



# The FDA and the Regulation of Medical Device Innovation: A Problem of Information, Risk, and Access

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ISSUE BRIEF

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Innovative new drugs and medical devices are often available in other countries long before they arrive (or don't) in the U.S., creating potentially frustrating access problems for U.S. citizens who would like to utilize these products but cannot due to the FDA's approval process, which demands not only product safety but effectiveness.

For this reason, among others, excitement in Washington, D.C. mounted in the summer of 2015, as representatives from across the political spectrum put forward the 21st Century Cures Act. The Cures Act was a major piece of rare bipartisan legislation that passed the House of Representatives in July but has since stalled in Congress. Touted as a law that would accelerate the "discovery, development, and delivery of life saving and life improving therapies," the Cures Act offers policies to improve research collaboration and access to funding, updates to the premarket clinical trials process, and incentives to enhance personalized medicine and the faster discovery of cures, especially for uncommon but deadly diseases.<sup>1</sup>

The Cures Act—as well as other recently proposed legislation<sup>2</sup> and regular editorials in reputable news publications—focus attention on the often debated tradeoff between consumer risk and access in the pharmaceutical and medical device sectors. An assumption shared by these proposals is that the current FDA approval process is somehow flawed. In this Issue Brief, we help to answer the question: Are FDA premarket trials actually

## SUMMARY

- This issue brief takes up the question of whether the current FDA approval process is somehow flawed. Specifically, are FDA premarket trials excessive and do they inhibit consumer access to new and much-needed technologies? Or may they actually be insufficient and expose consumers to too much risk?
- To address this question, the new research described here compares the regulatory approaches of the U.S. and the European Union for second and third generation coronary stents.
- The research supports the FDA's argument that reductions in their standards for device approval would reduce consumer welfare.
- Nevertheless, the research also suggests that in some circumstances, FDA reform proposals advocating for more relaxed premarket requirements but enhanced post-market surveillance would yield considerable welfare gains. But the gains from any such policy change would critically depend on the rate and cost of learning via post-market surveillance.



excessive (i.e., limit consumer access to an undue extent) or might they even be insufficient (i.e., expose consumers to unnecessary risk)? We also examine some of the questions imbedded in these reform proposals: Should different standards be applied to different disease areas? What is the potential for “post-market surveillance” to substitute for “pre-market” clinical trial requirements?

We studied the market for a widely utilized medical device, coronary stents, and created a model that captures the regulator’s tradeoff between consumer risk exposure and access to innovative products.<sup>3</sup> Our research sheds some much needed light on the consumer welfare implications of current FDA regulations and takes a useful step toward clearing up some of the confusion prevalent in the debate over the risk-access tradeoff.

## **MEDICAL DEVICE REGULATION IN THE U.S. AND THE EU**

The term “medical device” applies to a broad set of product categories, ranging from crutches to pacemakers to CT scanners. Regulation of medical devices in the U.S. began with the passage of the Medical Device

Amendments Act of 1976, prior to which there was little oversight of the sector. This law placed oversight authority within the Food and Drug Administration and mandated that the FDA use the dual standards of “safe and effective” when evaluating devices. The Act established a three-tiered classification system for devices (I, II and III), which are assigned based on the perceived risks associated with using a product. Class III devices are defined as those used for supporting or sustaining human life or are critical for preventing potentially unreasonable risk of illness or injury. Class I and Class II devices are lower risk devices. Our research concentrates on coronary stents used in angioplasties, which are themselves a blockbuster device in terms of sales and health impact. Stents are also typical of implantable devices that are deemed “necessary for the sustainment of life” and thus they are regulated as Class III devices in the U.S. and EU.

There are two basic regulatory pathways within the FDA to bring a device to market: Pre-Market Approval (PMA) and the 510(k). The PMA process applies to Class III devices, while the 510(k) process generally applies to Class II and some Class I devices. Under the 510(k)

process the manufacturer needs to demonstrate that the device is ‘substantially equivalent’ to a predicate device. Generally, bench testing data and perhaps a very small clinical study is all that is necessary for a device to demonstrate equivalency. While there is no standard timetable for 510(k) clearance, a straightforward clearance can typically be obtained within several months. Approval of a PMA device, on the other hand, generally requires the manufacturer to provide data from a pivotal study. These are large, multi-center, randomized clinical trials. These studies involve hundreds to thousands of patients and cost tens of millions of dollars to complete. In 2012, only 37 PMAs were approved by the FDA.

In the EU the device approval process for Class III devices is very different from that in the U.S. Medical devices are regulated by three EU Directives; chief among them is the Medical Devices Directive which passed in June 1993 and has been adopted by each EU member state.<sup>4</sup> A medical device is approved for marketing in the EU once it receives a ‘CE mark’ of conformity. The CE mark system relies heavily on third parties known as ‘notified bodies’ to implement regulatory control over

## **NOTES**

- 1 House Energy & Commerce Committee, <http://energycommerce.house.gov/press-release/21st-century-cures-act>.
- 2 Senators Ted Cruz (R-TX) and Mike Lee (R-UT) have a proposal, entitled the RESULTS Act of 2015, that would even more dramatically overhaul the system.
- 3 The main source for this Issue Brief is our paper “Regulating Innovation with Uncertain Quality: Information, Risk, and Access in Medical Devices,” 2015.
- 4 The Medical Device Directive was passed at a time when there was keen interest in a new approach to harmoniz-

- ing regulatory frameworks across EU member states. In contrast, the U.S. medical device regulatory framework was established after the Dalkon Shield injured several thousand women, garnering significant public outcry. At that time, a non-governmental approach to device regulation was never seriously considered by Congress.
- 5 In both the U.S. and EU, new-to-the-world devices may face the additional hurdle of gaining reimbursement from health-care insurance companies, but the devices we studied are second and third generation products, so coverage determi-

- nation has already been made prior to their introduction.
- 6 Boston Consulting Group, 2012, “Regulation and Access to Innovative Medical Technologies.”
- 7 BCC Research, 2015, “Stents: Technologies and Global Markets.”
- 8 The data used in this study consists of quantities and prices at the product-hospital-month level, collected by Millennium Research Group’s (MRG) MarketTrack survey of hospitals across the U.S. and EU from 2004-2013. This survey—covering approximately 10 percent of total market activity—is

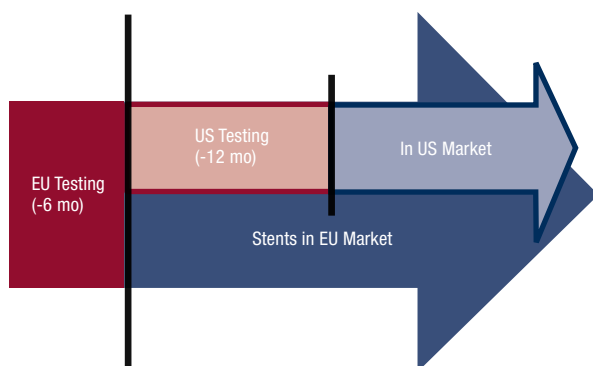
devices. Notified bodies are independent, commercial organizations that are designated, monitored and audited by the relevant member states via ‘competent authorities.’ Currently,

trials than required by the FDA.<sup>5</sup> For this reason, medical device manufacturers (many of which are U.S. based) typically introduce products in the EU well before they seek FDA

## CREATING AND EMPIRICALLY ESTIMATING THE RISK-ACCESS TRADEOFF MODEL

The standards that a regulatory body like the FDA uses to approve products, as well as the information they require from manufacturers, have the potential to fundamentally alter market outcomes. In order to determine the optimal regulatory testing requirements for the FDA, we needed to investigate a product with sufficient utilization under multiple regulatory regimes and one that also has experienced constant innovations over time. Coronary stents—particularly second and third generation stents—met this need. Notably, EU and U.S. regulatory approaches diverge most widely with respect to Class III devices, including stents, creating the variation we leverage in our research. The market for coronary stents, which treat ischemic heart disease (the leading cause of global death accounting for 7 million fatalities in 2010), is very large and the market data for these products is excellent. In 2013, total, worldwide sales of coronary stents exceeded \$7.9 billion, with the vast majority of those sales occurring in the U.S. and the EU.<sup>7</sup>

**FIGURE 1: TIMELINE OF EU/US TESTING AND MARKET INTRODUCTION. ALL DEVICES ENTER THE EU AFTER SAFETY TRIALS. SOME DEVICES THAT WISH TO ENTER THE US THEN RUN LONGER, LARGER EFFICACY TRIALS (CONCURRENT WITH BEING USED IN THE EU MARKET).**



there are more than 70 active notified bodies within the EU. A firm is free to choose any notified body designated to cover the particular type of device under review. To obtain a CE mark, a Class III medical device needs only to demonstrate safety and performance, not necessarily effectiveness. Compliance with this standard usually can be demonstrated with much simpler and cheaper clinical

approval, if they decide to enter the U.S. at all. Conditional on entry into both the U.S. and the EU markets, private reports have documented that medical devices are introduced into the U.S. on average approximately four years after the EU (Figure 1).<sup>6</sup>

### NOTES

the main source of detailed market intelligence in the medical device sector.

<sup>9</sup> It is important to note that our model applies best to markets like stents where interventional cardiologists are highly educated on new technologies. For innovations more broadly used by generalists, there could still be substantial value in the pre-market approval process, even with high-quality post-market surveillance.

<sup>10</sup> In 2009, over 640,000 stent procedures were performed in the U.S. (Auerbach, 2012).

<sup>11</sup> The amount of economic activity regulated by the FDA and the Notified Bodies is significant. In the U.S., sales in the medical device market exceeded \$150B in 2010, or 6 percent of total national health expenditures, and approximately \$130B (7.5 percent) in the EU (Donahoe and King, 2012; Medtech Europe, 2013). Further, the introduction of new medical technologies are responsible for significant reductions in mortality; and in so far as different regulatory regimes affect the availability of these technologies, their welfare impact extends beyond their direct impact on com-

merce.

<sup>12</sup> Wall Street Journal, 2015, “FDA Inspectors Call Theranos Blood Vial ‘Uncleared Medical Device’,” available at <http://www.wsj.com/articles/fda-inspectors-call-theranos-blood-vial-uncleared-medical-device-1445967607>. Note that blood tests are an area where excellent real-world data on efficacy could often be generated by requiring small amounts of redundant comparison tests.



We acquired monthly data on product-level prices, quantities, and diagnostic procedures in the U.S. and EU. These data were collected at the hospital level, which we then aggregated to the geographic area. The data come from Millennium Research Group, a medical device market research firm.<sup>8</sup> We then developed a model for capturing the regulator’s tradeoff between consumer risk exposure and access to innovation, the key feature of which is that when a new innovation is discovered, its true quality is uncertain, and the rate of learning about an innovation’s true quality in premarket clinical trials can be greater than the rate of learning after market entry.

Our data analysis documents multiple patterns consistent with the predictions of the model. The predicted greater access in the EU is evident in the fact that, on average, 49 percent of the stents used in the EU are unavailable in the U.S. at the points in time we studied. Meanwhile, the predicted greater risk in the EU is suggested by the facts that, on average, products in the EU experience less usage overall and higher volatility in usage patterns when first introduced. The U.S., by contrast, exhibits no such patterns. The estimated model also suggests that without any clinical trials, the stent market could virtually fail with very few patients selecting a stent due to the risk of receiving a low quality device.

## WELFARE IMPLICATIONS OF REGULATORY POLICY

So how much testing is enough? In our estimated model, we find that current FDA premarket testing for stents

falls within our confidence interval (seven to nineteen months) for the optimal regulatory policy conditional on the rate of observational learning. This result supports the FDA argument that reductions in their standards for device approval will reduce consumer welfare. The EU, however, despite being able to free-ride off of the information being generated in trials for U.S. entry, stands to benefit by up to 20 percent in welfare gains from increasing its premarket testing standards (at least for stents).

Some FDA reform proposals advocate for more relaxed premarket requirements but enhanced post-market surveillance. In regards to medical devices, the Cures Act would require the FDA to establish a program for priority review of breakthrough products based on case studies instead of clinical trials and it would provide several regulatory process improvements, including a third party quality assessment system through which the FDA would accredit third parties to assess device quality, safety and effectiveness. For the most part, the Cures Act is addressing the correct issues, especially with regard to devices with small markets.

In the context of our model, we find that if post-approval learning rates approach those we observe from clinical trials at a comparable cost, the benefits from such a policy change are substantial. In the extreme case where post-approval learning is fully informative and not too costly, the optimal policy is to require no pre-approval trials at all, which would yield a welfare increase of 24 percent.<sup>9</sup> The value of this increase is very large. Using baseline estimates of utilization

and a value of \$5,000 per treatment yields an estimate of nearly one billion dollars per year in increased welfare from this increase in post-market learning in the U.S. for stents alone.<sup>10</sup> Our analysis of the impact of different regulatory regimes not only speaks, therefore, to the broad questions of the economics of product quality regulation, but also clearly informs policy given these potentially large welfare consequences.<sup>11</sup>

There is merit, then, to the argument that requiring shorter trials with enhanced post-approval testing could improve consumer welfare, but the gains from this policy critically depend on the rate and cost of learning via post-market surveillance. For some products, observational learning from real world use may make it difficult to infer product quality (i.e., not having the randomization built into treatment and the control available in clinical trials). For other products, though—and likely for those in our sample—the problem is simply a lack of systematic data collection and sharing of information.

An important caveat of our analysis is that it holds the technology fixed and abstracts away from the feedback effects of the FDA’s regulatory approval regime on firms’ incentives to invest in new products. In other words, the analysis here cannot be assumed to hold for future generations of stents. However, an important takeaway from our analysis is that the value of a technological innovation to the marketplace depends to a large extent on the regulatory regime’s informational requirements for product testing. For example, coronary stents treat a narrower set of condi-



tions than cancer drugs; but scaled for market size, our findings suggest that the role of regulating information/testing can be comparable to the role of new technology innovation in affecting welfare. Thus a broader takeaway from our research is that the innovation process should be considered holistically from idea to consumer—the value of innovation can be significantly enhanced or diminished by the information regulators require technology firms to produce and disseminate.

Going forward, we plan to study private incentives, or what market forces are at play that would cause medical device manufacturers to run their own clinical trials and provide this information to the market on their own, and not through the

requirements of the FDA. We also want to explore asymmetric information, or what happens when a population less informed than, say, cardiologists must make decisions about which medical products to use. A longer term agenda would be to better understand how these regulations on the pathway from innovation to market approval affect the number and type of innovations discovered in the longer run. Such research would help to expound upon our current findings and have implications for everything from coronary stents to Theranos lab tests.<sup>12</sup>

## CONCLUSION

The efficacy requirements of FDA-required clinical trials provide valu-

able information to the marketplace. In some cases, better “post-market” surveillance can decrease the need for “pre-market” clinical testing, allowing access to more innovative new products while still protecting consumers from risk. The tradeoff between access and risk in regulating the market entry of new products is important in a variety of industries. Our empirical analysis is limited to coronary stents between 2004–2013, and repeating it is only feasible in the set of devices for which detailed market data is available. While our theoretical model provides guidance on how to consider extrapolating to policy in other cases, doing so should be done with care.



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