MEDICAL DEVICE RECALLS: THE NEED FOR AN UPDATED PROTOCOL IN THE 510(k) APPROVAL PROCESS FOR MEDICAL SAFETY AND EFFICACY

BY

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ABSTRACT

Title of Thesis: Medical Device Recalls: The need for an Updated Protocol in the 510(k) Approval Process for Medical Safety and Efficacy

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Signature of Thesis Advisor

Introduction:

A medical device is described as an instrument, machine, implant, software, reagent, or apparatus that is intended to be used for medical purposes, which include, but not limited to, diagnosis and treatment. [1] Medical devices vary with intended use and range from low risk (tongue depressors or elastic bandages) to moderate risk (Contact lenses and pregnancy kits) to high risk (artificial pacemakers and respiratory ventilators). The United States Food and Drug Administration (FDA) regulates all medical devices by a classification system based on the risks associated with their use. Devices are classified either Class I, II, or III. Class I devices are associated with lowest risk, Class II at moderate risk, and Class III the highest risk and are described as life sustaining. After classification, medical devices undergo a specific regulatory pathway for approval before market such as: Premarket Approval (PMA), Premarket Notification (510(k)), and Humanitarian Device Exemption (HDE). Overall, 35% of medical devices are categorized as Class I and roughly 90% are exempt from the pre-

market approval process. About 52% of the medical devices in Class II must be approved by the FDA. Of these devices, about 90% require FDA review but roughly 10% only have to go through pre-market approval or humanitarian device exemption. A 510(k) submission requires that there is a substantially equivalent device already on the market that has been through one of the three classifications prior to marketing to the public. The PMA process is more demanding; it must be demonstrated that the device is safe and effective when used. Most Class III devices require a PMA application; Class I and II require the 510(k). It has come to light that the current 510(k) approval process is not an effective approval process for devices any longer due to increasing recalls of medical devices.

Purpose:

The goal of my study was to determine whether the FDA has 510(k) process more stringent since three pivotal studies were published 5 years ago. I did this by identifying how often 510(k) and PMA devices were recalled in a three-month period between January and March 2019.

Hypothesis:

Medical devices approved by the 510(k) process are recalled more often than PMA approved devices.

Methods:

Data was collected from January 1, 2019-March 31, 2019 from the FDA Medical Devices Database. The following additional subcategories were added to each recall to determine a clear outcome of results: Product Code, Approval Process, Review Panel, and Class of Recall. The data was analyzed using SPSS and PRISM softwares for statistical testing and data visualization.

Results:

During the time of the study, the FDA approved 1247 new applications through the PMA and 510(k) process. During the same time, 392 devices were recalled. 94.6% (371) were classified as a 510(k) recall and 5.4% were a PMA recall. Chi-Square statistical testing was performed to check that variables are completely independent of each other. It shows that $p<0.001$. The top review panels were Radiology, Cardiology, General Hospital, Orthopedics, Clinical Chemistry, General and Plastic Surgery, and Gastroenterology/Urology. Each recall was identified as a Class I, II, or III along with describing if the recall is considered a malfunction, mislabeling, or sterilization issue. Out of the 392 total recalls, 43 are Class I, 330 are Class II, and 10 are Class III.

Conclusion:

In the past five years, there still hasn't been a change to the 510(k) process. The data proves there is still a need for a more rigorous approval process.

INTRODUCTION

Throughout history, rapid advances in science have led to the development of many new and different medical devices. Many of these devices were also unsafe and fraudulent, because of lack of federal regulation. In 1976, the Medical Device Amendments was passed by Congress, which granted the FDA's authority over medical devices. Congressional amendments to the Federal Food, Drug, and Cosmetic Act of 1938 (FDCA) were also expanded to give the FDA authority to clear devices before marketing. Until 1976, Congress has never enacted specific legislation governing the regulation of medical devices. Prior to that date, public protection from defective devices depended on FDA's enforcement of the limited provisions in the FDCA, and on legal interpretations that extended FDA's regulatory authority over drugs to devices. [2]

As new technologies continue to emerge, the challenges of determining how products will be regulated, and navigating the premarket clearance and approval process, continues and has its hindrances. The initial step includes deciding the medical device classification and regulatory pathway, which is not often straightforward. Once products are cleared or to market, companies face rigorous regulatory requirements to keep them there. The FDA's Center for Devices and Radiological Health (CDRH) is responsible for regulating companies that manufacture, repackage, re-label, and/or import medical devices sold in the United States. [3] A decision is solely made by the applicant depending on the classification and if a "substantially equivalent" medical device has been approved.

The FDA identifies medical devices into three classifications (Class I, Class II, or Class III). The classification is based on the device complexity, technical characteristics,

degree of invasiveness, and potential harm if misuse occurs. [4] Class I devices present minimal risk to patients. Examples are bedpans, tongue depressors, or stethoscopes. Class II devices are described as having a moderate risk to consumers and patients. Examples of Class II devices are syringes, contact lenses, surgical gloves and pregnancy test kits. About 52% of the medical devices in Class II must be approved by the FDA required 510(k) premarket notification. Class III devices are described as the highest potential harm or risk to a patient or consumer. These devices are described as life sustaining. Examples of Class III devices are pacemakers, breast implants, and implanted prosthetics.

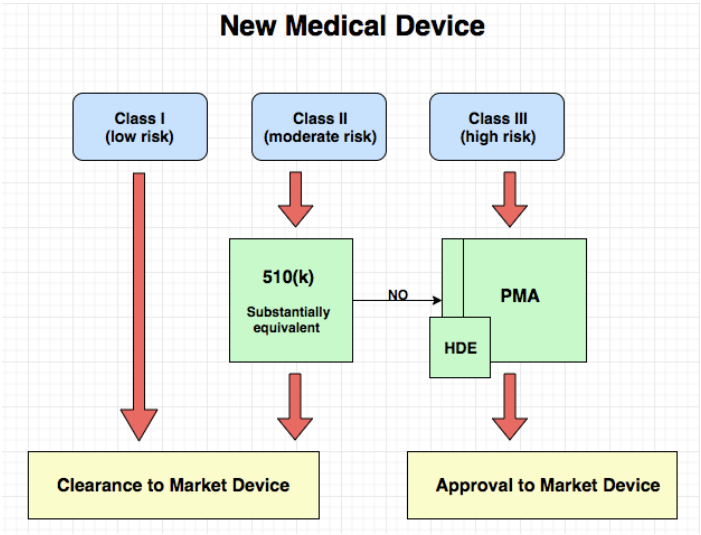
All medical devices are regulated in the United States by three different pathways, Premarket Notification (510(k)), Premarket Approval (PMA), and Humanitarian Device Exemption (HDE). A 510(k) submission requires that there is a substantially equivalent device already on the market that has been through one of the three classifications prior to marketing to the public. The PMA process is more demanding, it must be demonstrated that the device is safe and effective when used. Most Class III devices require a PMA application, whereas Class I and II usually require the 510(k). Extensive clinical trials, animal and laboratory studies are required for all PMA's. The exception is the humanitarian devices. On June 26, 1996, the FDA issued a final rule to carry out provisions of the Safe Medical Devices Act of 1990 regarding humanitarian use devices (HUD). A HUD is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. A device manufacturer's research and development costs could exceed its market returns for diseases or conditions affecting small patient populations, as such, necessitating the HDE. [5] For the purpose of my research, I excluded any HDE devices.

Recalls on the devices are rare and the studies included in my research also had none to report.

Table 1: Overview of FDA Classification and Regulatory Processes

Class	Risk	Example	Safety Controls	Regulatory Pathway
I	Low	Bedpans, tongue depressors, or stethoscopes	General	510(k)
II	Medium	Syringes, contact lenses, surgical gloves and pregnancy test kits.	General and Special	510(k) or PMA
III	High	Pacemakers, breast implants, and implanted prosthetics	General, Special, and Premarket Notification	PMA

Figure 1: Typical Device Approval Process



About 35% of all medical devices are associated in the Class I category but about 90% are exempt from the PMA process. About 52% of the medical devices in Class II must be approved by the FDA required 510(k) premarket notification. Of the Class III

devices, about 10% require the FDA review through PMA or HDE. The Institute of Medicine Committee on the Public Health Effectiveness of the FDA 510(k) Clearance process recommended to the FDA that the entire 510(k) is "fundamentally flawed" and should be replaced with a completely different system. [6]

All medical device recall information can be found on the FDA Medical Devices Database. The database was established in 2009 to provide information to the public about any medical device recall. The system is updated monthly.

Background

Several studies were conducted on recalled devices in order to determine whether there were issues with the device approval process. The first study, by John C. Somberg, MD et.al, was conducted between January 2005 to December 2012 and showed that 19% of all recalled medical devices were approved by the PMA process whereas 81% were approved by the 510(k) process. Half of the recalls were discovered within the first two years the devices were on the market. Cardiovascular devices represent the largest class of recalled devices during this time period. The proportion of recalled PMA and 510(k) cardiovascular devices were the same as for all medical devices until 2011, but 510(k) recalls dramatically decreased in 2012 to the lowest recall rate seen. The article suggests that the 510(k) process needs modification in order to become more rigorous, which could include, but is not limited to, a conditional 2-year approval and a mandatory registry in hopes of reducing 510(k) recalls. [7]

Another study by Diana M. Zuckerman, MD et al. details medical device recalls from 2005 through 2009. The investigators looked closely at category Class III recalls, which can result in serious health issues or death. One hundred thirteen recalls were

found and the FDA approved only 19% of these devices using the PMA approval process. Seventy-one percent were approved through the less stringent 510(k) process. Again, the researchers concluded the need for change in the approval process. [8]

In a third study, by Drs. Sheena Galhotra and Joseph Maurice, investigators took a closer look at one specific category of recalls, obstetrics and gynecologic devices. Their findings were very similar to the studies mentioned above which looked at a wide range of devices. Data was recovered from the FDA Medical Devices Database from November 1, 2002 to December 31, 2017 for devices with recalls using the PMA and 510(k) process for FDA approval. A total of 2,249 recalls were captured. Of those, 685 devices were approved through the PMA approval process and 1564 devices from the 510(k) approval process. "There was an overall increase in absolute device recall number over time in the 510(k) process, whereas the number of recalls in the PMA process did not change with time." [9] What was concluded is a call for improvement and increased scrutiny of the 510(k) approval process.

My research was conducted to see what changes, if any, have been implemented since the three pivotal studies regarding the lack of rigor in the 510(k) approval process to lower incidences of device recalls. I focused on device recalls during the period of January 1, 2019 to March 31, 2019. Information regarding device recalls was collected from the FDA approved medical device reported in the FDA Medical Device Database across all review panels. Of these recalls, 371 (94.6%) were classified as 510(k) and 21 (5.4%) were approved by the PMA process. The largest classification of recalls was in Class II, medium risk to patients. The Class II recalls resulted in 269 (82%) malfunctions, 44 (13%) mislabeled , and 17 (5%) with sterilization issues. Thus, it appears that even

though the three pivotal studies have clearly indicated the flaws in the 510(k) approval process these were not rectified or improved. What is especially alarming is the amount of recalls in the short period of time.

METHODS

Study Design:

My study design is an observational cross-sectional design. I was collected data from a representative subset (PMA & 510(k)) from January 1, 2019 to March 31, 2019. The FDA Medical Device Database is available to the public and cannot be traced back to the patient using the medical device; therefore approval from the Institutional Review Board was not needed. MAUDE is updated monthly.

Data was retrieved and analyzed from Medical Device Database from January 1, 2019 to March 31, 2019. The following information was noted: recall number, product description, recall classification, product code, approval process, review panel, class of recall, firm name, and finally, reason and description for the recall.

Statistical analysis:

Microsoft Excel, PRISM, and SPSS v26 were used for statistical analysis. There were a few double entries found in the data that were omitted. Descriptive analysis was performed on all variables in SPSS and PRISM. Chi-Square statistical testing was performed to check that variables are completely independent of each other. It shows that the p value is significant at $p<0.001$.

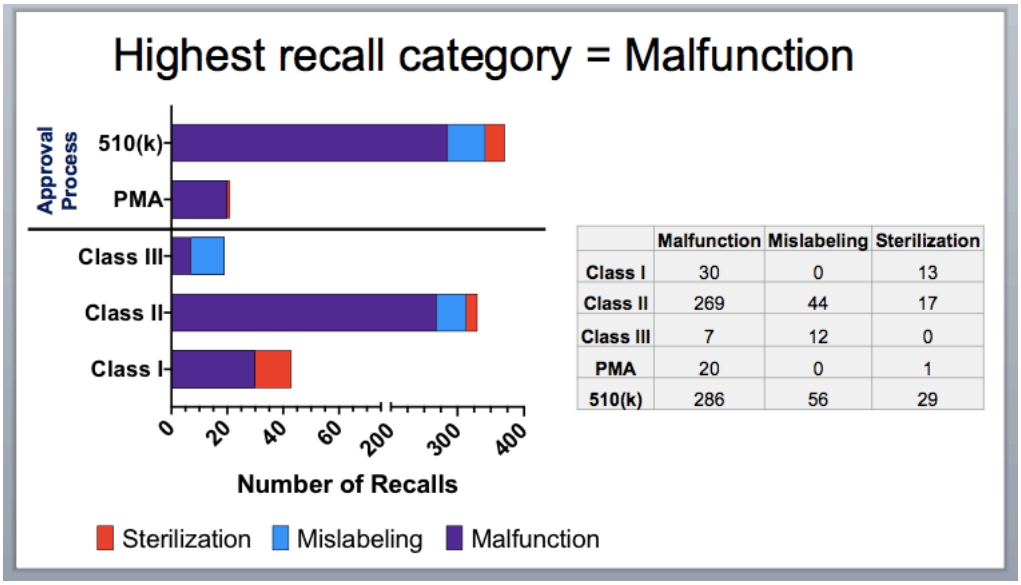
Hypothesis:

Medical devices approved by the 510(k) process are recalled more often than PMA approved devices.

RESULTS

The highest recall category among the device recalls was malfunctions. A few reasons given were false/positives with software, parts of devices not working properly, failing devices, or even missing pieces which in turn caused a malfunction in the device. Out of the 392 recalls, the 501(k) approvals reported 286 recalls because of malfunctions while the PMA approvals reported 20. The second highest category was mislabeling. Devices were simply mislabeled before marketing. The 501(k) reported 56 and the PMA reported none. There were not a significant amount of sterilization issues. The 510(k) approvals reported 29 recalls, and the PMA reported only one. When looking at these recalls by Category and Class, Class II devices are the highest which are approved by the 510(k)-approval process.

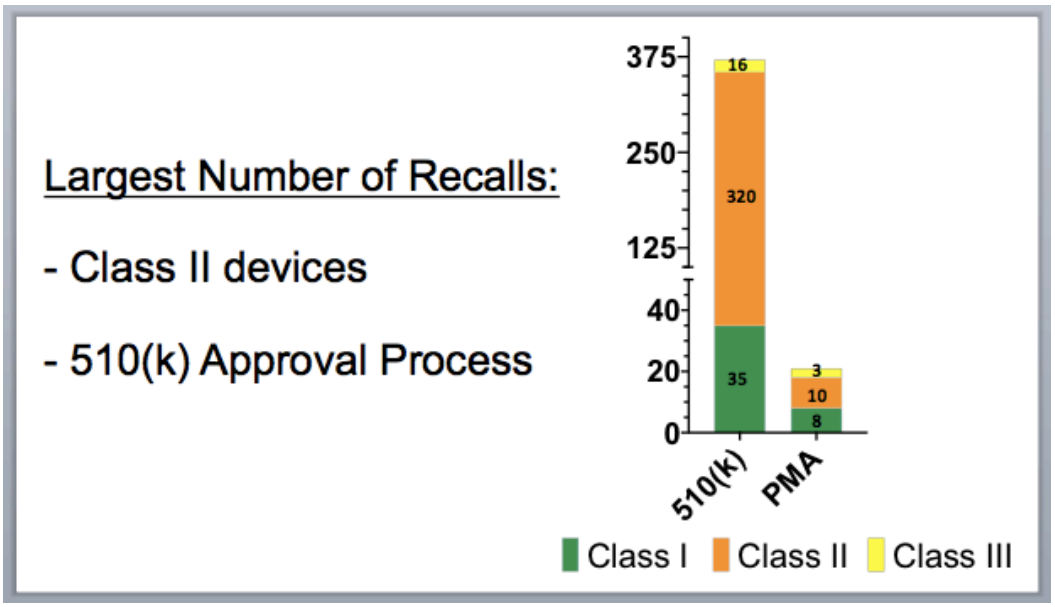
Figure 2: Number of Recalls by Category



	Malfunction	Mislabeling	Sterilization
Class I	30	0	13
Class II	269	44	17
Class III	7	12	0
PMA	20	0	1
510(k)	286	56	29

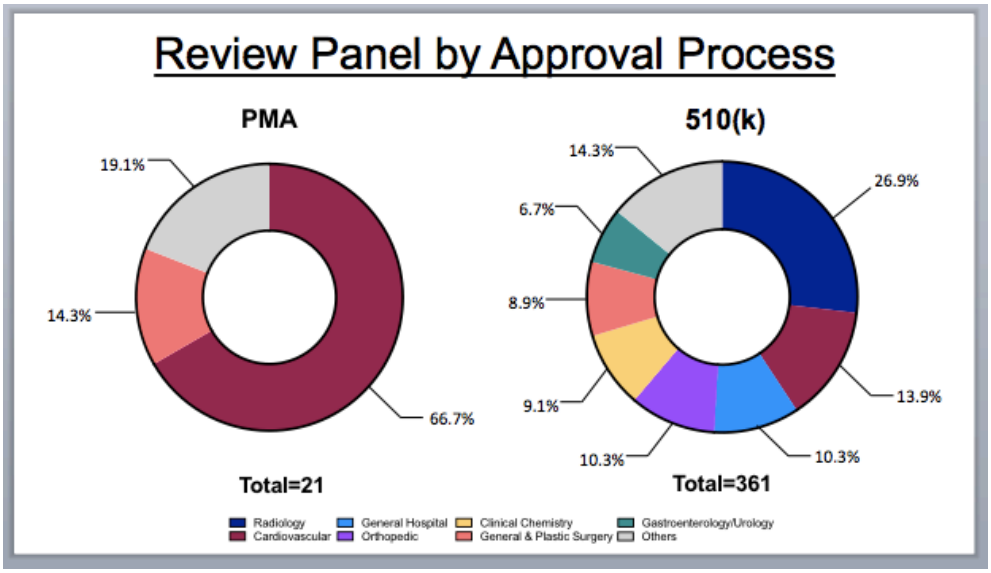
The 510(k) approval process reported 320 recalls from Class II devices, 35 from Class I and 16 in Class III. The more rigorous PMA approval process has far less recalls in all Class Categories. Only eight in Class I, ten in Class II, and three in Class III.

Figure 3: Largest Number of Recalls



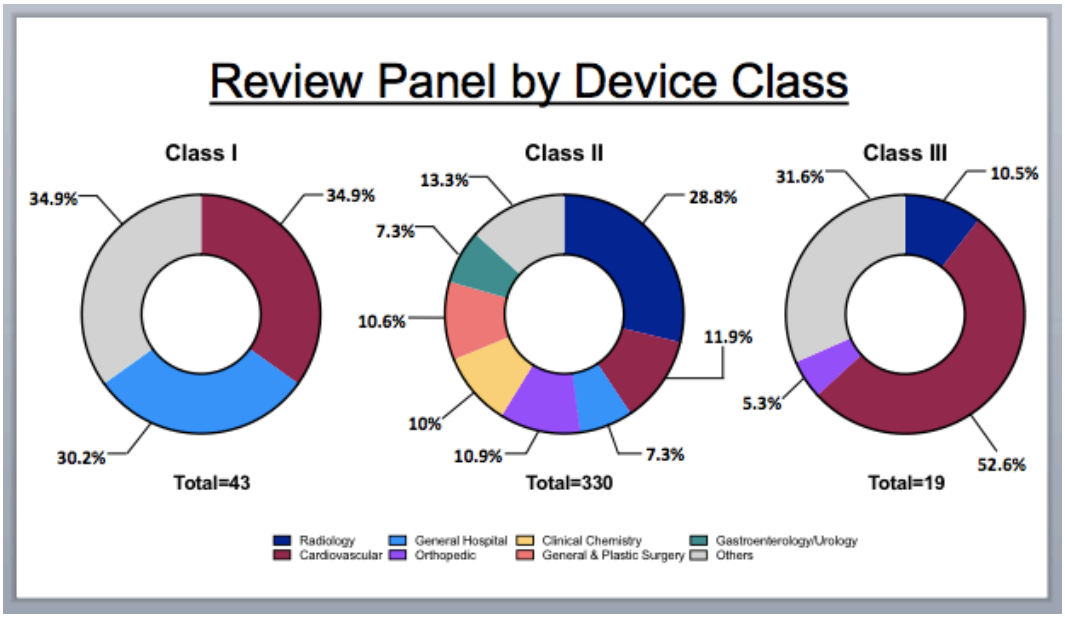
Studying recalls reported by the PMA and 510(k) process, the 510(k) reported a majority, 361 out of 392. Radiology was the highest class with Cardiovascular as second with 13.9% of the recalls. Compared to Dr. Somberg's study five years ago, this continues to be a very high rate. General Hospital and Orthopedics devices tied with 10.3% of the recalls and followed by Clinical Chemistry, General and Plastics Surgery, and Gastroenterology/Urology. There were about ten other review panels that fit into the "other" categories that accounted for 14.3%. The PMA approvals reported 21 recalls with Cardiovascular being the largest category with 66% and General and Plastic Surgery with 66.7%.

Figure 4: Review Panel by Approval Process



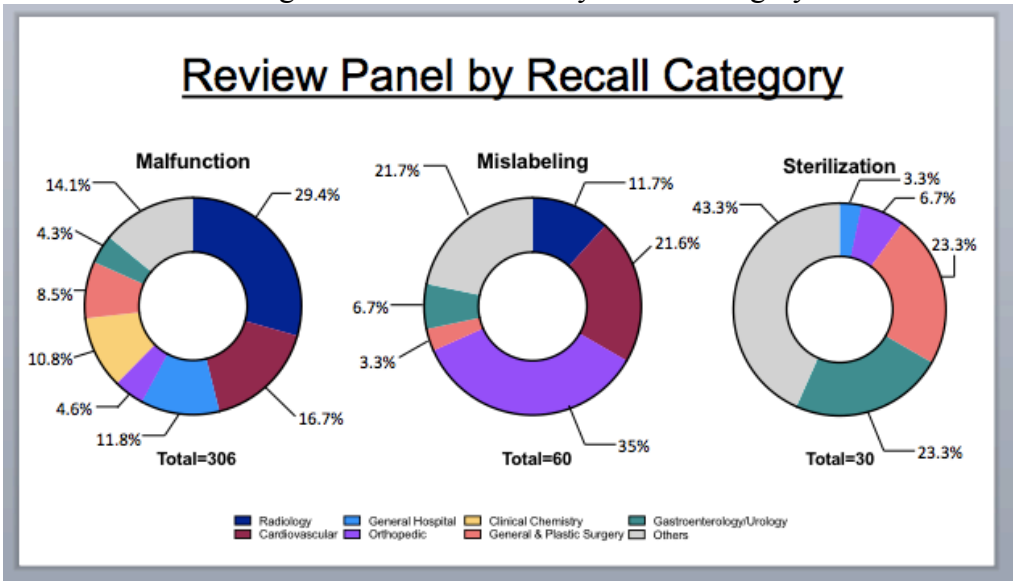
Review Panels are carefully reviewed when recalls are reported to the Medical Device Database. Class II devices are the highest among the device recalls. Radiology is the highest, and Cardiology is the second highest.

Figure 5: Review Panel by Device Class



When reviewing recall category, malfunction is the highest shown with Radiology reporting 29.4% and Cardiology reporting the second highest recalls at 16.7%. Mislabeling was fairly high reporting 60 recalls and most were from Orthopedics. Some of these recalls reported were mislabeled kits for knee and hip surgeries. Sterilization issues were more prevalent in the other ten review panels not shown, but Gastroenterology/Urology and General and Plastic Surgery report 23.3%.

Figure 6: Review Panel by Recall Category



DISCUSSION

A modification to the 510(k) approval process is recommended and requires a more rigorous and thorough process, similar to the PMA approval process. Most of the recalls in my research were Class II and the recall reason was malfunction. One suggestion could be, once a 510(k) medical device is approved, it would be on a conditional basis. Reviewers could ask for updated data and information after a six-month period to determine if the device is in fact safe for patients and consumers.

A second suggestion to regulate the 510(k) approval process would be to mandate all users to report any defective devices. Having clear data on all devices would provide health care providers, patients, and consumers of possible risks. In the future I would also suggest a new classification within all Class II medical devices. Depending on the use of the device and the use intended, some devices could be classified as Class II (b), which would require clinical trials and/or animal and laboratory studies to test the safety and efficacy for patients and consumers. Finding issues with this class of devices early would eliminate a good portion of recalls reported, especially in the malfunction category.

Lastly, a more robust system is needed for physicians and health care workers. National Evaluation System for Health Technology (NEST) is a database that is in the process of helping these device recall issues. NEST reflects the FDA's commitment to meaningful change within the post market surveillance system and adopts regulatory practices and reporting systems similar to those used in the aviation and nuclear industry. [10] NEST aims to address the drawbacks of the FDA Medical Device Database so physicians will have access to all devices that includes statistical analysis and recall information to make an informed decision whether to use the medical device or not.

CONCLUSION

The 510(k) approval process is not an effective medical device approval process. There must be a more effective process to reduce recalls and increase safety and efficacy. My research confirms that the approved process still is deficient today, as previously noted in earlier research. Class II devices continue to lead in recalls and this must be addressed. Patients and consumers have the right to know about devices that could potential cause harm. Hopefully NEST will help device reporting become more accurate

and streamline allowing the health care providers access to detailed information. Until there is change in the current practices, safety and efficacy will continue to be an issue.

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