The vast majority of medical devices are marketed in the United States based on one of two routes: 510(k) clearance or Premarket Approval (PMA). So it’s very easy to consider U.S. regulatory strategy in terms of “510(k) vs. PMA”. In reality, there are seven routes to get on the market legally. Let’s review the seven, but not just to increase your knowledge with trivia. Instead, knowing all seven paths may help you think “outside the box” when considering the regulatory path for a new device. A review of the seven routes will also give you a historical perspective on the U.S. regulatory process.

1. “Grandfathered” devices.
The Medical Device Amendments (MDA) to the Food, Drug and Cosmetic Act (FDCA) were enacted on May 28, 1976. As Congress was developing the amendments, they realized that it was neither feasible nor productive to insist that every single device currently on the market be required to obtain approval to stay on the market. So the MDA allowed that any device already on the market could stay on the market until further notice. The unofficial terms for such devices are “grandfathered” or “pre-amendment”.

It’s been almost 40 years since the enactment of the MDA, so there aren’t many pre-amendment devices still around. Proving that one of your company’s devices is grandfathered is difficult. One needs a sales brochure, shipping invoice, or similar document from before May 28, 1976. In lieu of documented evidence, FDA will accept an affidavit from a knowledgeable former employee. However, one may also need to establish that the device has not been significantly modified since May 28, 1976. Otherwise, a submission may be necessary.

2. 510(k) devices.
The 510(k) process started with the MDA. If a “new” device was “substantially equivalent” to a pre-amendment device or another similar device that had also been determined to be substantially equivalent (“predicate devices”), it could be marketed 90 days after notifying FDA of one’s intent to market the device. The term “510(k)” comes from the section heading of the Food, Drug, and Cosmetic Act. The official term is “premarket notification”.

Congress intended these to be very simple notifications, not approvals, so early 510(k) submissions were only a few pages long. However, over the years, the page length has grown, including 8% yearly growth for a period of 25 years. The complexities of the process and data requirements have also grown. Approximately 10% of 510(k)s include clinical data, a provision that was codified in the FDA Modernization Act of 1997 (FDAMA).

3. Exempt devices.
Some devices are sufficiently low-risk that premarket notification is not required (Class I devices). Congress introduced this provision in FDAMA so that FDA efforts could be directed towards review of medium- and high-risk devices. In general, Class I devices, which require only “general” controls to be regulated (e.g., proper labeling, good manufacturing practices), do not require a 510(k). However, the relationship isn’t one-to-one. Some Class I devices require a 510(k) and a few Class II devices do not require a 510(k).

Furthermore, even exemptions have limitations, including being exempt “only to the extent that the device has existing or reasonably foreseeable characteristics of commercially distributed devices

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1 [http://www.fda.gov/MedicalDevices/DeviceRegulationandG uidance/MedicalDeviceQualityandCompliance/ucm379552.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/MedicalDeviceQualityandCompliance/ucm379552.htm)

2 See Figure 4.7 at: [http://www.fda.gov/downloads/AboutFDA/CentersOffices/O fficeofMedicalProductsandTobacco/CDRH/CDRHHreports/UCM220784.pdf](http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHHreports/UCM220784.pdf)
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within that generic type.”3 But what is “reasonably foreseeable”? The regulation gives some helpful guidance, namely that the device has to operate, “using a different fundamental scientific technology” but the term is not further defined.

4. PMA devices.
When MDA was enacted, only “new” devices required PMAs. Existing devices required a PMA only after FDA classified the device into Class III and required a PMA by regulation. FDA still classifies several devices as Class III and yet doesn’t require PMAs, e.g., iontophoresis devices and shortwave diathermy, though they have been working through these over the past several years. In the meantime, one can obtain clearance of such devices through the 510(k) process.

5. De Novo devices.
What if your device is “new” because you can’t find an existing predicate, but it’s also not a particularly high risk device? Until FDAMA, all such devices automatically required a PMA, with the attendant significant increase in cost, time, and controls associated with PMAs. To remedy this gap in the law, the FDCA allows anyone who receives a “not substantially equivalent” decision due to lack of a predicate device to petition FDA for immediate (“de novo”) reclassification to Class I or II. With the FDA Safety and Innovation Act of 2012 (FDASIA), if it’s clear that no predicate device exists, one can now skip submitting the 510(k) and proceed directly to the de novo petition.

Use of the De Novo process has grown slowly. In 2004 (the first year De Novos were tracked separately from 510(k)s), only 7 petitions were granted. In 2014, 28 petitions were granted. The use of De Novo will continue to increase as more and more devices are new enough to have no predicates but still aren’t risky enough to need a PMA.

Some patient populations are so small that clinical trials to prove effectiveness are not feasible. In 1990, the Safe Medical Device Act (SMDA) introduced the HDE pathway for these devices. If your device serves less than 4000 new patients each year, an HDE approval can be granted based on reasonable assurance of the safety of the device (where probable benefits outweigh risks) and a demonstration of effectiveness isn’t required.

Two extra steps and one important limitation come with the HDE approval. Before you apply for the HDE, you must obtain a Humanitarian Use Device designation for your device. After you receive approval of an HDE, you still must obtain IRB approval at each facility where it’s used. Finally, you are allowed to make a profit on an HDE product in only limited situations: for pediatric uses and for adult uses where the development of the device for pediatric patients is impossible, highly impracticable, or unsafe.

This method comes last, because it is rarely used and will probably never be used. The PDP process is specified in Section 515(f) of the FDCA, but there are no implementing regulations. In essence, the submitter of a PDP submits the development process, including protocols for bench, animal, and clinical testing, along with acceptance criteria for those tests. FDA approves the PDP and, if everything goes as planned, the submitter can declare the PDP complete and market the device. However, because it requires an upfront commitment from FDA on what a successful study looks like and the development process rarely goes as planned, there have only been a few devices that have ever gone through the PDP process. With the various refinements in the IDE and PMA processes over the years (e.g., Pre-IDEs, Modular PMAs), the PDP will likely never be used.

Seven different paths, not just two. Perhaps your device will not qualify for the 510(k) route, but that doesn’t mean that it requires a PMA. The De Novo or HDE process may be better. Perhaps your device is simple enough that it can be exempt from 510(k) entirely. You can take a first try at determining your device’s class by searching here:

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3 See 21 CFR 862.9, 864.9, 866.9, and so on, to 892.9.
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Don’t forget to try some synonyms. Maybe you have a brand new device without a classification, in which case it will be a De Novo, PMA or HDE product. If you’re stuck, give us a call and we’ll see what we can do.

Our Services
Contact us so that we can work together to make products and therapies that will improve patient outcomes. www.medinstitute.com

If you have any questions or need any additional information, please contact:

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