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Bayer, Generic Firms Win In Antitrust Case

A federal appeals court has upheld a ruling that agreements between Bayer and four generic firms on the antibiotic Cipro did not violate the Sherman Antitrust Act or state antitrust regulations or laws.

In its decision, the U.S. Court of Appeals for the Federal Circuit agreed with the *In re Ciprofloxacin Hydrochloride Antitrust Litigation* decision made by the U.S. District Court for the Eastern District of New York in favor of Bayer, Hoechst Marion Roussel (HMR), Rugby Laboratories, Watson Pharmaceuticals and Barr Laboratories.

The appeals court found the companies did not engage in anti-competitive practices when they signed agreements with Bayer not

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Court Finds Against Sandoz In Biaxin XL Case

A federal appeals court upheld a preliminary injunction barring Sandoz from selling a generic version of Abbott Laboratories' extended-release antibiotic Biaxin.

The split decision by the U.S. Court of Appeals for the Federal Circuit moves the patent dispute back to the U.S. District Court for the Northern District of Illinois for further proceedings on the case, which started when Abbott sued Sandoz in 2005 for infringing on its '718, '616 and '407 patents on Biaxin (clarithromycin).

The FDA approved Sandoz's ANDA for Biaxin XL (extended release) Aug. 25, 2005, and Abbott filed suit the following month. Abbott subsequently withdrew the '407 patent from the complaint. Sandoz introduced its generic version of the drug after Abbott filed suit.

The court granted Abbott a preliminary injunction to stop Sandoz from selling its product in the U.S. and ordered the company to

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to challenge the validity of the '444 patent covering Cipro (ciprofloxacin HCl). In fact, "settlements in patent cases, however, frequently provide that the alleged infringer will not challenge the validity of the patent," the court says.

This ruling is the strongest yet in support of using reverse payments as a way to settle Hatch-Waxman cases, Michael Keeley, a partner at Axinn, Veltrop & Harkrider LLP who specializes in antitrust, told *Generic Line*. The Federal Circuit is, in effect, saying that reverse payment settlements are almost always lawful so long as they are not a sham, he noted.

Bayer first won Cipro approval from the FDA in October 1987. Barr filed an ANDA for generic Cipro in October 1991, asserting that the '444 patent was invalid and unenforceable. Bayer sued Barr in January 1992 in the U.S. District Court for the Southern District of New York. In 1996, Rugby, a subsidiary of HMR, agreed to help fund Barr's litigation against Bayer in exchange for half the profits from future sales of Barr's generic Cipro.

Bayer entered into settlement discussions with HMR and Barr and, just before the companies would have gone to trial, the generic firms agreed not to challenge the validity of the patent in separate agreements. The patent expired in December 2003 and enjoyed six months of pediatric exclusivity thereafter.

Under an agreement between Bayer, Barr and HMR, Barr said it would convert its Paragraph IV certification to a Paragraph III and would not manufacture a generic version of the drug. In exchange, Bayer said it would pay \$49.1 million and either supply Barr with Cipro for resale or make quarterly payments — referred to as reverse payments — until Dec. 31, 2003, according to court documents.

Payments from Bayer to Barr eventually totaled \$398.1 million, and Barr shared these payments equally with HMR, according to court documents.

Bayer also agreed to allow Barr to sell a competing ciprofloxacin product beginning at least six months before the patent expired.

In 2000 and 2001, direct and indirect purchasers of Cipro and advocacy groups filed suits challenging these agreements, saying they "constituted an illegal market allocation in violation of the prohibition on contracts in restraint of trade contained in sections 1 and 2 of the Sherman Act," according to court documents.

The cases were consolidated in the U.S. District Court for the Eastern District of New York, which ruled in support of the defendants, saying their agreements did not violate the Sherman Act or state antitrust laws, a position with which the appeals court agreed.

The Federal Circuit's opinion could have an indirect effect on other cases given the court's role in developing patent law, Keeley told *Generic Line*. He adds that of the four or five reverse payment cases that have come before circuit courts over the past few years, only the Sixth Circuit in its *In re Cardizem CD Antitrust Litigation* decision expressed significant skepticism about these agreements.

The Generic Pharmaceutical Association (GPhA) says in a statement that the decision demonstrates that patent challenge settlements are a lawful and valuable tool for bringing affordable medicines to market quickly.

"Patent settlements have proven to be a valuable component in providing consumers with affordable medicines, as they have brought more affordable products to market sooner than otherwise would have been possible," GPhA President and CEO Kathleen Jaeger says.

"The Appeals Court decision further supports our industry's position that the mechanisms for reviewing the appropriateness of settlements are already adequate, and that any initiatives, such as legislative action proposed in recent years

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ASK THE EXPERT

Recently, the U.S. Court of Appeals for the Federal Circuit handed down a decision in the case *In re Ciprofloxacin Hydrochloride Antitrust Litigation*, finding that Bayer and Barr did not violate antitrust laws in a case involving Cipro (*see story, page 1*). Michelle Seagull, an associate with Axinn, Veltrop & Harkrider LLP, discussed some aspects of the case with *Generic Line*.

What reasoning did the U.S. District Court for the Eastern District of New York use to reach its decision?

Seagull: The district court held that the settlement between Bayer and Barr did not violate the antitrust laws because it did not create a bottleneck on challenges to Bayer's patent, it did not have an adverse effect on competition that went beyond the scope of Bayer's patent and the settlement was not the result of fraud or sham litigation. As such, there was no anti-competitive harm and, therefore, the court did not need to consider whether the settlement had countervailing pro-competitive benefits and, if so, whether those benefits could be achieved through a less restrictive alternative.

Can you explain how the Federal Circuit arrived at its decision?

Seagull: The Federal Circuit arrived at its decision by adopting the reasoning of the district court. It agreed that the rule of reason applied and that, absent fraud or sham litigation, any settlement that did not expand beyond the facial scope of the patent would not violate the antitrust laws even in the event of a significant reverse payment.

What is the rule of reason and how did it apply in this case?

Seagull: Section 1 of the Sherman Act prohibits unreasonable restraints of trade. There are two methodologies courts use to assess whether an agreement unreasonably restrains trade. Some conduct is known to have such a pernicious effect

on competition that it can be deemed per se unlawful without further analysis. Price fixing, for example, is per se unlawful.

The rule of reason, on the other hand, applies to conduct that courts have less experience with or that does not present clearly anti-competitive harms. It requires an analysis of a restraint's actual competitive effects. The initial burden in a rule of reason case is on the plaintiff to demonstrate that a restraint harms competition. If the plaintiff meets this burden then the burden shifts to the defendant to show that the restraint has procompetitive benefits. If a restraint has anti-competitive and pro-competitive effects, the burden shifts back to the plaintiff to demonstrate that the harms outweigh the benefits or that the benefits could be obtained through a less restrictive alternative.

In this case, the court concluded that the settlement agreement did not result in any anti-competitive effects because it did not restrict competition beyond the exclusionary zone of the patent itself. In other words, it was the patent that enabled Bayer to exclude generic competitors, not the settlement agreement. Thus, the court did not need to assess whether the agreement had pro-competitive benefits or whether those benefits could be achieved through a less restrictive alternative in order to hold that it did not violate the antitrust laws.

Can you explain what sham litigation is?

Seagull: Sham litigation refers to a plaintiff's use of the process of litigating to obtain a competitive advantage as opposed to the outcome of the litigation. To constitute sham litigation, a lawsuit must be objectively baseless (i.e. no reasonable plaintiff could realistically expect to succeed on the merits). It also must be brought for an improper purpose, which requires a subjective determination. This is a difficult standard to

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to eliminate or restrict settlements, are unnecessary,” Jaeger says. “Limiting settlements would lead to fewer patent challenges and, in the end, delay market entry with a substantial loss in savings for consumers.”

Parties React

Plaintiffs’ attorney J. Douglas Richards of Pomerantz, Haudek, Block, Grossman & Ross told *Generic Line*, “Stark differences exist among legal positions taken on this issue by the Sixth Circuit, the Eleventh Circuit, and the Second and Federal Circuits.

“Despite those differences, the Supreme Court has declined three times to grant certiorari and clarify the law. It is time for it to do so,” he continued. “The position taken by the Second Circuit, and now also by the Federal Circuit, is irreconcilable with the views of other Courts of Appeals and of all antitrust authorities.”

Bruce Downey, Barr’s chairman and CEO, says in a statement, “This ruling provides additional legal precedent that will allow companies to settle patent challenge cases under terms that are both pro-competitive and pro-consumer. Barr continues to defend itself vigorously in a parallel appeal of the district court’s decision by direct purchasers that remains pending in the United States Court of Appeals for the Second Circuit, as well as similar cases in several state courts.”

FTC Concerns

The number of settlements in which brand companies compensate generic drugmakers that delay introducing less expensive medicines is on the rise, according to an FTC report released this year.

The FTC received 45 such agreements last year, 33 of which were final settlements of patent litigation brought by a brand company against a generic company. Of the 33 final settlements, 14 included both compensation and a

restriction on the generic drugmaker’s ability to market its product, the summary says. The brand company agreed not to sponsor or compete with an authorized generic for a period of time in 11 of the cases.

The report adds that 11 of the settlements with no compensation still restricted the generic drugmaker’s ability to enter the market. In six of these cases, the generic company withdrew its patent challenge, agreeing not to enter the market until the patent expired.

Only eight of the 33 final settlements did not explicitly restrict generic entry, the summary says. In five cases, the generic product was on the market; in two cases, the brand gave a covenant not to sue, allowing the generic to be marketed after final approval; and in one case, the generic company withdrew its ANDA after the brand company prevailed in district court against other challengers (*Generic Line*, May 28).

The FTC’s report is available at www.ftc.gov/os/2008/05/mmaact.pdf. — Elizabeth Jones

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FDA Proposes Withdrawal of MiraLax ANDAs

The FDA is proposing a withdrawal of approval for ANDAs for prescription versions of Braintree Laboratories' MiraLax after the agency allowed the brand drug to switch from a prescription laxative to an OTC drug in 2006.

Under the Federal Food, Drug and Cosmetic Act, prescription and OTC versions of a drug may not be marketed simultaneously. The generic MiraLax products (PEG 3350) are misbranded because they are labeled prescription-only and may not be marketed legally, according to the agency.

The FDA approved Braintree Laboratories' MiraLax NDA in February 1999 to treat occasional constipation in adults for up to 14 days. Kali Laboratories, Schwarz Pharma, Nexgen Pharma, Coastal Pharmaceuticals and Teva Pharmaceutical subsequently submitted separate ANDAs for prescription generics, all of which were approved.

In October 2006, the FDA approved Braintree's NDA for MiraLax that switched its status from prescription-only to OTC. The company received three years of exclusivity based on the studies necessary to establish the safety and efficacy of the OTC drug. Schering-Plough now holds the NDA for the MiraLax OTC product.

The FDA sent the ANDA holders a letter in April 2007 outlining the agency's position on the legality of marketing PEG 3350 for prescription. It informed the companies that if they intended to continue marketing the products, they must submit a new ANDA using the appropriate reference drug — MiraLax OTC — as the agency determined there was no meaningful difference between the prescription and OTC products.

The ANDA sponsors have not submitted new applications, nor have they voluntarily sought withdrawal of the approval of their respective ANDAs. However, the agency is offering the firms a chance to request a hearing Nov. 24 to explain why their applications should not be withdrawn.

Applicants also must file by Dec. 23 the information and analyses relied on to demonstrate there is a genuine and substantial issue of material fact that requires a hearing.

The notice is available at www.fda.gov/OHRMS/DOCKETS/98fr/FDA-2008-N-0549-nph.pdf. — Elizabeth Jones

UK Clears Second Insmed Follow-on Biologic Trial

Insmed has received approval from the UK's Medicines and Healthcare products Regulatory Agency (MHRA) to start a Phase I study of INS-20, the company's second follow-on biologic (FOB) product candidate.

INS-20 is a pegylated recombinant form of human granulocyte colony-stimulating factor (G-CSF) and an FOB of Amgen's Neulasta (peg-filgrastim), the treatment approved to reduce the risk of infection in patients with cancer receiving strong chemotherapy that decreases the number of infection-fighting white blood cells. Neulasta had U.S. sales of approximately \$2.4 billion last year, according to Insmed.

Preclinical studies demonstrated that INS-20 and Neulasta's pharmacological and toxicological profiles are comparable. The Phase I study will establish whether INS-20 is bioequivalent to Neulasta. Results from the trial are anticipated in 2009 and are expected to be used as part of a submission to establish a protocol with the FDA for a Phase III trial.

The Phase I trial is the second of two planned for this year as part of Insmed's development of a portfolio of follow-on biologics. In July, the company announced that a Phase I trial had demonstrated the bioequivalence of INS-19, the company's recombinant human G-CSF, compared with Neupogen (filgrastim), an approved G-CSF product for the treatment of neutropenia that had 2007 sales of about \$1 billion, according to Insmed.

Insmed intends to seek U.S. approval of both products and launch them when the relevant patents expire. — Elizabeth Jones

Mylan Gets FDA Tentative OK for Two Drugs, Faces Separate Suit

The FDA has granted tentative approval for two Mylan Pharmaceutical ANDAs — a version of the hypertension drug Benicar HCT and a generic Uroxatral to treat benign prostatic hyperplasia (BPH).

Mylan submitted its original application for generic Benicar HCT (hydrochlorothiazide/olmestartan medoxomil) to the FDA Feb. 14, 2007, and may be the first company to submit a substantially complete ANDA containing a Paragraph IV certification, according to a company statement.

Mylan also has received tentative approval for its ANDA for alfuzosin HCl extended-release 10-mg tablets, a generic version of Sanofi-Aventis' Uroxatral.

Benicar HCT, which is made by Daiichi Sankyo, had annual U.S. sales of about \$535 million for the 12 months ended June 30, according

to IMS Health. Uroxatral had annual U.S. sales of about \$168 million for the 12 months ended June 30, according to IMS Health.

Separately, Mylan is being sued by Novartis for infringing on a patent covering the cholesterol drug Lescol (fluvastatin sodium), according to court documents.

Mylan says in the filing that it is the first company to file a substantially complete ANDA containing a Paragraph IV certification for the product. The company filed an ANDA with the FDA in June, and Novartis filed its suit Oct. 10 in the U.S. District Court for the District of New Jersey, alleging infringement of the '772 patent.

Mylan maintains that the patent, which expires Oct. 11, 2011, and has pediatric exclusivity until April 11, 2012, is unenforceable, according to court documents.

The brand drug had approximately \$60 million in sales for the 12 months ended June 30, according to IMS Health. — Elizabeth Jones

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Par Reduces Workforce To Reassess Business

New Jersey-based Par Pharmaceutical is cutting 190 jobs and a portion of its generic portfolio as part of its reassessment of its businesses.

The company will eliminate the positions by the end of the year, and roughly 30 percent of them are in manufacturing, R&D and general and administrative areas. Par will cut back on its internal R&D to focus on completing products in development and will continue to look for opportunities with external partners, the company says in a statement.

“Over the past several years, Par’s generic R&D investment has yielded the company a very promising pipeline of current and future products. Those assets combined with a smaller, more profitable base business should generate significant cash over the next several years, improving Par’s ability to accelerate its investment in Strativa Pharmaceuticals,” says Patrick LePore, Par’s chairman, CEO and president.

Total expenses associated with these actions are expected to be \$28 million to \$38 million, including noncash charges of about \$20 million to \$28 million. Par anticipates these actions will generate operating-expense savings on an annualized basis from \$45 million to \$55 million. — Elizabeth Jones

Novator Reacts to Actavis Buyout Report

Icelandic drugmaker Actavis has received offers from other companies, but there is no sale under way, according to Novator, an investment firm that owns an 80 percent stake in the drugmaker.

An Oct. 17 article in *The Wall Street Journal* reported that the generic drugmaker might be for sale after Actavis Chairman Thor Bjorgolfsson’s investment, Landsbanki Islands, collapsed and was taken over by the Icelandic government.

“Actavis, as a global leader in the generics industry, is a highly valuable asset in a much sought after space,” a Novator spokesman tells *Generic Line* in an email. “Continued recent consolidation

in the global generics industry has led to the receipt of approaches and expressions of interest, as a result of which Merrill Lynch was appointed to advise the board on its strategic options.

“There is no sales process under way, though Novator of course continues to review all its investments in light of market conditions and opportunities to maximize value and remains committed to helping Actavis grow and achieve its potential.”

Bjorgolfsson founded the Novator investment firm. In July 2007, Actavis shareholders approved a Novator offer to acquire all Class A shares of the company.

Actavis issued a statement dated Oct. 14 saying the crisis in the Icelandic financial sector did not have an impact on the company’s normal course of business. The company says its banking operations are with international banks that were not exposed to the current events in Iceland. Actavis adds it generates only 1 percent of its revenue in Iceland. — Elizabeth Jones

Court Halts Online Drug Operation

The U.S. District Court for the Northern District of Illinois has issued an injunction prohibiting two operators from sending email advertising spam for products ranging from an herbal pill touted for male-enhancement to a weight-loss supplement, according to court documents.

The defendants said they were selling FDA-approved generic drugs from a U.S.-licensed pharmacy, including: Levitra (vardenafil HCl), Avodart (dutasteride), Cialis (tadalafil), Propecia (finasteride), Viagra (sildenafil citrate), Lipitor (atorvastatin calcium), Celebrex (celecoxib) and Zoloft (sertraline), according to court documents. The FTC says the drugs were potentially unsafe, unapproved imported products.

The FDA’s Office of Generic Drugs and Division of Pharmaceutical Analysis worked with the FTC to bring the operation to a halt after receiving more than 3 million complaints. — Elizabeth Jones

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recall all unsold product. Sandoz challenged the injunction in the appeals court, saying the lower court erred when it ruled that Abbott was likely to prevail on the issues of validity, infringement and inequitable conduct. The company also maintained the court abused its discretion in granting the injunction, a finding with which the appeals court disagreed.

Divided Court

The appeals court panel was not united in its opinion, however. Judge Glenn Archer joined Judge Pauline Newman's majority opinion except on Parts I and VI, which address issues of validity and conflicting precedent, respectively.

Judge Arthur Gajarsa dissented, saying there is "no legal basis for the granting of a preliminary injunction, and its issuance is an abuse of discretion." He cites *Cybor Corp. v. FAS Technologies, Inc.*, in which the appeals court found, "A district court abuses its discretion when its decision is based on clearly erroneous findings of fact, is based on erroneous interpretations of the law, or is clearly unreasonable, arbitrary or fanciful," according to court documents.

He adds that a preliminary injunction requires the movant (Abbott) to show four factors: a reasonable likelihood of success on merits, the prospect of irreparable harm, a balance of the parties' hardships in favor of injunction and no potential injury to an important public interest.

Gajarsa focuses his dissent on the likelihood-of-success factor, saying the district court did not properly consider evidence produced by Sandoz that established a substantial question of invalidity, rendering the '718 patent vulnerable to a challenge at trial.

"Given the strong dissent and some questions as to what the precedent says on this issue, it will be interesting to see if the Federal Circuit decides to hear this case en banc, which may provide some

further clarity," Chad Landmon of Axinn, Veltrop Harkrider, LLP told *Generic Line*.

Sandoz told *Generic Line* it had no comment on the decision because of ongoing litigation.
— Elizabeth Jones

Roche Amends Complaint Against Orchid in Boniva Dispute

Roche has filed an amended complaint against Indian drugmaker Orchid Chemicals & Pharmaceuticals in a '957 patent infringement lawsuit related to the once-monthly osteoporosis drug Boniva.

The U.S. Patent and Trademark Office awarded the '957 patent to Roche Aug. 12. Roche brought suit the same day because Orchid had filed an ANDA for a generic Boniva (ibandronate sodium). Roche asked the court to order Orchid to file a Paragraph IV certification against the patent, according to court documents.

Roche's amendment is a response to an October letter from Orchid that says it is filing a Paragraph IV notice related to the '957 patent covering Boniva 150-mg pills. Roche also is suing Teva Pharmaceuticals, Gate Pharmaceuticals, Cobalt Pharmaceuticals, Apotex, Genpharm and Dr. Reddy's for infringing the same patent, which expires May 6, 2023.

The suit is not the first Roche has brought against Orchid over its proposed generic Boniva. In August 2007, Roche received a letter from Orchid saying the Indian firm had filed an ANDA to manufacture generic Boniva before the expiration of Roche's '938 and '196 patents. The '938 patent expires May 6, 2023, and the '196 patent expires Oct. 7, 2019.

Roche filed a patent infringement suit in September 2007, and the case is pending before the same New Jersey court.

Boniva had sales of roughly \$664 million through the first nine months of the year, according to Roche. — Elizabeth Jones

EU System of Classifying, Labeling Substances Moves Forward

The European Parliament voted to adopt a compromise measure aimed at aligning the EU's regulations on classification, labeling and packaging of substances and mixtures with the United Nations' Globally Harmonised System (GHS).

The measure, which would replace current regulations on classification, labeling and packaging of hazardous substances, complements the regulation on the registration, evaluation, authorization and restriction of chemical substances (REACH). The European Council is scheduled to consider the measure Nov. 18 for final adoption.

This new regulation "will ensure that the same hazards will be described and labeled in the same way all around the world," the European Commission says in a statement following the vote. The rule's goal is to determine which components of substances and mixtures should be classified as hazardous and communicate the dangers to consumers.

All substances and mixtures supplied in the EU are covered by the regulation, except in cases in which other legislation — such as Directive 2001/83/EC on human medicinal products — spells out more specific provisions on classification and labeling.

According to the proposal, manufacturers, importers and downstream users have primary responsibility for identifying and classifying dangerous substances and mixtures.

"In fulfilling their responsibilities for classification, downstream users should be allowed to use the classification for a substance or mixture derived in accordance with this Regulation by an action in the supply chain, provided that they do not change the composition of the substance or mixture," the measure states.

Classification of hazardous substances not on the market but subject to registration and notification

is primarily the responsibility of manufacturers and importers, the regulation says.

But "there should be a possibility to provide for harmonised classifications of substances for hazard classes of highest concern and of other substances on a case-by-case basis, which should be applied to all manufacturers, importers and downstream users of such substances and mixtures containing such substances," the regulation says.

Specific industry sectors may establish networks to facilitate data exchanges, evaluate information and test data weight-of-evidence determinations and best practices to simplify compliance with the notification obligations, the regulation says.

Labeling must be in the official languages of the member states where the substance or mixture is placed on the market, unless otherwise specified by national authorities. Changes in labeling due to new information about the severity of the hazard or need for new supplemental labeling elements should be made "without undue delay," the measure says. All other labeling updates are supposed to be made within 18 months.

The measure also calls for the creation of a classification and labeling inventory to ensure harmonized protection of the public.

The threshold quantity of one ton per year for notification of the classification for imported or manufactured hazardous substances alone or in preparation, originally proposed by Parliament, is not included in Article 39 of the final text, Christoph Pescheck, chair of Eucomed's REACH Working Group, told *Generic Line*. "Thus any minute quantity of a hazardous substance, e.g. in an imported preparation, [would have] to be notified to the classification and labeling inventory" at the European Chemicals Agency.

Moreover, the measure sets no quantity limit for notification of the classification of research

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prove because even a slim possibility of success in the litigation would shield a plaintiff from a claim of sham litigation.

What, if any, impact will this decision have on future cases involving reverse payments?

Seagull: The Federal Circuit decision is another victory for the pharmaceutical industry and will likely further embolden brand and generic firms to settle their disputes with reverse payments. Nonetheless, the FTC can be expected to continue in its efforts to end this practice.

Earlier this year, the FTC sued Cephalon in the D.C. district court — the case was later transferred to the Eastern District of Pennsylvania — alleging that the company violated the antitrust laws by making reverse payments to several generic firms. Thus, the FTC may still obtain a victory in a Circuit that has not yet ruled on the issue and may eventually have this issue presented to the Supreme Court.

Watson Sues Barr Over Oxytrol

Watson Laboratories has filed a lawsuit alleging Barr Pharmaceuticals infringed on patents covering its Oxytrol patch, a treatment for overactive bladder.

Barr informed Watson in a Sept. 11 letter that it had submitted an ANDA for a generic Oxytrol (oxybutynin) transdermal system with Paragraph IV certifications on the drug's '839, '010, '441, '249, '250, '251, '252 and '483 patents.

Watson subsequently filed suit in the U.S. District Court for the District of Delaware and asked the judge to order Barr to convert its Paragraph IV certifications to Paragraph III certifications, court documents show.

Watson also asked the court to declare that FDA approvals of Barr's Oxytrol products may

not take effect before the brand drug's final patent expires. The '839 and '010 patents expire in April 2015, and the remaining patents expire in April 2020, according to the FDA's Orange Book.

Watson requested a copy of Barr's ANDA and samples from each lot of the product, but it has not received them, according to court documents. The drugmaker also alleges that Barr's Sept. 11 letter contains insufficient information regarding Barr's product; therefore, "Watson cannot fully evaluate, confirm or test the correctness" of the defendant's certification that the patents would not be infringed by the generic product, according to court documents.

The FDA approved Oxytrol in 2003. The system had annual sales of roughly \$39 million in the U.S., according to IMS sales data ending in August. — Elizabeth Jones

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and development substances that are "placed on the market," Pescheck said.

"This is crucial, as the REACH definition of 'placing on the market' also includes now providing it free of charge to a third party. Shipping an R&D substance from one company's site to another would require notification to the classification and labeling inventory," he added.

The benefits to business will grow as more countries adopt the GHS criteria, the proposal maintains. "The community should be at the forefront of this process to encourage other countries to follow and with the aim of providing a competitive advantage to industry in the [European] Community," it says. Presently, 65 countries are working to implement the GHS.

The deadline for substance classification under the new rules is Dec. 1, 2010, and is June 1, 2015, for mixtures.

The regulation is available at register.consilium.europa.eu/pdf/en/08/st11/st11206.en08.pdf. — Meg Bryant

Barr Confirms Patent Challenge of Opana ER

Barr Laboratories is being sued by Penwest Pharmaceuticals and Endo Pharmaceuticals for challenging patents covering the pain drug Opana extended-release (ER) in 5-, 10-, 20- and 40-mg strengths.

Barr filed its ANDA containing a Paragraph IV certification on the '933 and '456 patents for a 40-mg generic version of Opana (oxymorphone HCl) ER in September. It later amended its application to include the other three strengths, according to court documents.

Penwest owns the patents, which expire Sept. 9, 2013, and Endo is an exclusive licensee.

The plaintiffs filed their suit in the U.S. District Court for the District of Delaware in an effort to prevent Barr from proceeding with the commercialization of its product before the expiration of the patents.

Opana ER tablets had annual sales of approximately \$130 million in the U.S., based on IMS sales data. — Elizabeth Jones

Teva Gets FDA OK for Generic Fentanyl System

Teva Pharmaceutical Industries has begun shipping four strengths of its generic fentanyl transdermal system after receiving FDA approval to market the pain product.

The product is a generic version of Ortho-McNeil's chronic pain treatment Duragesic (fentanyl) patches in 25-, 50-, 75- and 100-mcg/hour strengths and was developed and made by Aveva Drug Delivery Systems, Teva says in a statement.

Teva's product uses a proprietary matrix design that incorporates the drug into an adhesive. It is indicated for the management of persistent moderate-to-severe chronic pain that cannot be controlled by other means and requires continuous opioid administration for an extended period.

Annual sales of brand and generic versions of the product were roughly \$1.2 billion in the U.S. for the 12 months ended June 30, based on IMS Health sales data.

A number of companies recalled fentanyl patches this year because of manufacturing problems that could have led to leaks of the active ingredient. Exposure to fentanyl gel may lead to serious adverse events, including respiratory depression and possibly fatal overdose.

Mylan subsequently issued a statement that its generic fentanyl patch is not affected by the recall because it is a matrix patch, not a patch in which a reservoir holds the gel containing the drug. Therefore, Mylan's patch does not leak, the company said (*Generic Line, March 5*). — Elizabeth Jones

Par Notifies Pozen, GSK of ANDA

Pozen and GlaxoSmithKline (GSK) have received a letter notifying them that Par submitted an ANDA to market a generic version of the migraine drug Treximet (sumatriptan succinate/naproxen sodium). Par tells the companies that it intends to market a generic version of Treximet tablets before the drug's '499, '458 and '183 patents expire.

GSK and Pozen are evaluating Par's letter and have full confidence in the intellectual property portfolio related to Treximet, according to Pozen. The companies signed an agreement in 2003 to co-develop the product.

The companies received FDA approval for the drug, a follow-up to GSK's blockbuster migraine drug Imitrex (sumatriptan), in April.

In clinical trials, Treximet performed better than Imitrex. The drug provided migraine relief at two hours for a greater percentage of patients than Imitrex 85 mg or naproxen sodium 500 mg alone, GSK said. In addition, Treximet provided more patients sustained migraine pain relief from 2–24 hours compared with the individual components. — Elizabeth Jones

Cypress to Market Generic Zyrtec For Children

The FDA has granted final approval to Cypress Pharmaceutical's ANDA to market generic prescription and OTC versions of McNeil Consumer Healthcare's Zyrtec oral solution, 1 mg/1 ml.

The prescription solution of Zyrtec (cetirizine HCl) treats symptoms associated with perennial allergic rhinitis in children age 6 months to 23 months and for chronic hives in children 6 months to 5 years.

The OTC version is an antihistamine used for the relief of sneezing, runny nose, itchy, watery eyes and itchy throat or nose due to indoor and outdoor allergies for adults and children older than 2 years and for the relief of itching due to hives for children age six years to adults.

Cypress' cetirizine HCl oral solution will be available through all the national drug wholesalers and chain drugstores and will be shipped immediately, the company said in an Oct. 14 statement. — Elizabeth Jones

Mylan Files Application for Generic Amrix

Cephalon and Eurand have received notice that Mylan Pharmaceuticals has submitted an ANDA to market a generic version of Amrix in 15- and 30-mg strengths.

Mylan filed a Paragraph IV certification with respect to the '793 patent covering Amrix (cyclobenzaprine HCl). The firm maintains the patent is invalid, unenforceable or will not be

infringed by the generic product. The patent expires Feb. 26, 2025, and covers extended-release formulations containing the muscle relaxant cyclobenzaprine. Cephalon has a three-year period of marketing exclusivity for Amrix, which Eurand developed, that ends February 2010.

Eurand and Cephalon are reviewing Mylan's notice letter and will work together to determine the most appropriate course of action, the companies say in a statement.

Amrix is indicated for short-term relief of muscle spasm as an adjunct to rest and physical therapy. It had sales of roughly \$17.1 million in the quarter that ended June 30, according to Cephalon. — Elizabeth Jones

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