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FDA Regulatory and Compliance Monthly Recap

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KEY FINDINGS

FDA replaces pregnancy labeling system with a new standard in a bid to provide more clarity

The regulator is discarding its decades-old system to explain the risks of prescription drugs to women who are pregnant or breast-feeding, in favor of a more-detailed explanation of potential risks and benefits.

Women currently rely on a system that uses the letters A, B, C, D and X to identify risks, with Category A describing prescription drugs considered relatively safe and Category X describing drugs that could cause fetal abnormalities.

However, the FDA acknowledges the lettered scale can be confusing. Dr. Sandra Kweder, deputy director of the Office of New Drugs in the FDA's Center for Drug Evaluation and Research, said the system was "overly simplistic and was misinterpreted as a grading system, which gave an oversimplified view of the product risk." Further, Dr. Joanne Stone, director of maternal and fetal medicine at The Mount Sinai Hospital in New York City, said the system fails to provide "detailed information relevant to making decisions about use in pregnancy and lactation."

To revamp how drug products are labeled with information about how a drug may be used during pregnancy, the FDA issued a new regulation, "Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling."

While drug companies already disclose the majority of the information now required by the regulator, Dr. Kweder said the data can be confusing, out of date and "scattered." Therefore, the aim is to organize the information in a clearer and more consistent format.

In an accompanying guidance document, "Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and

Biological Products — Content and Format," the FDA said the Pregnancy and Lactation Labeling Rule (PLLR) "provides a framework for clearly communicating information on the benefits and risks of using a drug during pregnancy and lactation to help facilitate prescribing decisions."

Under the rule, the FDA is abandoning its "pregnancy categories" — A, B, C, D and X — and is instead requiring companies to include a "risk summary" of potential risks, such as structural abnormalities, embryo/fetal/infant mortality, functional impairments or growth problems potentially caused by a drug.

Labels must also include information about "scientifically acceptable pregnancy exposure registries," which the FDA hopes will inform healthcare providers about the extent to which a product has been tested in pregnant women, and also encourage women to participate in those registries.

The rule bans the letter system for all drugs newly approved after June 2015, when it comes into effect. Labeling for existing prescription drugs approved on or after June 30, 2001, will be phased in gradually within three to five years. And in certain cases, drug companies will need to provide new information to doctors and patients.

The new system also breaks the risk into three sections: Pregnancy; Lactation; and Females and Males of Reproductive Potential.

The "pregnancy" section is a combination of the former "pregnancy" and "labor and delivery" sections, while the "lactation" section is meant to substitute the "nursing mothers" section. The FDA's guidance said the section on reproductive potential will contain information "on pregnancy testing, contraception and infertility." The FDA decided to include men in the pregnancy section because some drugs can cause fetal risk through men at the time of conception, or might lead to infertility.

The FDA estimates the transition into the new system will take "several years to complete, and will cost as much as $78.2 million."

FDA issues proposed regulations requiring electronic distribution of drug labeling to ensure healthcare providers have the most up-to-date prescribing information

The agency is proposing to require pharmaceutical firms to provide healthcare providers with real-time electronic updates of drug label changes, forgoing printed labels, a change the agency says is intended to ensure that healthcare professionals and patients have the most current version of prescribing information.

The proposed rule, "Electronic Distribution of Prescribing Information for Human Prescription Drugs, Including Biological Products," comes after years of development at the regulator.

Lawmakers called on the Government Accountability Office to study the advantages and disadvantages of largely discarding paper-based labeling for drug products to move to an electronic system. The GAO's report contained both likely benefits and potential disadvantages of an electronic-based labeling system. Stakeholders told the GAO that electronic labeling would ensure that all labeling had the safety risks, while currently, paper-based drug labels don't always reflect a new safety risk until new stock is produced, requiring prescribing entities to recall specific safety alerts.

Additionally, contrary to many types of communications that have a single intended audience, FDA-approved labeling normally serves two audiences at the same time: patients and healthcare providers. Transitioning to an electronic-based system could enable both groups to view information in a more user-friendly format, the GAO was told.

The GAO was also told, however, that there was concern that electronic labeling wouldn't benefit the elderly, who may not know how to access the drug labeling online, or may not even be able to access

the Internet. The GAO also said that counseling patients could become more challenging for doctors who would stop having access to printed package inserts.

The FDA's proposed rule appears to be designed to dodge most of the potential disadvantages noted in the GAO report, instead placing focus on "prescribing information intended for healthcare professionals." The electronic requirements don't pertain to patient labeling, only to a product's "professional labeling."

In a Federal Register notice, the agency proposed requiring manufacturers to submit prescribing information intended for healthcare professionals to the FDA, which would subsequently post it on its labels.fda.gov website every time there is a modification in the labeling.

The rule requires that container labels and outside packaging of products include a link that brings the prescribing physician to the publicly accessible online repository containing the label's most up-to-date instructions, forcing pharmaceutical companies to keep vigilantly monitoring their repository listing and notify the FDA of any changes in labeling that have yet to be displayed on the site.

Container labels must also include a toll-free number for physicians who lack Internet access, although inserts and medical guidelines meant for patients and often slipped into packaging, as well as labeling appearing on promotional materials, are exempt from the regulation. The FDA said products meant for use in emergency rooms or that may be stockpiled for an emergency are examples of cases where it could be appropriate to exempt a product.

The agency anticipates the rule will save the industry between $5 million and $74 million over a 10-year period, primarily in printing costs, with pharmacies expected to incur costs of between $47 million and $89 million over 10 years in access costs, increased search time and the printing of labels when requested.

FDA publishes guidance meant to help firms understand the labeling section related to patient counseling

The regulator issued guidance containing recommendations meant to ensure that the "Patient Counseling Information" section of labeling is clear and useful, as well as consistent.

In 2006, the FDA issued a final rule amending the requirements for the content and format of drug labeling, and creating a section in labeling called "Patient Counseling Information."

This month, the agency published guidance titled "Patient Counseling Information Section of Labeling for Human Prescription Drug and Biological Products – Content and Format," which is aimed at helping applicants in developing that particular labeling section. In the document, the FDA covers how to choose topics to include in the Patient Counseling Information section, how to present it and how to organize it.

The document states that since regulatory requirements for the section are "broadly worded" and that multiple different presentations have been used in labeling, the FDA is publishing guidance to offer recommendations on selecting the information to include, and to increase consistency as it relates to the content and format of the section.

The guidance elaborates on the FDA's thinking on the content of the section, including its purpose and aim — which is to allow healthcare providers to identify topics for a counseling discussion with a patient once a prescribing decision is made.

The FDA also includes specific recommendations regarding content, starting with the reference statement language as well as where it should appear. The guidance also contains the FDA's recommendation concerning counseling topics, describing how the information should be presented and listing the types of information to include, as

well as information that should not be included in the patient counseling section.

Lastly, the FDA informs applicants of its recommendations relating to the format of the section, elaborating on the subject of subheadings, cross-referencing and appending.

Stryker to undertake compliance efforts as part of the DOJ settlement over OtisMed's unapproved marketing of devices before the company was acquired

As OtisMed pleads guilty to selling unapproved devices, current parent company Stryker must pay $80 million and carry out compliance efforts for violations that occurred prior to Stryker's acquisition of OtisMed.

Stryker will pay around $80 million to settle civil and criminal charges related to the illegal sale of OtisKnee products by its subsidiary OtisMed, before the company was bought. OtisMed admitted to never obtaining FDA approval before selling devices used by surgeons to make accurate bone cuts to implant prosthetic knees, pleading guilty in federal court in Newark, N.J., to one felony count of distributing misbranded medical devices with the intent to defraud.

OtisMed applied for FDA approval in October 2008, and 13 months later the regulator determined the company had failed to show it was safe and effective. Nevertheless, former CEO Charlie Chi then shipped 218 devices to surgeons, overruling his advisers and board.

According to prosecutors, OtisMed generated $27.1 million by selling more than 18,000 OtisKnee devices between May 2006 and September 2009, 75 percent of which were sold alongside a Stryker knee replacement system. However, OtisMed was acquired by Stryker in November 2009, and the DOJ acknowledged that the criminal conduct took place while OtisMed was still a privately held business, and "without Stryker's prior knowledge or acquiescence."

A lawyer who represented Stryker at the plea hearing said the company learned about the shipments only after it bought OtisMed. Stryker deputy general counsel Michael Cartier said the company will need to spend approximately $100 million to "try to make this right."

OtisMed is set to pay a fine of $34.4 million and forfeit $5.16 million in a criminal case, while paying a civil fine of $41.2 million. It is also being barred from participating in federal healthcare programs for 20 years. Though Stryker is not being barred, the company agreed to cooperate with the government's probe and maintain a compliance program. It will also conduct a review and audit concerning whether other marketed devices have the appropriate FDA approvals, providing the government with the results. Stryker also agreed to annual certifications from the president of Stryker's orthopedics group and from Stryker's board of directors on the subject of the effectiveness of the compliance program. Those measures are explained in a 40-page side agreement that states that the U.S. won't prosecute Stryker as long as OtisMed fulfills its obligations within 90 days of the sentencing.

OIG semiannual report to Congress shows enforcement number of $4.1B in investigative receivables

In issuing its report, the watchdog said that of the $4.9 billion in expected recoveries for this year, $4.1 billion came from investigative work.

The Office of Inspector General of the Department of Health and Human Services said the agency will return $4.9 billion in improperly spent federal healthcare dollars to taxpayers from oversight and probes conducted this year, mostly through fraud investigations that targeted Medicare and Medicaid abuse.

The head of HHS' Office of the Inspector General, Daniel R. Levinson, informed Congress in the watchdog's semiannual report that probes revealed $4.1 billion in misspent federal funds and that about

$834.7 million was discovered missing via program audits. Levinson said $1.1 billion of the full amount would be allocated to Medicare restitution for states.

According to the report, 533 civil and administrative cases were filed in 2014, with certain false claims and unjust enrichment suits being transferred to federal district court, while others looked at civil monetary penalties through administrative procedures.

The report also highlighted other OIG accomplishments, including its Medicare Fraud Strike Force efforts leading to the filing of charges against 228 individuals or entities, 232 criminal actions and $441 million in investigative receivables.

Additionally, the report showed that whistle-blower lawsuits serve as a frequent source of Medicare and Medicaid recovery for the OIG, underlining the $85 million settlement with Halifax Hospital Medical Center, which allegedly provided physicians with kickbacks for unnecessary referrals that were subsequently billed via Medicare, in violation of the Stark Law.

For more information on any of these FDA regulatory and compliance updates, please contact Scott S. Liebman at sliebman@loeb.com.

Loeb & Loeb LLP's FDA Regulatory and Compliance Practice

Loeb & Loeb's FDA Regulatory and Compliance Practice comprises an interdisciplinary team of regulatory, corporate, patent and litigation attorneys who advise clients on the full spectrum of legal and business issues related to the distribution and commercialization, including marketing and promotion, of FDA-regulated products. Focusing on the health and life sciences industries, including pharmaceuticals, biologics, medical devices, wellness products, dietary supplements and organics, the practice counsels clients on regulatory issues, compliance-related matters and risk management strategies; advises on laws and regulations related to product advertising and labeling; counsels on FDA exclusivity policies and related Hatch-Waxman issues; and provides representation in licensing transactions and regulatory enforcement actions.