
How to make the most of IP due diligence in deals involving generics

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Abstract Due diligence is a necessary component of any transaction. One way or another — before the deal or during litigation involving the circumstances of the deal — a company involved in a transaction is going to have to do its due diligence. The objectives of due diligence are: (1) to identify risk to an appropriate level of detail in a due diligence report by understanding the assets of the target, issues relating to the target and how those issues may affect its ability to continue to operate its business and (2) to ensure informed drafting of the transaction documents so that they both shield the parties from liability and ensure the worth/value of a proposed transaction. Risk is identified by recognising hidden or unexpected liabilities and/or major regulatory obstacles to the acquisition. Intellectual property (IP) due diligence is a key component of technology-driven deals. Its purpose is to assess the scope, validity and enforceability of the target company's IP. A due diligence investigation involving generic medicines has specialised requirements. This paper will serve as a guide on how to make the most of IP due diligence in such deals.

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INTRODUCTION¹

It is no secret that consolidation is the name of the game in the generics industry today. In May 2007 alone, Mylan announced signing of a definitive agreement to acquire the generic drugs business of Merck KgA in a deal valued at more than \$6.7bn,² and Taro and Sun Pharmaceuticals announced the signing of a definitive agreement by which Sun is to acquire Taro in a deal worth \$454m.³

Due diligence is a necessary component of transactions — whether the transaction is an acquisition of stock or assets of a target company, a partnership, a minority investment, a merger, a private offering, a joint venture or a license. One way or another — before the deal or during litigation involving the circumstances of the deal — a company involved in such transactions is going to have to do its due diligence.

What is due diligence? It is both the investigation that is part of nearly every transaction and an affirmative duty to ensure compliance with obligations of disclosure. Several types of due diligence play a role in transactions: for example, financial due diligence (which often is conducted by investment banks, financial specialists and/or

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accountants), business due diligence (which often is conducted by senior representatives of, eg an acquirer and/or its consultants) and legal due diligence (which is the subject of this paper).

The objectives of due diligence are twofold: (1) to identify risk to an appropriate level of detail in a due diligence report (report) by understanding the assets of the target, issues relating to the target and how those issues may affect its ability to continue to operate its business and (2) to ensure informed drafting of the transaction documents so that they both shield the parties from liability and ensure the worth/value of a proposed transaction.

Risk is identified by recognising hidden or unexpected liabilities (eg environmental, employment-related or litigation-related liabilities), change of control triggers in key agreements (such as licenses-in or licenses-out, employment agreements, noncompetition agreements or restrictions on business (eg settlement agreements)), anti-assignment clauses in major agreements and/or major regulatory obstacles to the acquisition.

Due diligence to evaluate a target company's intellectual property (IP or IP due diligence) is a key component of technology-driven deals. Its purpose is to assess the scope, validity and enforceability of the target company's IP. Every IP due diligence investigation should be customised by the characteristics of the transaction. Factors include the type of IP involved, the budget/size of the transaction, the nature of the products of the target company and the relative importance of IP to the transaction. The scope of an IP due diligence investigation for a transaction involving a single patent will be different from that for a transaction involving a patent portfolio of more than 100 US and international patents. A large IP due diligence investigation may be conducted in phases, with the decision to proceed to phase II dependent on the satisfactory completion of phase I. For example, the decision may be made to

evaluate the risks involved in litigation(s) in process before proceeding to in-depth due diligence. The scope of the investigation necessarily is greater when the transaction involves securities because of the potential for criminal liability under the securities laws of the United States for making statements that are materially misleading.

SOURCES OF INFORMATION

A company has not conducted a reasonable due diligence investigation if it merely accepts information provided by the target company as fulfillment of its due diligence obligation. It always is necessary to conduct an independent investigation and then compare the results of this investigation to company-provided information.

Sources of information needed to conduct a due diligence investigation include publicly available information, company provided documents and interviews with company personnel.

The internet is a ready source of public statements made by company representatives relating to litigation positions, deals, IP issued, IP challenged and changes to key personnel. The target's website is a good place to start. Examples of official websites also offering useful information include the United States Patent and Trademark Office (USPTO, www.uspto.gov, for published US applications, issued US patents and trade marks); World International Patent Organization (WIPO, www.wipo.org, for international patents and patent applications); the European Patent Office (EPO, www.epoline.org, for European patents); the US Copyright Office (www.copyright.gov); and the US domain name registry (www.nic.us). PACER (<http://pacer.psc.uscourts.gov>) is an electronic public access service of the United States Judiciary that allows users to obtain case and docket information from US federal courts. For public companies, the website for the Securities and Exchange Commission (SEC, www.sec.gov) provides access to public filings, such as 10K, 10Q and 8K reports, which are

good sources of public statements made by a company. There is one caveat: while documents filed with the SEC often include material agreements, such as license agreements, these attachments usually are redacted to protect the company's confidential information.

Paid subscription services can be used for worldwide trademark searches and domain name registrations. Based on current knowledge, there is no service providing a global copyright search.

The target company is the best source for documents not obtainable from public sources, such as non-redacted material agreements and pending, but not yet published, patent applications. Typically the parties will conclude a confidentiality agreement in advance to ensure access to such information.

In view of the need for company trade secrets to be kept highly confidential, company management probably is the only source of trade secret information. In-house and outside counsel can provide insight into patent and litigation strategy.

Kinds of information to include in the report

IP assets

US and international patents, trade marks, copyrights, domain names and trade secrets are IP assets. The scope of IP assets always must be evaluated in view of the product(s) that they are supposed to protect.

Patents — A generic manufacturer may invest significant effort in research and development (R&D) to design around innovator patents, resulting in patents of its own. If a particular product/process is the value driver of the transaction, IP due diligence should focus on identifying IP that protects that product/process. This is particularly important to identify (and if necessary correct) any missed patent opportunities.

The report should tabulate information identifying patent applications, their inventors,

related applications, ownership, publication dates, issue dates, expiration dates and maintenance fees. For some due diligence investigations, the prosecution file histories of key patents may be reviewed to determine whether the claims of these patents were narrowed for reasons related to patentability or whether the target has taken inconsistent positions that can undermine its litigation position elsewhere.

(i) *Patent ownership*: State law, rather than federal patent law, generally governs ownership rights in patentable inventions, including the rights as between an employer and an employee. The general rule under US law is that an individual owns the patent rights in subject matter of which he/she is a sole or joint inventor even though the subject matter was conceived and/or reduced to practice during the course of employment.⁴ An employer, however, owns employee inventions if the employee is a party to an express contract or 'if the employee was specifically hired to exercise his/her "inventive faculties"'.⁵ An employer also may have a non-exclusive and non-transferable royalty-free license or 'shop right' to use the employee's patented invention.⁶ A person who occupies a position of responsibility, such as an officer of a corporation, may be under a fiduciary duty to transfer rights in patentable inventions.⁷

Under US law, title to a patent can pass only by written assignment.⁸ An assignment vests the assignee with legal title in the patent, which includes the right to sue infringers.⁹ Since an assignment of an interest in an invention secured by patent is a contract, it is to be construed to carry out the intent of the parties.

The report should indicate whether each inventor of each US patent or published patent application has assigned his/her rights, and if so whether title is clear. If there is a recorded security interest, for example, against a key patent, the transaction documents may require the company to clear title by a certain date.

Joint ownership situations may occur where a patent arose as a result of collaborations, sponsored research or development

agreements. Under US law, each joint owner owns an equal and undivided interest in a patent and therefore can license or transfer his/her interest without the consent of other joint owners. Normally each joint owner must join a suit to enforce a patent, but this requirement is waived if one joint owner has granted another the right to sue unilaterally. Furthermore, a joint owner's grant of a license may limit litigation damages. International law may be different; for example, UK and Japanese law require a joint owner's permission to grant a license.

(ii) *Patent expiration dates/priority*: The report should identify patent applications related to each patent in order to determine priority and expiration dates. Patent term-shortening mechanisms include terminal disclaimers and abandonment for failure to pay maintenance fees. Patent term extensions are available under US law for USPTO prosecution delays (up to five years); for regulatory delay (up to five years, to a maximum 14 years from date of approval); and for paediatric exclusivity, which adds six months to the patent term, even if the patent is subject to a terminal disclaimer.¹⁰ The due diligence investigation should determine whether an application for patent term extension due to regulatory delay was timely even though it may take years for the USPTO to grant a patent term extension for regulatory delay.

(iii) *Patent searches*: For some due diligence investigations, an independent freedom-to-operate search should be performed to determine whether the company will have freedom to use key IP covering the product/process that is the value driver. The search should cover the product/process, known indications, possible additional indications, dosage forms and dosages, and the claims of patents identified by the search need to be compared to the proposed product/process. In cases where the product/process is not fully developed, the freedom to operate analysis may wind up being broader than desirable, but this broad analysis may help direct the development process.

For some due diligence investigations where key IP has not yet been granted, an independent patentability search also may be desirable.

Trademarks: Wherever possible, the report should document each mark by country, application serial number, filing date, registration number, registration date, class/description, status (live or dead), owner and comments. International trademark searches can be conducted using free, online international databases or using professional search vendors where available.

Copyrights: It is worth noting that unlike the situation for patents, a joint owner of a US copyright may exploit that copyright without permission of other joint owners but has a duty of accounting to the other joint owners and must share royalties.

Domain names: The report should confirm that domain names for key products are registered in key markets.

Licenses/agreements involving IP

The report should contain such key information as the parties to each agreement, whether the license is a license-in or license-out, whether it is exclusive or non-exclusive, a definition of the licensed technology or field, IP covered by the license (eg does the license cover improvements?), whether it is assignable and/or sub-licensable, the license term, termination events and status.

Patent due diligence, including an assessment of how critical the licensed-in IP is to the product that is the value-driver, and an assessment of whether there are potential third-party challenges relevant to that IP, often is indicated for licensed-in IP. Licensees have greater freedom to challenge validity in the aftermath of the Supreme Court's decision in *Medimmune v Genentech*, which held that a licensee does not have to breach its licensing agreement to challenge the validity of a patent.¹¹

The report also should summarise change-of-control triggers and anti-assignment clauses in license agreements, confidentiality

agreements and non-competition agreements or other restrictions on business. Settlement agreements that prevent patent challenges are likely to be upheld, while no challenge clauses may be unenforceable.

Litigation exposure

The report should assess the risk associated with litigations in process based on existing abbreviated new drug application (ANDA) filings. Interviews with executives involved in decision-making may be desirable in order to evaluate, in each case, whether the target's positions are realistic and whether the certifications and factual and legal basis memorandum filed in support of each certification is appropriate. The cost of litigation, the profitability of the product at issue, the litigation strategy and the likelihood of success in litigation should be considered in evaluating the risk associated with ongoing litigation. For example, the target may have good legal positions but may need to make a highly technical case in a highly unfavourable litigation venue.

The report also should address factors involved in product selection. The investigation should review searches performed by the target, the target's efforts to design around, formal opinions, cease and desist letters (if any) received by the target, failed licensing/partnering negotiations, settlement agreements and outsourcing agreements.

(a) *Searches*: The report should assess the company's diligence in monitoring the patent landscape. To decrease exposure to infringement risk, a search should provide a reasonable level of assurance that all patents relating to a particular generic product have been identified. The investigation therefore should include not only Orange Book patents but also non-Orange Book patents. Again, the target's product/process must be compared to the claims of each patent identified in the search. Opportunities to submit requests for re-examination or for oppositions also may be identified during the investigation.

(b) *Efforts to design around*: To account for patent problems in the development schedule, it is best to identify key patents early, that is, as soon as a particular active ingredient is identified as a development candidate. Generics that then patent their own innovations will have a less advanced prior art base. Because more patents are being filed earlier in the lifecycle by innovators and because a larger number of interested parties are filing those patents, generic manufacturers may be forced to make a significant R&D effort to design around these patents. Patents hard to design around should be recognised early to allocate resources and avoid redevelopment costs. It also is important to recognise the need to continually monitor the patent position for an active ingredient under development because slight changes to reaction conditions may change a non-infringing product into an infringing one. The best source of information sufficient to understand the target's patent position probably will be senior management in the regulatory R&D and manufacturing areas. A common interest agreement may be required in order to gain access to this information, but the target may be hesitant to execute such an agreement unless the transaction is at a sufficiently advanced stage.

(c) *Formal opinions*: The target may be hesitant to share opinions of counsel because it does not want to risk waiving the attorney-client privilege. If such opinions are sufficiently important to become a deal-breaking issue, an independent search should be performed and new opinions developed.

(d) *Cease and desist letters*: The report should summarise the company's efforts to address letters from third parties. Any cited IP should be evaluated to determine whether the transaction documents will need to have provisions requiring good faith negotiations to result in a license for key IP.

(e) *Settlement agreements*: The report should address efforts to identify any potentially anticompetitive agreements that could place 180-day exclusivity at risk (eg settlements

involving reverse payments and agreements with competing generic entrants). It also should identify provisions and conditions that provide that IP, particularly key IP, is to be returned to the other party.

(f) *Outsourcing agreements*: 35 U.S.C. §271(f) creates a cause of action for patent infringement due to foreign sales when a component of a patented invention is supplied from the United States with knowledge that the component will be combined in an infringing manner outside the United States. It is unknown whether court decisions in *Eolas v Microsoft*¹² and *Research In Motion, Ltd. v NTP, Inc.*,¹³ both of which concern the meaning of the term ‘component’ in the context of information technology, will be extended to include shipment of DNA or other genetic material out of the United States for replication and incorporation into an invention that is patented in the United States and thereby give rise to infringement liability.

Two basic principles have emerged from each case. The court’s decision in *Eolas v Microsoft* resulted in the principles that (1) there is no physicality requirement for a component of a patented invention to fall within the statute and (2) a foreign-produced copy of the shipped component can create infringement liability when the copy is to be used in an infringing manner.¹⁴ The court’s decision in *Research in Motion, Ltd. v NTP* resulted in the principles that (1) the plain language of 35 U.S.C. §271(a) does not preclude infringement where a system is used within the United States even though a component of that system is physically located outside the United States and (2) the test to determine infringement is whether control and beneficial use of the infringing system was within the United States.¹⁵

(g) *Declaratory judgment actions*: The report should note whether the company has filed, or should file, any Declaratory Judgment (DJ) Actions, or has made, or should make, other attempts to revoke or invalidate patents. *Medimmune* represents a lowering of the bar regarding the standard necessary to establish

DJ jurisdiction to merely require an actual controversy based on a totality of the circumstances.¹⁶

DJ actions offer certain strategic advantages: they allow the filer to file suit rather than to wait to be sued, to choose a convenient forum, to open and close at trial, to resolve specific issues (eg ownership, license rights, laches, estoppel) and to avoid a jury trial, since a DJ is historically equitable in nature.

It always is a good idea to monitor and weigh the impact of pending legislation that may change the rules of the game. For example, patent reform legislation pending in the US Senate¹⁷ provides venue restrictions that apply not only to claims for infringement but also to DJ actions. The legislation provides, for example, that venue for a foreign infringer will be the foreign corporation’s residence, which is where its main US subsidiary is located. This proposal therefore would provide a foreign corporation with incentive to locate its US subsidiary in the most infringer-friendly forum.

Regulatory obstacles to the transaction

Internal Review Board (IRB) endorsements, regulatory submissions (including investigational new drug applications (INDs), new drug applications (NDAs), ANDAs, 505(b)(2)¹⁸ applications (ie applications in which the applicant relies on safety and effectiveness data in another applicant’s NDA), annual reports and correspondence, particularly with regulatory agencies, should be examined to help identify regulatory obstacles to the transaction.

Third-party consents: The report should identify what, if any, regulatory or third-party consents are necessary. For example, a drug manufacturer that is seeking to buy a plant in another state, operate it for a short time and then relocate the plant, would be required to submit information to the Secretary of Health and Human Services to register changes in the prior registration for the facility. The transaction documents consequently would need to contain a provision requiring the

target to provide the purchaser with its registration so that the registration could be updated in a timely manner to reflect the change in control.

Regulatory approvals: The report should consider the risk that the federal Food and Drug Administration (FDA) will reconsider its policy regarding the extent to which a 505(b)(2) application can rely on innovator data. A 505(b)(2) application allows sponsors that do not have a right of reference to all the data needed for an approval to rely on the FDA's findings of safety and efficacy for an approved drug or on published literature, rather than conduct their own studies.¹⁹

In 2001, Pfizer filed a Citizen's Petition seeking amendment of CDER's 'Guidance for Industry: Applications Covered by Section 505(b)(2)' so as not to permit a Section 505(b)(2) applicant to rely on another applicant's non-public data and not to permit findings of therapeutic equivalence between a 505(b)(2) NDA drug and the innovator drug it copies. On 14th October, 2003, the FDA issued a partial response denying Pfizer's citizen petition in which the FDA addressed the legal bases and policy reasons for its interpretation and application of Section 505(b)(2) but reserved for further review the issue of whether there is a subset of applications that should be exempted from the scope of Section 505(b)(2) of the federal Food, Drug and Cosmetic Act (FDCA).²⁰ Although Pfizer, Inc. subsequently sued the FDA, the suit was terminated as not ripe on 30th September, 2005.²¹

Furthermore, even if the target believes that its products will be regulated as medical devices and therefore will have a shorter regulatory path, the report should assess the risk that the FDA could decide that the target will need to comply with the drug approval process under the FDCA if the FDA decides to regulate the product as a drug and not as a medical device.

Market exclusivities: The report also should provide sufficient information to assess the effect on the target's proprietary and generic

products in development of market exclusivities available to NDA holders in the United States. With the exception of Orphan Drug exclusivity,²² exclusivity is not automatic, that is, the FDA requires that each NDA applicant submit information to allow the agency to determine whether the application qualifies for a period of 'market exclusivity'.²³ The regulation is explicit on the information that must be submitted.

The exclusivity provisions of the Hatch–Waxman Act limit the ability of a generic manufacturer to obtain FDA approval of a drug based on the approval of a pioneer product. A second manufacturer can still obtain approval of its version of the same drug, for example, through submission of an NDA or a new animal drug application (NADA), which includes full safety and effectiveness data. While these provisions do not provide an exclusive right to market the drugs to which they apply in the United States, because of the expense and time involved in generating such data, 'exclusivity' effectively does provide exclusive marketing rights for the applicant that so qualifies.

The exclusivity provisions provide that an applicant may claim five years of exclusivity against submission of an ANDA or 505(b)(2) NDA for the first approval of a new chemical entity.²⁴ This applies only to applications for drugs that contain no active ingredient that has been approved previously by the FDA in any other application under FDCA Subsection (505)(b). According to a respected treatise, this includes prior approvals of alternative chemical forms of the active ingredient (ie ester or salt) in the condition for exclusivity.²⁵ Thus, a previous approval of the active ingredient or a salt or ester of that ingredient would bar exclusivity for that ingredient, while prior approval of the active ingredient in the acid form would not bar exclusivity for the salt or ester form.

In one instance, the five-year exclusivity period becomes a four-year period. If the ANDA, ANADA or 505(b)(2) application contains a certification of patent invalidity or

non-infringement (Paragraph IV Certification), the ANDA, ANADA or 505(b)(2) application may be submitted four years after FDA approval of the application accorded exclusivity under this provision.²⁶ Approval of the ANDA, ANADA or 505(b)(2) application is held up if an action for patent infringement is commenced during the year after the four-year exclusivity period expires.

The exclusivity provisions also provide that the FDA can approve three years of 'exclusivity', during which no ANDA or 505(b)(2) application can be approved on the basis of the subject NDA or supplement for new NDAs for previously approved drugs when the NDA is supported by new clinical investigations, conducted by the applicant, that are essential to approval.²⁷

To show that the application contains 'new clinical investigations', an applicant claiming a three-year exclusivity under 21 C.F.R. 314.108(b)(4) or (b)(5) must certify that to the best of its knowledge, each of the clinical investigations (meaning any experiment other than a bioavailability study in which a drug is administered to, dispensed to, or used on, human subjects) included in the application is 'an investigation in humans, the results of which have not been relied on by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety for a new patient population, and do not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness or safety in a new patient population of a previously approved drug product'.²⁸ For purposes of this section, data from a clinical investigation previously submitted for use in the comprehensive evaluation of the safety of a drug product but *not* to support the effectiveness of the drug product would be considered 'new'.²⁹

To show the 'conducted or sponsored by' element, an applicant for exclusivity must identify the IND by number if the applicant was the sponsor named in Form FDA-1571 for an investigational new drug application

(IND) under which the new clinical investigation(s) essential to the approval of its application was conducted. If the applicant was not the sponsor of the IND under which the clinical investigation(s) was conducted, it must certify that the applicant or its predecessor in interest provided 'substantial support' for the clinical investigation(s) essential to the approval of its application, and information supporting the certification. To show 'substantial support', it must provide either a certified statement from a certified public accountant that applicant provided 50 per cent or more of the cost of conducting the study or provide an explanation of why the FDA should consider the applicant to have conducted or sponsored the study if its financial contribution is less than 50 per cent or the applicant did not sponsor the investigational new drug.³⁰

'Essential for approval' means that there are no other data available that could support approval of the application.³¹ To satisfy the 'essential to its approval' requirement, an applicant claiming a three-year exclusivity must conduct a literature search and submit (i) a list of all published studies or publicly available reports of clinical investigations relevant to the conditions for which it seeks approval; (ii) a certification that it has thoroughly searched the scientific literature; that to the best of its knowledge, the list is complete and accurate; and that, in its opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval of the conditions for which it is seeking approval without reference to the new clinical investigation(s) in the application; and (iii) an explanation as to why the studies or reports are insufficient.³² Paediatric exclusivity³³ (reauthorised by Congress as part of the Food and Drug Administration Amendments Act of 2007 (FDAAA))³⁴ is available to patents covering an approved drug substance (active ingredient), drug product (formulation and composition) or method of use. It provides the patent holder with six months of additional

protection from generic competition after expiration of a patent as a reward for studying drugs in children.

Thus, where a Paragraph III certification has been filed, it may be possible for an innovator to keep generic competition out for five years, plus three additional years for new indications, plus six months for studying its approved drug substance (active ingredient), drug product (formulation and composition) or method of use in children, for a total of eight and a half years. Where a Paragraph IV certification has been filed, it may be possible for an innovator to keep generic competition out for four years, plus three additional years for new indications, plus six months for studying its approved drug substance (active ingredient), drug product (formulation and composition) or method of use in children, for a total of seven and a half years.

An additional Orphan Drug Exclusivity (which was enacted before Hatch–Waxman) prohibits approval of generic copies of an orphan drug (an orphan drug is a drug (both new drug and biologics) for a rare disease or condition) through an ANDA or a 505(b)(2) application and delays approval of a second company's version of the orphan drug even if the second company submits a full NDA containing a new set of safety and effectiveness investigations to the FDA for that drug for seven years.³⁵ The seven-year period reflects the time it will take to recover the cost of developing an orphan drug from sales of such drug in the United States. The exclusivity only applies to the disease or condition for which the approved drug was designated.³⁶ The seven-year exclusivity period can be extended for an additional six months by paediatric study. Orphan Drug Act exclusivity is automatic when the statutory criteria have been met, without further FDA action.

Follow-on biologics: If the transaction is driven by the desire to acquire follow-on biologics capability, the uncertainty regarding a statutory mechanism for filing abbreviated applications in the United States (Congress

failed to approve follow-on biologics legislation in 2007) should be weighed against the cost of filing under the existing statutory scheme. Currently, biologics in the United States are approved and licensed under §351 of the Public Health Service Act and not the FDCA, which lacks any statutory mechanism for filing an abbreviated application. The 505(b)(2) pathway was used by Sandoz to gain marketing approval in the United States for Omnitrope, its 'generic' human growth hormone product.³⁷ The European Medicines Agency's (EMA's) guidelines on regulation of biosimilars are instructive.³⁸ The EMA (1) requires comparability studies, which will impact the number of non-clinical and clinical studies required; (2) requires clinical studies to show safety and effectiveness, in particular addressing immunogenicity concerns; and (3) expects postmarket pharmacovigilance plans as part of approval commitments.

180-day exclusivities: The report furthermore should contain an evaluation of all 180-day exclusivities to ensure that no events have occurred or will occur that could lead to the target's forfeiture of its 180-day exclusivity opportunities.

The 180-day exclusivity provisions of the Hatch–Waxman Act were amended in 2003 by the Medicare Modernization Act of 2003³⁹ (MMA). The MMA amendments permit 180-day exclusivity only for ANDAs containing a Paragraph IV certification made on the first day in which any such certification is made for the drug, certifying that such patent is invalid or will not be infringed by the manufacture, use or sale of the new drug for which the application is submitted. There is no similar 180-day exclusivity period applicable to 505(b)(2) applications.

The MMA amendments require that the ANDA containing a Paragraph IV certification be a 'substantially complete application' (meaning one that on its face is sufficiently complete to permit a substantive review and contains all the information required in an ANDA) in order to qualify for

180-day exclusivity.⁴⁰ The various ‘first applicants’ with ‘substantially complete applications’ have a potential for 180-day exclusivity but may have to share the market with any other first applicant.⁴¹

The 180-day exclusivity period begins on the date of first commercial marketing of the drug by any first applicant. The MMA states that marketing of the innovator drug under the innovator’s NDA by any first applicant (which sometimes occurs as a result of settlement of patent litigation) begins the 180-day period.⁴² This recognises that a generic applicant may, in some cases, be willing to launch at risk after the 30-month period expires. It also provides a useful trigger when there has been no patent suit. A decision dismissing a declaratory judgment action for lack of case or controversy also can start the 180-day exclusivity period.

For ANDAs containing a Paragraph IV certification filed after 8th December, 2003, the 180-day period will no longer be triggered by a court decision finding a patent invalid or not infringed. For any product for which there was an ANDA containing a Paragraph IV certification before 8th December, 2003, and for which the exclusivity was not already triggered before 8th December, 2003, a court decision can still trigger the 180-day exclusivity period. In this case, the triggering court decision must be one from which no appeal has been or can be taken (generally a decision of an appellate court).

An ANDA applicant entitled to 180-day exclusivity will lose that exclusivity if any of the following forfeiture events occur:⁴³

(a) *Failure to market*: An ANDA applicant entitled to 180-day exclusivity will lose that exclusivity if that applicant fails to market its drug by the later of (1) 75 days after the first applicant’s approval is made effective or 30 months after the date of the submission of the application, whichever is earlier or (2) 75 days after at least one of the following occurs with respect to the first applicant or any other applicant that has tentative approval and with

respect to each patent for which the applicant qualifies as a first applicant: (i) a final decision that the patent is invalid or not infringed is entered by a court from which no appeal (other than a petition for certiorari to the US Supreme Court) has been or can be taken in an infringement case or a DJ action; (ii) an infringement or DJ action is settled and the court signs an order or consent decree that enters a final judgment, including a finding that the patent is invalid or not infringed; or (iii) the NDA holder withdraws the patent information for the patent.

(b) *A change in patent certification*: A first applicant may lose 180-day exclusivity if the first applicant amends or withdraws its Paragraph IV certification for all patents for which it was eligible for 180-day exclusivity.

(c) *Failure to obtain tentative approval*: A first applicant may lose 180-day exclusivity if it fails to obtain tentative approval within 30 months after the ANDA is filed, unless that failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

(d) *Illegal settlement agreement*: A first applicant may lose 180-day exclusivity if the first applicant enters into an agreement with another ANDA applicant, with the NDA holder or with the patent holder and the US Federal Trade Commission or US Attorney General files a complaint leading to a final decision that the agreement violates the antitrust laws of the United States or Section 5 of the Federal Trade Commission Act.

(e) *Patent expiration*: A first applicant forfeits its exclusivity if all the patents that form the basis for its exclusivity expire.

In conclusion, the worst outcome of a due diligence investigation is that the target is so afraid that the investigation will block the deal that it holds back vital information. A due diligence investigation often does not produce a thumbs up or a thumbs down on the deal. Instead, its purpose is to identify the risks involved in the deal; and, if possible, help to mitigate those risks with the proper terms

and price so that the transaction can go forward.

References and Notes

1. This paper is based on a presentation given by the author during the Eighth Annual Generic Drugs Summit in Washington, DC, 17th–19th September, 2007.
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11. *Medimmune, Inc. v Genentech, Inc.*, 127 S. Ct. 764 (2007).
12. *Eolas Technologies, Inc. v Microsoft Corp.*, 457 F.3d 1279 (Fed. Cir. 2006).
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14. *Eolas Technologies, Inc. v Microsoft Corp.*, 457 F.3d 1279 (Fed. Cir. 2006).
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17. Senate Bill No. S1145, The Patent Reform Act of 2007.
18. 21 U.S.C. §355(b)(2).
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20. Letter from Janet Woodcock, MD, Director, Center for Drug Evaluation and Research, Food and Drug Administration, to Katherine M. Sanzo, Esq., *et al.*, Docket Nos. 2001P-0323/CP1 & C5, 2002P-0447/CP1, and 2003P-0408/CP1 (14th October, 2003), www.fda.gov/ohrms/dockets/dockets/04p0231/04p-0231-c000001-toc.htm; Exhibit 29, accessed 11th February, 2008.
21. *Pfizer, Inc. v Food & Drug Administration et al.*, Docket 1:03-cv-02346-RCL (filed 13th November, 2003), Dismissed 30th September, 2005 (Docket documents 19 and 20). In its complaint (document 1, filed 13th November, 2003), Pfizer alleged that the FDA's final agency action in approving Dr Reddy's NDA for amlodipine maleate, which relied on non-public proprietary data in Pfizer's NDA for Norvasc®, was a violation of the FDCA, the Administrative Procedure Act, 5 U.S.C. § 706(2)(A), and the Trade Secrets Act, 18 U.S.C. § 1905, because the FDA improperly referenced and relied on Pfizer's proprietary, trade-secret data to support the approval.
22. 21 U.S.C. §360aa- §360ee.
23. 21 C.F.R. § 314.50(j); 59 Fed. Reg. 50388 (1994).
24. 21 U.S.C. §355(j)(5)(F)(ii).
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26. 21 U.S.C. § 355(j)(5)(F)(ii).
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28. 21 CFR 314.108(a); 21 C.F.R. 314.50(j)(4)(i).
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30. 21 C.F.R. 314.50(j)(4)(iii).
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37. Sandoz press release, www.us.sandoz.com/site/en/company/news/pool/20060531_omnitrope_media_release.pdf, accessed 11th February, 2008.
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42. 21 U.S.C. § 355(j)(5)((iv)(I)).
43. 21 U.S.C. § 355(j)(5)(D).