FDA Regulatory and Compliance Monthly Recap

AUGUST 2014

KEY FINDINGS

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.

Mobile health industry could get a boost as FDA draft guidance exempts certain medical devices, including digital health devices

The FDA's decision to not require a number of mobile health devices to go through the 510(k) process could make it easier for these types of devices to make it to market, thus encouraging manufacturers to venture into the world of digital medical devices.

In a draft guidance, the regulator proposed to largely deregulate a considerable list of Class I and Class II medical devices and no longer require their manufacturers to go through the 510(k) process, though the move would not necessarily exempt the device makers from other steps such as appropriately registering and labeling their wares as medical devices or quality systems requirements. The FDA said it would not enforce 510(k) requirements for the devices it listed - many of which fall into the mobile health spectrum - and it doesn't expect companies that make these devices to submit 510(k)s for them in the meantime.

The guidance comes amid debate about mHealth device and app regulatory oversight between federal agencies, lawmakers and industry advocacy groups, including the FTC and FCC, with, for example, Sen. Charles Schumer (D-N.Y.) calling on the FTC in August to require fitness device and app companies to provide consumers with the ability to opt out before their personal information is sold, and FTC Commissioner Julie Brill saying she supports new laws for boosting healthcare data privacy and protection measures, though the agency is not mulling any new regulations.

Mobile healthcare device vendors are paying close attention to FDA guidance and other regulatory proposals as they prepare and roll out tools in the market in rapid fashion, and are looking to be part of the decision-making process.

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Items covered in the guidance would include apps that convert a mobile phone into an electronic stethoscope, a hearing aid or a thermometer, as well as talking first aid kits, fertility diagnostics and other devices. The FDA determined these devices are adequately well-understood and don't pose risks requiring premarket review to guarantee their safety and effectiveness, consequently reducing the regulatory burden on medical app developers. The decision to exempt a number of mobile health devices from the 510(k) process broadens opportunities for development and distribution of mobile health tools.

FDA issues guidances, launches and expands programs to encourage medical device innovation

The regulator's bid to simplify the approval process for novel devices, enhance medical device development, accelerate clinical studies and better understand the industry reflects its efforts to support innovative medical device development and promote regulatory science, which it says bridges the gap between research and discovery and actual marketing of devices.

The regulator issued a draft guidance document describing how manufacturers of novel medical devices can avoid having to win clearance along its toughest approval pathway, fleshing out a process overhauled by Congress two years ago. In the guidance, the agency details how manufacturers can take advantage of the de novo process, which enables new products that aren't substantially equivalent to previously cleared devices to nonetheless be sold without re-obtaining premarket approval.

Though premarket approval typically applies to new products involving distinctive technology or presenting unexplored questions related to safety and effectiveness, the de novo process was created to enable quicker approval of novel devices that are low risk or moderate risk. In the Food and Drug Administration Safety and Innovation Act, lawmakers went beyond that, eliminating the requirement to first go through the 510(k) process and allowing device makers to go straight to a de novo application, which the De Novo Classification Process document solidifies.

Also pointing to the FDA's efforts to encourage new devices is the agency's focus on the device development and clinical trial processes. The regulator said it is seeking participants for a pilot program aimed at accelerating approval of new medical devices. The FDA said it plans to accept no more than 15 candidates, who will ideally have Medical Device Development Tools (MDDTs) that are mature, are intended to meet a public health need, have the potential to affect many device development programs or are COA/BT/NAM tests.

Regulators have long been interested in ensuring tools and measures employed during the medical device development process are proper for use and fit for purpose within a specific context. Many clinical trials are ultimately abandoned or criticized by regulators when it is determined that a measurement tool fails to take into account an important variable, is imprecise or is otherwise inadequate for its specific purpose. Therefore, companies and regulators are both looking to make sure tools are validated, saving time and resources in quality regulatory reviews.

In November 2013, the FDA released a draft guidance document, Medical Device Development Tools, which it said would lead to faster, more efficient medical device development and promote the creation and qualification of new MDDTs.

The process, however, is currently voluntary and in need of participants. The FDA said it is seeking participants for the program under its newly created MDDT Pilot Program, under which the regulator says it hopes to gain experience that it can then use to "help inform the final guidance document and processes." The proposed MDDT qualification process is aimed at facilitating timely development of tools

that manufacturers and the FDA use to assess and measure the performance, safety and effectiveness of medical devices. The agency expects that manufacturers can better rely on MDDTs reviewed and accepted by the FDA and made available through this voluntary program.

The FDA also issued a final guidance document aimed at "promoting" clinical studies of new medical devices under the FDA's Investigational Device Exemption (IDE) regulations. "Conditional" approvals are the focus of the final guidance document, Decisions for Investigational Device Exemption Clinical Investigations, in which the FDA describes the intent of the conditional approval process as creating a more timely and efficient process for starting IDEs for certain devices, "even when outstanding issues remain regarding the IDE submission."

In addition to attempting to make it easier for the industry to develop, test and market new medical devices, the FDA also wants its regulators to learn more about emerging device topics and announced its plan to add a new general training program component to its Experiential Learning Program (ELP), which will help the Center for Diagnostics and Radiological Health officials better understand "the policies, laboratory practices, and challenges faced in broader disciplines that impact the device development life cycle," like biocompatibility testing and emerging manufacturing methods - such as 3-D printing. The component will be known as the "ELP General Training Program" and is aimed at improving communication and facilitating the premarket review process.

FDA puts focus on clinical trials, moves to improve data quality, encourage participation and increase transparency

The FDA published a plan designed to strengthen the demographic composition of clinical trials that drug and device makers perform as studies are increasingly being conducted outside the U.S. and interest in personalized medicine grows.

The FDA released an "Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data" in a bid to improve the gathering of clinical trial data on specific patient populations based on gender, race/ethnicity and age. The plan - which Congress ordered under the 2012 user fee law - has three main goals: improving the completeness and quality of the data and its analysis; identifying obstacles to subgroup participation in clinical trials and increasing participation; and making subgroup data more easily accessible and transparent.

In conjunction with the plan, the agency posted a final guidance document titled Evaluation of Sex-Specific Data in Medical Device Clinical Studies, which outlines specific recommendations for considering sex and other variables during the study design stage. The action plan centers on three priorities: data quality, subgroup participation and data transparency. The final guidance comprises recommendations to the medical device industry and FDA staff on enrollment, analysis, reporting and decision frameworks for sex-specific study design.

When the FDA issued a draft of its Section 907 report to the public in 2013, it said that while it found most companies were doing a good job at reporting differences experienced between men and women, the report found they did less well on analyzing or reporting factors like race and ethnicity. The agency also warned about the usefulness of certain data received, saying that though some companies submit data on age or sex differences, the size of the trial can limit the power and usefulness of that data, particularly when subgroups are underrepresented to begin with.

In addition, trials are frequently conducted outside the U.S., which complicates efforts to match a study's racial makeup to the demographics of a particular disease in America. The issue has drawn more attention amid scientists increasingly pushing into the frontier of personalized medicine.

The two new documents, the guidance and the plan, are aimed at introducing solutions to the deficiencies

identified by the report. Among a list of action items, the FDA said it is revising three guidance documents, including Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs, Collection of Race and Ethnicity Data in Clinical Trials, and ICH E7 Studies in Support of Special Populations: Geriatrics. According to the plan, regulators will also revise medical product applications to improve information on demographic subgroups, and the Center for Devices and Radiological Health intends to examine how health professionals view labeling to improve understanding and use.

Senators' call for biosimilars guidance highlights debate over naming issue; regulations could clear a path for market boom

U.S. senators are pushing for a formal policy on biosimilar medicine naming as drugmakers and generic drugmakers clash over the issue amid a possible looming market boom worldwide. The naming issue could prove consequential for the U.S. industry, with regulations potentially triggering a surge of biosimilars in the market.

One week after the FDA received its first request to approve a biosimilar medicine, senators called on the HHS to publish guidance on biosimilars, while an FDA guidance document is said to be awaiting government approval. Sens. Lamar Alexander (R-Tenn.), Richard Burr (R-N.C.), Orrin Hatch (R-Utah), Mike Enzi (R-Wyo.) and Pat Roberts (R-Kan.) wrote a letter to the Department of Health and Human services, urging it to immediately issue guidance pending within the organization related to the implementation of the biosimilar pathway. In their letter, the five Republican members of the U.S. Senate Committee on Health, Education, Labor & Pensions said they believe the FDA sent its naming guidance to the HHS for approval.

At issue is whether biosimilars should be given the same International Non-Proprietary Name (INN) as brand-name biologics. The World Health Organization oversees the global INN system, but individual regulatory agencies in each country are not bound by the latest WHO proposal.

In Europe, biosimilars were approved using the same INN as the related innovator biologic, though there is still debate over whether this is sensible. Other countries believe each biosimilar should have a unique non-proprietary name since they are not identical to the original drug.

The debate has divided the U.S. pharmaceutical industry, with brand-name drugmakers and biotechs pushing for biosimilars to have unique or generic names to distinguish the medicines from the original biologics. Generic drugmakers and other proponents of using the same INN contend that not to do so would hinder substitution of the branded generic with a cheaper alternative and result in a lack of harmonization between the U.S. and other parts of the world.

Amid changing regulations and an impending biotech patent cliff, the global market for biosimilars is poised to boom, according to a report from Allied Market Research, which projected that worldwide sales for copycat biologics will swell to $35 billion by 2020 from $1.3 billion last year as new products penetrate the market in North America, Europe and Asia. AMR found that the European market is making some of the greatest strides in biosimilar development, with clear regulations on development, which are now considered the industry "benchmark" for the world. Though the U.S. market may be the richest in the world, AMR analysts noted that a number of major-league pharma groups have been teaming up to exploit expected openings in the Asian market amid growing demand for cost-effective treatment due to the prevalence of chronic diseases.

The FDA has issued five biosimilars guidances concerning quality, scientific considerations, meetings with drugmakers, clinical pharmacology data and implementation of the biosimilars pathway, with the most recent being released in May. An FDA

spokeswoman would say only that the regulator is “currently considering the appropriate naming convention” and that it will weigh all comments received as it moves forward in crafting future policies, including naming. According to AMR, though biosimilars developers have been taking advantage of emerging markets with less IP protection as their launch pad for established markets, the regulatory framework is maturing in established markets, like the U.S., and it will become easier for biosimilars manufacturers to quickly enter such markets.

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

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