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FDA statement underscores continued emphasis on use of real-world evidence in active postmarket device surveillance

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On 20 November 2018 Food and Drug Administration (FDA) Commissioner Scott Gottlieb and Center for Devices and Radiological Health (CDRH) Director Jeffrey Shuren released a joint statement regarding updates to the Medical Device Safety Action Plan (safety plan) announced in April. The FDA's statement, released after receiving and reviewing public feedback, reiterates and embellishes on certain aspects of the safety plan, including areas of recent progress, while also providing some new information related to the monitoring of a number of device types for women's health. Issuance of the joint statement came shortly before the FDA issued another joint statement regarding the 510(k) premarket review pathway, and both statements come on the heels of increasing scrutiny of FDA postmarket controls for medical devices in protecting public health. The joint statement provides an overarching vision of how the FDA sees the role of postmarket surveillance, but it does not provide details related to how these actions will directly affect the medical device industry, patients, or other stakeholders.

A new goal for the FDA

The FDA's April 2018 safety plan announcement included an overview of certain enhancements undertaken to modernize the agency's ability to evaluate the premarket and postmarket benefits and risks of medical devices. In the joint statement, the FDA touches on many of these initiatives under the umbrella of a new goal: "Ensuring that the FDA is consistently first among the world's regulatory agencies to identify and act upon safety signals related to medical devices."

The statement emphasizes the necessity of such innovations given the massive FDA workload: regulating more than 190,000 different devices manufactured by more than 18,000 firms in over 21,000 facilities worldwide and weighing the risks and benefits for the approval, clearance, or grant of marketing authorization of 12 new or modified devices each business day. The FDA's new goal is framed as an important milestone in the culmination of steps the agency has taken in recent years to strengthen and implement new postmarket monitoring tools in the medical device space.

The FDA also describes the evolution of the agency's thinking on these types of tools and resources, pointing out the following over recent years:

- A 2012 vision statement seeking to establish a postmarket surveillance program that quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearances.
- A corresponding 2012 strategy statement for active medical surveillance using newly developed tools and modernized medical device reporting (MDR).
- Establishment of the unique device identification (UDI) system for tracking devices.
- Greater use of real-world evidence in both premarket and postmarket decision-making.

Use of real world evidence in active postmarket device surveillance

With regards to using real-world evidence in postmarket surveillance, the FDA particularly emphasized the agency's commitment to broadening available resources for the National Evaluation System for health Technology (NEST). NEST is a national system for gathering real-time, real-world information on the performance of medical devices by accessing a wide range of data systems, including data from patient registries, Medicare claims, and electronic medical records. Leveraging NEST as an active surveillance and evaluation system that complements the approaches currently in use is core to the FDA plan.

As noted in the statement, on 5 November 2018 the FDA announced that the NEST Coordinating Center (NESTcc), NEST's independently run public-private coordinating center, had initiated eight NEST test cases as demonstration projects in premarket submissions, label expansions, and postmarket surveillance across five different disease areas. The FDA emphasizes that NEST's objective is to use real-time device safety information to improve on patient outcomes and the projects are intended to show proof-of-concept for the use of real-world evidence in preparing regulatory submissions and meeting postmarket surveillance requirements.

These test cases, and the NEST program, are partially funded by industry as part of the latest Medical Device User Fee Amendments (MDUFA IV), and, in September, the FDA allocated an additional US$3 million in agency funding to the project. Along with this, the statement indicates the president's 2019 budget includes an additional US$46 million to support NEST (and other FDA-sponsored postmarket studies that address device-specific safety concerns). Nevertheless, the agency expressed the belief that NEST can ultimately be financially self-sustaining.

Focusing on women's health

The statement also describes a particular focus on clinical questions about device therapies that are unique to women. As part of the effort to implement a more active surveillance system, the FDA plans to further Coordinated Registry Networks (CRNs) that link disparate real-world data sources to generate more robust medical device clinical evidence.

The women's health technologies pilot CRN (WHT-CRN) project began on 29 September 2017 with a projected end date of 30 September 2019. The data gathered through the CRN project, according to healthit.gov, are anticipated to be used for evaluating effectiveness and safety associated with differing treatment options; assessing the effectiveness and quality of life associated with varying treatment options; providing a framework for clinical studies to be conducted within a registry (e.g., studies required to fulfill the FDA's request for postmarket surveillance); and allowing health care providers to track measures for quality improvements.

The FDA asserts that the pilot program has thus far shown excellent progress. Over the past six months, the WHT-CRN has succeeded in developing, and internationally integrating, data sets for uterine fibroids, pelvic floor disorder, female sterilization, and long-acting reversible

contraception. The agency states that the next step is to develop an implementation guide for participating registries that will allow for efficient extraction of data from electronic health records.

The statement also details other FDA achievements related to real-time surveillance of women's health care issues such as the National Breast Implant Registry, launched in September 2018 to provide a platform for evaluating real-world data on the safety and performance of breast implants.

The FDA also used the statement to make a few new announcements. The statement provides an update to the FDA's safety communication "Warn[ing] Against Use of Energy-Based Devices to Perform Vaginal 'Rejuvenation' or Vaginal Cosmetic Procedures," and related marketing concerns. The statement notes that all manufacturers contacted have responded with adequate corrections, though the agency intends to actively monitor related marketing practices as well as complaints and adverse event reports.

As a follow-up to action taken by the agency in January 2016, when it up-classified a surgical mesh indicated for transvaginal pelvic organ prolapse repair, the statement also announces a plan to convene a special advisory committee meeting on 12 February 2019. The 2016 reclassification triggered a requirement for device premarket approval applications that stymied marketing activities for the device until approval could be received. The meeting is intended to solicit expert opinion about the safety and effectiveness of the device in practice.

Next steps and conclusion

By and large, the next steps described by the FDA in the statement are consistent with the agency's overarching goals: foster innovation that spurs the development of safer, more effective technologies to which patients are assured timely access while, at the same time, maintaining a vigilant postmarket surveillance system for quick identification and evaluation of new or increased safety concerns.

While these are not new goals, the efficient use of real-world evidence to help alleviate the inherent tension between them is. The statement provides some insight into the progress that has been made to this end and the ongoing efforts to further an active, rather than passive, postmarket surveillance system. We anticipate continued efforts by the agency to use big data tools to gather and evaluate data and also for the agency to consider whether there are additional types of data that it needs from the industry in order to fully evaluate its existing data sources.

The FDA indicates an intention to seek new authority for faster and more efficient imposition of postmarket safety mitigations and to undertake new efforts to further assure the safety and effectiveness of devices reviewed under the 510(k) process. This effort includes potential changes to the 510(k) clearance pathway, announced by the FDA on 26 November 2018. Read more about the FDA's proposed changes in our companion client alert. This is consistent with what has already been seen in the premarket context where the agency is evaluating its existing postmarket data sets for safety signals seen in previously cleared/approved devices that could be relevant to a pending submission and then pre-emptively asking questions during its review.

The FDA's statement does not provide much detail on or timelines for any broad new initiatives being undertaken for postmarket surveillance. Rather, the statement focuses on efforts currently underway and the results to date of such efforts. The agency likely will have further updates as the NEST program and additional registries continue to be implemented and additional information on the progress of these programs becomes available. Given the increased scrutiny of the agency's oversight of medical devices, we can expect the FDA will look for opportunities to demonstrate

that it is working hard to protect patients and make well-founded clearance and approval decisions.

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