

Bloomberg

BLOOMBERG LAW REPORTS®

Health Law

VOL. 3, NO. 2

February 2010

Daughter Had Capacity to Contractually Bind Mother to Arbitration

Lumpkin first asserted that her daughter lacked capacity to bind her to arbitration when acting as a health care surrogate under the Uniform Health-Care Decisions Act, [Miss. Code § 41-41-201](#). The court noted that this issue was decided in a previous case, *Covenant Health Rehab. of Picayune, L.P. v. Brown*, [949 So.2d 732](#) (Miss. 2007). Just as in that case, the court found that because there was no dispute that McDaniel was acting as Lumpkin's health care surrogate, she had authority to contractually bind Lumpkin to the arbitration provision.

Arbitration Clause Had Sufficient Consideration

Lumpkin then argued that the arbitration clause lacked sufficient consideration and that it should be stricken from the agreement. She based this argument on the testimony of the facility administrator who stated that Lumpkin would not have been refused admission if she objected to the arbitration provision.

The court noted that the administrator's statement did not determine whether there was sufficient consideration, although it did indicate that McDaniel could have negotiated a better arrangement for her mother. Moreover, the court noted that the statement would not be admissible due to the parol evidence rule, which provides that a written contract cannot be changed by prior oral agreements. Although parol evidence may be admissible when a contract is ambiguous, the court stated that there had been no showing or suggestion that the admission agreement was ambiguous.

The court explained that consideration is present when there is either a benefit to the promisor or a detriment to the promisee. The court found clearly sufficient consideration to support the arbitration agreement. The court noted that both parties performed duties to each other under the admissions agreement. Covenant provided care and Lumpkin paid for the services provided. Thus, the court found that the admissions agreement did not fail for lack of consideration.

Court Finds Dispute Within Purview of Arbitration Clause

The court further found that the claims of negligence and malpractice fell within the purview of the arbitration clause. The arbitration clause specifically required that any and all "claims, disputes and/or controversies" between the parties be resolved through binding arbitration.

Arbitration Provision Unenforceable

The court then examined whether the arbitration clause was invalidated by any external legal constraints such as fraud, duress or unconscionability. The court concluded that it was not.

First, the court rejected Lumpkin's contention that Covenant fraudulently misrepresented that the arbitration clause was a necessary condition for admission to the facility. The court explained that fraud in the inducement occurs when a party asserts information he knows is untrue to induce the other party to enter into the contract. In this case, the court noted, the admission agreement did not contain any false information. The mere fact that Covenant would have altered the terms if asked did not constitute fraud.

Second, the court found that although the admission agreement contained several unconscionable provisions (e.g., a provision requiring a resident to forfeit all claims except those for wilful acts and a provision requiring a resident to waive liability for criminal acts). The court observed that these provisions were the same as those struck in the *Brown* case as well.

The court noted that, in its original opinion, it concluded that the unconscionable provisions in the contract were severable and did not require it to declare the entire contract — or even the arbitration provision — unenforceable. However, the court explained that *Estate of Moulds* examined the issue and surveyed other court rulings on similar contracts. In *Estate of Moulds*, the court overruled its prior precedent because it found an arbitration clause identical to that in Lumpkin's admission agreement to be unconscionable and unenforceable. That decision prompted the court to re-examine its own decision. The court then ruled that, in light of *Estate of Moulds*, the arbitration clause at issue was unconscionable and the trial court did not err in refusing to compel arbitration. The court thus affirmed the lower court and remanded the case for further proceedings.

Pharmaceuticals, Medical Devices & Biologics

Labeling

Efficacious and Safe Drug Labeling Strategies - The Access to Affordable Medicines Act

Contributed by Kimberly Weinreich and Jeffrey A. Wolfson, Haynes and Boone, LLP

This article discusses U.S. drug labeling strategies used by brand (also referred to as innovator) and generic pharmaceutical companies, including the most recent proposed drug labeling changes in the Access to Affordable Medicines Act (AAMA).

In particular, the overlap of patent protection, labeling, and Food and Drug Administration (FDA) approval are discussed in the context of the regulatory framework and history of drug labeling, and the currently pending health care legislation.

A Brief Drug Labeling History

Historically speaking, drug labeling may have begun with drug labels in the mid 15th century on recovered Italian apothecary jars, the use of which spread to France, Germany and The Netherlands throughout the 16th and 17th centuries.¹ By the late 16th century, there was a growing concern that all apothecary jars be correctly labeled, evidenced by extensive published writings on the subject² and the case of a Barcelona pharmacist who falsely labeled his products and was forever barred from the pharmacy profession.³ The first formalized drug warning label regulation appears to have been when a group of London druggists adopted a set of regulations for marking poisons in 1818, which required a label still recognizable today as the skull and crossbones.⁴

The present U.S. labeling requirements arose as a result of similar concerns over mistaken drug identity and intentional false labeling, as well as efforts to regulate unproven, far-fetched or untruthful therapeutic or curative claims such as healing disease through appeals to the mind⁵ or curing drunkenness through scientifically unsupported and unproven methods.⁶ As a result, current [section 502](#) of the Federal Food, Drug and Cosmetic Act (FD&C Act) was enacted in 1906. Section 502(a) provides that a drug or medical device “shall be deemed to be misbranded . . . if its labeling is false or misleading in any particular.” Although still valid law today, the FDA primarily uses other legislation, e.g., the Drug Amendments of 1962, [Pub. L. No. 87-781](#), [76 Stat. 780](#), (1962) to regulate drug labels.

The Drug Amendments of 1962 require premarket proof of a drug’s effectiveness before allowing the drug to enter the market in the form of FDA approval of a [New Drug Application](#) (NDA). As part of the NDA approval process for any drug, the FDA must review and approve the labeling, i.e. all of the printed information that accompanies a drug including the label, the wrapping and the package insert.⁷ The drug label is the pharmaceutical company’s and the FDA’s representation to the consumer that the drug is sufficiently safe and effective for public consumption. At a minimum, labels typically include dosage information, directions for administration, the conditions for which the drug is effective, contraindications, and warnings about side effects and adverse reactions.⁸ If a drug label is considered by the FDA to be false or misleading in any particular, the NDA will be rejected and the drug banned from entering the market unless and until the label is suitably corrected. Should any errors be made in labeling and harmful new drugs be placed on the market, both the drug

company and the FDA, under the Federal Tort Claims Act, [28 U.S.C. § 2671](#), *et seq.*, can be held liable to the affected consumers. Naturally, innovator drug companies and the FDA take great care in accurately labeling, and in reviewing and approving, drug labels.

The scrutiny of the label continues after the drug is marketed. Typically, if a drug claim is false, lacking in fair balance or otherwise misleading,⁹ the FDA will negotiate with the drug company and sometimes require a “corrective” advertisement through the same channel(s) as the original, or a revised warning label that reflects any newly obtained information, or possibly both.¹⁰ Rarely does this issue go to court at the behest of the FDA. Rather, competitor pharmaceutical companies typically bring a Lanham Act lawsuit for unfair competition based on false or misleading competitive claims in labeling or advertising.¹¹

Generic Drug Labeling Loophole

The drug approval process, including labeling, is considerably less arduous for generic drug companies to incentivize the entry of low cost generic drugs onto the market quickly. The increasing use of required generic drug substitution by health programs and insurance agencies, as well as state generic substitution laws, has also added to the generic market share. In 1984, the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act, [Pub. L. No. 98-417](#), [98 Stat. 1585](#) (1984), amended the FD&C Act to establish the current streamlined FDA approval process for generic drugs.¹² Generic drugs regulated by the current FDA approval process are restricted to those having small chemical molecules, as contrasted with typically larger structures found in biologic drugs now beginning to enter the marketplace. While Congress is presently considering biologics legislation that would authorize biogenerics, i.e., generic-type follow-on applications to biologic-type drugs, the discussion here relates to the existing generic drug labeling regulatory framework for small chemical molecule generic drugs.

Generic companies file an [Abbreviated New Drug Application](#) (ANDA), where generally preclinical and human clinical data is not required to establish safety and effectiveness since that was previously done by the innovator company. Instead, generic applicants can “piggyback” their ANDA by submitting scientific data that their drug is bioequivalent to the original one. Generally, bioequivalency means that the generic drug has the same active ingredient, route of administration, dosage form and strength as the original drug.¹³

An ANDA applicant must also certify that, to the best of the applicant’s knowledge, either (I) the original drug has not been patented, (II) the patent(s) has already expired,

(III) the generic will not be commercialized until the patent(s) expires, or (IV) the patent(s) is not infringed or is invalid (*i.e.*, a paragraph I, II, III, or IV patent certification respectively).¹⁴ To streamline this analysis and create the best possible public notice of patents covering each original drug product, the FDA publishes the “Orange Book,” which contains all NDA and ANDA approvals, as well as patent and exclusivity information and product changes.

After conducting their research and submitting bioequivalence data and a patent certification, among other parts of the ANDA, generic drug manufacturers typically have to label the generic for the same indications as that of the original, with exceptions for differing manufacturer information or if some information on the original drug label was covered by patent or market exclusivity.¹⁵ Recently, courts have begun broadening these exceptions to ensure that generic drug labels are permitted to truthfully include up-to-date safety data and warnings, even if their original counterparts do not.¹⁶ Legislation that would prohibit lawsuits against generic manufacturers for not including such information on their labels was pending before Congress but has apparently been dropped in legislation that would prohibit original drug manufacturers from giving “reverse payments” to generic manufacturers to defer generic entry onto market.¹⁷

Generic companies can also take a different approach when seeking FDA approval. Instead of certifying that a product covers the same “method of use” or “indication,” as the original product, generic companies can submit a so-called “section viii statement” that the patent(s) owned by the brand company is inapplicable to the generic company’s desired use.¹⁸ In effect, a section viii statement asserts that the labeling in the ANDA does not include one or more uses claimed by one or more of the original drug company’s method of use patent(s). A section viii statement is only appropriate when an applicant can “carve out” information protected by the use patent from the labeling for the proposed ANDA product, yet still have the product remain safe and effective.¹⁹ This is sometimes referred to as “skinny labeling.”²⁰ If truly different usage and indications are sought to be treated than those covered by patent rights, or if a different patient population is sought to be treated, there is no possibility for a patent infringement action because no infringement of the method of use patent rights would occur. There can be intertwining patent claims throughout the label, however, so deciding what can and should be safely “carved out,” if anything, can lead to citizen petitions to the FDA and litigation threats from brand drug owners. Such petitions and litigation, in turn, can delay market entry of generic drugs—sometimes improperly. Infringement claims can be direct assertions that commercialization of a generic drug will result in a patent violation, or they can be assertions that inducement

to infringe is occurring or will occur, such as by instructing others, *i.e.* physicians, pharmacists and patients, on the label how to violate patent rights. Skinny labels limit the potential market for the generics to fewer than all the approved uses of the original drug product, thereby providing a balance in protecting the patent rights of the original drug developer.

The use of section viii statements and skinny labels has, however, gained increasing importance for generic drug companies, both because doctors and pharmacists have increasingly prescribed drugs for “off label” uses,²¹ and because various original drug patents are expiring leaving protection only for more recently developed and patented indications. The FDA does not have the authority to regulate the practice of medicine, which permits physicians to prescribe drugs off-label, *i.e.*, for uses not approved by the FDA, even though drug companies are not permitted to legally advertise or market such off-label use. Even with billions of dollars worth of fines for violation of this mandate, promoting off-market use remains profitable for some drug companies.²² Indeed, a new FDA rule that allows pharmaceutical sales representatives to distribute peer-reviewed journal articles promoting off-label drug use to physicians, and a recently filed lawsuit challenging the FDA restrictions on promoting unapproved use based on free-speech grounds could further complicate the management of off-label use.²³

At this time however, mandatory state substitution laws plus the ability to prescribe off-label uses essentially permit physicians to prescribe drugs for off-label uses, such as giving a patient a generic drug not labeled for one of the brand company’s labeled, approved uses.²⁴ As off-label use has broadened, some brand drug companies have more actively policed their patents, particularly unlisted patents not in the Orange Book. Such patents are sometimes enforced even if they are just tangentially related to the pharmaceutical product, which is possibly the best way for a brand drug company to seek to prevent potential carve outs by generic companies. Depending on the approved indications and related series of method of use patents filed by some brand drug companies (*i.e.* by use of patent “evergreening”), there can be few, if any, indications available as a carve out for a generic company to seek section viii approval.²⁵ At least one brand company has tried to alter its Orange Book listings so as to avoid carve outs, but this has met with no success in the courts so far.²⁶ Section viii statements will surely become even more profitable to generic companies if recent proposed legislation, the Drug Price Competition Act of 2009, S. 1315,²⁷ and its companion House bill H.R. 3777,²⁸ are enacted. The Drug Price Competition Act of 2009 provides 180-days of market exclusivity to the first generic company to file either a section viii statement, or a more traditional paragraph IV certification.²⁹

Innovator Drug Labeling Loophole

As generic drugs have increased in market presence, particularly in the present era of greater public consciousness over health care costs and proposed health care legislation, brand drug companies have had to develop strategies to compete. One useful tactic some brand companies use in prolonging their dominant, or solo, presence on the market has been to amend or update product labeling both before and after the drug has entered the market. If a brand drug and a generic drug are already on the market, the brand company can seek patent protection for claims that are designed to appear on an updated label. Generics must then copy the updated label under current law, if it relates to one of the covered indications, and when the patent issues the generic faces infringement liability.³⁰ To avoid this liability danger, generic drug companies can remove the indication at issue on the revised label. However, this has a tendency to drastically minimize profits as there are fewer approved indications. Whether or not this tactic will prove effective in most cases remains to be seen, because recent Supreme Court patent jurisprudence limits the patentability of modest variations in claimed inventions such as revised drug labeling. Although this will make brand company patents on drug labeling information more difficult to obtain, the loophole in the Hatch-Waxman Act still permits brand drug companies to pursue the tactic.

Another tactic has been to make many last minute, almost meaningless, changes to the brand label before the generic is approved by the FDA, thereby delaying generic drug entry onto market while the FDA evaluates the situation and the generic considers whether it can revise its label in an approvable fashion but without running afoul of brand company patent rights. Some generic drugs have had delayed market sales as the result of merely one sentence differences between the generic and the brand labels.³¹

Closing a Loophole — The Access to Affordable Medicines Act

On October 14, 2009, Senators Jeanne Shaheen (D-NH) and David Vitter (R-LA) introduced Senate bill S. 1778, the Access to Affordable Medicines Act, which is designed to address this exact labeling issue.³² If enacted, the bill would affect the labeling requirements of the FD&C Act's ANDA provisions at section 505(j). The bill, nicknamed the "Generic Loophole Bill," is purported to close the loophole in the current legislation that enables brand drug companies to make last minute labeling changes, which generic drug companies must also then make before their generic drug is approved and introduced in the market.³³ Should a brand drug company make one or more last minute labeling changes when a generic is near receiving approval, it can

delay the introduction of the less expensive generic drugs into the market. This proposed bill would provide generic drug companies a 60-day grace period to seek FDA approval of a changed label, so long as such changes are not to the 'Warnings' section of the label and the application otherwise meets the standard requirements for approval. The proposed amendments arose as a result, in part, of a report from the Generic Pharmaceutical Association (GPhA) that found that the generic version of AstraZeneca's Casodex[®] (bicalutamide), a drug used to treat prostate cancer, was delayed entry onto the market by more than three months. This occurred because AstraZeneca made last-minute labeling changes to the pediatric section of the label, which were basically nonessential changes given that prostate cancer is a rare condition in men under age 45. The three-month delay resulted in an estimated additional \$75 million profit for AstraZeneca and cost consumers at least an estimated \$15 million that would likely have occurred with the price drop from two-party competition on such sales.

If passed, this legislation would certainly reduce the profit margins of brand-name drug manufacturers who have used the loophole to defer generic drug entry into the marketplace. The effect of this loophole closure will be amplified once the patents on blockbuster drugs like Pfizer's Lipitor[®] begin to expire.

Conclusion

While the Access to Affordable Medicines Act would close one loophole present in current law, many others remain open and unaddressed by Congress, the courts, or the FDA. For example, a recent Lanham Act false advertising case before the Seventh Circuit Court of Appeals was dismissed without prejudice because, the Court reasoned, the generic drug at issue was not yet deemed "misbranded" by the FDA, and any judicial action would therefore interfere with the FDA's authority.³⁴ As the brand company's drug went off-patent, the brand manufacturer got an ANDA approved for the generic version alongside the true generic manufacturing defendants. The brand company then obtained FDA approval for an over-the-counter version of the drug, which required a "take for no more than 7 days" warning label. At least the one defendant's generic version retained the "Rx only" label as required by law³⁵ and the brand company sued for false advertising since it had obtained approval for its over-the-counter version at the last minute.

The FD&C Act dictates that the "same" drug cannot be dispensed both by prescription and over-the-counter. The generic manufacturer in that case contended that the instructions for "no more than 7 days" use for the

over-the-counter product must therefore make it a different drug than the generic manufacturer's prescription drug. Although the court did not rule on the substantive issue in this case, the court did hypothesize that "it is not obvious that the goal of protecting consumers is furthered by making sure that [doctors and pharmacists] are aware of the existence of an over-the-counter equivalent," suggesting that the Director of the Office of Generic Drugs in the FDA's Center for Drug Evaluation and Research may want to rethink his initial position on the issue and the FDA may want to preserve the rights of the generic manufacturers in its final agency action.

In addition, the Access to Affordable Medicines Act does not address other basic questions, such as whether the regulations for making changes in drug labels actually apply to generic drugs. For example, minor and moderate label changes, such as changes that are merely editorial in nature, or that strengthen warnings, do not require pre-approval. Although courts seem to indicate that these regulations apply universally,³⁶ a proposed amendment to FDA regulations suggests that they only apply to brand drugs.³⁷ Such gaps in drug label legislation can lead to potential profits for brand-name drug manufacturers but can also lead to disputes with generic manufacturers and potential legislative action.

The drug labeling issue and delay of generic drug entry due to gamesmanship is an important one in the present climate of excessive health care costs in the U.S. Indeed, shortly after being elected, the current President said that "[w]e will lower drug costs by allowing the importation of safe medicines from other developed countries, increasing the use of generic drugs in public programs and taking on drug companies that block cheaper generic medicines from the market."³⁸ President Obama may hold true to that promise, as both the Obama administration and some members of Congress have made clear their intention to expedite generic approvals and sales, thus minimizing health care costs and tipping the balance of scales decidedly away from big pharma. This will be reflected on the drug labels the FDA approves for brand and generic companies, as well as the possibility for decreased labeling litigation and disputes. Ultimately, closing the various labeling loopholes will favor generic drug manufacturers and the drug prices for end-user consumers. On the other hand, such changes in the labeling regulatory framework will likely have a skull and crossbones effect on the brand pharma company business models and profits—and it will not require a black box warning to see that.

Kimberly Weinreich is an associate in the Washington, D.C. office of the law firm of Haynes and Boone, LLP. Her practice emphasizes patent law, including patent procurement and

counseling. She may be reached at kimberly.weinreich@haynesboone.com or 202.654.4532.

Jeffrey A. Wolfson is a partner in the Washington, D.C. office of the law firm of Haynes and Boone, LLP. His practice emphasizes patent and trade secret law, with a focus on strategic client counseling, patent procurement and management, and due diligence and IP-related agreements. He may be reached at jeff.wolfson@haynesboone.com or 202.654.4565.

¹ Griffenhagen, G.B., et al., History of Drug Containers and Their Labels, 3–34 (American Institute of the History of Pharmacy, 1999).

² Griffenhagen, G.B., et al., *supra* note 1, at 13–14 citing De Renou, Jean, Oeuvres Pharmaceutiques (1926). ("The names of the medicaments must be inscribed upon every vessel and bag wherein they are included, that the medicament to be exhibited may soon be seen and not mistaken for another.")

³ *Id.* at 13.

⁴ Bauer, E., Pharmaceutical Packaging Handbook (Informa Healthcare, 2009).

⁵ See, e.g., *American School of Magnetic Healing v. McAnnulty*, 187 U.S. 94 (1902).

⁶ *United States v. 11 ¼ Dozen Packages ... "Mrs. Mofat's Shoo Fly Powders for Drunkenness,"* 136 F.2d 868 (9th Cir. 1943).

⁷ FD&C Act § 505; 21 U.S.C. § 355.

⁸ For a full list of information to be included, see FD&C Act § 502; 21 U.S.C. § 352.

⁹ FD&C Act § 502(n); 21 C.F.R. § 202.1(e)(1).

¹⁰ See, e.g., Heavey, S., "US FDA: Amgen, Wyeth's Enbrel drug to carry warning," Reuters, May 1, 2008, <http://www.reuters.com/article/governmentFilingsNews/idUSWB00891220080501>.

¹¹ 15 U.S.C. § 1125(a).

¹² FD&C Act § 505(j); 21 U.S.C. § 355(j).

¹³ 21 U.S.C. § 355(j)(2)(A).

¹⁴ *Supra* at note 12.

¹⁵ 21 U.S.C. § 355(j)(2)(A)(v); 21 C.F.R. § 314.93(b).

¹⁶ See, e.g., *Mensing v. Wyeth, Inc.*, No. 08-3850, 2009 BL 255053 (8th Cir. Nov. 27, 2009).

¹⁷ Preserve Access to Affordable Generics Act, S. 369, 111th Cong. (2009).

¹⁸ FD&C Act § 505(j)(2)(A)(viii); 21 U.S.C. § 355(j)(2)(A)(viii).

¹⁹ 21 C.F.R. § 314.127(a)(7).

²⁰ Mahn, T.G., "Generics Behaving Badly: Carve Outs, Off-Label Uses," *IPLaw360*, (2009) available at <http://www.fr.com/Files/Uploads/attachments/Generics%20Behaving%20Badly%20by%20Terry%20Mahn%20205%204%2009.pdf>.

²¹ *Id.*

²² "Fines Unlikely to End Off-Label Drug Marketing," Sept. 4, 2009, available at http://www.msnbc.msn.com/id/32694936/ns/business-us_business

²³ Allergan, Inc., "Allergan Filed Federal Lawsuit to Allow It to Share Relevant Information with the Medical Community on the Safe Use of BOTOX® for Common Therapeutic Off-Label Treatments," Oct. 1, 2009 available at <http://agn.client.shareholder.com/releasedetail.cfm?ReleaseID=413218>.

²⁴ See, e.g., FDA Decision Letter, *Camptosar*®, July 28, 2008 available at <http://www.drugs.com/pro/camptosar.html> The FDA has stated it "has no control over the operation of these substitution laws" and that just because the brand drug company can fore see off label use, doesn't mean that the FDA has authority to interfere with the practice of medicine.

²⁵ Mahn, T.G., *supra* at note 19.

²⁶ See, e.g., *Novo Nordisk v. Caraco Pharmaceutical Laboratories, Ltd. and Sun Pharmaceutical Industries, Ltd.*, Case No. 05-40188, 2009 BL 203529 (E.D. Mich. Sept. 24, 2009).

²⁷ S. 1315, 111th Cong. (2009).

²⁸ H.R. 3777, 111th Cong. (2009).

²⁹ *Id.*

³⁰ Mahn, T.G., *supra* at note 19.

³¹ For example, ribavirin, the generic version of Rebetol, a drug used to treat hepatitis C, was delayed onto market because of a one sentence difference on the physician's insert.

³² S. 1778, 111th Cong. (2009).

³³ Karst, K.R., "Senators Introduce Access to Affordable Medicines Act to Close Labeling Change 'Loophole'; Companion Bill to Senate Drug Price Competition Act of 2009 Introduced in House," *FDA Law Blog*, October 15, 2009 available at http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2009/10/senators-introduce-access-to-affordable-medicines-act-to-close-labeling-change-loophole-companion-bi.html.

³⁴ *Schering-Plough Health Care Products, Inc. v. Schwarz Pharma Inc.*, Case Nos. 09-1438, 1462, 1601, 2009 BL 233473 (7th Cir. Oct. 29, 2009).

³⁵ 21 U.S.C. § 353(b)(4)(A).

³⁶ See, e.g., *Foster v. American Home Products Corp.*, 29 F.3d 165 (4th Cir. 1994) and *Mensing v. Wyeth, Inc.*, No. 08-3850, 2009 BL 255053 (8th Cir. Nov. 27, 2009).

³⁷ 73 Fed. Reg. 2848, 2849, n. 1 (Jan. 16, 2008).

³⁸ Dawber, A., "Obama Battles Big Pharma," *Independent.ie*, Jan. 27, 2009 available at <http://www.independent.ie/business/world/obama-battles-big-pharma-1616183.html>.