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FDA Regulatory and Compliance Monthly Recap

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KEY FINDINGS

In an unusual move, the FDA takes issue with the accuracy of Sciecure's studies in a warning letter over sales promotion material for the company's sleeping pill

In addition to criticizing the pharmaceutical company for leaving out risk information from its sales materials and making unsupported superiority claims, the regulator unusually disputed the accuracy of the sources Sciecure used to bolster its assertions.

The regulator's advertising oversight division warned Sciecure Pharma about materials used to promote its Doral sleeping tablets, writing in a warning letter that by omitting risks associated with Doral, Sciecure's sales aid deceptively suggests that the product is safer than has been shown. The Office of Prescription Drug Promotion (OPDP) also found the materials contained claims about the drug's superiority that failed to hold up to the FDA's close scrutiny.

While the FDA sending a warning letter citing the omission of risk information or the exaggeration of the efficacy of a product in advertising isn't unusual, the FDA rarely challenges the accuracy of studies referenced in ads. What makes this letter unusual is the focus on the actual reliability of the studies cited in Sciecure's ads.

The FDA's letter also addresses a number of "unsubstantiated superiority claims" made by Sciecure, including the characterization of Doral as "unique" and the claims "Discover a surprisingly unique sleep agent" and that the drug is "uniquely selective."

The regulator contends that the issue is that the drug hasn't been proven to be safer or more effective than other insomnia treatments, even though the company claims it has a "unique mechanism of action," which the OPDP notes "had not been demonstrated by substantial evidence," the key word being "substantial." Though Sciecure provided evidence of this claim, the FDA contested the accuracy of its sources.

The OPDP wrote that two of the four references were review articles that contained pharmacokinetic information and information about quazepam's efficacy but didn't include information on controlled clinical trials. Therefore, there wasn't anything explicitly supporting that Doral sleeping tablets are superior.

Additionally, the FDA found that one reference was an algorithm that lacked actual abuse data in human subjects and wasn't validated, and the fourth consisted of a study of the drug in nine healthy volunteers, the main issues being that they didn't suffer from insomnia and the sample size was too low.

The FDA wrote that the studies don't account for "substantial evidence" to support that Doral is safer or more effective than other drugs for treating insomnia. The letter states that the studies fail to describe acceptable and well-controlled thorough clinical trials that compare appropriate doses for the drug and comparable products in an appropriate patient population.

Office of Inspector General's 2015 work plan shows agency will examine medical device security, FDA's regulation

The Department of Health and Human Services' watchdog agency released a 2015 work plan that calls for federal auditors to assess medical device cybersecurity amid intensifying scrutiny in the area, as well as areas that may be in need of some revamping by the FDA.

The work plan outlines a number of information security-related reviews for 2015, including examining whether the DHHS Centers for Medicare and Medicaid Services' oversight of hospitals' cybersecurity of networked medical devices is sufficient. The OIG wrote that computerized medical devices that are interconnected with electronic medical records and the broader health network "pose a growing threat to the security and privacy of personal health information." The review of medical device cybersecurity comes amid increasing scrutiny in the area, with the FDA hosting a related workshop and issuing voluntary guidance for device makers to deal with cybersecurity risks in the design and development of products.

The OIG is also planning on honing in on FDA regulation areas. The agency will examine the FDA's requirements for post-marketing studies and clinical trials, saying it is interested in studying how the regulator deals with firms that do not complete the studies. Many drugs are granted approval along with conditions, namely that the companies carry out trials to find potential issues with the drugs. However, the problem is that firms don't always conclude the studies once the drugs hit the market, with some companies contending it's challenging to recruit patients for the proposed studies because they are able to avoid the studies entirely and get a hold of the drugs from their physician. The OIG wants to look at the FDA's level of monitoring and, in the event that a company fails to comply with requirements, how it's disciplined.

The DHHS agency will also review the implementation of the drug identification system as it relates to drug supply chain "trading partners," such as drug makers and wholesale distributors, with plans to talk to them about how they have effectively exchanged information. The national system to track pharmaceutical products to allow them to be traced throughout the supply chain, created under the Drug Supply Chain Security Act, is still in early stages, with the law's transaction requirements coming into effect Jan. 1. The OIG is looking to hear about their "early experiences" with the requirements.

The OIG also intends to assess the extent to which clinical trials comply with the reporting requirements established by the Food and Drug Administration Amendments Act as well as the manner in which the FDA is making sure that these requirements are satisfied.

The Department of Health and Human Services proposes tougher reporting rules in a bid to increase clinical trial transparency

The DHHS is seeking to expand the scope of information on clinical trials that must be submitted to the NIH's online data set of experiments in the midst of ongoing concerns that too many trial results are withheld.

The DHHS unveiled proposed requirements for its online clinical trials register, ClinicalTrials.gov, which will require pharmaceutical and medical device companies to provide more information about patient enrollment, the progress of trials and the results of those trials – even if a product is never granted approval in the U.S.

The move comes amid ongoing criticism that public health may be harmed due to many trial results remaining concealed. For example, a 2012 study in the BMJ showed that fewer than half of all National Institutes of Health-funded trials were published in peer-reviewed journals within 30 months of completion, with a third of completed trials remaining unpublished after nearly four years.

It has been a heated issue, particularly for the pharmaceutical industry, which has endured scandals as a result of disclosures that trial data containing safety or effectiveness information was not previously disclosed.

Under Section 801 of the Public Health Service Act, as amended by the Food and Drug Administration Amendments Act of 2007, the DHHS was ordered to create a clinical trial registry data bank. That data bank, www.ClinicalTrials.gov, is run by the National Institutes of Health (NIH) National Library of Medicine (NLM). The website works as a unified center for the oversight of clinical trials, and provides information about the sites where a trial is conducted, the general design of a study and information about its sponsor.

The NIH said it hopes the proposed rules will at least double the number of summary results published on the website per week to between 200 and 250. To achieve this, the DHHS is looking to expand the scope of information required to be submitted to cover summary results for products not currently approved or licensed in the U.S., in addition to main results and additional tables presenting breakdowns of adverse events. The regulations also clarify who is responsible for posting data and the timing for providing the information, along with needed updates.

The new proposal calls for multiple changes to how clinical trial results are recorded and reported. For instance, under the proposal, only one entity can be responsible for the submission of information regarding an "applicable clinical trial." Also, the information provided to ClinicalTrials.gov would need to include information on obtaining "expanded access to investigational drugs used in applicable clinical trials," but only if those drugs are available through an expanded access program.

The proposed changes are also heavily focused on the submission of results, with the rule proposing to "extend the requirement for results submission to applicable clinical trials of drugs, biological products, and devices that are not approved, licensed, or cleared by FDA."

Under the proposed rule, companies would be required to submit tables of data that summarize demographics and baseline characteristics of enrolled participants and primary and secondary outcomes. The results would need to be submitted within one year following the completion date of the clinical trial.

Additionally, the rule would require the inclusion of the number of adverse events suffered by patients in the results submitted to the ClinicalTrials.gov register, which, according to RAPS, is unusual given that the FDA already accepts and analyzes much of that information.

FDA proposes three studies on direct-to-consumer prescription drug ads in a bid to better understand the impact of ad exposure frequency, spousal influence and risk understanding

The agency announced three proposed studies on how people view direct-to-consumer advertising, as it continues to assess factors that influence assessments of risks and benefits in a bid to ensure its regulations adequately protect public health.

As it announced its first proposed study this month, the FDA said it is interested in studying whether consumers who view the same drug ad several times perceive the safety or efficacy of the advertised drug differently than those who view it only once. The FDA said that perceptual and cognitive effects of increased ad exposure frequency have been studied extensively using nondrug ads, and that it has generally been argued that first exposure to an ad causes attention, while second exposure leads to the learning of the advertised message, and third and subsequent exposures strengthen the learning effects of the second exposure. For example, one study showed that a commercial message repeated twice results in better recall than a message broadcasted only once, while another study found that ads viewed multiple times "improve product attitudes and recall for product attributes."

For regulators, that information could lead to some concerns since drug ads are meant to portray an accurate assessment of a product's benefits and risks. The FDA's standard that companies dedicate equal time, prominence and space to a drug's benefits and risks stands in contrast to most consumer product ads, which solely focus on a product's benefits. Because of this, coupled with that fact that research about ad exposure frequency doesn't include prescription drug ads, the FDA is looking to test its hypothesis that consumers who view the same drug ad multiple times will have a slightly different view of the product each time.

In its notice announcing the study, the FDA appears to imply that if a consumer is bombarded with drug ads, he or she may eventually perceive the product as being safer than it actually is. The agency does note, however, that prominent risk information in drug ads may actually reduce the positive effects of repeated advertising. In the event that the FDA's study showed that increased exposure to an ad improves consumers' attitudes toward it, consumer advocates and regulators could consequently push for revised rules to reflect and address that.

The agency is also proposing a study of consumers who view drug ads on TV in a bid to evaluate spousal influence on how consumers understand the risks and benefits of drug products. The FDA said that while consumers are often considered individual targets for prescription drug ads – as though they are always shown DTC ads individually and thus make judgments about advertised products on their own – judgments related to prescription drugs represented in DTC ads are likely made in social contexts much of the time. Because social interactions can lead to unique reactions relative to people who view DTC prescription drug ads alone, the OPDP wants to look at differences between consumers viewing prescription drug ads with a spouse or partner as opposed to alone. The FDA said such outcomes have noteworthy public health implications.

The agency is also planning a study on how patients understand the risks and benefits of drug products. The FDA said research indicates that consumers struggle with the concepts of risk and efficacy, often overestimating drug efficacy. Because of this, the agency is proposing a study in the hope of understanding and accurately gauging how consumers are understanding information and how it affects decisions about prescription drugs.

While the FDA's OPDP actively examines how direct-to-consumer advertising impacts consumer knowledge, perception measures have a tendency to vary by study. As a result, the FDA wants to

create a “pool of reliable and valid measurement items for assessing consumers’ drug risk and benefit perceptions” in a way that’s consistent across studies. The regulator said the aim of the study is to create that pool of reliable measures and increase the rigor and efficiency of its research.

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.