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BRADLEY ARANT BOULT CUMMINGS

Where is your principal place of business?

In *Hertz Corporation v. Friend*, No 08-1107, __ U.S. __ (Feb. 23, 2010), the Supreme Court clarified where corporations have access to federal courts by defining the location of a corporation's "principal place of business." For most product liability or contractual disputes, federal courts are available only when the dispute is between citizens of different states. A corporation is deemed to be a citizen of any state it is incorporated in "and of the State where it has its *principal place of business*." 28 U.S.C. § 1332(c)(1). In *Hertz*, the Supreme Court concluded that a corporation's "principal place of business" is the "place where a corporation's officers direct, control, and coordinate the corporation's activities," or its "nerve center."

Hertz is important for multi-state corporations -- such as life science corporations -- that may have research, manufacturing, and sales operations in different states because it provides certainty as to where federal courts will be available. Prior to *Hertz,* a corporation's "principal place of business" was dependent on the law of the jurisdiction where a particular lawsuit was filed. In determining the principal place of business, some courts relied on the location of the nerve center, or corporate headquarters, while others used multi-factor tests to determine the "center of gravity" of the corporation's operations. For example, in California a corporation's "principal place of business" was California if that company's activities in California were "significantly larger" than in any other state. Under that test this often meant that corporations selling goods or services in California were citizens of the state due simply to the size of California's market. Under this prior standard, a corporation's "citizenship" depended on where the case was filed, not where a corporation chose to locate its headquarters.

Under *Hertz*, a corporation can control and know in advance where it will be deemed a "citizen" for purposes of federal jurisdiction. The location of a corporation's headquarters, where its operations are controlled and coordinated, will be it "principal place of business" for jurisdictional purposes. Federal courts will be available for most lawsuits brought by citizens of states other than the state in which the corporation is incorporated and where the corporation is headquartered, assuming the other standards for federal jurisdiction are also met.

Statutory Pathway for FDA Approval of Biosimilar Biologics -- New Territory

Buried within the pages of the Patient Protection and Affordable Care Act of 2010 is the "Biologics Price Competition and Innovation Act of 2009" (the "Biologics Act"), the statutory pathway for FDA licensure approval of biologic products that are biosimilar to (and interchangeable with) biologic products (called "reference products") which received a license under the Public Heath Service Act.

The Biologics Act frequently was described immediately following adoption of the 2010 health care reform legislation as establishing substantially the same treatment for approval of biosimilar biologics ("biosimilar products") as the Hatch-Waxman statute created for generic drugs for traditional (small molecule) pharmaceuticals in 1984, and a 12-year data exclusivity

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period for reference products which begins when the reference product is first licensed and during which the FDA may not approve applications for a biosimilar product. Whether or not the Biologics Act will have the economic spur that the Hatch-Waxman Act gave generic drugs will be determined as the Bioloigcs Act is implemented. At the threshold of this implementation, however, references to "equity" or similarity between the licensure approval requirements for generics and biosimilar biologics are misleading. "Yes", there are two statutory pathways for approval of generics and biosimilar biologics; but, "No", these pathways are not the same. Perhaps most importantly, the economic consequences flowing from these two pathways may be different: the generic drug pathway has led to cost savings, increased consumer access, and greater competition; whether or not the biosimilar product pathway will do the same is an open question.

While the Hatch-Waxman Act and the Biologics Act may include several types of features that appear to be similar (such as data exclusivity), the Biologics Act contains several important differences, including requirements of "interchangeability" and exchanges of significant proprietary trade secret and patent information.

1. The chemical formula of a traditional small molecule drug can be readily stated, confirmed, and described in a patent, while the process for making such drug may vary. However, as long as the same chemical formula is confirmed in the drug, the process (while important for cost control or other reasons) usually is of relatively less importance.

Biologics, on the other hand, are the product of living organisms and the process used to create a biologic is at the core of its efficacy, purity, and safety. Small, seemingly inconsequential changes to a biologic drug production process may result in substantial changes in the drug, its efficacy or its purity and safety.

In short, determining that a generic drug has exactly the same chemical structure and identity as its "brand name" predecessor is relatively easy and, consequently, there are good reasons for allowing generic drug applicants to rely on the clinical trials and post-approval data related to a "brand name" drug. The same level of certainty currently does not exist in the realm of biosimilar biologics.

It generally is difficult to determine whether or not a biosimilar product is the same as a biologic reference product without thorough analysis of the processes used to create each specific product. However, because there is no assurance that the process used to make a biosimilar product will result in a product which is the same as (or is "interchangeable" with) the reference product, a biosimilar product applicant may not be able to rely on the clinical trial and post-approval data of the reference product, a widely used and cost-effective short cut in the generic drug arena. The biosimilar product applicant may be required to conduct its own clinical trials and provide this and other data to the FDA.

And, from the perspective of biosimilar product development (and the related development and FDA licensure approval costs), therein lies the rub--under the Biologics Act, the FDA makes two determinations. First, whether or not a biological product is a "biosimilar product" if it is "highly similar to the reference product notwithstanding minor differences in clinically inactive components" and "if the biological product has no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product." And, second, assuming the biological product is a "biosimilar product", whether or not it is "interchangeable" with the reference product. The statutory definition of "interchangeable" requires the FDA to determine whether the biosimilar product "can be expected to produce the same clinical result as the reference product in any given patient" and, for a biological product that is administered more that once to an individual, whether the risk in terms of safety or diminished efficacy of alternating of switching between use of the biological product and the reference product is not greater than the risk of using the reference produce without such alternation or stitch." It is after a biosimilar product is approved as "interchangeable" that it can be used instead of the reference product without another prescription -- the pharmacist may make the substitution as occurs with generics.

Because the Biologics Act provides an opportunity for the public to comment on any proposed regulations, policies or guidelines that the FDA proposes to adopt with respect to Biologics Act applications and licensure, those addressing biological drugs should be alert to the April 22 statements by Janet Woodcock, Director of the FDA's Center for Drug Evaluation and Research ("CDER"), that the FDA plans to issue guidance on biosimilar products and has established a working group comprised of officials from CDER and the Center for Biologics Evaluation and Research. Ms. Woodcock also noted in her comments that the "interchangeable" standard in the statute meant there could be no clinical difference between the reference drug and the biosimilar drug. "That is a scientific bar that we have to figure out how to demonstrate," she said.

The FDA will announce its proposed schedule for public comments regarding its guidelines and those in the

scientific, drug manufacturing, healthcare and other communities should not overlook their opportunity to comment.

2. FDA approval also requires the biosimilar product applicant's disclosure to the FDA of the applicant's process information, which usually is trade secret information and related patent information. A similar disclosure requirement pertains to applications for approval of generic drugs. But, the Biologics Act goes farther than the Hatch-Waxman Act by also requiring (i) the biosimilar product applicant to deliver a copy of its application and additional detailed information relating to the method of manufacturing the biosimilar product to the reference product sponsor (under a duty of confidentiality) within 20 days after filing the application with the FDA and (ii) a complex exchange by the biosimilar product applicant and reference product sponsor of lists of patents and possible claims of infringement which could reasonably be asserted by either the reference product sponsor in connection with the making, using, offering to sell, selling or importing of the biosimilar product or by the biosimilar product applicant with respect to the reference product, as well as detailed information regarding each of the patents in question and reasons for the alleged infringement, invalidity, or unenforceability or the alleged non-infringement, validity, or enforceability, as the case may be.

The Biologics Act also includes penalties for non-compliance with the exchange of information procedures, including the reference product sponsor's loss, if it omits a patent, of its cause of action for infringement by the biosimilar product. In addition, the Act includes a complex arrangement for the biosimilar applicant and the reference product owner to litigate certain patents and seek a judicial resolution of possible infringement issues before beginning marketing of the biosimilar product.

Both reference product sponsors and biosimilar product applicants should note the relatively limited periods of time (generally no more than 60 days) to respond to the exchange of patent information and the statutory penalties. These relatively quick turnaround periods for the information exchanges indicate that sponsors and applicants should have a review and response structure, background information for each relevant patent, and working groups of internal patent managers and scientists and patent counsel in place to handle the information exchange activities. Those that wait until an information exchange occurs may be substantially disadvantaged.

The Bureau of Economic Analysis: Filing Requirements for Foreign Direct Investment in the U.S.

In an effort to compile statistics on the level and nature of foreign direct investment in the U.S., the U.S. Department of Commerce Bureau of Economic Analysis (the "BEA") requires the filing of periodic reports pursuant to the International Investment and Trade in Services Survey Act, as amended[1]. The BEA's various filing requirements pertaining to foreign direct investments allow the U.S. Government to track foreign investment in U.S. companies by receiving reports (which are called "surveys") of the initial direct foreign investment, and quarterly, annual, and "five year" surveys of financial and operating information of U.S. entities in which a direct foreign investment has been made. The BEA is allowed to use reported information only for analytical or statistical purposes and is required to keep such information confidential. The penalties for failing to file the required surveys include civil fines of $2,500 to $25,000, injunctive relief, and in the event of willful failure to report, imprisonment and/or fines. Officers, employees, or agents who knowingly participate in the willful failure to file a survey also may be subject to these penalties.

The BEA requires a U.S. business enterprise (a "U.S. Affiliate") in which a foreign entity or person (a "Foreign Parent") directly and/or indirectly owns a 10% or more voting interest to make periodic reports: (i) when a foreign direct investment is made and thereafter (ii) quarterly, (iii) annually, and (iv) at five-year intervals. The BEA's filing requirements are imposed on the U.S. Affiliate. In addition, a U.S. Affiliate must file on a fully-consolidated domestic U.S. basis and include in the full consolidation all U.S. business enterprises (if any) in which the U.S. Affiliate directly or indirectly owns more than 50% of the outstanding voting interest.

The required surveys include:

I. Form BE-605 (*Initial* and *Quarterly* Survey of Foreign Direct Investment in the United States): Beginning in January, 2010, Form BE-605 must be filed regarding the initial direct foreign investment. Thereafter, Form BE-605 also must be filed quarterly unless an exemption from filing is available. The initial survey of a direct foreign investment generally must be filed within 30 days after

1 The rules and regulations implementing the Act can be found in the Code of Federal Regulations (15 CFR Part 806). Amendments to the regulations are published in the Federal Register.

the direct investment is made. The quarterly survey must be filed within 30 days after the end of each of the first three calendar quarters, and within 45 days after the end of the fourth calendar quarter.

Exemption: A U.S. Affiliate is exempt from filing a Form BE-605 quarterly survey (but not the initial survey of a direct foreign investment) if one of the following conditions applies:

a. the value of the U.S. Affiliate's total assets, sales or gross operating revenues, and net income (loss), each, were equal to or less than $60 million (or negative $60 million if a loss) for the most recent financial reporting year;

b. the U.S. Affiliate was consolidated, merged into, or re-organized into another U.S. Affiliate which files a Form BE-605 survey;

c. the U.S. Affiliate is indirectly foreign owned through another U.S. Affiliate and has no direct transactions with the Foreign Parent(s) or any of its (their) affiliates; or

d. the Foreign Parent's voting interest in the U.S. Affiliate was sold to a U. S. entity that does not have foreign ownership of 10% or more, or the U.S. Affiliate was liquidated or dissolved, or the Foreign Parent's 10% or more ownership in the U.S. Affiliate was diluted so that the Foreign Parent's total voting interest in the U.S. Affiliate is below the 10% threshold required for filing.

To obtain an exemption from quarterly filing, the U.S. Affiliate must file a Certification of Exemption with respect to the quarter to in which the exemption became available. Assuming the U.S. Affiliate continues to meet the requirements for an exemption, the U.S. Affiliate is not required to file additional Certifications of Exemption for subsequent quarters.

II. Form BE-15 (Annual Survey of Foreign Direct Investment in the United States): Form BE-15 should be filed on or before May 31 each year. There are three BE-15 forms: Form BE-15A, Form BE-15B and Form BE-15EZ. The required form will depend on the U.S. Affiliate's total assets, sales or gross operating revenue, and net income.

Exemption. An exemption from filing Form BE-15 is available if either (i) foreign ownership in the U.S. Affiliate has fallen below 10%, or (ii) the U.S. Affiliate is fully consolidated or merged into another U.S. Affiliate, or (iii) the total assets, annual sales or gross operating revenues, and annual net income (after U.S. income taxes) for the U.S. Affiliate are $40 million or less (positive or negative). After an initial Form BE-15 Claim for Exemption is filed, the U.S. Affiliate is not required to make subsequent annual filings of the Claim for Exemption, so long as it continues to meet the exemption criteria each year.

III. Form BE-12 ("Benchmark Survey") is a survey conducted once every five years (in lieu of the annual survey) and is the most comprehensive filing required by the BEA. The most recent benchmark survey occurred in 2007 and a 2007 BE-12 survey is required for each U.S. Affiliate whose fiscal year ended in 2007.

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Bradley Arant Boult Cummings LLP Recognized Among Top Patent Firms

Bradley Arant Boult Cummings has been listed in Intellectual Property Today magazine's annual compilation of Top Patent Firms for 2010. The listing ranks law firms according to the number of patents issued in 2009 where the firm is the legal representative on an issued patent. The firm also was listed as a Top Trademark Firm in the same publication's trademark listing in 2009. Intellectual Property Today, published monthly since 1994, focuses on legal issues in patent, trademark and copyright law.

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