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A Broken Regulatory System: Only 2% of Medical Devices used in the United States are FDA-Approved

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Introduction

When most people think of medical devices that are legally marketed in the United States and implanted or otherwise used by trained and licensed surgeons, they are very likely thinking of FDA-Approved medical devices. FDA Approval incorporates rigorous pre-clinical research such as: cadaver, animal, mechanical, materials and stress testing followed by human subject trials that are aimed at proving that a device is safe and effective. The trials may include a pivotal trial preceded by one or more pilot studies, and an adequate number of months for clinical follow-up. Many devices (e.g., hip-replacement systems) usually require at least 24 months' follow-up. In order for a company to pursue this pathway, it must first obtain an Investigational Device Exemption (IDE) which allows it to use the product in an investigational setting. Obtaining an IDE usually involves several rounds of discussions with the FDA during which the study protocol, statistical approaches and safety considerations are discussed. The results of the IDE trial are submitted by the company to the FDA as part of a 510 k *de novo* or a Premarket Approval (PMA) application. The FDA has 180 days to review the application and confirm or deny the company to begin marketing its device [1]. Overall, this is a fairly rigorous approach that can take up to seven years depending on the type of device and the required testing [2]. One may think of it as the equivalent of the approval process for new drugs. Before a drug can be marketed, extensive pre-clinical testing is needed. Successful molecules may be moved into Phase 1 trials, followed by Phase 2 trials and eventually one or more Phase 3 trials that may or may not result in FDA approval. Even though the FDA device approval process is less cumbersome than the process for drug approvals, it still provides a high level of confidence that a device is safe and effective for its indication(s).

However, unbeknownst to most, the overwhelming majority of medical devices in the United States, including implantable devices, are not FDA-approved. Instead, they are FDA-cleared. In fact, up to 98% of medical devices [3] are marketed and used by means of what is essentially a legal loophole known as the 510 k pathway. This legal pathway does not require any clinical testing. In order to understand how this is possible, one must first understand the history of the 510 k regulations.

The 510 k pathway is a result of the 1976 Medical Device Amendment to the Food, Drug and Cosmetics Act. The Amendment established a three-tier low to high-risk system for medical devices (Class I to Class III). High-risk Class III devices are those that require the abovementioned IDE approach. They are defined by the FDA as devices that "usually sustain or support life, are implanted, or present potential unreasonable risk of illness or injury" [4]. Knee replacements, hip replacements or spine disc replacements would, by definition, fit this classification.

The legal loophole comes into play as all pre-1976 devices are not covered by the Medical Device Amendment. At the time, it was considered unreasonable to require mandatory clinical trials for devices that had already been marketed for many years, even if they met the new Class III definitions. This essentially meant that any pre-1976 device was a Class I or Class II device as per the new classification system.

In order to allow manufacturers of the pre-1976 devices to make modernizations and improvements to their products without going through an IDE trial, the 510 k pathway was put in place. 510 k refers to the FDA technical dossier which describes Class II devices. 510 k allowed manufacturers to argue that their modified device is "substantially equivalent" to the pre-1976 device and therefore it is not subject to the rigorous IDE process. However, the ability to make a 510 k substantial equivalency claim was not limited to the company which manufactured the original pre-1976 device. Any business entity could present to the FDA a new medical device and argue that it is substantially equivalent to a device that is already on the market – thus allowing it to skip the IDE trial process. As described in 2018 by Dr. David Kessler, the former Commissioner of the U.S. FDA, the 510 k process "became the rule, so that the vast majority of devices today regrettably are regulated under this framework." Dr. Kessler also confirmed that the 510 k process was intended as an exception but that it is now in essence a loophole [5].

Today, there is an entire industry of companies, lawyers, consultants, regulatory affairs specialists and others who specialize in helping medical device companies argue to the FDA that their new devices are in fact substantially equivalent to a pre-1976 product. In fact, many former FDA employees go to work for these organizations after retiring from their government jobs [6].

The discrepancy between approvals and clearances is astounding. In January 2018, the FDA-cleared 234 new medical devices *via* the 510 k pathway [7]. This included devices such as the Everest ® Deformity Spinal System designed to "address the most difficult correction maneuvers for complex spinal pathologies" [8] and the Cervical Spine Truss System ™ which is a cervical spine implant that is marketed as an "innovative" product developed using 3D printing technology [9]. Both companies were able to successfully argue that their products are substantially equivalent to medical devices that were already on the market 40+ years ago. This is despite the fact that 3D printing had not yet been invented in 1976 [10] and spinal surgery using instrumentation was still in its infancy in 1976 [11]. None of the 234 products that were approved in January 2018 underwent clinical trials that would satisfy the minimum requirements for an IDE study.

One may think that it is impossible to successfully argue that a 21st century medical device is substantially equivalent to a pre-1976 product. Even the most skilled lawyers and regulatory consultants would have a difficult time arguing that a 3D-printed spine implant is even remotely comparable to a product that existed before 3D-printing was invented. However, there is a legal loophole for that too. Any device that is cleared by the FDA can be used as a predicate for future submissions. In fact, the FDA encourages this "since medical science has advanced greatly since 1976, it is recommended that you use a

recently cleared device under 510 k as your predicate device" [7]. Further, the FDA allows companies to present "more than one predicate device to help demonstrate substantial equivalence in certain circumstances" [7].

Without a doubt, FDA-cleared and FDA-approved are vastly different classifications and the quality and completeness of data required to obtain FDA approval is vastly superior to the level of data required for the FDA Clearance.

Better education by the FDA to both the general public and to physician/surgeons is needed. Patients deserve to know whether their new hip or knee has been clinically tested and proven safe and effective, or if it is merely substantially equivalent to a medical device that was approved pre-1976.

From a regulatory perspective there is also a strong argument to be made for a reconsideration of the 510 k pathway. It is being misused as a way to skip otherwise important medical device clinical trials. On an annual basis, several dozen medical devices are recalled from the market by the FDA [12]. It is possible that many of these would have never passed the FDA PMA approval or 510 k *de novo* processes, and therefore they would have never entered the market.

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