510(K) Applications and the Risks associated with the Medical Device Regulatory Pathway

A Research Paper submitted to the Department of Engineering and Society

Presented to the Faculty of the School of Engineering and Applied Science

University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements for the Degree

Bachelor of Science, School of Engineering

Josephine Johannes

Spring 2022

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

ADVISOR

Sean M. Ferguson, Department of Engineering and Society

510(K) Applications and the Risks associated with the Medical Device Regulatory Pathway

Countless companies and startups submit an application for medical devices each year with the hopes that their respective medical devices will be approved by the Food and Drug Administration (FDA). There are numerous types of medical devices, such as those that are used to monitor patients or others that are embedded within the body. For medical devices that are placed into the human body, strict regulatory standards must be upheld to keep patients safe. In general, the FDA has classifications for medical devices, such as Class I, II, and III. Class I devices are the lowest hazard and Class III devices are high risk devices that pose a significant risk of illness or injury (FDA, 2020). Depending on the device's classification, a company must submit a Premarket Notification (510(k)) or a Premarket Approval (PMA) for the device to be released onto the market. A 510(k) is "a premarket submission made to the FDA to demonstrate that a device to be marketed is safe and effective, that is, substantially equivalent, to a legally marketed device" (FDA.gov, 2020). However, if the prior art used to approve such medical devices had caused serious patient harm and was not removed from the list of approved medical devices, this could enable lower quality medical devices to be released onto the market. The risks involved with the approval process of medical devices begs the question: what is considered safe enough to be implanted within the human body?

I will be using a framework based on risk and standards by discussing the background of medical devices and their approval process, the status of the medical device industry, the role of the media in bringing light to device defects, the source of legitimate expertise in the domain, and lastly, how the medical device approval process should be refined to make products safer. This study investigates the thesis surrounding the 510(k) used to expedite the approval of medical devices based on prior innovation. As various professionals and groups of medical

experts have commented on suggestions to improve the Medical Device Amendments to increase the stringency of the accelerated approval process, this research explores the various comments and suggestions given by such professionals and continues an ongoing conversation about the regulation of medical devices.

Background

Medical Device Regulations and the Medical Device Amendments

The first comprehensive federal consumer protection law was the 1906 Food and Drugs Act which was intended to prohibit misbranded and adulterated food and drugs in interstate commerce. However, there were still flaws in the act, and many consumer items considered hazardous were sold on the market legally. This led to an increasing amount of dangerous consumer products that poisoned, maimed, and killed many people; the breaking point that led to a change happened in 1937, when an untested pharmaceutical killed numerous patients, including many children, right after it was sold on the market (Commissioner, 2021a). This devastated the state of medical devices and so a new regulation was created.

The first mention of any kind of regulation for medical devices occurred in 1938 when the Federal Food, Drug, and Cosmetic Act (FD&C Act) was passed (Health, 2021). This act authorized the FDA's regulation and oversight of medical products as well as extended the prohibition of interstate commerce to misbranded and adulterated cosmetics and therapeutic medical devices. The FD&C was essential in securing controls over drugs and food, including new consumer protection against unlawful cosmetics and medical devices, and enhancing the government's ability to enforce the law. In context, the amendments were drafted at the end of the "consumer decade" which was a period of time when numerous pro-consumer laws were

enacted (Adler, 1988). As more devices were being created and sold on the market, regulations were made again in 1976, with the Medical Device Amendments to the FD&C Act. The Medical Device Amendments served six purposes: (1) to provide reasonable assurance of the safety and effectiveness of medical devices, (2) to create a three-class, risk-based classification system for all medical devices, (3) to establish the regulatory pathways for new medical devices, (4) to create the regulatory pathway for new investigational medical devices to be studied in patients (Investigational Device Exemption (IDE)), (5) to establish several key post market requirements including registration of establishments and listing of devices with the FDA, Good Manufacturing Practices (GMPs), and reporting of adverse events involving medical devices, and lastly (6) to authorize the FDA to ban devices (Health, 2021). These modifications served to make medical devices safer and more effective for users while increasing somewhat stringent regulations for medical devices.

Post Medical Device Amendment Devices

Derived from the Medical Device Amendments, the FDA currently stratifies medical devices according to risk, where Class I is minimal, Class II is moderate, and Class III is high. An example of a Class III device would include a pacemaker and a Class I device would be a tongue depressor. This classification is critical in determining the appropriate pathway in which a novel device gains approval from the FDA to reach the market (Rubin et al., 2020). However, there were still improvements to be made in terms of regulation and device innovation. In 1990, the Safe Medical Devices Act (SMDA) was written for several purposes. The first was to improve post market surveillance of devices by requiring user facilities such as hospitals and nursing homes to report adverse events involving medical devices and authorizing the FDA to require manufacturers to perform post market surveillance on permanently implanted devices if

permanent harm or death could result from device failure. This act was also important in authorizing the FDA to order device recalls and impose civilian penalties for violations of the FD&C Act and modifying the procedures for the establishment, amendment, or revocation of performance standards. Most importantly, this act defined substantial equivalence, which was the standard for marketing a device through the 510(k) program.

The standards for a 510(k) are that it is a premarket submission, proving that a device is marketed as safe and effective and also known as "substantially equivalent" to a legally marketed device (Health, 2020). Class I and II devices are allowed to undergo the 510(k) pathway, which does not require the proof of clinical testing if the device's manufacturers can prove that the device is "substantially equivalent" to an approved device. Substantial equivalence is defined as the new device being as safe and effective as a predicate device. The requirements for determining if a device is substantially equivalent to a predicate is if the new device has the same intended use and same technological characteristics as the predicate or has the same intended use as the predicate, has different technological characteristics and does not raise different questions of safety and effectiveness, and the information submitted to the FDA demonstrates that the device is as safe and effective as the legally marketed device (Health, 2020). This new modification to the regulatory pathway was created to "enable newer versions of existing devices to enter the market" and reduced the amount of time a product was released to a market (Kahan, 1984). Post-1976 devices of lower complexity and risk that are substantially equivalent to a marketed "predicate" device may be cleared through the 510(k) premarket notification process and clinical data is not necessary (Jarow & Baxley, 2015). The only other evidence that a 510(k) requires is nonclinical and beiomachinal benchtop testing and descriptive data.

To understand the importance of a medical device being approved by its "substantial equivalent", it is essential to delineate the differences between a PMA and a 510(k). The PMA process for devices is like the new drug application process used for pharmaceuticals. Extensive testing including valid scientific evidence is necessary for PMA submission and the intended use for the PMA was to "prevent impairment of human health or which present a potential risk of illness or injury" (*Medical Device Recalls and the FDA Approval Process | Medical Devices and Equipment | JAMA Internal Medicine | JAMA Network*, n.d.). The process of gaining premarket approval is a lengthy, meticulous process and requires that the applicant provides full reports of all information concerning investigations undertaken to show whether the device is safe and effective (Kahan, 1984).

Although the Medical Device Amendments do not require adequate and well-controlled investigations for proof of effectiveness, efficacy is proved by scientific evidence. Such scientific evidence means that sponsors of a medical device are required to conduct clinical trials with the device before the PMA is submitted as well as a significant amount of research. Not only must the device undergo clinical trials, but the sponsor of the medical device must obtain approval from the FDA to conduct a clinical investigation (Kahan, 1984). The purpose for a 510(k) is for a more streamlined device approval application compared to the elements required in a PMA application which normally take an extensive amount of time to be approved. As there are more requirements for a PMA application, companies strategically choose to submit a 510(k) application to be more efficient and quickly make profit.

During the drafting of the Amendments, Congress had determined that it would be unfair to subject a post-amendment device to the full extent of regulations if the device were substantially equivalent to a pre-amendment device. This system was deemed better than

previous regulations but increased the chance for low quality medical devices to be approved for consumers and patients. As regulations for medical devices had not been classified before the Medical Device Amendments in 1976, medical devices that had been approved prior to Medical Device Amendments can serve as predicate devices for modern devices. Congress however, found that this was unfair to subject a substantially equivalent post-amendment device to the stringent regulations of the PMA process while the pioneer pre-amendment device was not subject to the same regulations (Kahan, 1984). Although Congress had found this arbitrary, the "regulatory value of close scrutiny of substantially equivalent post-amendment devices is questionable, for it would still leave the pre-amendment device on the market – a device whose safety and effectiveness had not yet been subjected to close FDA review" (Kahan, 1984). If an older device was used as a predicate for a modern device developed currently, the standards for a new device would not be upheld to stringent modern regulations. Such lower standards could allow for less safe and effective devices to be released onto the market as they could contain defects and faulty features like those based on the predicate.

State of the Medical Device Industry

In the first year after the Medical Device Amendments, 2,433 requests to market new devices were submitted to the FDA. Of those applications, only 11 requests were a premarket approval application (PMA) (Kahan, 1984). The remaining applications were 510(k) applications and for experts, it seemed like an increasingly large amount of 510(k) applications would be filed if given the choice between submitting a PMA or 510(k) (Kahan, 1984). After the first decade in which the Amendments were approved, it was noticed by professionals that the provisions considered the most innovative of the Amendment were proven to be the least workable (Adler, 1988). A collaboration from a group of Orthopedic Surgery departments created a study from

2008-2017 that examined the risk of recall and high-risk recall for devices undergoing 510(k) clearance compared with premarket approval (PMA). The definition of risk used in the article is the combination of probability of occurrence of harm and the severity of that harm (MATRIX, 2020). The study reviewed 28,556 devices from varying specialties and did not specifically state the risks of the medical device sample size. However, 97.3% of the recalled devices had received 510(k) approval and 2.7% of the recalled devices had PMA clearance (Dubin et al., 2021). To reduce the number of recalled devices, the authors of the study also agreed with multiple other authors that post marketing surveillance strategies should be increased to supplement the Manufacturer and User Facility Device Experience (MAUDE) database and the MedWatch program, the FDA's medical product voluntary and mandatory safety reporting program for health professionals, patients, and consumers. The authors also suggested increasing the quality of evidence used in pivotal trials performed for devices with PMA (Commissioner, 2021b; Dubin et al., 2021).

In the current situation, whereas most industries have suffered from the pandemic, the biotech industry (which includes the medical device industry) experienced the opposite and experienced a high. From a McKinsey analysis performed by interviewing 20 C-level executives from small and midsize biotechs and venture-capital firms, overall biotech was found to outperform pharmaceuticals and other household-name consumer-goods and technology companies (*Biotech Is Riding a Wave of Growth in Funding. What's next? | McKinsey*, n.d.). As the biotech industry increases in size, more medical devices applications will be submitted and reviewed by the FDA. The 510(k) application process reduces the amount of time it takes for a product to be released onto the market, setting the projection for the medical device industry to go up.

Sources of legitimate expertise in the Medical Device Industry

The FDA has the most influence on the regulation of medical devices and knowing how the FDA was created is critical in understanding its role in regulating medical devices. The introduction of a new regulatory pathway was intended to accelerate the application reader's approval process, which became beneficial for both FDA employees and medical device companies. This acceleration enabled businesses to streamline their product onto the market and highly encouraged innovation amongst startups and new inventors.

Regarding the opinions of leaders in the medical device industry, more companies would rather scale back on oversight of implants and other devices, claiming that it is necessary to promote innovation to more easily approve new devices (*Poll*, n.d.). One of the most well-known medical device companies in the U.S. market is Stryker Corporation. In an interview with John Brown, the chairman of Stryker in 2007, when asked about the lenient FDA approval process or post release oversight and monitoring of a device, Brown responded that the manufacturers are already concerned about potential liability costs, acting as another obstacle to the approval of a new device (Burns, 2007). Overall, Brown expressed that the 510(k) process works well and that the industry does well with proving the safety and efficacy of medical devices through clinical trials (Burns, 2007). Other well-known figures in the biotech industry have expressed a similar sentiment. Although consumer rights' advocates believe that the regulations should be tightened, CEOs would rather alleviate regulations or maintain them (Burns, 2007). In the case of more stringent regulations, companies would undergo greater restrictions to obtain medical device approval. The effect of more stringent regulations would require more resources, such as funding to create and test more prototypes, and the approval process would be prolonged and less streamlined for companies trying to produce their product as fast as possible.

Furthermore, sources of expertise are derived from the developers and manufacturers of medical devices. The responsibilities of the developer and manufacturer are to develop, test, manufacture, and market products that are safe and effective. The most critical goal during the research and design phase is to reduce unavoidable risks to a minimum, as there will always be risk associated with a device. For the developers in the design ideation phase, some teams will receive input from users in the targeted patient population. Expertise provided from the physicians and surgeons that use the device in an operation is also valuable. Synthesizing information from the patient population and the professionals that use the equipment allows for a more comprehensive device design. During the premarket phase, the biomedical product is usually tested within a small and well-defined set of healthy volunteers and patient subjects (Engineering (US) et al., 1988). For the 510(k) pathway, clinical testing is not required, but frequently uses benchtop (nonclinical and biomechanical) tests and descriptive analysis (Dubin et al., 2021). Once the product is approved, the product is marketed with its indications for use, its benefits, and the known risks associated with its use. However, with the limited experience and knowledge gained from a small subset of patients, there are few known serious risks (Engineering (US) et al., 1988).

Role of the Media in exposing Device Defects and Public Opinion

The media has an essential role to play in how it frames the medical device industry for the public. More specifically, risk professionals and scholars have long recognized the media as a key player in the social construction of risk (Dan & Raupp, 2018). When journalists cover risks, they use frames to divide the issue into perspectives that are important and those that are not. An example of a frame that is utilized in the medical device industry is the health severity frame (Dan & Raupp, 2018). The health severity frame presents the impact of a health risk on human

life, which defines the boundaries of the problem and is also issue-specific (Dan & Raupp, 2018). For instance, the news media has utilized progress and generic risk frames at the inception of the nano industry, and after a decade has passed, the frames involving regulation and interplay of market incentives, including regulatory responsibility are the majority of frames used to describe the nanoscience industry (Weaver et al., 2009). In terms of risk, the media can display essential evidence that some medical devices are extremely harmful and can cause life-threatening conditions. Numerous and journalists and patient advocates have discussed the importance of medical device regulations, and the FDA has promised to make "transformative" changes to medical regulations.

The media can similarly be recognized as a central arena for the actors challenging government practice, as those who succeed in publicly defining issues can influence public perceptions and policy outcomes (Fredheim, 2021). One of the most well-known cases of medical device failures covered by the media was the use of Essure. Essure was a form of hysteroscopic sterilization and a surgical mesh that was intended to replace interval laparoscopic sterilization (Rubin et al., 2020). The device was marketed to be safe and effective, however, there were many complications that came with the implantation of the device. The Netflix documentary, "The Bleeding Edge", provided another form of media that presented critical background information and expertise surrounding the Essure device as a risk case study, while analyzing the 'rapid innovation' objective encouraged by the FDA. Not only did the documentary spread awareness, but patient groups and consumer rights' advocates also informed the public of issues with Essure. After the device had garnered attention for its complications, the FDA released a statement saying that the FDA themselves would conduct a more thorough post market evaluation of Essure (Health, 2022). This event signified that the FDA listened to the

demands of those working directly and indirectly with the device. The increase of medical device coverage and digital media in general, allows the general public to produce knowledge, including their own experiences, and advocate for changes in health-related policies and practices, in particular, the changes that affect treatment (Petersen et al., 2019).

As mentioned previously, the media can highly influence public opinion, and public opinion acts as an influential factor in the government's policy making. One of the earliest media stories about a faulty medical device was the Dalkon Shield (Pisac & Wilson, 2021). The Dalkon shield was a contraceptive device inserted into a woman's uterus for pregnancy prevention and was marketed as a better alternative to contraceptive pills. Three years after its release onto the market, 2.2 million devices were implanted in American women, but due to the limitations in regulatory requirements, there was no federal oversight of the device's premarket assessment (Pisac & Wilson, 2021). However, post market research revealed that the device had a 4.7% pregnancy rate and a 6.3% rate of device expulsion in Dalkon Shield users and these statistics did not match those provided by the manufacturer. Even worse, women who became pregnant were also at a higher risk for complications, which included septic pregnancy and maternal death. As a result of the Dalkon Shield post market research, the government found that pre- and post market regulation were critical and that a decentralized regulatory authority could be dangerous. Therefore, amendments were made to the Medical Device Amendments of 1976 (Pisac & Wilson, 2021).

Improvements to the Medical Device Application Process

Congress made amendments to the FD&C Act as a response to focus its resources on medical devices that present the greatest risk to patients (Commissioner, 2018). After 1990,

Congress passed the Food and Drug Administration Modernization Act (FDAMA) in 1997, which created the "least burdensome" provisions for premarket review, permitted the use of data from studies of earlier versions of a device in premarket submissions for new versions of the device, and created the option of accredited third parties to conduct initial premarket reviews for certain devices (Commissioner, 2018). The last option seemed to allow for a more stringent testing process, which was in favor of device users. However, to increase innovation, the De Novo program was also established in which novel low-to-moderate risk devices could be classified into Class I or II instead of automatically classifying them into Class III.

In 2010, the Institute of Medicine (IOM) Committee on the Public Health Effectiveness of the FDA 510(k) Clearance Process conducted a workshop on medical devices. The IOM committee had decided that changes in the 510(k) process potentially would better foster innovation and ensure confidence that the process results in safe and effective medical devices (Medicine et al., 2010). The committee also recommended that the Class II medical device approvals should not reference pre-amendment products and should be based on objective performance criteria that ensure safe and effective use (Medicine et al., 2010). Patient and consumer advocates agreed with the report and Michael Carome, MD, deputy director of Public Citizen's health research group has long asserted that the 510(k) process allows potentially unsafe devices on the market (*IOM Device Report Gets Strong Response*, 2011).

The most recent amendment was the Food and Drug Administration Reauthorization Act (FDARA) which reauthorized the medical device user fee program (MDUFMA), authorized risk-based inspection scheduling for device establishments and prescribed other process improvements related to device establishment inspections, decoupled accessory classification from classification of the parent device, and lastly, required the FDA to conduct at least one pilot

project to explore how real-world evidence can improve post market surveillance (Health, 2021). The MDUFMA granted the FDA the authority to collect user fees for select medical device premarket submissions to help the FDA improve efficiency, quality, and predictability of medical device submission reviews and helped the FDA regulate more premarket submissions (Health, 2021). Mentioned previously, one of the methods of improving medical device regulation is using post surveillance mechanisms. The FDA has created various systems such as the Adverse Event Reporting System and the MedWatch program which take in input from both volunteers and from records of adverse events. Such programs would require thorough fact checking to ensure that only the most accurate information appears on the database.

From a business standpoint, companies could include human factors engineering as a critical piece in the medical device development process. The human factors engineering perspective, also known as user-centered usability engineering methods) ensures that the development of high quality and well designed medical devices are in tune with patient and user needs (Money et al., 2011). Companies should also prioritize a Failure Mode & Effects Analysis (FMEA) that identifies and addresses potential problems in the device's mechanism before an adverse event occurs (Kane & Kane, n.d.). Another component to be prioritized is the risk analysis conducted by the medical device company working alongside the manufacturer. Based on the previous amendments, the FDA takes into consideration both the opinions of the medical device companies and the public.

Although many amendments have been made to the FD&C Act, it is nevertheless important for the media and users to be cognizant of the risks associated with a device. After controversies with ineffective contraceptive devices and surgical meshes as well as devices that did not uphold the standard at which they were marketed with, patients and users of medical

devices should be wary of the risks that come with the use of a medical device. It would be important for users to research and investigate the known risks behind the use of a medical device.

Discussion

This paper aimed to synthesize the conversation of modifying medical device regulations to make devices safer for consumers. In this paper, I discuss the current challenges with the medical device approval process by defining the biotech industry's regulatory history, by defining the period before the FD&C Act, and the period after. I also analyzed the state of the medical device industry by looking at the FDA application statistics as well as included the expertise of professionals in the industry such as the CEOs of major medical device companies and their engineers. Finally, I discuss the improvements to the FDA's approval process and the solutions from experts and advocate groups.

Furthermore, previously the FDA highly encourages rapid innovation, more so than the safety of users as these devices are intended to increase a patient's quality of life. However, as more people become aware of the risks posed by medical devices, this led to a shift in how the FDA currently perceives the cost-benefit analysis of innovation vs safety. The FDA is striving toward a balance between rapid innovation and consumer safety. Many journal articles have been released discussing the perspectives of both industry leaders and consumer advocates and have criticized the FDA for not having stringent regulations.

Current improvements have increased the regulations placed upon the medical device industry and the FDA has released updated medical device regulations that address concerns of scholars and professionals in the medical device industry. Further research on improving the

regulation of the medical device industry can be done but are limited by the governing bodies mentioned in this study. Lastly, it is essential that consumers are aware of the risks that medical devices might have using adverse event databases and other programs that the FDA offers.

References

Adler, R. (1988). The 1976 Medical Device Amendments: A Step in the Right Direction Needs Another Step in the Right Direction. *Food, Drug, Cosmetic Law Journal*, *43*(3), 511–532.

Biotech is riding a wave of growth in funding. What's next? | McKinsey. (n.d.). Retrieved March 11, 2022, from https://www.mckinsey.com/industries/life-sciences/our-insights/whats-ahead-for-biotech-another-wave-or-low-tide

Burns, L. R. (2007). Growth And Innovation In Medical Devices: A Conversation With Stryker Chairman John Brown. *Health Affairs*, *26*(Supplement 2), w436–w444. https://doi.org/10.1377/hlthaff.26.3.w436

Commissioner, O. of the. (2018, November 3). *Food and Drug Administration Modernization Act (FDAMA) of 1997*. FDA; FDA. https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-administration-modernization-act-fdama-1997

Commissioner, O. of the. (2021a). How did the Federal Food, Drug, and Cosmetic Act come about? *FDA*. https://www.fda.gov/about-fda/fda-basics/how-did-federal-food-drug-and-cosmetic-act-come-about

Commissioner, O. of the. (2021b, December 16). *MedWatch: The FDA Safety Information and Adverse Event Reporting Program*. FDA; FDA. https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program

Dan, V., & Raupp, J. (2018). A systematic review of frames in news reporting of health risks: Characteristics, construct consistency vs. name diversity, and the relationship of frames to framing functions. *Health, Risk & Society*, *20*(5–6), 203–226. https://doi.org/10.1080/13698575.2018.1522422

Dubin, J. R., Simon, S. D., Norrell, K., Perera, J., Gowen, J., & Cil, A. (2021). Risk of Recall Among Medical Devices Undergoing US Food and Drug Administration 510(k)

Clearance and Premarket Approval, 2008-2017. *JAMA Network Open*, *4*(5), e217274. https://doi.org/10.1001/jamanetworkopen.2021.7274

Engineering (US), N. A. of, Medicine (US), I. of, & Ekelman, K. B. (1988). Perspectives of Industry, the Physician, and Government. In *New Medical Devices: Invention, Development, and Use*. National Academies Press (US). https://www.ncbi.nlm.nih.gov/books/NBK218287/

Fredheim, N. A. G. (2021). Life, death or drugs: Actor framing power on the news media coverage of health care policy. *European Journal of Communication*, *36*(3), 270–285. https://doi.org/10.1177/0267323120978721

Health, C. for D. and R. (2020, March 13). *Premarket Notification 510(k)*. FDA; FDA. https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k

Health, C. for D. and R. (2021). A History of Medical Device Regulation & Oversight in the United States. *FDA*. https://www.fda.gov/medical-devices/overview-device-regulation/history-medical-device-regulation-oversight-united-states

Health, C. for D. and R. (2022). Essure Benefits and Risks. *FDA*. https://www.fda.gov/medical-devices/essure-permanent-birth-control/essure-benefits-and-risks

IOM Device Report Gets Strong Response. (2011, July 29). https://www.medpagetoday.com/publichealthpolicy/fdageneral/27806

Jarow, J. P., & Baxley, J. H. (2015). Medical devices: US medical device regulation. *Urologic Oncology: Seminars and Original Investigations*, *33*(3), 128–132. https://doi.org/10.1016/j.urolonc.2014.10.004

Kahan, J. S. (1984). Premarket Approval versus Premarket Notification: Different Routes to the Same Market. *Food, Drug, Cosmetic Law Journal*, *39*(4), 510–525.

Kane, R., & Kane, R. (n.d.). *Guidance for Performing Failure Mode and Effects Analysis with Performance Improvement Projects*. 14.

MATRIX, O. S. A. (2020, May 1). ISO 14971 Medical Device Risk Management | Oriel STAT A MATRIX. *Oriel STAT A MATRIX Blog*. http://www.orielstat.com/blog/iso-14971-risk-management-basics/

Medical Device Recalls and the FDA Approval Process | Medical Devices and Equipment | JAMA Internal Medicine | JAMA Network. (n.d.). Retrieved October 17, 2021, from https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/227466

Money, A. G., Barnett, J., Kuljis, J., Craven, M. P., Martin, J. L., & Young, T. (2011). The role of the user within the medical device design and development process: Medical device manufacturers' perspectives. *BMC Medical Informatics and Decision Making*, *11*(1), 15. https://doi.org/10.1186/1472-6947-11-15

Petersen, A., Schermuly, A. C., & Anderson, A. (2019). The shifting politics of patient activism: From bio-sociality to bio-digital citizenship. *Health*, *23*(4), 478–494. https://doi.org/10.1177/1363459318815944

Pisac, A., & Wilson, N. (2021). FDA Device Oversight From 1906 to the Present. *AMA Journal of Ethics*, *23*(9), 712–720. https://doi.org/10.1001/amajethics.2021.712

Poll: Public wants strong medical device oversight. (n.d.). CR Advocacy. Retrieved March 10, 2022, from https://advocacy.consumerreports.org/press_release/poll-public-wants-strong-medical-device-oversight/

Rubin, A., Chen, J.-F., Veade, A., & Hagemann, I. S. (2020). Pathologic findings in fallopian tubes of women with chronic pelvic pain after Essure placement. *Contraception*, *102*(2), 133–136. https://doi.org/10.1016/j.contraception.2020.04.010

Weaver, D. A., Lively, E., & Bimber, B. (2009). Searching for a Frame: News Media Tell the Story of Technological Progress, Risk, and Regulation. *Science Communication*, *31*(2), 139–166. https://doi.org/10.1177/1075547009340345