Shook, Hardy & Bacon L.L.P.

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LIFE SCIENCES & BIOTECHNOLOGY LEGAL BULLETIN

SCIENCE • TECHNOLOGY
ENGINEERING • ENERGY
PHARMACEUTICAL

CONTENTS

IP NEWS

NGOs Request March-in Rights for Patented Drug

Four non-governmental organizations (NGOs) have filed a petition with the National Institutes of Health (NIH) requesting that it grant march-in rights under the Bayh-Dole Act for a patented drug that they claim is "a federally funded invention that is much more expensive in the United States than in Canada, Europe or other high-income countries." At issue is an antiretroviral protected by six patents. The NGOs are Knowledge Ecology International, the American Medical Students Association, U.S. Public Interest Research Group, and Universities Allied for Essential Medicines. Noting that in the 31 years such rights have been available, the NGOs claim that "NIH has never granted a march-in request."

Under the law, an agency that funds the research leading to a patented invention may on its own initiative or at the request of a third party ignore the exclusivity of a patent awarded under the Act and grant licenses to other "reasonable applicants." This right is strictly limited to instances such as where (i) the patent holder fails to achieve "practical application" of the invention, defined as making the invention's benefits "available to the public on reasonable terms"; (ii) action is necessary to alleviate health or safety needs that are not "reasonably satisfied" by the patent holder; or (iii) action is necessary "to meet requirements for public use specified by Federal regulations," and that use is "not reasonably satisfied" by the patent holder. When exercising march-in rights, the government may require the contractor/patent holder to issue a license "upon terms that are reasonable under the circumstances" or may itself grant a license.

The petitioners urge NIH to find that a product's price should be considered when assessing whether a patent holder has failed to make benefits available to the public on reasonable terms. To that end, they also recommend that NIH adopt two policy rules: first, that U.S. prices presumptively be considered unreasonable and licenses be granted to competitors to supply the product to consumers, if U.S. prices are higher than seven of 10 comparison countries or 10-percent higher than the median price of the reference countries; and second, that march-in rights be awarded if a product based on a patented

invention is a drug, medical device, diagnostic, or similar invention, and it is used or is potentially useful "to prevent, treat or diagnose medical conditions or diseases involving humans, and its co-formulation, co-administration or concomitant use with a second product is necessary to effect significant health benefits from the second product, and the patent holder has refused a reasonable offer for a license." *See Knowledge Ecology International News Release*, October 25, 2012.

NEW BIO BUSINESS VENTURES

Biotechs Merge to Develop Oncolytic Adenoviruses

DNAtrix, Inc., a Houston-based biotechnology company that develops oncolytic virus technology to treat cancer, has reportedly merged with VectorLogics, Inc., which develops complementary products for ovarian cancer. Merged company DNAtrix, Inc. will continue clinical trials for stage IV brain tumors at the University of Texas M.D. Anderson Cancer Center with its lead cancer product, DNX-240, described as "the culmination of over a decade of work and . . . the first oncolytic virus capable of killing cells with defects at any point in the retinoblastoma (Rb) pathway." CEO Frank Tufaro said, "The merger makes strategic sense, and we are now a much stronger company in all respects." *See DNAtrix, Inc. Press Release*, October 23, 2012.

INVESTOR NEWS

Biopharma Company Raises $30.9 Million to Advance Treatments for Diabetes Complications

Biopharmaceutical company Cebix Inc. has reportedly closed a $30.9-million Series B financing round involving prior investors Interwest, Sofinnova Ventures and Thomas, McNerney & Partners. Newly appointed president and CEO Joel Martin said that Cebix, which just successfully completed a trial of its lead investigational drug ERSATTA™, "is well-positioned to launch our Phase 2b trial in early Q1 2013." The self-administered drug has apparently been shown to be well tolerated with no serious adverse effects. It is a C-peptide replacement therapy used to treat long-term diabetes-related microvascular problems, such as neuropathy, nephropathy and retinopathy. *See Cebix Inc. News Release*, October 17, 2012.

Synthetic Biologics Developer to Sell Stock in Private Placement Financing

Synthetic Biologics, Inc. has reportedly entered into private stock purchase agreements to raise about $10.8 million to fund its monoclonal antibody and synthetic DNA programs as well as provide general corporate financing.

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If you have questions about this issue of the Report, or would like to receive supporting documentation, please contact Mary Boyd (mboyd@shb.com) or Dale Walker (dwalker@shb.com); 816-474-6550.

According to CEO Jeffrey Riley, "We are very pleased to receive such solid support from both our new and existing investors, who share our vision of the emerging field of synthetic biologics." The Rockville, Maryland, biotech develops products designed to "address serious diseases and unmet medical needs." The company also has in its research pipeline drugs to treat infectious diseases and therapies for pulmonary arterial hypertension, relapsing-remitting multiple sclerosis (MS) and cognitive dysfunction in MS, and amyotrophic lateral sclerosis. *See Synthetic Biologics News Release*, October 29, 2012.

Series C Financing Brings $34.5 Million to Mirna Therapeutics for MicroRNA Therapeutics

Austin, Texas-based biopharmaceutical company Mirna Therapeutics Inc. has apparently completed a $34.5-million Series C financing round, which will enable it to further develop and commercialize its lead microRNA therapeutic product candidate MRX34. President and CEO Paul Lammers called the funding round "significant" and said that Mirna is "now positioned to be the first company in the pharmaceutical and biotechnology industry to advance therapeutics based on miRNA mimics towards the clinic in cancer. We believe that miRNAs represent a powerful and innovative approach to cancer therapy which has the potential to provide renewed hope for many cancer patients."

According to the company, miRNAs "are small oligonucleotides that affect gene expression by interacting with messenger RNAs"; they can "function as 'master-switches,' efficiently regulating and coordinating multiple cellular pathways and processes. By coordinating the expression of multiple genes, miRNAs are responsible for guiding embryonic development, immune and related inflammatory responses, as well as cellular growth and proliferation. . . . [R]eplacement of down-regulated miRNAs in tumor cells results in the destruction of cancer cells." *See Mirna Therapeutics Inc. News Release*, October 24, 2012.

Michael J. Fox Foundation Awards Grant to Evaluate Treatment for Parkinson's Disease

The Michael J. Fox Foundation has reportedly awarded a grant to Avanir Pharmaceuticals to evaluate the safety and efficacy of its AVP-923 to treat levodopa-induced-dyskinesia in Parkinson's Disease. The California-based biopharmaceutical company develops medicines for patients with central nervous system disorders "of high unmet medical need." Avanir will use the grant to enroll Parkinson's Disease patients at three study centers in the United States and Canada; they will receive the studied drug (45 mg of dextromethorphan and 10 mg of quinidine) and a placebo at two-week intervals in a random order. The patients will be monitored for side effects and tested to determine the drug's effect on dyskinesia. *See Avanir Pharmaceuticals Press Release*, October 23, 2012.

$4 Million in Series C Equity Raised to Grow Drug-Discovery Technologies Company

HemoShear LLC, a Charlottesville, Virginia, biotech research company that develops human and animal cell-based replicas of organ systems and diseases for use in the discovery and assessment of new drug compounds, has reportedly closed its fourth equity financing round for a total exceeding $4 million. This apparently brings private investment in the firm since 2008 to more than $13 million. HemoShear CEO Jim Powers said, "The enthusiastic support of our investors has permitted the company to establish outstanding laboratory facilities, recruit highly trained scientists and technicians, and expand commercial operations. Our customer base and revenues are growing rapidly as the pharmaceutical industry recognizes HemoShear's leadership in human-relevant systems for new drug discovery and development." The new funds will be used for a 2013 move to a larger laboratory and to expand the company's science and business staff. *See HemoShear LLC Press Release*, October 24, 2012.

BUSINESS CLIMATE

Increase in Health-Care M&A Deals Anticipated

Investment bankers are reportedly looking for health-care companies, and pharmaceutical companies in particular, to enter more business deals during the next year. Industry giants are apparently flush with cash reserves and ready to build product lines. In the past 12 months, more than 2,000 deals were announced in the health-care products, services and pharmaceutical sectors. They were valued at approximately $166 billion, with drug makers near the top of the acquiring companies at $37.1 billion invested, mainly in biotechnology and genetics companies. *See Bloomberg*, October 25, 2012.

LEGISLATIVE AND REGULATORY DEVELOPMENTS

Congressional Staff Report Shows Gaps in Compounding Drug Regulation

In the wake of a hepatitis outbreak linked to a New England compounding pharmacy, Representative Edward Markey (D-Mass.) has released a **staff report** exploring "the nature of regulatory oversight and gaps in legal authority that led to one of the worst public health tragedies in recent U.S. history." Titled, "Compounding Pharmacies, Compounding Risk," the report details federal and state regulatory roles and concludes that while U.S. Food and Drug Administration (FDA) efforts to ensure the safety of compounded pharmaceuticals have been "challenged at every juncture by some members of the compounding pharmacy sector," state pharmacy boards have not taken a consistent enforcement role.

According to the report, state regulators either do not or cannot "perform the same sort of safety-related oversight of compounding pharmacy practices that FDA has historically undertaken. But it is also clear that absent clear new statutory authority, FDA efforts will ultimately be constrained by gaps in regulatory oversight authority." Markey said that the hepatitis outbreak "is clearly just the tip of an industry iceberg that has long needed reform and federal oversight. This tragedy demands the strongest response from Congress and federal and state authorities to ensure safeguards are in place to protect patients." *See Representative Ed Markey News Release*, October 29, 2012.

Meanwhile, the Congressional Research Service (CRS) has updated its review of FDA authority to regulate drug compounding. In its October 17, 2012, report, CRS examines FDA guidance documents on the issue, a 1997 amendment to the Federal Food, Drug, and Cosmetic Act (FFDCA) and conflicting decisions from the Fifth and Ninth Circuits to determine the extent of that authority in an era when pharmacies are no longer compounding drugs to create medication for an individual patient, but are instead producing drugs on a much larger scale.

FDA compliance guides of 1992 and 2002 outline the factors the agency will consider in exercising pharmacy-compounding enforcement discretion. CRS notes that such guidance does not establish legally enforceable rights or responsibilities and does not legally bind the public or FDA. Congress addressed FDA's role in the regulation of drug compounding as part of the FDA Modernization Act of 1997, generally exempting compounded drugs from FFDCA requirements on drug adulteration, misbranding and new drug approval, if certain conditions are satisfied. "The compounded drug must comply with standards of an applicable U.S. Pharmacopoeia, or made from FDA-approved drug ingredients, meet certain manufacturing criteria, and the drug compounded must not be one that appears on a list of drugs or drug products that have been withdrawn or removed from the market because the product, or components of the product have been found to be unsafe or not effective." The pharmacy also may not compound regularly or in inordinate amounts "any drug products that are essentially copies of a commercially available drug."

The law also included provisions on advertising, stating that drugs may be compounded and subject to the exemptions if they are based on a valid prescription that was not solicited and if the pharmacy, licensed pharmacists or licensed physician does not advertise or promote the compounding of any particular drug. The advertising provisions and whether they are severable from the remainder of the statute were at issue before the Fifth and Ninth Circuits, and were found unconstitutional by the U.S. Supreme Court, which did not address the severability issue.

According to author Jennifer Staman, "the cases have created an interesting scenario of non-uniform enforcement throughout the U.S. In the Fifth Circuit, compounded drugs are specifically exempted from new-drug, adulteration, and misbranding requirements of the FFDCA if certain criteria are met; while in the Ninth Circuit (and, according to the FDA, the rest of the United States), compounded drugs are subject to these requirements, but the FDA may exercise discretion in taking action against an entity that violates these provisions." The **report** may be purchased from CRS. *See Health Legislation* (a CRS blog), October 23, 2012.

Data Standards Partnership Launched

The U.S. Food and Drug Administration (FDA) has launched a partnership with the Clinical Data Interchange Standards Consortium and Critical Path Institute to develop standardized definitions for individual diseases and the therapeutic approaches to treat them in an effort to transform the massive data streams from drug studies on specific diseases into usable information. Dubbed the Coalition for Accelerating Standards (CFAST), the initiative brings together clinical data experts from FDA and the pharmaceutical and information technology sectors to develop and maintain data standards. According to FDA's Center for Drug Evaluation and Research Director Janet Woodcock, "We at the FDA are excited to be a member of this important partnership. We believe that CFAST will provide an important resource for drug development and research that will result in enhancements in the evaluation of safe and innovative therapies for the public." *See ExpressPharmaOnline,* October 25, 2012.

FDA Brings Successful Enforcement Actions Against Dietary Supplement Makers

The U.S. Food and Drug Administration (FDA) has obtained a permanent injunction against Truman Berst who sells, as Alternative Health & Herbs Remedies, herbs and dietary supplements with disease-treatment claims. A federal court in Oregon determined in September 2012 that Berst had violated federal law by claiming that the company's herbal tinctures, capsules, topical products, eyewashes, and compresses could address serious diseases, such as cataracts, viral and bacterial infections, and cancer. According to an FDA spokesperson, "This company has ignored previous FDA warnings and has continued to produce and distribute products in violation of federal law. The FDA continues to protect public health by seeking enforcement action against companies that are identified as violating our manufacturing and drug approval requirements."

FDA had apparently warned the company as early as 2004 that its products were being distributed as unapproved and misbranded drugs. According to an agency press release, Berst has taken an appeal from the injunction to the Ninth Circuit Court of Appeals.

In a related development, Venus Pharmaceuticals International, Inc. and its CEO Bharat Kakumanu have agreed to cease producing and distributing dietary supplements in the United States, and to recall and destroy products made before January 2012, according to the terms of a consent decree approved by a federal court in New York. FDA accused the company of repeatedly violating current good manufacturing practice regulations thus rendering its products adulterated under the FFDCA. The company will also be required to implement corrective actions before it can resume dietary supplement production and must hire an outside auditor to oversee and review its progress in implementing the required changes. *See FDA Press Releases*, October 25, 2012.

Max Planck Institute Issues Paper Criticizing EU Unitary Patent Package

The Max Planck Institute for Intellectual Property and Competition Law has issued a **paper** that criticizes the unitary patent package currently under consideration in the European Union (EU).

Although the Institute generally supports "a balanced, innovation-friendly and uniform patent system" in the EU, it lists 12 reasons for concern about the proposed reforms. Among them are that the package may lead to unnecessary complexity and further, that it is unbalanced and lacks legal certainty. The Institute calls for reconsideration of the entire package.

EC Proposes Limits on Food Crop-Based Biofuel

The European Commission (EC) has **proposed** limiting the amount of food crop-based biofuel that can count toward the European Union's 2020 renewable energy targets. A 2009 EC Directive has set mandatory consumption targets of 20-percent renewable energy overall and 10-percent renewable energy in the transport sector. The proposal would cap the contribution of so-called "first-generation" ethanol and biodiesel at 5 percent of the transport sector's target.

The EC has determined that greenhouse gas performance calculations for biofuels should consider the indirect land-use change that occurs when biofuel crops displace food or feed production onto non-agricultural land. The EC's proposal thus aims to address this discrepancy and "start the transition to biofuels that deliver substantial greenhouse gas savings."

"For biofuels to help us combat climate change, we must use truly sustainable biofuels," said Commissioner for Climate Action Connie Hedegaard in an October 17, 2012, press release. "We must invest in biofuels that achieve real emission cuts and do not compete with food. We are of course not closing down first generation biofuels, but we are sending a clear signal that future increases in biofuels must come from advanced biofuels. Everything else will be unsustainable."

Indian Drug Industry Disputes Prohibition on Brand Names

According to a news source, the Indian Drugs Manufacturing Association is gearing up to challenge action taken by the country's drug controller to prevent the sale of medicines under brand names as part of an effort to accelerate sales of less-expensive generics. The association's secretary general reportedly said, "Our legal experts are studying the matter. We don't think the government has jurisdiction over the branding of drugs. We will also be taking a presentation to the government, asking it to consult the stakeholders on such a matter." The government's proposal would evidently require all drug makers applying for licenses to manufacture or market fixed-dose combination drugs to submit the generic name for the product and not the brand names. *See Pharmalot.com*, October 19, 2012.

Scientists Oppose SCI's Recommended Moratorium on Biotech Crops

After an expert committee appointed by the Supreme Court of India (SCI) recommended halting field trials of transgenic food crops for 10 years, biotechnologists, agricultural scientists and agribiotech-industry heads reportedly gathered in Bangalore to oppose the recommendations. Noting that genetically engineered crops will be needed to produce enough to feed a growing population, the scientists suggested that the committee relied solely on the views of select scientists and activists who oppose biotechnology in agriculture. They also claimed that the committee exceeded its mandate by making sweeping recommendations on a wide range of issues without accounting for the scientific rigor of methods in use in the country.

Biocon Ltd. Chair and Managing Director Kiran Mazumdar Shaw was quoted as saying, "I am here to express my solidarity with scientists and support to biotechnology. Innovations happen only through research and experimentation. No one has a right to ban research and experimentation. Those who oppose scientific research are not intellectually right and would take the country on a wrong path. Science and technology have done a lot to the country." *See Business Standard*, October 29, 2012.

LITIGATION

Vascular Graft Patent Dispute Heads to SCOTUS for Review of Heightened Willful Infringement Standard

Medical supply manufacturer W.L. Gore & Associates, Inc. has filed a petition before the U.S. Supreme Court seeking review of a Federal Circuit ruling remanding to the district court a long-running patent-infringement dispute over a prosthetic vascular graft, with instructions to reconsider its denial of W.L. Gore's motion for judgment as a matter of law of no willful infringement. *W.L. Gore & Assoc., Inc. v. C.R. Bard, Inc.*, No. 12-458 (U.S., petition for *certiorari*

filed October 12, 2012). Details about the Federal Circuit's ruling appear in Issue 37 of this *Bulletin*.

According to a news source, W.L. Gore contends that the Federal Circuit's ruling makes it more difficult to prove that a defendant acted despite an objective risk that its actions constituted infringement. The appeals court held that "a patentee must show by clear and convincing evidence that the infringer acted despite an objectively high likelihood that its actions constituted infringement of a valid patent." And while the trial court may "allow the jury to determine the underlying facts relevant to the defense in the first instance, for example, the questions of anticipation or obviousness, . . . the ultimate legal question of whether a reasonable person would have considered there to be a high likelihood of infringement of a valid patent should always be decided as a matter of law by the judge."

The dispute involves the man who made the graft and first conceived its use and the man who was asked to test the graft and was awarded the patent for it after a 28-year interference proceeding. The jury that found willful infringement awarded Bard Peripheral Vascular $185 million in damages. The district court doubled the damages verdict and added $19 million in costs and attorney's fees. W.L. Gore reportedly argues that the Federal Circuit's willful infringement standard expected a joint-inventor to meet the same standard as a sole inventor to prove willful infringement. Its petition apparently states, "In addition to its many legal defects, the Federal Circuit's misinterpretation . . . will have a severe negative impact on scientific collaboration, recognized by Congress as 'an essential pillar of the economy of the United States.'" *See Law360*, October 19, 2012.

Federal Circuit's Patent Infringement Ruling Conflicts with USPTO Re-Examination on Validity

The Federal Circuit Court of Appeals has denied a request for an en banc rehearing by a medical-device patent holder which argued that the U.S. Patent and Trademark Office's (USPTO's) Board of Patent Appeals had effectively nullified a previous Federal Circuit decision on the validity of its patent. ***In re Baxter Int'l, Inc.*, No. 2011-1073 (Fed. Cir., decided October 26, 2012)**.

As dissenting Judge Pauline Newman framed the issue, "The patent was granted in 1993. The [patent invalidity] litigation was initiated by [admitted infringer] Fresenius in 2003 by declaratory action. The action was decided by the district court in 2007, sustaining patent validity, and the appeal to the Federal Circuit was decided in 2009, sustaining patent validity. [A jury had determined that the patent was obvious, but the courts determined that Fresenius failed to show the patent was obvious, and it was ordered to pay $23.5 million in damages.] A reexamination request was filed by Fresenius in 2005, and in 2012 the Board of Patent Appeals and Interferences, stating

that 'the agency is not bound by the court's determination,' decided the same issues of patent validity on the same evidence, to contrary result."

Newman continued, "The appeal is again in the Federal Circuit, with this court deferring to the PTO's decision as 'substantially' supported, and refusing to recognize our own final decision three years earlier on the same evidence. Although patent validity is a question of law, the court declines *de novo* review, refuses to be bound by our prior decision, and authorizes the agency to overrule the court, all without a nod to finality, or correctness, or res judicata, or the Constitution."

According to the three judges concurring in the Federal Circuit's denial of rehearing, "the panel opinion [upholding the board's finding of obviousness] does not, as the dissent claims and the petition for rehearing en banc assumes, endorse 'administrative nullification of a final judicial decision.'" The concurrence contends, "The majority here concludes—rightly in my view—that a prior court decision in which a party has failed to prove a patent invalid does not bar the Patent and Trademark Office (PTO) from subsequently reexamining that same patent. And, it concludes that, despite a final court judgment reaching a contrary conclusion as between the patent holder and one alleged infringer, the PTO is free to conclude that the patent is, indeed, invalid. That proposition is an unremarkable one."

The concurring judges maintain that a patent is not found "valid" in a court proceeding. "A judgment in favor of a patent holder in the face of an invalidity defense or counterclaim merely means that the patent challenger has failed to carry its burden of establishing invalidity by clear and convincing evidence in that particular case—premised on the evidence presented there. If the PTO later considers the validity of that same patent, it does so based on the evidence before it and under the lesser burden of proof that applies in reexamination proceedings."

NEWS BYTES

The U.S. Patent and Trademark Office **proposes** an update to its professional conduct rules to conform to the American Bar Association's Model Rules of Professional Conduct as amended through 2011. Some specific language would be tailored to "circumstances particular to practice before the office." Comments are requested by December 17, 2012.

The U.S. Patent and Trademark Office (USPTO) **launches** two new regional pro bono patent programs to assist "financially under-resourced independent inventors and small businesses" that might otherwise be unable to afford patent protection. The new programs in California and the District of Columbia region, including Virginia and Maryland, join four others already established under the America Invents Act. USPTO plans to get 10 started by the end of 2013.

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The U.S. Patent and Trademark Office (USPTO) **seeks** comments on an information collection relating to patent applications containing nucleotide sequence and/or amino acid sequence disclosures. It estimates that it will take the public six minutes to six hours "to gather the necessary information, prepare the form or sequence listing, and submit it to the USPTO" at an estimated annual cost burden of $2.5 million. Comments are requested by December 28, 2012.

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LIFE SCIENCES & BIOTECHNOLOGY LEGAL BULLETIN

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