



Recent Trends in Orthopedic Device Regulation

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Controversy has swelled in recent years regarding the US Food and Drug Administration's (FDA) methodology by which novel medical devices are advanced to market.¹⁻⁴ The debate permeates well beyond the medical literature, repeatedly appearing in widely read editorials, such as *The New York Times*' contemporary article, "The Device Makers' Shortcut."⁵ Much of the scrutiny targets the complex and occasionally inconsistent FDA approval process, which primarily follows one of two major tracts: 510(k) clearance and premarket approval (PMA).⁶

Most devices are cleared for marketing through the 510(k), which stipulates that a new device must demonstrate "substantial equivalence" to an existing, or predicate, device.⁶ Most often, device manufacturers accomplish this through bench-top research, and there is little need for any corroborating clinical trial. Mahomed et al⁷ revealed that up until 1995, only 15% of the 701 total hip replacement devices cleared by the 510(k) had published data regarding clinical effectiveness. Premarket approval, conversely, typically demands clinical trials demonstrating efficacy and safety, but not necessarily randomized, controlled trials. Dhruva et al⁸ found that studies in support of cardiac devices undergoing PMA were randomized trials only 31% of the time and blinded in just 13% of cases.

The determination of which approval pathway a device must undergo typically follows a 3-tiered classification system according to perceived safety: Class I devices present minimal risk and simply require "general controls," such as manufacturer registration and product listing (eg, nonpowered goniometer); Class II devices have moderate risk and require "special controls," such as standardized testing protocols and corroborating research data of some form (eg, intramedullary nails, screws, and most total joint arthroplasty devices); and Class III devices carry higher risk, represent a completely new design, and may support or sustain human life (eg, intervertebral body fusion devices that include any therapeutic biologic, cardiac ventricular assist). Many Class I devices are exempt from undergoing any formal clearance, whereas others, along with most Class II devices, require clearance through the 510(k). Class III devices undergo the more demanding PMA.⁹

This schema, however, is not always so clear. In 2006, the Birmingham Hip Resurfacing System—a Class III metal-on-metal hip resurfacing device—was approved for market via PMA.¹⁰ Two years later, the DePuy ASR XL total hip, also a Class III metal-on-metal hip implant, navigated its way to market through the 510(k) with the claim that its constituent components each demonstrated substantial equivalence to specific components of various antecedent devices, although no prior "equivalent" device constituted the sum of the parts. Furthermore, some of the cited predicate devices themselves received clearance with the claim of substantial equivalence to formerly recalled and/or pre-amendment devices (devices legally marketed before May 28, 1976, that have not been significantly modified).^{2,11} Ultimately, the ancestry of the ASR XL can be traced to 95 progenitor devic-

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es, and it was recalled in 2010, at which time there was a reported 49% failure rate at 6-year follow-up, after 100,000 devices had already been implanted.^{2,12}

Another infamous tale is that of the ReGen Menaflex collagen scaffold, which was designed for use in medial meniscus pathology. In 2004, the Menaflex fell short of an initial attempt at PMA, but subsequently became eligible for 510(k) consideration. After a tenacious third 510(k) submission in 2008, the device was found to demonstrate “substantial equivalence” to surgical meshes used elsewhere in the body, and advanced to market. However, this transaction seemed to move forward with apparent disregard for prior clinical data that demonstrated potential safety concerns and questionable efficacy.^{13,14} This dubious chain of events led to several indictments against the FDA, and even elicited a formal internal investigation, which ultimately resulted in rescindment of the FDA’s decision to award substantial equivalence. Ivy Sports Medicine, the successor of the now bankrupt ReGen, subsequently filed suit against the FDA, but eventually lost.¹³⁻¹⁵

Orthopedic devices account for \$33 billion (16%) of the \$200 billion medical device industry worldwide, falling just \$2 billion shy of cardiovascular revenues.¹⁶⁻¹⁸ Between 2000 and 2011, 3485 orthopedic devices entered the marketplace through the less-stringent 510(k) clearance process, which demonstrated an overall annual increase of 52%, largely attributable to the field of spine.¹⁹ This increase stands in the face of a downward trend observed across all medical specialties between 1999 and 2009.²⁰ On the other hand, a mere 34 devices fulfilled the more rigorous PMA between 2000 and 2011. Of these 34 devices, 11 were ceramic total hips, 5 were total disk replacements, and 3 were hyaluronic acid derivatives for injection.²¹ Undoubtedly, the quantitative discrepancy between 510(k) and PMA approvals is due, in part, to the more demanding checkpoints required for PMA.

Schemitsch et al,²² addressing the device regulation dispute, proffered that orthopedic surgeons should practice in a cost-conscious, evidence-based, and patient-centered manner. To this end, they proposed a 4-tiered system, similar to the checkpoints required in the more rigorous drug industry, involving multiple research trials for market advancement. Multiple other authors have called for randomized, controlled trials to demonstrate *superiority* to existing treatments—not just proof of efficacy and safety—attributing device cost inflation to newer, unproven, and possibly dubious technology.^{1,22,23} Such ambitious changes, however, do not come without a cost of their own.

A 2010 survey of more than 200 unique US medical device companies found that devices undergoing the 510(k) pathway required an average of 31 months from first communication to clearance. Devices undergoing PMA required an average of 54 months from first communication to approval. Interestingly, these US companies reported their time to approval in the European market as just 7 and 11 months, respectively, for an equiva-

lent device review. The survey also addressed the cost of bringing products from concept to market, reported to be \$31 million for 510(k) and \$94 million for PMA devices.²⁰

Although these temporal and monetary costs may seem staggering to some, a minority of currently implanted medical devices carry sufficient clinical data to prove their efficacy and safety.^{1,7,8} If the solution to the broken FDA regulatory system is more robust clinical data and checkpoints, as proposed by Schemitsch et al²² and others,^{1,23,24} costs may skyrocket to the order found in the more demanding drug industry. These costs were recently reported to be \$350 million for a single drug to reach market, and up to \$5 billion when taking into account the multiple failed attempts that accompany the development of one safe and effective new medication.^{1,22-24}

Orthopedic surgery is intimately intertwined with technology and innovation. Although patient safety is of paramount importance, we believe that aggressive attempts to reform the currently disputed FDA regulatory framework need to be met with prudence to ensure that checkpoints and guidelines are refined but do not suffocate the lifeblood of our specialty.

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