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White Paper

Three expected changes to the FDA medical device approval process in 2019

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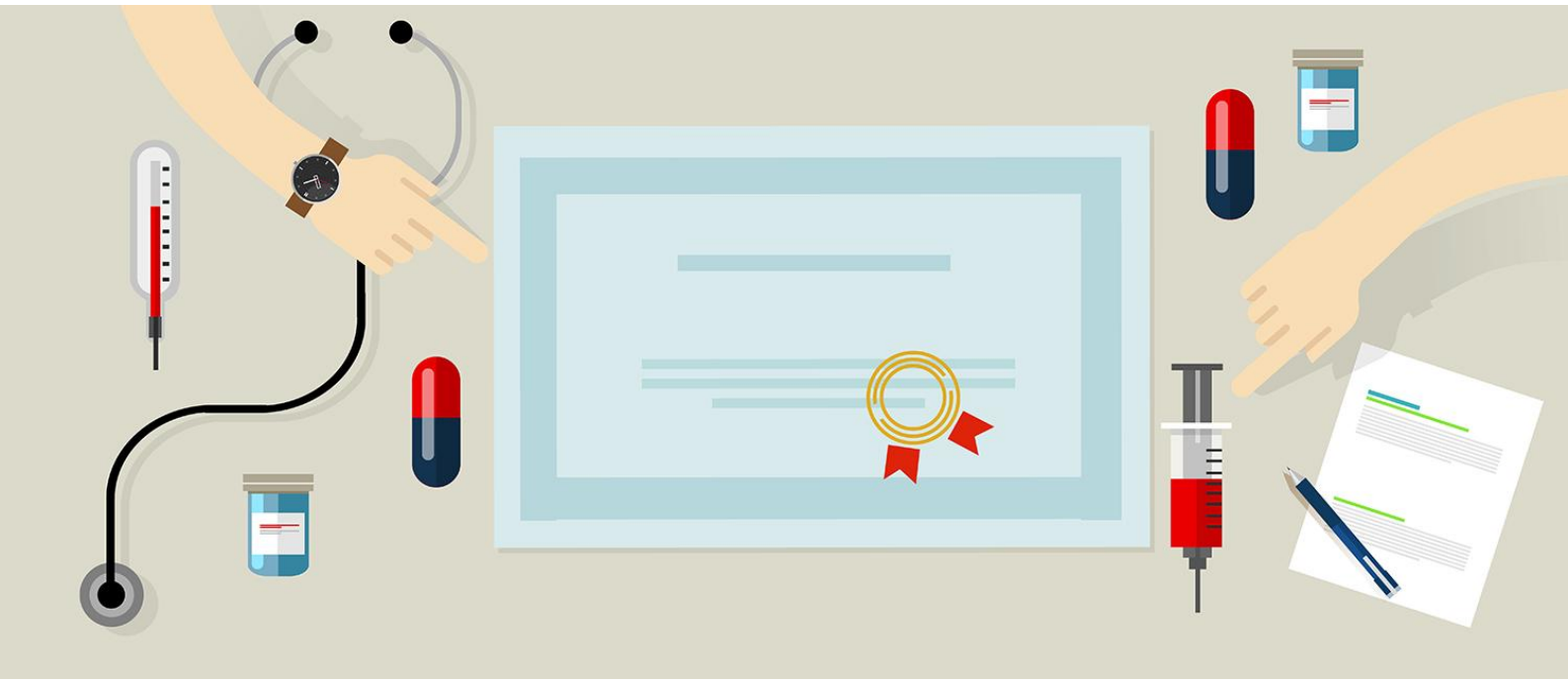
2019 is set to be another interesting year for medical device companies. In our previous blog articles, we discussed the complete overhaul of medical device regulations in Europe. The industry is also facing impactful changes across the pond. At the end of 2018, the FDA announced several upcoming changes to the way medical devices are approved in the United States. In this white paper, we will discuss three expected changes to the FDA medical device approval process in 2019.



How are medical devices currently approved by the FDA?

In the United States, the approval of new medical devices is centrally organized through the FDA's Center for Devices and Radiological Health (CDRH). The CDRH oversees approximately 190,000 devices. The FDA's goal is to protect public health by assuring the *safety and effectiveness* of the products under its supervision. Unlike the rules-based classification system in Europe under the Medical Device Regulation (MDR), medical devices in the US are classified using a predicate-based system. This means that new devices are compared with existing devices on the market. The risk that a new device will pose in comparison to a predicate device will determine its classification and thus its premarket approval pathway.

Similar to Europe, the FDA uses a tiered system to classify medical devices, where Class I is considered low-risk devices, Class II moderate-risk, and Class III high-risk devices. However, new devices without a predicate on the market are automatically considered to be Class III devices, unless the manufacturer can show otherwise. There are four main ways new devices can obtain FDA approval:

- **The PMA process** is the most extensive process and is required for devices that represent the highest risk to patients. Premarket Approval (PMA) submissions will require the manufacturer to produce clinical evidence, typically from a randomized controlled trial. Most devices undergoing PMA submission are long-term invasive devices such as heart valves, breast implants, or pacemakers. However, under this system, devices based on new technology are automatically designated as Class III. However, in practice, only a few companies pursue the PMA pathway. In 2007, PMA submission made up only 1% of all submissions.

- **The 510(k) process** allows low-to-medium risk devices to receive market clearance based on *substantial equivalence* to an existing device on the market. In this case, the manufacturer can piggyback on the submission dossier of the *predicate device*. Substantial equivalence can usually be demonstrated without obtaining new clinical data. Only about 10% of 510(k) applications include clinical data. This route is therefore by far the preferred route for most device companies.

- **The *de novo* 510(k) process** has been created for medium-risk devices for which no suitable predicates exist. The *de novo* process requires more clinical data than a 510(k), but its requirements are significantly lighter than that of a PMA. The FDA will determine if a device is Class I or II. If rejected, the device will be classified as a Class III and will require a full PMA.

- **Exemption** from premarket notification requirements can be obtained by most low-risk devices falling under Class I. Similar to Class I devices in Europe, these devices will be able to self-certify.

By far, the largest amount of devices are submitted under the 510(k) process. However, the FDA recently announced plans to significantly modernize the 510(k) process. What exactly will be changing?

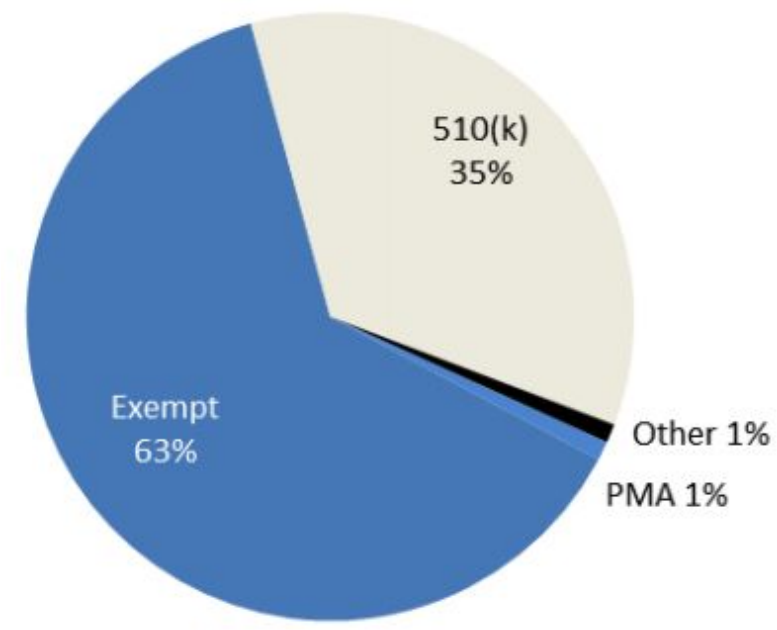


Figure: Medical devices listed with the FDA by Premarket Review Process.
Congressional Research Service, 2016

1) The proposed revision to the 510(k) process

Increased scrutiny by the FDA and changes in device regulation are often a reaction to high-profile incidents and the resulting public backlash. In particular, the FDA has recently been under fire for unsafe products that received approval under the 510(k) process. For example, several brands of vaginal surgical meshes approved under the 510(k) process have been linked to severe adverse events. In addition, the FDA has received criticism that many devices containing completely novel technology received market approval through the 510(k) process despite limited clinical testing. Adding to the fire, the "International Consortium of Journalists" in December 2018 published a highly critical report outlining many alleged flaws in the FDA's 510(k) process.

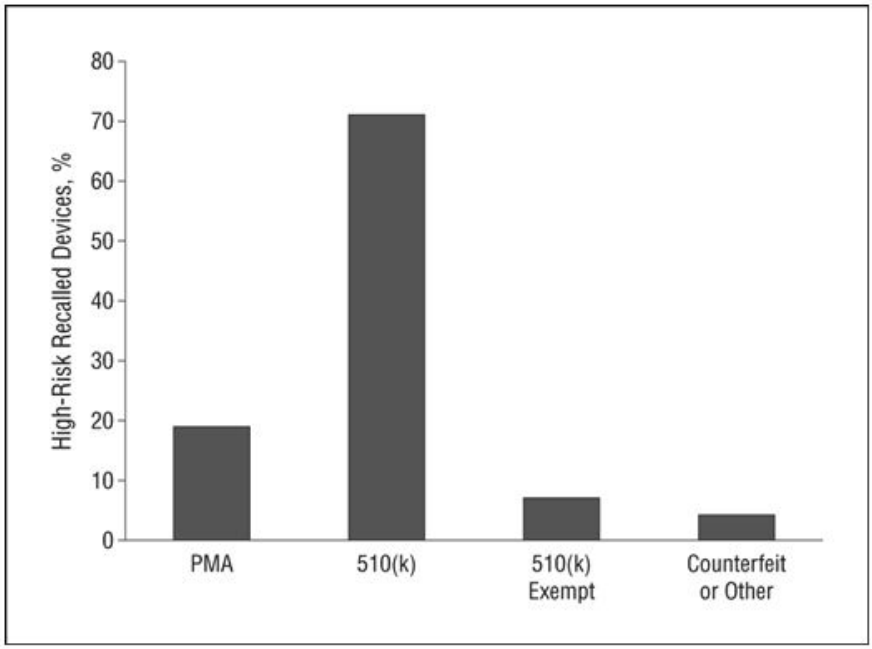


Figure: Recalled devices by FDA review process, 2005-2009. JAMA

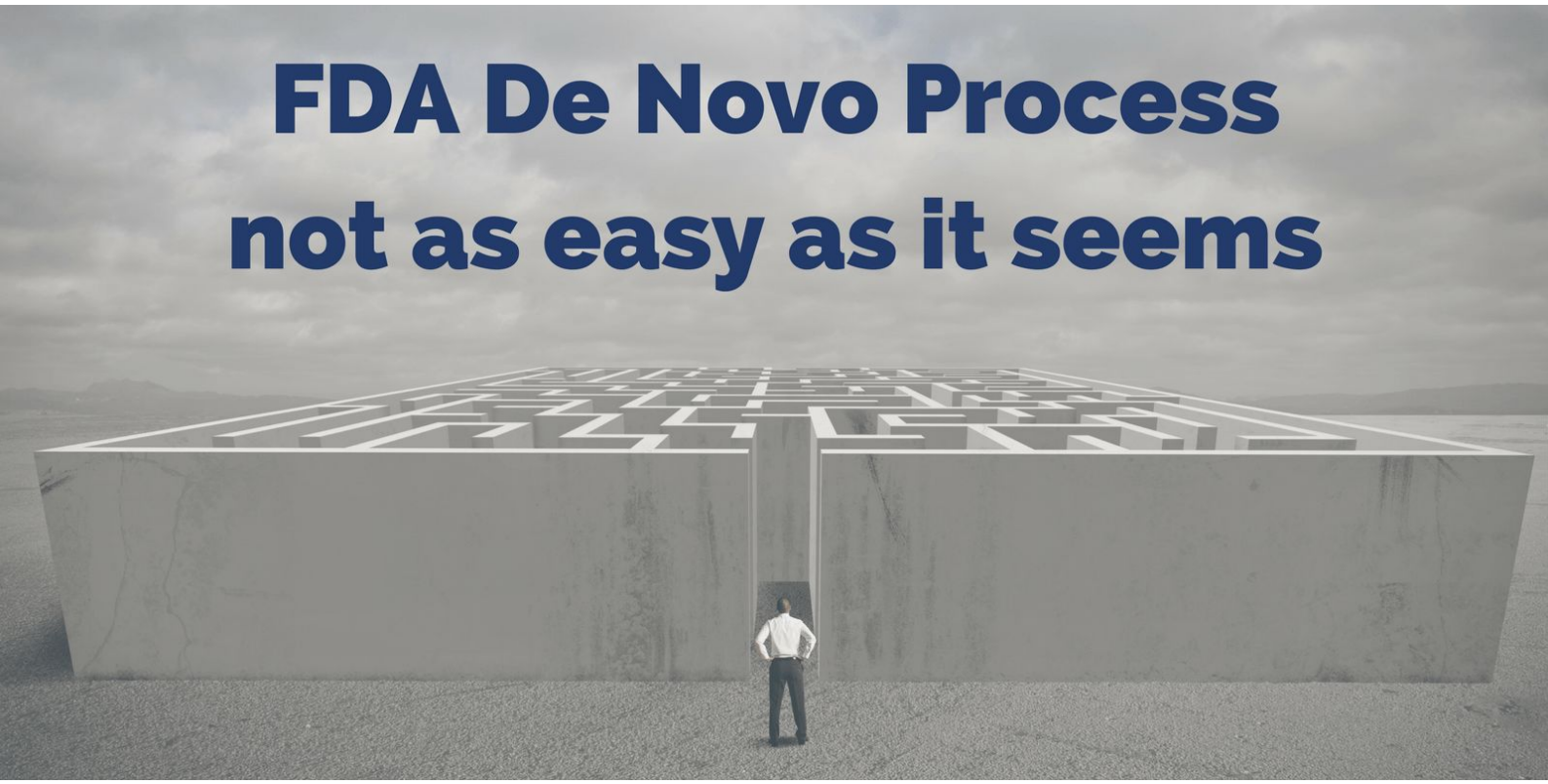
Soon after this report, the FDA announced that it plans to modernize the 510(k) process. In a new guidance that the FDA plans to publish in early 2019, manufacturers should expect that the FDA will no longer accept predicate devices older than 10 years. Currently, around 20% of 510(k)s are based on older predicates.

The FDA's announcement has already received opposition from several medical device associations. They pointed out that older devices sometimes offer valuable information that may help improve the safety of more modern devices. Also, it is questionable whether the FDA's proposed changes will be able to move forward without approval from Congress.

Equivalent, but Different

2) Changes in the *de novo* pathway

In addition to the changes in the 510(k) process, the FDA is proposing improvements to its *de novo 510(k)* process. Class II devices for which no predicates are available can receive clearance through the *de novo* pathway. Such devices are thus exempt from the lengthy PMA process. The newly proposed set of rules aims to provide clear standards, expectations, and processes for the *de novo* pathway. The proposal includes clear requirements on the format and content of the requests, and provides more transparency under what conditions requests will be accepted or rejected. For example, manufacturers will be able to submit a *de novo* request with or without first filing a 510(k). Making the rules more transparent will increase the accessibility of the *de novo* pathway. With this new proposal, it appears the agency is making the 510(k) process more geared towards innovative devices.



Source : fdazolla.com

3) Changes in the way e-health technologies will be evaluated

With more and more medical devices outfitted with computerized components and some software applications now considered medical devices, the FDA needs to change its processes for market clearance and cybersecurity.

One fundamental difference between hardware and software is that software applications release new versions much more frequently. This creates tension with the traditional regulatory process. Software applications iterate often, and cannot file a resubmission for every release. To deal with this, the FDA is currently running a pilot on a 'precertification' program as part of its Digital Health Innovation action plan. The program will precertify trusted manufacturers and will allow manufacturers to streamline their approval under the 510(k) *de novo* pathway. As part of precertification, manufacturers will be required to actively collect real-world data to monitor how the software performs.

The FDA plans for the precertification program to be overseen by a new Center of Excellence for Digital Health. The center will also likely become responsible for managing cybersecurity for medical devices, as well as providing guidance and new requirements for manufacturers.

A compromise between limiting patient risk and enabling innovation

Even though the FDA's mission includes "advancing the public health by helping to speed innovation," its mandate for protecting the public has always taken precedence. The FDA has more incentives to be as certain as possible about the safety of a device than it has to quickly approve submissions. Needless to say, the FDA is more affected by public outcry over harmful devices that it approved, than by any lost opportunity in patient health by not approving a device. However, this can be frustrating for innovators. Each time a new regulation is adopted, it is added to all of the previously existing regulations. This means that medical device regulation is inherently becoming more stringent, and device development more costly. Although the FDA will argue it needs these regulations to ensure patient safety, they will most certainly affect investment in medical device innovation.

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Links to other useful resources:

- 4 ways the Medical Device Regulation will impact your device studies
- Why having a single EDC system for your device company makes sense
- In-vitro diagnostics regulation: From oversight to overhead
- 4 myths about the benefits of paper-based CRFs
- ePRO: the electronic solution for questionnaire surveys in medical research
- Randomization in medical research