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IN THIS ISSUE

Supreme Court Ruling Strengthens Patent Holders' Claims in Infringement Cases

A U.S. Supreme Court ruling last week that patents should be presumed valid could make it easier for medical devicemakers to sue for patent infringement, a patent law attorney said.

The 6-2 ruling, with one abstention, in *Commil USA v. Cisco Systems* means plaintiffs will no longer need to prove their patents are good to bring a claim, says Jonathan Losk, a partner with Knobbe Martens. Previously, defendants could not be held liable for infringement if they had a good faith belief the patent was invalid.

The case involved allegations by Commil that Cisco infringed upon a patent for a method of implementing short-range wireless networks. The case went to trial, and Cisco was held liable for direct and induced infringement, despite the defendant's claim that it had a "good-faith belief" that the patent was invalid. The U.S. District

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FBI Wants to Know if Devicemakers Knew of Morcellation Cancer Risk

The Federal Bureau of Investigations has launched an investigation into whether major devicemakers and their customers routinely broke the law by failing to report adverse events related to uterine morcellation, a cardiac surgeon interviewed by bureau agents says.

Dr. Hooman Noorchashm of Philadelphia told *IDDM* that he approached the FBI with his concerns after his wife's cancer spread throughout her body following a morcellation procedure at Boston's Brigham & Women's Hospital in 2013. The couple finally got a response from the bureau's Newark, N.J., district office earlier this year, with agents interviewing Noorchashm, his wife and several other patients and physicians.

Power morcellators, which are used to remove uterine fibroids, came under scrutiny in April 2014 when the FDA issued a safety

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Patents, *from Page 1*

Court for the Eastern District of Texas deemed Cisco's supporting evidence inadmissible, and the Federal Circuit affirmed the decision.

In upholding the appeals court and lower court rulings, the Supreme Court said "a defendant's belief regarding patent validity is not a defense to an induced infringement claim."

While this is good news for devicemakers, there are steps they can take better protect intellectual property, says Losk. For starters, companies should file separate patents on the device, the device system, the method for treating patients with the device and the manufacturing process. The patent applications should "give breadth and length to your intellectual property protections," Losk says. He spoke at an FDAnews webinar last week.

Protect Critical Assets

Companies should take extra care to protect critical assets — those that, if usurped by competitors, could disrupt the business, Losk says. This normally involves identifying an asset owner, implementing primary and secondary safeguards and restricting access based on the need to know. In addition, firms should forensically capture and review every computing asset when it is replaced or when an employee leaves.

Losk also recommends correlating patents with business value models by developing a list of key clinical value features and mapping patent claims against these features. He further advises adding restrictive labeling to devices, such as one-time use restrictions, or restricting implied licenses for use.

Once patents are attained, companies should monitor the landscape for possible infringement, which can be done by searching the USPTO database, watching key foreign markets and watching for FDA clearances, CE marks, or other regulatory authorizations for products similar to your own, Losk says.

Losk also recommends establishing a firm internal policy that any unsolicited product concepts be channeled to a single individual or office, normally patent counsel or business development. He cites the example of a physician sharing an invention with a devicemaker's sales rep, who then takes the product to the corporate office where in-house R&D staff have been working on the same concept. Without any internal policy, the physician might expect a lucrative business agreement, and failure to get one could lead to loss of a customer or a lawsuit, the attorney says.

Companies can further protect themselves if they accept only copies of filed patent applications, which will require inventors to protect their concepts before disclosing them. When accepting a concept, the firm should issue a nondisclosure agreement limiting access to the product idea to a few company representatives.

View the decision in *Commil USA v. Cisco Systems* at www.fdanews.com/06-01-15-CommilvCisco.pdf. — Elizabeth Orr

China FDA Exempts 'Equivalent' Devices from Clinical Trials

Devicemakers won't have to stage new clinical trials of their devices to gain approval in China if they can demonstrate that they're basically equivalent to devices already on the market, Chinese regulators say.

To get around the trial requirement, devicemakers must submit data from a trial of an older device to which the newer one is being compared. Two devices may be deemed equivalent if the differences in their operating principles, structures, materials, production processes, safety evaluation, applicable national or industry standards and intended use are so minor as to not affect the device's safety or efficacy, a new guideline released by the China Food and Drug Administration says.

The guideline also exempts so-called catalog products from clinical trials. Evidence shows they are equivalent to items on the CFDA's formal list of devices exempted from clinical studies.

For most devices requiring clinical trials, the manufacturers may submit data from overseas studies as long as the trial design meets Chinese standards for sample size, control group selection and end point. The data must also show that the device is equally effective across different ethnic groups. That does not apply to certain Class III devices, which require Chinese trial data, the CFDA says.

For lower-risk products, literature reviews conducted in major scientific databases and empirical data collected from clinical use of the device, including adverse event reports, may be acceptable, the agency adds.

View the guideline, in Chinese, at www.fdanews.com/06-01-15-china.pdf. — Elizabeth Orr

Guidance on Pediatric Extrapolation Applies to New and Existing Devices

New draft guidance on extrapolating existing data to gain approval for pediatric indications applies to new devices as well as those already approved for adult use, an FDA official says.

"We certainly did not intend to limit the application of this guidance to only products that already have an approval for adult indications," says Kathryn O'Callaghan, acting associate director for science and strategic partnership in the Center for Devices and Radiological Health. Companies that think they can leverage adult data or data from another pediatric population should speak with the agency early in the preapproval process about their plans and the rationale, she says.

Before extrapolating data, devicemakers should ensure that the existing adult response data or population characteristics are similar to the intended pediatric population and that the adult data is of good quality. They should also verify that the data can be used fairly and responsibly to determine the safety and effectiveness of the device, O'Callaghan says.

Partial data extrapolation, combined through a statistical model with pediatric data sources to demonstrate a reasonable assurance of effectiveness, is preferred over full extrapolation of data from adult studies, O'Callaghan says. She spoke at a recent FDA webinar on the guidance.

The draft guidance applies to PMA and HDE devices only because 510(k) devices fall outside the scope of the original regulation. However, the principles behind the guidance might apply to certain 510(k) devices as well, O'Callaghan says. She encourages sponsors of 510(k)s to contact the FDA during the presubmission process and file comments on the draft to alert the agency to concerns about the scope of the guidance.

CDRH issued the draft guidance to address ongoing challenges in pediatric device trials,

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Interoperability Growing Despite Lack of Incentives

Governments and standards organizations worldwide are moving toward a healthcare delivery system where devices work together, but devicemakers may need better incentives to get on board, an analyst says.

Shruthi Parakkal, a senior research analyst with Frost & Sullivan, says governments in the U.S., EU and other jurisdictions have been encouraging interoperability by issuing standards and guidance documents. "It's not that the standards have not been set. It's that they have not been utilized to the proper level due to a lack of incentives," she says.

Governments will need to step in with regulations before interoperability among medical devices becomes routine, because it's not always clear to companies what the benefits are, Parakkal told *IDDM*. Devicemakers typically use proprietary technology that blocks their devices from communicating with other products, and they often lack the expertise or willingness to change, she adds.

Factors preventing the design of interoperable devices include:

- A perception that the devicemaker is primarily a software developer and can better spend R&D funds on other efforts;
- Reluctance to involve the FDA or other regulatory authorities;
- The lack of a strong industry culture of interoperability, such as is found in aerospace; and
- The need to invest in fast-changing new technologies like WiFi and Bluetooth to maintain interoperability.

Meanwhile, hospitals and caregivers want devices that talk to one another, but are often constrained by cost considerations and lack of in-house expertise, says Parakkal, who authored a recent Frost & Sullivan report on healthcare and medical device connectivity and interoperability. To get around those issues, many opt for third-party connectivity that is vendor-neutral. An example is a software vendor that designs products allowing devices used in hospitals to feed into a common medical record system.
— Elizabeth Orr

China Announces Registration Fees; Class III Imports to Cost $50K

The China Food and Drug Administration Wednesday announced registration fees for locally made and imported medical devices aimed at speeding up the processing of applications.

Sponsors of imported Class III devices must pay approximately US $49,802 for initial registration, while locally made Class III devices are charged $24,772. For Class II devices, registration fees are set at the provincial level for locally made products, and at $34,008 for imports.

In addition, devicemakers must pay a continuing registration fee of $6,579 every five years for imported Class II devices and all Class III devices. Continuing fees for locally made Class II devices are set at the provincial level.

There is also a $6,966 fee for clinical trials of Class III devices.

Devicemakers can still register Class I devices for free, and fees may be waived on a case-by-case basis for small and micro businesses with innovative technologies, the CFDA says. To apply for the waiver, companies must submit a copy of their business license, recent tax returns and a notice from the CFDA stating the device is innovative.

AdvaMed's China staff is discussing the new fees with the CFDA under the auspices of the Joint Commission on Commerce and Trade, says Ralph Ives, executive vice president of global strategy and analysis.

View the fees notice, in Chinese, at www.fdanews.com/06-01-15-registration.pdf.
— Elizabeth Orr

Morcellators, *from Page 1*

alert saying the devices' blades could spread cancerous tissue throughout the abdomen. At least 21 cases of cancer attributed to morcellation were known to the FDA as of a summer advisory panel hearing, with the suspicion being that many more had gone unreported.

After retired pathologist Dr. Robert Lamparter warned morcellator maker Johnson & Johnson that he believed the devices could spread malignancies because of the number of unsuspected uterine cancers at his small hospital, J&J edited the packaging of Morcellex to specifically warn of the risk of disseminating malignant tissue, J&J spokesman Matthew Johnson told *IDDM*.

The packaging suggests that physicians who suspect cancer use a special tissue extraction bag during morcellation procedures.

But Noorchashm says manufacturers and healthcare facilities failed to alert the FDA or take other steps to protect patients from morcellation's dangers, even as they knew of the risks.

"The bottom line is that a specific federal law has been violated, and a lot of people have been harmed or died," he says. "I think the FBI and Congress will take an interest in how something like that could happen."

Specifically, Noorchashm said hospitals and devicemakers violated the medical device reporting regulation (21 CFR 803) by failing to report cancer risks even though morcellators have been used for 20 years.

J&J recalled its morcellators last summer and is among manufacturers facing lawsuits from patients who say their cancer spread after undergoing procedures involving morcellation (*IDDM*, May 25).

The FDA required a black box warning on the devices in December 2014 and recommends against their use for most women, but has not requested the devices be removed from the market.

Johnson says J&J hasn't been contacted by the FBI, and he doesn't believe the firm or its Ethicon subsidiary are being targeted specifically in what might be a broader survey of the industry.

The FBI won't confirm investigations until charges are filed. — Elizabeth Orr

Pediatric, *from Page 3*

such as small sample sizes and anatomy. For example, a reference draw may require more blood than is safe to take from a child.

The draft also applies to biologics-device combination products that are partially regulated by the Center for Biologics Evaluation and Research.

Comments on the draft guidance are due Aug. 4 to docket no. 2015-10482. Read it at www.fdanews.com/05-11-15-pediatric-device.pdf. — Elizabeth Orr

AE Reporting by Devicemakers Up Significantly, TGA Says

The number of adverse events reported by devicemakers in Australia jumped by more than a thousand in 2014, compared with the previous year, regulators say.

In 2014, companies submitted 3,697 AERs to the Therapeutic Goods Administration, or 85 percent of the total 4,337 device-related reports, according to postmarket vigilance data released May 26. This was significantly more than the 2,456 adverse events devicemakers reported in 2013.

The TGA attributes the spike to greater awareness among device users to report incidents to the manufacturer.

The remainder of the reports — 640 — were filed by doctors, allied health professionals, nurses and consumers. Unlike devicemakers, these groups aren't required by the TGA to report adverse events.

The number of reports by doctors dropped to 115 in 2014, from 376 the previous year when a major breast implant recall was underway, the TGA notes. Allied health professionals and nurses filed 232 and 167 reports, respectively — up from 158 and 93. Consumers accounted for just 122 reports, down from 178 in 2013 when a total of 3,000 AERs were logged.

View the TGA report at www.fdanews.com/06-01-15-TGApostmarket.pdf. — Elizabeth Orr

Report: FDA Should Move Slowly To Regulate Genomic Medicine

The FDA will need to change its approach if it wants to regulate genomic medicine while encouraging the field to grow, a special report in the *New England Journal of Medicine* concludes.

The authors, from the University of Houston Law Center and the University of Washington's bioethics and humanities departments, argue that rushing to regulate the growing field "could subject genomic testing to counterproductive regulatory burdens that may – ironically – diminish consumer safety and chill innovation."

A more limited approach to regulatory reforms, however, could bring the FDA's genomic oversight up to snuff, the authors say.

For example, they suggest the FDA work with the National Institutes of Health and private industry to create and fund a genomic database that sponsors could use in validating their diagnostics. Not enough genomic information is publicly available to discern the full effects of unusual genetic variants, they say.

Some resources used to develop the FDA's Sentinel system for postmarket monitoring could also be diverted to a genomic database.

View the report at www.nejm.org/doi/full/10.1056/NEJMsr1501194. — Elizabeth Orr

Michigan Devicemaker Warned Over Unapproved Hip Implants

The FDA slapped Signal Medical with a warning letter for marketing a hip implant system that had never been approved.

During a July 31 to Aug. 11, 2014, inspection of the firm's Marysville, Mich., facility, the investigators from the Detroit district office found that MicroSeal Total Hip Acetabular System was adulterated because Signal didn't have an active PMA or other marketing clearance on some system components.

Specifically, the hip system includes a hood feature integrated with two separate liner models that were never cleared. In addition, the company sells two other liner sizes beyond the three available when the product was cleared for marketing.

The products are misbranded because Signal changed the device shell and liner without getting FDA approval, the warning letter says. The company responded to the Form 483, but did not address the issue of misbranding, the FDA says.

Signal Medical did not respond to a request for comment by press time.

View the Dec. 15 warning letter posted online recently, at www.fdanews.com/06-01-15-signal.pdf. — Elizabeth Orr

BRIEFS

TGA Finishes Morcellator Review

Australia's Therapeutic Goods Administration has updated the instructions for use on all laparoscopic morcellators approved for use in the country to ensure doctors and patients understand the potential risks. Specifically, the IFU warns that morcellators should not be used in patients with suspected uterine tumors and specifies that physicians be credentialed and trained on the devices. The TGA undertook a review of laporascopic morcellators in April 2014 after U.S. regulators warned that morcellation during certain uterine surgeries could spread cancer cells into surrounding tissue. In safety advisories issued last year, the TGA put the risk to Australian women undergoing morcellation at about one in 1,000.

Cook Undergoes IMDRF Single Audit

Cook Medical's Limerick, Ireland, plant has signed on with the International Medical Device Regulators Forum's single audit program, making it the first Irish facility to do so and one of just six companies worldwide to have MDSAP audits since the program launched last summer. The site underwent a two-day initial certification audit in April. MDSAP is based on a three-year audit cycle, with initial audits followed by partial surveillance audits each of the next two years and a complete recertification audit at the end of three years. Regulators participating in the MDSAP pilot include the FDA, Health Canada, Australia's Therapeutics Goods Administration, Brazil's Anvisa and Japan's Pharmaceuticals and Medical Devices Agency.

Silk Road's Stent System Approved

Silk Road Medical's Enroute transcarotid stent system has secured FDA approval, making it the first of its kind to be implanted in the carotid artery using a direct common carotid access point. The stent is indicated for high surgical risk patients and intended for use alongside the Enroute transcarotid neuroprotection system, which won FDA 510(k) clearance in February. The neuroprotection system provides access to the common carotid artery to reverse high rates of temporary blood flow, protecting the brain from stroke.

Guided Therapeutics' PMA Rejected

The FDA has rejected a July 2014 amendment to Guided Therapeutics' PMA for the LuViva advanced cervical scan, saying it needs to see more patient data before signing off. LuViva, Guided's first product, is a noninvasive device that uses spectroscopy to measure light interaction with tissue to identify chemical and structural markers for cervical cancer. The device is available in Europe.

Sunshine Heart Resumes Trial Enrollment

Sunshine Heart said Tuesday it has resumed patient enrollment in a clinical trial of its C-Pulse heart assist system, following FDA approval. The devicemaker paused enrollment March 6 after four patients died. However, an independent committee ruled the deaths weren't device-related. The multicenter trial will test the system's safety and efficacy in the treatment of NYHA Class III and ambulatory Class IV heart failure. Sunshine plans to enroll patients across 40 clinical sites. The device, which is investigational status in the U.S. and Canada, received CE Mark approval in 2012.

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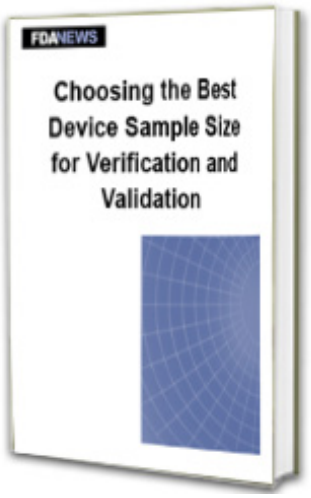

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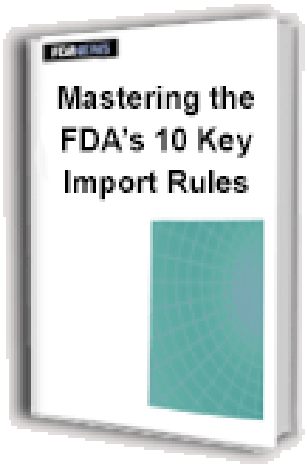

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