, 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"[4]. The court held that "an adequate written description of a generic DNA . . .'requires a precise definition, such as by structure, formula, chemical name, or physical properties . . .'"[5]. The court also found that detailed description of only one species of cDNA (rat insulin cDNA) was not a sufficient description of the claimed genus (mammalian or vertebrate insulin cDNA), because, at the time, one skilled in the art could not readily identify other members of the genus (insulin DNA from other mammalian or vertebrate species) from a knowledge of only the rat insulin cDNA[6]. To uphold broad claims directed to a previously unknown group or genus of materials or products, defined in the claims in functional terms, *Eli Lilly* and subsequent decisions require "a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus"[7].

After *Eli Lilly,* the US Patent and Trademark Office (USPTO) issued guidelines for the examination of patent applications for compliance with the written description requirement[8]. These guidelines reflect the USPTO's understanding of the current law on written description and provide insight into how a US patent examiner will review an application in light of *Eli Lilly*.

Patents with broad generic claims issued before *Eli Lilly* and before the USPTO guidelines, thus raise a "red flag" and may merit a close examination as to whether, in view of recent case law, they would be found in compliance with the written description requirement if challenged in court today. Many of the early biotechnology patents have extraordinarily broad claims and scanty disclosure, and are, therefore, particularly vulnerable to a validity attack on grounds of either an inadequate description of the claimed subject matter or inadequate "enablement" information, as explained below.

The enablement requirement. A patent might also be challenged for noncompliance with "the enablement requirement"[9]. In order to satisfy this requirement, the disclosure in a patent specification must be sufficient to enable a person skilled in the art to practice the invention as broadly as it is claimed without "undue" or excessive experimentation[10]. As the United States Court of Appeals for the Federal Circuit has stated, "[t]ossing out the mere germ of an idea does not constitute enabling disclosure"[11]. The patent specification may therefore also be reviewed to determine whether it discloses representative working examples, and/or detailed instructions and guidance as to how to make and use the claimed invention, including where applicable, any starting materials or conditions under which a process or method can be carried out.

As with the written description requirement, biotech patents are held to a rigorous standard of disclosure with respect to enablement. This is evident from court decisions such as *Genentech, Inc. v. Novo Nordisk A/S*[12], where a Genentech patent directed to a cleavable fusion expression process for making human growth hormone was declared invalid for failure to satisfy the enablement requirement. The court noted that the specification was devoid of any detailed discussion of the cleavable fusion process: it did not describe a specific material to be cleaved or any reaction conditions under which this expression method would work.

Of particular relevance to biotechnology is the court's statement in *Genentech*, followed in later decisions[13], that "[w]here, as here, the claimed invention is the application of an unpredictable technology in the early stages of development, an enabling description in the specification must provide those skilled in the art with a specific and useful teaching"[14]. This pronouncement suggests that the earlier in the invention development process that an application is filed, the more difficult it may be to enable the claims.

This again raises particular concerns regarding older biotechnology patents. Not only were older patents written without any awareness of the stringent written description requirements, but they may face an additional hurdle in overcoming a challenge based upon non-enablement. An enablement determination is made retrospectively by looking back to the date that the patent application was filed and determining whether undue experimentation would have been required to make and use the invention at that time. Thus, what may seem enabled today given the current state of the art may not pass muster when evaluated against the knowledge that existed at the time of filing.

Freedom from infringement

Product (or process) clearance. Perhaps the most important aspect of any IP due diligence investigation is to assess and, if possible, to reduce the risk that present and future business activities of the target will infringe patent rights of third parties, a process known as "product clearance" or "process clearance". When "clearing" a product, it is also necessary to examine the process for making the product, as well as the method or methods for its use, because these could have been patented by others, and could form the basis for investor liability (for inducing or contributing to infringement) even if the target merely sells the product and does not make or use it[15].

Clearance involves obtaining a complete description of the activities (products or processes) to be "cleared", conducting searches of issued patents and published applications to uncover any claims that may be infringed, and analyzing the patents that are uncovered to assess the risk of infringement. Each component of a product, each process that is or will be used to make it, and each use to which it may be put, should be researched separately. The objective is to identify as many of the relevant patents as possible in order to assess accurately the risk that the investor or its customers may be blocked from commercializing or using the product at a later date. It is not uncommon in such cases to analyze third-party published patent applications in order to assess the likelihood that they will issue as patents with claims that will be infringed by post-transaction activities of the investor or its customers. Product clearance is particularly important in biotechnology, where many of the patents directed to basic developments in this field are still in force.

First inventor defense. The patent laws of many countries provide that a prior use of a later patented invention does not give rise to infringement liability if it began before the date the application for a patent was filed. Recently, the United States also enacted a law protecting from infringement liability both the developer and the first commercial user of an invention later patented by someone else, provided that the invention is directed to a method of doing or conducting "business", a term left intentionally broad and vague in the statute[16]. Needless to say, this freedom to operate can be very valuable. For example, a prior developer of an efficient bioinformatics method for resolving or mining genomic research data may be the only entity who can practice that technique without fear of liability if the method is later patented by another party. In that event, the due diligence team should carefully examine the records of development and first commercial use of the technique by the target, because freedom from infringement liability is contingent upon

the competence, completeness, and credibility of these records.

Third-party agreements

All agreements involving patents or other proprietary information to which the target is a party should be reviewed, both to identify additional IP assets (if the target is the grantee of rights) and to identify liabilities of the target's IP estate. If the target has granted even limited-scope licenses to the investor's competitors, for example, the investor may be foreclosed from exclusivity in a particular field. Unlike assignments, licenses are not required to be recorded, and a review of the relevant agreements is often the only way to obtain such information.

License agreements. A review of all license agreements in which the target has granted rights to others is therefore important. This review can help (1) determine whether all license agreements survive the contemplated transaction, and do not, for example, terminate if the target is acquired by another company; (2) compute the royalties that the investor may expect to pay out or to receive after the closing; (3) determine if any critical agreements are about to expire; (4) identify any potential liabilities created by representations and warranties made by the target in various agreements or by the presence (or omission) of indemnification provisions; and (5) identify products of the target that may not be covered by license and therefore may threaten the target's relationship with the licensor and expose the target to infringement liability.

Supply, distribution, and marketing agreements. All agreements that enable the target to use or to market its products must be reviewed. Consideration must be given to whether the target company is making use of goods or materials that incorporate patented technology or other intellectual property owned by third parties.

For example, if the target sells nucleic acid array kits packaged in packages with a patented design, and the packaging is supplied by a third party, the due diligence team may need to determine whether the target's supplier has secured the necessary authorization from the owner of the packaging patent to supply the packaging to the target company for the specific use.

Other agreements. Other important agreements that should be reviewed include collaborative, contract, and sponsored research, funding and development agreements, and employee and independent contractor (e.g., consultant) agreements. These agreements should provide for the transfer to (or retention by) the target of all relevant intellectual property rights and have adequate and enforceable confidentiality and other restrictive provisions. The employee or consultancy agreements may be especially important when the target expects to terminate employees or consultants before completion of the transaction. If a company does not have agreements with R&D contributors that include enforceable (e.g., not too restrictive) noncomplete or confidentiality provisions, the company's entire research effort toward development of a new product could be jeopardized if a key researcher terminates his/her employment with the company, takes his/her knowledge elsewhere, and is free to compete with the former employer .

Examination of agreements may reveal other liabilities, such as a consultancy with an individual who also consults for a competitor of the investor. In due diligence involving university-developed technology, agreements to which a principal investigator is a party (including consulting agreements) could also reveal any failures of the investigator to safeguard the proprietary nature of biological materials and information, or to avoid conflicts of interest. Accordingly, where the key technology was developed in a university, the investigators must be interviewed and all relevant agreements (even agreements in which the institution is not a party) carefully examined.

Litigation or other disputes

Claims by third parties against the target or its IP are always a concern for the investor. Due diligence should therefore identify any pending or threatened infringement action involving any assets of the transaction, as well as any future liability that the investor might be subject to as a result of actions of the target. Such information can be used by the investor in the valuation of the transaction as well as in risk assessment.

The investor should require the target to disclose any information regarding judgments, claims, orders, oppositions[17], settlements or even correspondence with an adverse or potentially adverse party that may affect the value of the patent rights being conveyed.

When potential claims are identified early, the transaction can often be restructured to account for them (as reflected, e.g., in a lower transaction valuation or an indemnification provision) or to avoid them (e.g., by excluding from the transaction activities, products, or intellectual property tainted by potential liability).

Report of findings

A report on the due diligence investigation should include a summary of the IP estate, including patent expiration or potential expiration dates, relevant agreements, royalty payments, and other obligations associated with the use of the proprietary technology to be transferred. Problems and/or risks should be identified, including claims for infringement as well as other pending or threatened litigation by or against the target and the products with respect to which claims or threats have been made or which are otherwise a source of potential liability for infringement. Where possible, the damages exposure and the likelihood that the adverse party would prevail should also be specified. Other items that should be noted are any new products for which patent protection must be obtained and any agreements currently being negotiated.

The report should also advise the investor about what it needs to do after the deal closes and provide recommendations for future actions, such as maintaining key patents, expanding patent coverage where this is feasible, and executing noncompetition and confidentiality agreements as well as agreements allocating IP rights with employees and consultants.

Conclusions

A strategically conducted IP due diligence review can elicit information useful in the adjustment of the acquisition purchase price, the renegotiation of key terms of the acquisition agreement, and an accurate assessment (and possibly reduction) of risks associated such a transaction.

Acknowledgments

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1. 35 USC §251.
2. 35 USC §112, ¶1; *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997).
3. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997).
4. Id. at 1568. (emphasis added)
5. Id. at 1566.
6. Id. at 1569.
7. Id.
8. Revised Interim Guidelines for Examination of Patent Applications Under the 35 USC Sec. 112, para. 1 "Written Description" Requirement, 64 Fed. Reg. 71, 427-71,440 (1999), updated Fed. Reg. 1099.
9. 35 USC §112, ¶1.
10. *In re Goodman*, 11 F.3d 1046, 1050 (Fed. Cir. 1993).
11. *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997).
12. *Genentech*, 108 F.3d 1361.
13. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362 (Fed. Cir. 1999).
14. Id. at 1367-8.
15. 35 USC §§ 271(b) and (c).
16. 35 USC § 273.
17. A patent opposition is a proceeding available in many countries in which an administrative tribunal within the patent office decides the merit of objections to a patent by one or more third parties. Even when a patent has survived such a proceeding, the record (and even any settlement agreement with one or more of the challengers of the patent) may reveal a potential weakness or infirmity of a corresponding patent in another country (such as the United States, where opposition is not available).