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Dueling Records: Are Statements in Your 510(k) Putting Your Patents at Risk?





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EXECUTIVE SUMMARY

Laboratory developed test (LDT) providers, previously exempt from U.S. Food and Drug Administration (FDA) oversight, under a new FDA proposal, must now consider if their LDTs constitute moderate-risk (Class II) or high-risk (Class III) devices that will be subject to FDA oversight.

If so, LDT providers will have to seek FDA approval or clearance through a premarket approval application (PMA) or a 510(k) premarket notification submission. During the 510(k) process, a company asserts that its new device is substantially equivalent to an existing predicate device for the purpose of establishing the safety and effectiveness of the new device.

However, undiscerning statements of ''substantial equivalence'' that are not narrowly tailored to the safety and efficacy of the new device may seem inconsistent with the company's prior statements before the United States Patent and Trademark Office (USPTO) regarding the patentability of the device. These apparent discrepancies can be exploited during patent litigation to undermine the enforceability or validity of the patent asset.

Thus, companies can inadvertently jeopardize patent assets in an attempt to secure expedient regulatory clearance for a new device.

This dilemma is partly attributable to the often large temporal gap between the patent procurement stage and market clearance stage of the life cycle of most companies. This article provides companies (e.g., LDT providers) with practical solutions for mitigating the risk of losing valuable patent rights, while securing regulatory clearance prior to entering the market.

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FDA'S TRADITIONAL ENFORCEMENT DISCRETION OVER LDTS

''Personalized medicine'' or ''precision medicine'' refers to the ''use of genomic, epigenomic, exposure and other data to define individual patterns of disease''[1] and covers a vast array of innovative products and services that tailor medical treatments to the specific characteristics, needs, and preferences of each patient.

One goal of personalized medicine is to streamline clinical decision-making by facilitating the advance identification of patient subpopulations that will most likely benefit from a given treatment regime, while sparing others from the unnecessary expense and side effects associated with the same regime.[2] Personalized medicine promises to advance medical product devel-

[1] National Research Council: Committee on a Framework for Developing a New Taxonomy of Disease, *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*, National Academies Press (2011).

[2] U.S. Food and Drug Administration, *Paving the Way for Personalized Medicine – FDA's Role in a New Era of Medical Product Development*, FDA 6 (October 2013), http://

opment by uncovering the underlying causes of variability in patient response, and ushering in a larger number of drugs that are safe, effective, and commercially viable.[3]

Targeted therapeutics[4] and their complementary ''companion diagnostics''[5] are two fundamental components of products and services that drive personalized medicine. *In vitro* diagnostic products (IVDs) refer to ''reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae.''[6] IVDs are typically developed by a conventional device manufacturer and are sold to labs, hospitals, or clinics.[7]

In contrast, a laboratory developed test (LDT) is ''an IVD that is intended for clinical use and designed, manufactured and used *within a single laboratory*.''[8] The FDA classifies IVD products into Class I (low-risk), Class II (moderate-risk), or Class III (high-risk) devices according to the level of regulatory control that is necessary to assure safety and effectiveness.[9] Class II (moderate-risk) or class III (high-risk) devices require FDA premarket review. During this review process, the FDA often requires the manufacturer to submit evidence of the accuracy, precision, and reliability of the test, as well as clinical data validating that the test performs as intended and labeled for the specific clinical use.[10] The premarket review process can take from several months to years to complete, and is often accompanied by significant costs for collecting the information required for FDA clearance or approval.[11]

IVD PRODUCT CLASSIFICATION

CLASS I(low-risk) —subject to general controls

CLASS II(medium-risk) —subject to general and special controls

CLASS III(high-risk) —subject to most stringent regulations

Many existing diagnostic tests are offered as LDTs[12] that facilitate the evaluation of alterations in biomarker levels or the presence/absence of genetic susceptibility mutations in patients. While the FDA maintains that it has had the authority to regulate all IVDs since the 1976 enactment of the Medical Device Amendments (MDA) to the Federal Food, Drug, and Cosmetic Act (the FD&C Act), it ''has *generally not enforced* applicable provisions under the FD&C Act and FDA regulations with re-

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www.fda.gov/downloads/ScienceResearch/SpecialTopics/PersonalizedMedicine/UCM372421.pdf.

[3] U.S. Food and Drug Administration, *supra* note 2, at 13 (''many drugs under development never reach the stage of being submitted to FDA in an application requesting approval for marketing. High attrition rates stem largely from failure of drugs to meet expected efficacy levels, to demonstrate improved outcomes over a comparator drug, or to demonstrate sufficient safety to justify their use'').

[4] ''Targeted therapeutics, usually drugs or biologics, are treatments designed to benefit a particular subpopulation, or whose use in another subpopulation might be especially disadvantageous or require different dosing.'' Personalized Medicine Coalition, *Personalized Medicine Regulation – Pathways for Oversight of Diagnostics*, PMC 3 (January 2013), http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc_pathways_for_oversight_diagnostics.pdf (hereinafter, ''Pathways'').

[5] The FDA's Center for Drug Evaluation and Research, Center for Devices and Radiological Health, and Center for Biologics Evaluation Research define a companion diagnostic device as ''an in vitro diagnostic device that provides information that is essential for the safe and effective use of a corresponding therapeutic product.'' U.S. Food and Drug Administration, *Guidance for Industry and Food and Drug Administration Staff - In Vitro Companion Diagnostic Devices*, FDA 7 (August 6, 2014), http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm262327.pdf.

An IVD companion diagnostic device could be essential for the safe and effective use of a corresponding therapeutic product to: identify patients who are most likely to benefit from the therapeutic product; identify patients likely to be at increased risk for serious adverse reactions as a result of treatment with the therapeutic product; monitor response to treatment with the therapeutic product for the purpose of adjusting treatment (e.g., schedule, dose, discontinuation) to achieve improved safety or effectiveness; and identify patients in the population for whom the therapeutic product has been adequately studied, and found safe and effective, i.e., there is insufficient information about the safety and effectiveness of the therapeutic product in any other population.

FDA does not include in this definition *in vitro* diagnostic tests that are not essential to the safe and effective use of a therapeutic product.

Id.

[6] 21 C.F.R. § 809.3.

[7] U.S. Food and Drug Administration, *supra* note 2, at 32.

[8] U.S. Department of Health and Human Services, U.S. Food and Drug Administration, Center For Devices And Radiological Health, *Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs)* – draft guidance, FDA 5 (October 3, 2014), http://www.fda.gov/downloads/medicalservices/deviceregulationandguidance/guidancedocuments/ucm416685.pdf (8 MELR 643, 10/1/14) (hereinafter, ''LDT draft guidance'') (emphasis added). The FDA provides the following as an example of an LDT: ''A laboratory uses peer reviewed articles to guide development of a new diagnostic device. The laboratory uses general purpose reagents and analyte specific reagents combined with general laboratory instruments and develops a testing protocol, that together constitute a test system which is then verified and validated within the laboratory. Once validated this device is used by the laboratory to provide clinical diagnostic results.''

Id.

[9] Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360c(a)(1). See *also* Pathways, *supra* note 4, at 8-9 (internal citations omitted):

CLASS I DEVICES are subject to general controls, such as requirements for device labeling, device listing with the FDA, 510(k) premarket notification, and compliance with the FDA's quality systems regulations (QSR). General controls apply to all devices. Most Class I devices are exempt from 510(k) premarket review requirements, and in some cases, are also exempt from compliance with FDA's quality systems regulations, other than minimal record keeping and reporting requirements.

CLASS II DEVICES are subject to general and special controls, such as performance standards, postmarket surveillance, and FDA guidelines. Most class II devices require premarket review by the FDA through the 510(k) clearance process prior to commercialization.

CLASS III DEVICES are generally implantable devices; devices represented to be used for life-sustaining or life-supporting purposes; or, new devices that have not been found substantially equivalent to legally marketed Class I or II devices. Class III devices require approval of a PMA application and are the most stringently regulated.

[10] Pathways, *supra* note 4, at 9.

[11] *Id.*

[12] U.S. Food and Drug Administration, *supra* note 2, at 32.

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spect to LDTs.''[13] The FDA's traditional practice of exercising enforcement discretion over LDTs grew out of the fact that LDTs comprised a relatively small volume of tests developed by local laboratories that were either relatively simple or were intended for use in diagnosing rare diseases or to meet the needs of a local patient population.[14] Further, LDTs were historically manufactured using components that were legally marketed for clinical use.[15]

However, the increasing reliance on LDTs in clinical decision-making, combined with the complexity of LDTs being offered, poses increasing risks to patients,[16] thereby motivating the FDA to revisit its stance regarding its oversight of moderate- to high-risk LDTs.

FDA'S CURRENT ACTIVISM IN OVERSIGHT OF CERTAIN LDTS

The FDA has recently determined that some modern LDTs pose an increased risk to patient safety in the absence of more rigorous oversight.[17] The sheer pace of technological advancements in the IVD space over the past decade has been staggering. Information arising out of the human genome project, along with the decreasing costs of whole genome sequencing, have led to a plethora of publications linking particular biomarkers to different diseases, and the rapid integration of this information into new molecular diagnostic tests.[18] The growing reliance on molecular diagnostic tests in guiding critical treatment decisions, combined with the dramatic increase in the number and complexity of LDTs, create legitimate concerns over the safety and effectiveness of certain LDTs. Estimates suggest that tens of thousands of diagnostic tests, including the majority of genetic tests, are currently offered as LDTs.[19]

Moreover, the business models for laboratories have changed. In contrast to the hospitals or public health laboratories of 1976, in which LDTs comprised relatively simple tests that were generally used to diagnose rare diseases or meet the needs of the local community, modern LDT manufacturers are oftentimes large corporations that have an international reach and can provide diagnostic results for high-risk diseases,[20] such as breast cancer and Alzheimer's disease.

Thus, unlike traditional LDTs, modern LDTs are typically:

> More complex;
>
> Widely used to screen for common diseases rather than rare diseases;
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> Manufactured in high volume and offered beyond local patient populations;
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> Manufactured with components that are not legally marketed for clinical use; and
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> Present higher risks that are similar to those of other IVDs that have undergone premarket review (e.g., used in guiding critical treatment decisions).[21]

The FDA has also determined that regulatory oversight of LDTs under the Clinical Laboratory Improvement Amendments (CLIA) alone does not address patient safety concerns, primarily because CLIA accreditors neither validate these tests prior to marketing nor do they assess the clinical validity of an LDT.[22] In light of the profound shifts in the technology and business practices with respect to the use of LDTs, the FDA ''believes the policy of general enforcement discretion towards LDTs is no longer appropriate.''[23]

Despite opposition from segments of industry, including the laboratory testing industry, hospitals, and medical societies, regarding the FDA's authority to regulate LDTs,[24] the agency maintains that the Medical Device Amendments of 1976 grants it the authority to regulate LDTs as devices and has strengthened its stance in this regard. In October 2014, the FDA issued the draft guidance proposing a regulatory framework for oversight of LDTs, breaking the nearly 40-year status quo of enforcement discretion.[25]

The FDA's draft regulatory framework for LDTs is based on the risks to patients if the device were to fail rather than whether the LDTs were made by a conventional manufacturer or a single laboratory.[26] The FDA would rely upon the existing medical device classification system to evaluate the risk of an LDT category, evaluating the potential for severe therapeutic consequences brought on by the initiation of unnecessary treatments or a decision to delay or forego treatment altogether for a condition.[27]

Under the FDA's proposed framework, low-risk LDTs (defined as Class I medical devices) and LDTs for rare diseases or unmet medical needs will continue to experience enforcement discretion for applicable premarket review and quality systems requirements.

However, the applicants for these devices will be required to comply with registration and listing (with the option to provide notification) and adverse event reporting within six months after issuance of the FDA's final guidance on LDTs.[28]

Under the new guidance, a company is only required to comply with the registration and listing requirements if it does not provide notification information to the FDA with respect to its LDTs.[29] Most companies would likely go through the FDA notification process. In addition to satisfying the registration and listing and reporting requirements for low-risk LDTs, moderate-risk

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[13] LDT draft guidance, *supra* note 8, at 6 (emphasis added). Although rare, there have been several past examples of the FDA's varying oversight of LDTs. See Pathways, supra note 4, at 10-11.

[14] LDT draft guidance, *supra* note 8, at 7.

[15] *Id*.

[16] U.S. Food and Drug Administration, *supra* note 2, at 32.

[17] LDT draft guidance, *supra* note 8, at 8-13.

[18] U.S. Food and Drug Administration, *supra* note 2, at 30.

[19] R. Sachs, *The Complex Effects of the FDA's Proposal To Regulate Laboratory-Developed Tests*, Health Affairs Blog (April 10, 2015), http://healthaffairs.org/blog/2015/04/10/ the-complex-effects-ofthe-fdas-proposal-to-regulate-laboratory-developed-tests/.

[20] LDT draft guidance, *supra* note 8, at 8.

[21] *Id*.

[22] *Id*. at 7, 8-9.

[23] *Id*. at 8.

[24] J. Evans & M. Watson, *Genetic Testing and FDA Regulation*, JAMA 313(7):669-670 (2015).

[25] LDT draft guidance, *supra* note 8.

[26] LDT draft guidance, *supra* note 8, at 11. The FDA intends to apply the same risk-based framework to any IVD that is being marketed as a LDT by a CLIA-certified laboratory, even if they do not meet the FDA's definition of a LDT. *Id*. at 6.

[27] *Id*. at 11-12.

[28] *Id*. at 12, 14.

[29] *Id*. at 17-18.

(Class II) and high-risk (Class III) LDTs will be subject to more onerous regulatory oversight than low-risk LDTs.

Moderate-risk LDTs will be subject to premarket review requirements (i.e., premarket notification or 510(k) submissions) within five to nine years after the FDA's final guidance is implemented.[30] High-risk LDTs will be subject to premarket review requirements beginning one year after the FDA's guidance on LDTs is finalized.[31] The FDA will focus its initial efforts on reviewing LDTs that have the same intended use as an FDA-approved or -cleared companion diagnostic or Class III medical device, as well as LDTs that determine the safety or efficacy of blood or blood products.[32] The FDA intends to continue to exercise enforcement discretion with respect to Quality System regulation requirements, codified in 21 C.F.R. 820, until a manufacturer of a given LDT submits a PMA or the FDA issues a 510(k) clearance order for the LDT.[33]

The FDA's recent interest in regulating moderate to high-risk LDTs is also underscored by its recent approval of the BRACAnalysis CDx test, which represents the FDA's first approval of an LDT under a premarket approval application and is the first approval of an LDT companion diagnostic.[34] The BRACAnalysis CDx test is designed to detect specific BRCA gene mutations in patients with advanced ovarian cancer to determine who may be candidates for treatment with Lynparza™ (olaparib).[35]

Further, the FDA recently outlined its plans for $10 million in funding that it expects to receive under the president's Precision Medicine Initiative to continue to fuel its regulatory oversight of moderate- to high-risk LDTs, particularly those involving next-generation sequencing (NGS) platforms.[36,37] Under the Precision Medicine Initiative, the FDA will be charged with establishing oversight standards for NGS testing, and to develop the bioinformatics infrastructure necessary to facilitate the curation and sharing of the information that can be gleaned from NGS technology.[38] Indeed, the FDA has already taken preliminary steps towards exploring alternate approaches to regulating NGS-based tests.[39]

AN EMERGING AREA OF REGULATION FOR LDT PROVIDERS

Should the FDA implement its proposed guidelines concerning the regulation of moderate-risk and high-risk LDTs, it is likely to have a profound impact on the market for companion diagnostics and other tests that support personalized medicine. Around 11,000 tests developed by 2,000 different laboratories are predicted to fall under the FDA's proposed framework for regulatory oversight of moderate-risk and high-risk LDTs.[40]

Thus, it is becoming increasingly evident that providers of moderate-risk and high-risk LDTs that were once largely shielded from FDA oversight, must now seek FDA approval or clearance.

Medical devices generally reach the market in one of two ways:

1. A premarket approval application (PMA) — a difficult and expensive pathway that requires clinical data to support an application

2. A premarket notification 510(k) application[41]

The 510(k) premarket-clearance pathway requires manufacturers to demonstrate that the device to be marketed is at least as safe and effective, or ''substantially equivalent,'' to an already legally marketed ''predicate'' device.[42] The term ''substantially equivalent'' means that the device: (a) has the ***same intended use*** as the predicate device; and (b) either has the ***same technological characteristics*** as the predicate device, or different technological characteristics with information demonstrating that the device is at least as safe and effective as the predicate device.[43]

In order to secure clearance via the 510(k) pathway, the manufacturer must demonstrate how the new device compares to the predicate device with respect to a variety of elements, including clinical indications, technological characteristics, method of operation, and a summary of comparative preclinical performance testing.[44] A 510(k) notification must also include an expla-

[30] *Id*. at 13.
[31] *Id*. at 13.
[32] *Id*.
[33] *Id*. at 28-29.
[34] *FDA Approves Lynparza to Treat Advanced Ovarian Cancer*, FDA (December 19, 2014), http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427554.htm (9 MELR 20, 1/7/15).
[35] *Id*.
[36] Ray, *FDA Outlines Plan for Expected $10M Under President's Precision Medicine Plan*, GenomeWeb (February 18, 2015), https://www.genomeweb.com/regulatory-news/fda-outlines-plan-expected-10m-under-presidents-precision-medicine-plan.
[37] Thus far, only one NGS instrument (Illumina MiSeq DxTM) and two accompanying assays for diagnosing cystic fibrosis (Illumina MiSeqDx Cystic Fibrosis 139-Variant Assay and Illumina MiSeqDx Cystic Fibrosis Clinical Sequencing Assay) have been FDA-approved. A. Konski, *FDA Considering New Regulatory Approaches for NGS*, Personalized Medicine Bulletin (December 28, 2014), https://www.personalizedmedicinebulletin.com/2014/12/28/.
[38] A. Konski, *Details Emerge for President's Precision Medicine Initiative*, Personalized Medicine Bulletin (February 2, 2015), https://www.personalizedmedicinebulletin.com/2015/02/02/.
[39] *Optimizing FDA's Regulatory Oversight of Next Generation Sequencing Diagnostic Tests—Preliminary Discussion* Paper, FDA (Dec. 29, 2014), http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM427869.pdf.
[40] M. Herper, *FDA To Regulate Thousands Of Cancer, Genetic, And Other Diagnostics*, Forbes (July 31, 2014), http://tinyurl.com/p7rp5xg.
[41] A 510(k) notification is used where premarket approval is not required because the device is substantially equivalent to a device legally marketed in the United States. For instance, 510(k) submissions are used where there is a modification in intended use, or where there is a modification of a legally marketed device and that change could significantly affect its safety or efficacy.
[42] *See* 21 C.F.R. § § 807.81-807.100.
[43] Federal Food, Drug, and Cosmetic Act § 513(i); 21 C.F.R. § 807.100(b).
[44] ''Technological characteristics'' can include aspects such as design, material selection, chemical composition, or energy source. If the device has the same technological characteristics, a summary of the technological characteristics of the new device in comparison to those of the predicate device is included in the 510(k) summary. If the device has different tech-

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nation of why differences between the new device and predicate device do not affect the safety and effectiveness of the new device.[45]

510(k) SUBMISSIONS

Indiscriminate statements could compromise a manufacturer's market standing

At first blush, the 510(k) pathway seems rather appealing as it circumvents the significant costs and clinical data requirements of PMAs. But 510(k) submissions can operate as a double-edged sword for manufacturers — specifically, undiscerning statements of ''substantial equivalence'' that are not restricted to the safety and efficacy of the device can be seemingly contradictory when viewed in conjunction with statements or arguments regarding the patentability of the device before the USPTO.

Patent litigators can, and often will, exploit these apparent discrepancies as part of their arsenal to undermine the enforceability or validity of the patent asset. In other words, a manufacturer can unwittingly compromise its monopoly in its niche market on account of indiscriminate statements in a 510(k) submission regarding the substantial equivalence of the new device to an existing predicate device.

510(k) STATEMENTS: REAL WORLD CONSEQUENCES TO PATENT ASSETS

Patents allow a company to maintain its competitive stance in a niche market by protecting its valuable intellectual property assets. To acquire patent protection, patent applicants must overcome a number of hurdles before the USPTO, including demonstrating substantive differences between the prior art and the device being patented. A 510(k) application may impact the validity and/or enforceability of patents in at least one of the following three scenarios:

1. BREACH OF THE DUTY OF CANDOR

Patent applicants have a duty to disclose any information ''material to patentability'' to the USPTO during the patent application process.[46] Failure to comply with this duty can result in the entire patent being unenforceable, even if otherwise valid and infringed. *Bruno Independent Living Aids, Inc. v. Acorn Mobility Services, Ltd.* is a cautionary tale of how 510(k) notifications can serve as evidence of an applicant's breach of the duty of candor to the USPTO.[47]

In this case, Bruno, a device manufacturer, filed its 510(k) notification after filing its patent application, but before the patent issued. The 510(k) contained information on several prior art devices that were never disclosed to the USPTO. Bruno later sued its competitor Acorn for infringement of its patent. Acorn, in turn, accused Bruno of intentionally withholding material prior art on the predicate device from the USPTO.

Despite Bruno's position that its 510(k) was only relevant to the FDA (and thus did not need to be disclosed to the USPTO), the court agreed with the defendant that Bruno's 510(k) demonstrated knowledge of material prior art, i.e., the predicate device, that it failed to disclose. The court ultimately determined that Bruno had breached the duty of candor to the USPTO and held the patent unenforceable.

As shown above, failure to disclose the predicate device described in the 510(k) notification may leave a patent holder vulnerable to allegations of breach of the duty of candor with respect to the patent asset. At worst, a finding of breach of the duty of candor can jeopardize the rights of an entire family of related patents, and not just the patent at issue.

2. INVALIDITY BASED ON A LACK OF NOVELTY OR ON OBVIOUSNESS GROUNDS

An accused infringer may attempt to use a 510(k) submission for a new device as a means to invalidate the corresponding device patent by demonstrating that the predicate device anticipates or renders the claimed new device obvious. A manufacturer is likely to fall into the trap of undermining the novelty and technological advancements of its new device when providing factual statements of the technological characteristics of the new device and predicate device that do not pertain to the safety or efficacy of the new device.

The case of *Sunrise Medical HHG, Inc. v. AirSep Corp.* illustrates the importance of carefully wording a substantial equivalence assertion to limit its scope to safety and efficacy.[48] Here, Sunrise sued AirSep for infringing its patented EX2000 device, an electronic oxygen conserving device for respiratory patients with therapeutic oxygen needs. AirSep, in turn, challenged the validity of Sunrise's patent based on Sunrise's 510(k) assertion of substantial equivalence between the EX2000 device and the prior art. Specifically, the Sunrise 510(k) summary stated:

> The PulseDose series devices are *fundamentally repackaged* versions of the OMS 20 and 50, DeVilbiss current oxygen management system. There are no *significant* changes in the materials or features. Therefore, based on the abovementioned similarities, *especially the dosage methodology*, the PulseDose Series devices and the OMS 20 and 50 are substantially equivalent devices. . . . The *gas dose methodology* oxygen delivery specifications and performance of the device in the PulseDose series are *identical* to those of the OMS 20 and 50. . . .Previous designs of the DeVilbiss OMS 50 and 20 had similar components except for the integral regulator and pressure relief.[49]

The *Sunrise* court ruled that the 510(k) submission was not dispositive of patent invalidity because the substantial equivalence assertion focused on the gas dose methodology, which was not the claimed subject matter of Sunrise's device patent. Further, the patentable differences of the EX2000 device were omitted from the

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nological characteristics than the predicate device, then the summary must explain how the technological characteristics of the device compare to the predicate device. 21 C.F.R. § 807.92(a)(6).

[45] 21 C.F.R. § 807.92 (a)(5).

[46] 37 C.F.R. § 1.56.

[47] *Bruno Independent Living Aids, Inc. v. Acorn Mobility Services, Ltd.*, 394 F.3d 1348 (Fed. Cir. 2005).

[48] *Sunrise Medical HHG, Inc. v. AirSep Corp.*, 95 F. Supp. 2d 348 (W.D. Pa. 2000).

[49] *Id.* at 405-406 (emphasis added) (quoting plaintiff's exhibits 154 and 155) (internal quotation marks omitted).

510(k) notification because they were not essential to the safety or efficacy of the device.

Given that there is no precedential decision about how 510(k) notifications should play into determining the validity of a patent during litigation, manufacturers would be well-advised to avoid overbroad statements of equivalence that extend beyond safety and efficacy. Factual assertions in a 510(k) submission are more likely to cause harm when they are focused toward the patent claims. Strategies to mitigate these risks include selecting a predicate device that permits the manufacturer to claim equivalence in ways oblique to patentability or expressly disclaiming patent issues in the 510(k) notification.

PROTECT YOUR PATENT VALIDITY

Consider avoiding overbroad statements of equivalence that extend beyond safety and efficacy

3. EVIDENCE OF PATENT INFRINGEMENT

A 510(k) notification may be used as evidence of infringement, as well as willfulness. In particular, ''technological characteristics'' and other specific assertions in a 510(k) submission may be used to develop or refute a patent infringement case.

For instance, in *U. S. Surgical Corp. v. Hospital Products International Pty. Ltd.*, the plaintiff brought an action against the defendant Hospital Products International Pty. Ltd (HPI) for infringement of its stapling device.[50] HPI had submitted a 510(k) notification to the FDA stating that the ''devices were equivalent to their USSC counterparts.''[51] Further, HPI's second 510(k) notification asserted that ''[b]oth devices utilize the same type of disposable cartridges . . . [which] utilize similar staples, similar anvils, similar staple line configurations, and the same tissue-joining methods.''[52]

The court ultimately determined that HPI infringed the plaintiff's device patents. While the court's decision did not solely rely on the information disclosed in the 510(k) notification, the 510(k) statements were admissible as evidence for the plaintiff to prove infringement of the device patent.

Moreover, even where a 510(k) notification is not admissible in court, its assertions may nonetheless provide a patent owner with a road map to claims analysis against the later device discussed in the 510(k) notification. In light of the above considerations, manufacturers should carefully deliberate over the information that is included in their 510(k) notifications, lest they become unsuspecting targets of an infringement action.

PRACTICAL SOLUTIONS FOR MITIGATING RISK

An underlying theme in each of the above three scenarios is that loss of exclusionary rights and/or infringement liability may occur as a result of information asymmetry between the IP and regulatory legal teams, who are separately tasked with two distinct legal objectives for the same device. Part of this problem is attributable to the fact that the cycles of patent procurement and market clearance within most businesses are temporally misaligned, and in many cases may be up to a decade apart. The absence of temporal coordination between these two key business objectives thus lures manufacturers into believing that patent asset creation and FDA clearance operate as completely separate and distinct processes.

Fortunately, LDT providers (as well as device manufacturers in general) can mitigate the risk of falling prey to their 510(k) assertions and unintentionally jeopardizing their patent rights by implementing at least some, if not all, of the practice tips outlined below.

Acknowledge that patent asset management and market clearance do not occur in a vacuum. Indeed, LDT providers would be well-advised to keep these dual objectives in mind when assembling their core legal teams.

Rather than having IP and regulatory counsel operate as two autonomous entities, LDT providers can structure an arrangement that permits these service providers to collaborate and devise an integrated strategy for patent asset creation and market clearance.

A key aspect of this model is that the IP and regulatory legal teams would have simultaneous access to the same information at any given point of time, which in turn fosters active collaboration between the two teams.

Invest in an integrated, yet diverse, team of legal experts at the outset; it will inevitably pay dividends in the long run. Indeed, coordinated efforts between IP and regulatory counsel can influence critical discussions throughout the life cycle of the company, ranging from coordinating the timing of different filings to selecting the optimal predicate device to tailoring the content of the 510(k) notification to fortifying the company's patentability position.

IP AND REGULATORY COUNSEL

Coordinating efforts is critical

Minimize the risk of any potential breach of the duty of candor and safeguard valuable patent assets through active collaboration between IP and regulatory counsel. For example, in addition to citing the predicate device (or corollary patent) before the USPTO in a timely fashion, IP counsel is likely to disclose and carefully characterize the predicate device in a way that supports patentability, without undermining the position the company has taken with the FDA. This would severely weaken an accused infringer's attempt to allege a breach of the duty of candor based on inconsistent statements made in the 510(k) submission and before the USPTO.

Moreover, IP counsel would be able to work in concert with regulatory counsel to identify a predicate device that can be used to produce a robust FDA submission, while simultaneously shielding patent assets. Ideally, the predicate device would be unable to serve as the basis of an alleged infringer's invalidity arguments *and* does not run afoul of a third party's exclusionary IP rights.

Coordinated efforts between IP counsel and regulatory counsel also permit companies to monitor potential threats of liability in a commercial space that is highly litigious. The ability to assess and manage risk in the personalized medicine arena is especially important in

[50] *U. S. Surgical Corp. v. Hospital Products International Pty. Ltd.*, 701 F. sup. 314 (D. Conn. 1988).
[51] *Id.* at 347 (emphasis added).
[52] *Id.*

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light of evolving case law[53] and access to alternate administrative proceedings such as *inter partes* review (IPR).

Finally, collaboration between regulatory and patent experts would lead to fortified portfolio diligence efforts, which may result in the rapid identification and remediation of vulnerabilities within a company's portfolio. These interactions would ultimately drive the successful monetization of patent assets or lead to the identification of licensing opportunities that would generate additional revenue streams.

Accordingly, LDT providers that deploy the above model would benefit from counseling that is multidimensional, well-informed, and creative, with an eye towards their evolving commercial objectives. Such an approach creates and maintains a situation where ''each hand is cognizant of what the other is up to.''

One possible option to reasonably achieve these objectives would be to engage the services of a single law firm that possesses both patent and regulatory expertise, as well as the experience to navigate the jagged interface between these two legal regimes. Indeed, many clients prefer hiring a single legal service provider to handle these complex and intertwined issues because of the inherent communication between the different stakeholders, as well as the internal management of risk in real-time.

Although by no means a substitute for actual counsel, the following diligence checklist includes a non-exhaustive list of queries that are geared towards flagging many of the issues discussed above, and serves as a baseline tool to ensure that both regulatory and IP counsel are on the same page with respect to their client's patent assets.

Exemplary Diligence Checklist to Identify Potential Conflicts Between Patent Assets and 510(k) Applications

1. Was a 510(k) application submitted for a particular patent asset? If yes, what was the basis for selecting the predicate device listed in the 510(k) submission? When does the term of the patent asset expire?

2. What are the relevant similarities/differences between the predicate device and the patent asset? Do these identified criteria impact patentability of the asset in any way?

3. a. Was the recited predicate device subject to patent protection in the U.S.? If yes, when does the patent(s) of the predicate device expire?

   b. Does the new device read on the claims of the predicate device? Does the 510(k) contain disclosure that distinguishes the new device from an essential patentable feature of the predicate device?

   c. Were the USPTO maintenance fees for the predicate device patent paid?

   d. Is the predicate device patent subject to a terminal disclaimer? Are the predicate device patents commonly owned?

   e. Was a non-infringement/invalidity opinion concerning the patented predicate device obtained?

   f. Was a license concerning the manufacture or use of the patented predicate device obtained?

4. a. Was the language of the 510(k) submission vetted by IP counsel for potential inconsistent statements between the 510(k) submission and the patent asset?

   b. Are the assertions in the 510(k) narrowly directed to the safety and efficacy of the device? Were patentable features of the device included in the 510(k), and if yes, do they relate to the safety or efficacy of the device?

   c. Does the 510(k) notification contain language that explicitly disclaims patent issues?

   d. Does the 510(k) submission contain any broad teachings regarding the technological features or operation of the patent asset?

   e. Was the 510(k) disclosure analyzed by IP counsel for potential impact on other patent filings within the portfolio?

5. Were the corollary patents or publications regarding the predicate device cited as prior art during the prosecution history of the patent asset?

6. When was the 510(k) application filed relative to the patent filings associated with the device?

7. Verify integrity of foreign rights in absolute novelty jurisdictions:

   a. Did publication of the 510(k) submission occur prior to filing in a foreign jurisdiction?

   b. Was there a priority claim to an earlier U.S. or international application that preceded the publication of the 510(k) summary? Was the priority claim perfected?

8. Monitor FDA guidelines on alternative regulatory strategies for NGS-based LDTs.

9. Does the 510(k) notification assert substantial equivalence to multiple predicate devices? What is the rationale for doing so? Does the combination of the recited predicate devices include all the elements of the claimed device?

[53] *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, slip op. 2014-1139 (Fed. Cir. 2015).