Medical Devices in the Regulatory System: Factors Contributing to the Recall Crisis

A Research Paper in STS 4600

Presented to the Faculty of the School of Engineering and Applied Sciences
University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science in Engineering

Author

Kayla Prose-Craig
May 12, 2021

On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

Signature _Kayla Prose-Craig_____ Date 05/12/20

Approved _____ Date _____
Tsai-Hsuan Ku, Department of Engineering and Society

Introduction

The Food and Drug Administration (FDA) is responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices sold in the United States as well as regulate devices set to be released to the public market. The FDA's approval process involves clinical testing and the device manufacturer has to prove that the device is effective and safe for use. In more recent years, though, the number of devices being recalled and the number of complaints from the public has increased (Ball, 2019). Recipients of medical devices, especially ones that are implanted, hope that the devices administered to them will be safe and aid them in their lives. The FDA receives push-back from the public for its regulation of medical devices that could cause harm to their recipients. However, the FDA also wants to facilitate scientific advancement and not put so much strain on researchers and developers while keeping the public safe. Due to this paradoxical situation, public opinion of the FDA continues to go down as more device failures occur and more developers complain about the strict processes (Kaganov, 1980).

The FDA's primary focus is to ensure that the devices being distributed to patients and doctors are effective and safe, which can take some time to do. Developers want to make a profit and produce innovative devices. They are questioning whether or not the FDA's regulations are impairing their ability to create novel devices. The disparity between the FDA and device developers is what contributes to this paradoxical relationship, with neither side being completely at fault. The recall issue is more than this surface-level argument and is the reason for discussion on this thesis. The complex network of FDA regulation includes the FDA regulators, device companies, politicians, and the people who come into contact with the devices after their release to the public. I propose that this system is deserving of an STS approach to research why

this relationship is contributing to a higher rate of recalls and what can be done to reduce the number of recalls moving forward.

Literature Review

In recent years, the number of recalls has been steadily increasing (Ball, 2019). This could be because the number of applications to the FDA for medical devices has increased over the years or it could be an issue with the regulatory system. In a study done by Zuckerman et. al.(2011), they analyzed the recalls issued from January 2005 through December 2009 and found that there were 113 Class I, or low-risk, recalls. Of those 113 device recalls, 80 of them were devices cleared through the 510(k) process, which is 71%, and an additional 8% were exempt from the FDA regulations. In this time frame at least, the majority of recalls were due to the 510(k) process and the FDA has been criticized as a result by health system advocates. This is a process that is intended to be less "burdensome" to allow improvements on previous devices (D. M. Zuckerman et al., 2011). The devices that undergo premarket notification are not approved, they are only "cleared" for patient use. The FDA relies heavily on the 510(k) process and one reason for this is that this process is much less expensive and enables the relatively small Center for Devices and Radiological Health (CDRH) to review thousands of devices each year (Government Accountability Office, 2009). Additionally, the 510(k) process stimulates competition amongst manufacturers, which is valued heavily in America's capitalistic market. If there are more generic drugs or devices on the market, then those products can be made cheaper. However, cheaper is not always better in the realm of healthcare. Research shows that this competition to produce a cheaper product leads to manufacturers "cutting corners", especially in manufacturing, which can result in harmful outcomes (Ball, 2019).

Other factors affecting the number of recalls include the disconnect between manufacturer and patient, the rush to test, minimizing negative data collected, faulty designs, software hacking, insufficient warning system, and off-label use by doctors and manufacturers (Sharp, 2016). Some broader reasons are influenced by political, technical, or mechanical factors which is the main focus of the three case studies presented in my research. Another point to note is that a majority of medical devices on sale in the U.S. market today, over 90 percent, are only cleared by the FDA through the 510(k) process (*A Delicate Balance*, 2011). Additionally, these devices are 11.5 times more likely to have an issue that forces a recall than a device that went through the PMA approval process (Silvestrini, 2021). This is important to note since two of the three device cases being researched were cleared based on the 510(k) process. The one device that was approved via the PMA pathway still resulted in a total recall due to falsifying reports (U.S. Food & Drug Administration, 2021).

The FDA is also responsible for monitoring medical devices after they have gained approval or clearance to ensure product quality and safety are maintained. During development, clinical trials are devoted to a subset population in a controlled environment with the intention that the device will apply to the general market after its approval. Many funds are allocated at the onset of development but once the device hits the market, funding tends to dwindle into a fraction of the original testing cost (Mehran Roxana et al., 2004). The Quality System Regulation 21 CFR 820 requires that device developers report any device-related deaths, serious injuries, or certain malfunctions to their manufacturers for quality assurance and the FDA for regulatory action (Whittaker, n.d.). This means that the clinicians and patients who use the device must report their complaints to the company first, which makes it difficult to obtain reliable information (Mehran Roxana et al., 2004). For example, clinicians and patients may be reluctant

to report any failings if the use of the device involved off-label usage. Therefore, the statistics may not be accurate for device failure. Even when there have been reports of adverse events, the FDA can take up to 36 months to research and build a review on the device (Mehran Roxana et al., 2004). The FDA can also order what is known as a post-approval study (PAS) on high-risk devices after approval to evaluate post-market performance (Reynolds et al., 2014). In a review done by Reynolds et al. (2014), PSAs that were authorized between January 2005 and December 2011 were evaluated and the FDA has not recalled a device based on the developers' failure in post-marketing surveillance. The most common outcome that was seen in this particular study was that rather than recalling the device, its label of use was changed. However, since the PSAs don't seem to do much and that there is little information on the PSAs themselves, the effect of this post-marketing surveillance method is undermining the authority of the FDA to order these studies (Reynolds et al., 2014).

Upon review of the previous studies being done, it is fairly clear that a majority of researchers look at the FDA as a governmental agency that needs to be changed via new regulatory statutes and laws. The perspective of the patient and physician is addressed only when the researchers highlighted the practice of off-label use, but that is not their only influence. The social and technical components of the issues relating to device regulation should both be addressed in order to get a fuller scope of the issue and make regulatory changes. This is the reason for my proposed research using an STS framework.

STS Framework/Research Method

What is it about the relationship between the FDA, companies, and medical practitioners that contributes to a higher rate of recalls? To better understand this, the framework of a large

technical system (LTS) proposed by Thomas Hughes can be employed. The LTS approach allows a broader connection to be formed between the more technical components associated with recalls and the social components (Gökalp, 1992). Three case studies, Essure, DePuy, and Menaflex, will be discussed and for each, a technical or social component will be highlighted. Essure showcases the patient side of the process and the social implications associated with a recall. DePuy's hip replacements describe more of the technical and regulatory interactions. Finally, Menaflex shows how the influence of politics can affect the regulatory process. All three of the studies, unfortunately, end with a device recall, and people were hurt in the process.

To establish these studies, I will be sourcing mainly secondary sources as well as official documents like court hearings. Additionally, interviews regarding the device recalls that were aired on various news programs will give further insight into the patient perspective. Upon investigating a variety of sources, I hope it will provide further insights into the incidence of recalls occurring and aid in finding a solution to this situation.

Data Analysis

The Food and Drug Administration (FDA) is the oldest consumer protection agency in the United States. Originating in the U.S. Patent Office in 1848, it was ultimately codified in the Pure Food and Drug Act of 1906 (Van Norman, 2016). In 1938, the U.S. Congress required all drugs to be approved through the FDA for safety, and medical devices weren't regulated to this extent until 1976 (D. M. Zuckerman et al., 2011). The FDA is tasked with ensuring that medical treatments demonstrate both safety and efficiency before they are released to the public, ideally as quickly as possible. For much of its existence, the FDA has faced criticism. Compared to other westernized countries, the FDA approval process is lengthy and expensive. There are calls

from the public that implore the FDA to loosen its regulation process to not stifle innovation (Van Norman, 2016). However, the FDA must ensure that new medical treatments are safe or effective to protect the public from pre predatory marketing practices. This requires more testing and development, which can be costly. The FDA has faced this paradox and provided shorter avenues to seek out clearance or approval.

The FDA categorizes the medical devices into three risk-ascending classes, with Class I being the most low-risk devices and Class III being the most high-risk (Health, 2020). There are four methods for a device to undergo the regulation process: Investigational Device Exemption, Premarket Approval, 510(k) clearance, and De Novo Classification. Investigational Device Exemption (IDE), is only a precursor method for the other three methods. IDE allows the device being investigated to be used in a clinical study to provide data for approval or clearance. Clinical studies with devices of significant risk, class III, must be approved by FDA and by an Institutional Review Board (IRB) before the study can begin. Other devices, class I or class II devices, only need to get approval from the IRB (Health, 2020).

Premarket Approval (PMA) is the pathway in which medical devices prove that they "support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury." (D. M. Zuckerman et al., 2011) PMA usually requires extensive testing and is the most expensive and time-consuming pathway of the four. The devices that undergo PMA are categorized as high-risk Class III devices that pose a significant risk of illness or injury. They are required to submit clinical data to support claims made for the device before they can receive approval (Health, 2020). The cost of taking a new drug from concept to market as of 2014 is now above $1.3 billion (Van Norman, 2016). PMA usually has a development time of 4-8 years and costs between 50 to 200 million

dollars. The FDA is usually able to review PMA applications, depending on how many times it needs to be revised, within a year after submission (Fast Forward Medical Innovation, 2015). The following case study, Essure, was a device that went through the PMA application process.

Essure, a birth control implant, was a device that showed several mechanical failures. The main issue, in this case, was the failure to report testing complications and patient complaints to the FDA (LastWeekTonight, 2019). According to news outlets, 80 women got pregnant (the device did not perform as intended) and 91 women had to get hysterectomies (ABC Action News, 2013). There were many reports from test subjects that said they experienced pain and bleeding as well. The company, Bayer, knew about the patient complaints and failed to report back to the FDA. There were 168 complaints about pain or chronic pain, including pain caused by perforation, and only 22 of these complaints were known by the FDA (News 5 Cleveland, 2014). There was reason to suggest that the clinical data given to the FDA for the PMA application was not an appropriately designed study. The FDA was not aware of the negative feedback so they were delayed in seeing the warnings and issuing a recall for the device. In the lawsuits against Bayer, it was revealed that Bayer had failed to report hundreds, if not thousands, of Essure complaints and that there was extensive evidence that questioned the safety of the birth control device (Fulmer & Searcy Law, 2020). This doesn't only affect the company. Many of the women who had complaints had permanent damage, even infertility, because of the testing protocol failures (ABC Action News, 2013). If the women had been able to voice their complaints, then they could have gotten earlier assistance or notified the developers of design complications. The recalls are only what happens after the patients have used the device. The patients are the ones who on an individual level experience the most adverse effects of poor testing and FDA recalls.

The remaining case studies, DePuy and Menaflex, consisted of devices that went through premarket notification, also called PMN or 510(k). This is a process that is intended to be less "burdensome" and costly to allow improvements on previous devices (D. M. Zuckerman et al., 2011). The devices that undergo premarket notification are not approved; they are only "cleared" for patient use. Devices that can be cleared have to be in the lower-risk class I and class II classification and they must prove to be "substantially equivalent to a previously approved or cleared device. Over time, the definition of substantial equivalence has expanded to include devices made from different materials and devices using a different mechanism of action, if they were determined to have a similar safety profile (D. M. Zuckerman et al., 2011). Additionally, a predicate device does not have to be limited to approval status. The predicate device itself could have been "cleared" as long as it is already circulating in the public. Figure 1 (Government Accountability Office, 2009) details the FDA's decision-making process when it comes to 510(k) clearance. Compared to the PMA process, the 510(k) is substantially cheaper and faster. The estimated development time for 510(k) devices is 4-8 months depending on complexity and

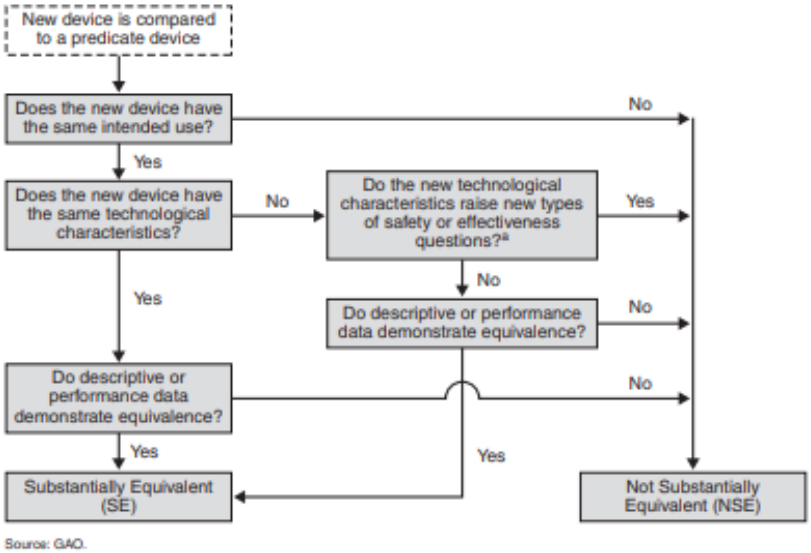

Figure 1: FDA's 510(k) Decision-Making Process. In cases where the FDA determines that a new device has new technological characteristics that could affect safety and effectiveness, FDA requires performance data to demonstrate substantial equivalence (Government Accountability Office, 2009).

how substantially equivalent the device is to its predicate device. The "user fee" that the FDA collects with the 510(k) clearance application is about $5,000 or half that for smaller businesses (Fast Forward Medical Innovation, 2015). If the device is low-risk but does not have a substantially equivalent predicate device, then the medical device companies can submit a De Novo request. The De Novo classification must also provide reasonable assurance of safety and effectiveness for the intended use (Health, 2019).

Device failure is a factor that is not so easily ignored. DePuy Synthes is a company that was acquired by Johnson & Johnson in 2008 and produces products relating to skeletal injuries and joint replacements (Surgical Watch, 2016). Three of DePuy's hip replacements were recalled because they resulted in injuries to patients, some of which required replacements and additional surgery. In particular, the recalls only affected the metal-on-metal versions of the hip replacements, which resulted in serious medical complications including metallosis (metal poisoning), implant dislocation, chronic or severe pain, and the need for hip revision surgery (Surgical Watch, 2016). Two of the three devices were cleared on basis of being substantially equivalent to a predicate device and the last device did not qualify for 510(k) clearance and required an IDE for clinical testing (Surgical Watch, 2016). The patients in the study also experienced a high number of fractures so the device was not approved to the American market but was allowed in the European market (Surgical Watch, 2016). In 2009, DePuy started to phase out these particular devices "as a result of declining demand and the intention to focus on the development of next-generation hip replacement"(Johnson & Johnson, 2010) and not as a result of the failure rate of their devices. Very few devices, at the time, were in circulation worldwide when there was a full recall in 2010. DePuy found that 49% of all implants required replacement and they admitted to a higher-than-average recall rate (Surgical Watch, 2016). DePuy covered

many costs for the treatment of people impacted by the faulty hip replacement, but they still managed to accrue many lawsuits in this period. Company documents showed that De Puy had reports of the ASR's flaws as early as 2008 and did nothing about them (Surgical Watch, 2016). Facing these pressures from the FDA and legal challenges, De Puy decided to discontinue their metal-on-metal versions of the Pinnacle Systems by August of 2013. To this day, PINNACLE® Revision Acetabular Cup System is still in circulation, but the metal-on-metal variations have been phased out (J&J Medical Devices, 2021).

Politics can also be a huge social factor in the approval or clearance process. Menaflex was approved through the 510(k) clearance path, despite it having failed approval twice already due to poor results from IDE studies (Milfred, 2012). Menaflex, an "implantable porous meniscus scaffolds composed of collagen fibers" (Aetna, 2020), was evaluated by a team of orthopedic scientists and was rejected as having little benefit to patients and being an injury risk. The commissioner was convinced to push it through on the third attempt for approval because the commissioner was petitioned by four congressmen to approve the device, all of whom receive funding from ReGen Biologics. Medical device companies can lobby Congress members and can be very influential in the status of new laws or bills that get assessed relating to the regulatory process. In 2013, Menaflex was pulled from the market due to the FDA finding that it was not similar enough to the function of the device they claimed as a predicate, with a court hearing upholding the FDA's claim (Aetna, 2020). The court determined that the previous FDA under a different administration had wrongfully cleared the device because of outside pressure, namely congressional lobbying (Aetna, 2020). This is a loophole that can easily be taken advantage of by device companies. Many politicians are influential in governmental agencies, of

which the FDA is included, and can be motivated by financial pressure. This particular problem is not solely related to device regulation, so it would need an STS investigation on its own.

Discussion/Conclusion

Two of the three previously discussed cases were recalls resulting from the 510(k) process. A device was 11.5 times more susceptible to being recalled in this way than a device that was approved via PMA according to Silvestrini (2021). This unusually high rate is partly due to the lack of testing needed for the 510(k) clearance but is also partly caused by the ambiguity in which a device can qualify for 510(k) clearance. As can be seen in Figure 1, there is a decision tree to help FDA regulators determine if a device is "substantially equivalent" to another regulated device already on market. The decisions, however, are qualitative and can vary from regulator to regulator. The social, technical, and political factors that were discussed in the case studies show how much a decision can be affected. There is also the question of whether a device is "equivalent enough" which can raise some interesting responses. There is no metric currently to evaluate these decisions and companies can take advantage of this fact through regulatory loopholes, like the ones shown with the DePuy study. The 510(k) system is not simple but is a very complex regulatory machine. Given that we already know this to be true, the next question is what can be done? The proposed solution by Milfred (2012) is to de-emphasize the pursuit of efficiency by either tightening or discarding programs like 510(k), which emphasize the need for efficiency over safety. If the FDA is found slower than its peers, reinforce the FDA overall by increasing the agency's budget rather than cutting corners and skipping steps of regulatory review (Milfred, 2012).

On a different note, Essure was a device that went through the more stringent PMA process but still required a huge system recall. The clinical study process is an important step in the PMA approval but it appears to be easy enough to "fake" positive results like Bayer did with Essure. This could be remedied by either the FDA sending a representative to oversee clinical testing or doing all the testing within the FDA. The government would have to increase the FDA's budget, which is not very likely to happen soon. However, by having the FDA invest more into clinical trials, the medical manufacturing companies would also benefit as they would not have to spend as much on resources required for trials. The FDA is already understaffed, as most regulatory agencies tend to be, so when a company lies about testing results, they don't catch it until it's too late. If the government won't increase the budget for the FDA for the sake of clinical testing, then they should increase the number of staff the FDA can take on. Another suggestion by Fineberg (2007) to help with the issue of post-marketing surveillance, was to add a special symbol to products upon release that would be removed after two years in order to bring special attention to the drug or device. Better post-surveillance of newly approved devices could also aid in catching companies who falsified testing results in the early stages. This doesn't help those affected adversely, though. There are compensation programs to aid those affected but the trauma and pain aren't always easy to compensate in patient injuries. The best way to prevent injury is to provide better infrastructure to the early phases of regulation, which is why the most common suggestions for reform involve the 510(k) process rather than on PSAs.

The device industry pushes back hard when reforms to FDA regulations are presented, so changes are not easily made. Medical device manufacturers don't want the regulations to become more stringent or expensive because it is bad for business. This is why so many companies will lobby or fund multiple congresspeople to keep the politician's viewpoints aligned with their own.

These politicians are presented with conflicting interests and will usually do whatever is in the best interests of their sponsors, as was shown in the case of Menaflex. Device manufacturers should not be allowed to lobby politicians and the FDA's regulations should be based fully based on scientific methods. When money and conversation become involved, the focus is on the device as something that can produce capital rather than on the device as something that can help people.

Conclusion

It is evident that the FDA system has its flaws and its perks, but as with any agency or government facility, it is not perfect. The different factors that contribute to how the FDA is run and how it can function are complex systems that affect one another. In the future, the FDA will need to make some changes to help decrease the number of recalls issued and it needs to start with the device companies and manufacturers. Congress should aim to increase the budget for the FDA to make sure they can do their job with the appropriate number of staff. Changes to the 510(k) process to include testing or clear up the ambiguity around it would also be of benefit. Even though other issues need congressional attention, the number of injuries caused to the American public will not decrease on its own without introspection.

References

ABC Action News. (2013, October 4). *Serious issues over Essure birth control*. https://www.youtube.com/watch?v=lfplsmWNT2E&ab_channel=ABCActionNews

Aetna. (2020, December 15). *Menaflex*. http://www.aetna.com/cpb/medical/data/700_799/0786.html

Ball, G. (2019, April 26). *Recalls of medical devices and drugs are up—Can anyone predict when it will happen next?* The Conversation. http://theconversation.com/recalls-of-medical-devices-and-drugs-are-up-can-anyone-predict-when-it-will-happen-next-115832

Fast Forward Medical Innovation. (2015, February 28). *FDA Regulation of Medical Devices (Part 1 of 3)*. https://www.youtube.com/watch?v=yZAG51ogVhE&t=35s&ab_channel=FastForwardMedicalInnovation%E2%80%93CommercializationEducation

Fineberg, H. V. (2007). Reinventing the US Food and Drug Administration. *Medscape General Medicine*, *9*(2), 6.

Fulmer, B., & Searcy Law. (2020, July 29). *Did Bayer Hide Behind Sealed Court Documents To Tout Essure? | Searcy Denney Scarola Barnhart & Shipley—JDSupra*. https://www.jdsupra.com/legalnews/did-bayer-hide-behind-sealed-court-51326/

Gökalp, I. (1992). On the Analysis of Large Technical Systems. *Science, Technology, & Human Values*, *17*(1), 57–78.

Government Accountability Office. (2009). *Medical Devices: FDA Should Take Steps to Ensure That High-Risk Device Types Are Approved through the Most Stringent Premarket Review Process* (GAO-09-190). Government Accountability Office. https://www.gao.gov/assets/gao-09-190.pdf

Health, C. for D. and R. (2019). De Novo Classification Request. *FDA*. https://www.fda.gov/medical-devices/premarket-submissions/de-novo-classification-request

Health, C. for D. and R. (2020, September 4). *Overview of Device Regulation*. FDA; FDA. https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/overview-device-regulation

J&J Medical Devices. (2021). *Hip Replacement*. https://www.jnjmedicaldevices.com/en-EMEA/specialty/hip-replacement

Johnson & Johnson. (2010, August 26). *DePuy Orthopaedics Voluntarily Recalls ASR™ Hip System—DePuy | J&J Medical Devices*. Johnson & Johnson - Medical Devices. https://www.jnjmedicaldevices.com/en-US/news-events/depuy-orthopaedics-voluntarily-recalls-asrtm-hip-system-depuy

Kaganov, A. L. (1980). Medical Device Development: Innovation versus Regulation. *The Annals of Thoracic Surgery*, *29*(4), 331–335. https://doi.org/10.1016/S0003-4975(10)61480-4

LastWeekTonight. (2019, June 3). *Medical Devices: Last Week Tonight with John Oliver (HBO)*. https://www.youtube.com/watch?v=-tIdzNlExrw

Mehran Roxana, Leon Martin B., Feigal David A., Jefferys David, Simons Michael, Chronos Nicholas, Fogarty Thomas J., Kuntz Richard E., Baim Donald S., & Kaplan Aaron V. (2004). Post-Market Approval Surveillance. *Circulation*, *109*(25), 3073–3077. https://doi.org/10.1161/01.CIR.0000134694.78653.B6

Milfred, J. (2012, November 4). *The Politics of FDA Approval*. Yale Scientific Magazine. https://www.yalescientific.org/2012/11/the-politics-of-fda-approval/

News 5 Cleveland. (2014, November 13). *Essure birth control inspections uncovered*. https://www.youtube.com/watch?v=VaP5sGGUm2w&ab_channel=News5Cleveland

Reynolds, I. S., Rising, J. P., Coukell, A. J., Paulson, K. H., & Redberg, R. F. (2014). Assessing the Safety and Effectiveness of Devices After US Food and Drug Administration Approval: FDA-Mandated Postapproval Studies. *JAMA Internal Medicine*, *174*(11), 1773–1779. https://doi.org/10.1001/jamainternmed.2014.4194

Sharp, M. (2016, July 11). Top 8 Reasons For Medical Device Recalls. *Matthew L Sharp*. https://mattsharplaw.com/news/top-8-reasons-medical-device-recalls/

Silvestrini, E. (2021). *FDA 510(k) Clearance*. Drugwatch.Com. https://www.drugwatch.com/fda/510k-clearance/

Surgical Watch. (2016, March 30). *DePuy Hip Replacement*. http://surgicalwatch.com/depuy-hip-replacement/

U.S. Food & Drug Administration. (2021, March 22). *Premarket Approval (PMA)*. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P020014

Van Norman, G. A. (2016). Drugs, Devices, and the FDA: Part 1: An Overview of Approval Processes for Drugs. *JACC: Basic to Translational Science*, *1*(3), 170–179. https://doi.org/10.1016/j.jacbts.2016.03.002

Whittaker, M. A. (n.d.). *IMPACT ASSESSMENT OF THE QUALITY SYSTEM REGULATIONS FOR MEDICAL DEVICES - ISO 13485.2003 AND 21 CFR 820 AND THE CAPA SYSTEM*. 91.

A Delicate Balance: FDA and the Reform of the Medical Device Approval, Senate, 112–4 (2011) (testimony of Diana Zuckerman). https://www.govinfo.gov/content/pkg/CHRG-112shrg67694/html/CHRG-112shrg67694.htm

Zuckerman, D. M., Brown, P., & Nissen, S. E. (2011). Medical Device Recalls and the FDA Approval Process. *Archives of Internal Medicine*, *171*(11), 1006–1011. https://doi.org/10.1001/archinternmed.2011.30