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The Use of Predicates in FDA Regulation of Medical Devices: A Case Study of Robotic Surgical Devices

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ABSTRACT

In the last decade, a number of high profile medical device recalls have drawn attention to the regulatory approval process, particularly the streamlined process for devices considered "lower risk" known as the 510(k). Approval of medical devices through the 510(k) Process is not based on clinical data, but rather on "substantial equivalence" to predicate devices approved pre-1976 or legally marketed thereafter. A predicate device is one that shares the same intended use as the new device and technological characteristics which are either the same or different without introducing new safety hazards. Many scholars believe that the premise of approving medical devices based on similarity to existing devices is inherently flawed. In particular, there is worry that presence of technology creep between predicate devices can lead to the approval of medical devices which ultimately do not resemble the original device for which clinical evidence exists, even as that evidence is used to validate device safety.

Given these concerns about the safety of the established regulatory process, this thesis explored the impact of predicate creep within the 510(k) Process through a case study of a Robotic Assisted Surgery (RAS) devices, with particular focus on the Intuitive Surgical Da Vinci Surgical System. Through the development of new methodologies using publicly available data to measure predicate creep, this research traces the predicate ancestry of several RAS devices to assess the current impact and implications of predicate creep on the current regulatory process. The study concludes that there is significant evidence of predicate creep within the approval process and recommend new guidelines for classifying device risk and subsequent evidentiary requirements within the 510(k) Process, to reduce the number of devices with high levels of potential risk to public safety released onto the market.

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GLOSSARY/ABBREVIATIONS

Cryosurgery - Surgical procedure utilizing extreme cold to destroy abnormal or diseased tissue

Direct Predicate – The predicate device to which a subject device claims first generation equivalence; the predicate device listed on a 510(k) approval application

Endoscope - an instrument that can be introduced into the body to give a view of its internal parts

Endoscopic and Laparoscopic Instruments - Surgical instruments specifically designed for use in laparoscopic or endoscopic surgical procedures. Typically featuring elongated shafts and cable-controlled mechanisms to allow the surgeon a range of motion inside the body through a small incision.

Laparoscope - A small fiberoptic instrument inserted through the abdominal wall to view the interior of the abdominal cavity

Laparoscopic Surgery - A surgical procedure performed using small incisions in the body, usually with the aid of a camera. Also known as minimally invasive surgery (MIS)

Originating/Ultimate Predicate - The oldest device to which substantial equivalence can be traced in a branch line

Predicate - A device upon which a determination of substantial equivalence is made

Predicate Creep – The introduction of technology creep over time in medical devices cleared via the 510(k) Process. Typically refers to instances where new technological characteristics are introduces without significant scientific evidence to support claims of safety and efficacy

Subject - The device receiving approval based on a given predicate

Trocar - A pen-shaped medical device used in laparoscopic surgery to provide an access port for endoscopic instruments into the abdomen. The device consists of three components, an obturator (the pointed tip), a cannula (a hollow tube), and a seal.

Technology Creep – The development of new technological advancements over time through a cumulative series of incremental changes from preceding technologies

Table 1: Definitions of commonly used abbreviations

Abbreviation	Term	Definition
510(k)	510(k) Process	The process used to clear Class I and II medical devices for market
CDRH	Center for Devices and Radiological Health	The Office of the FDA specifically in charge of medical devices
FDA	United States Food and Drug Administration	The government agency responsible for medical device regulation
MDA	Medical Device Amendments of 1976	The law which created the current regulatory structure and classification system for medical devices
NSE	Not Substantially Equivalent	A declaration that a device is not cleared via the 510(k) Process
PMA	Pre-market Approval Process	The process used for approval of Class III medical devices
SE	Substantially Equivalent	A declaration that a device meets the requirements for clearance via 510(k)

1 INTRODUCTION

The current FDA regulatory guidelines for medical devices were created by the 1976 Medical Device Regulation Act (MDRA), which was passed by Congress in response to concerns about the safety of approved medical devices. The purpose was to create a standardized regulatory approval framework that would ensure safety, efficacy, and proper labeling of medical devices. The MDRA established a classification system for medical devices based on their intended use and level of potential risk to patients. Class I contains low risk devices, such as dental floss or tongue depressors. Class II contains moderate to high risk devices that are not considered life sustaining or supporting, ranging from acupuncture needles to robotic assisted surgical platforms. Class III contains the highest risk devices, those which are life sustaining or supporting, such as pacemakers and most medical implants.

Devices which fall into Classes I and II may use a streamlined approval process, known as the 510(k) Process. The process is based on "substantial equivalence" to devices approved pre-1976 or legally marketed thereafter, known as predicate devices. The FDA determines the amount of testing performed based on the level of substantial equivalence to the identified predicate device(s) for both function and technological characteristics and any existing standards applicable to the device. Devices in Class III are required to go through a more stringent and individualized approval process, known as the Pre-Market Approval (PMA) process; this includes clinical trials and more extensive testing requirements.

In the last decade, several high profile device recalls have drawn attention to the regulatory approval process. After studies found that 71% of high risk recalls (those issued due to serious health risks or deaths) involved devices approved through the 510(k) Process, researchers began to raise questions about the validity of the 510(k) Process as a broad approval mechanism (Zuckerman, Brown & Nissen, 2011).

One of the issues raised as a potential flaw is the use of "predicates" to streamline the approval process. A predicate is any existing legally marketed device which possesses the same intended use as the new device and either the same or, if specific criteria are met, different technological characteristics. The additional criteria for validation of a predicate possessing different technological characteristics is sufficient evidence to determine that the new device does not raise additional questions of safety or efficacy past those addressed in the predicate, and that it is at least as safe and effective as the established predicate (FDA, 2014).

The use of a predicate device to establish safety and efficacy for a new device, when there are no substantial differences between the form or function of the two devices, is straightforward and logical. However, this same approval mechanism is also used under a clause in the definition of substantial equivalence permitting "different technical characteristics" for many Class II devices which possess significant differences in form or function, both physically and technologically, compared to the predicate device. Although the FDA does require some evidence of safety and efficacy in these cases, many scholars believe that the existing measures are insufficient to ensure the safety of the public (CDRH, 2010; Heneghan & Thompson, 2012; Hines, Lurie, Yu, & Wolfe, 2010). In a 2011 report conducted at the request of the FDA to evaluate the 510(k)

Process, the Institute of Medicine (IOM) concluded that the premise of approving medical devices based on similarity to existing devices was inherently flawed, and recommended that the 510(k) Process should be replaced in its entirety (Institute of Medicine [IOM], 2011).

In addition to concerns about the validity of the 510(k) Process as a whole, many scholars have expressed concerns that new devices approved based on another device previously approved via 510(k) and so on, may create a cycle whereby devices are continually approved without introducing any new clinical evidence to support claims of device safety (Hines, Lurie, Yu, & Wolfe, 2010; Zuckerman, Brown, & Das, 2014). If these devices were all identical to each other, the risk of repeated, cumulative approvals via substantial equivalence would be mitigated by the evidence provided through the successful function of the predicate device on the market. However, the FDA permits manufacturers to use this same process for approval of devices with different technological characteristics than the identified predicate, thereby introducing technology creep into the approval process. This cycle of technology creep through repeated approval of devices based on predicates with slightly different technical characteristics is known as predicate creep. Researchers worry that the combination of predicate creep and minimal evidentiary requirements for the 510(k) Process will allow devices to be approved which are completely different from the original predicate device, even as they rely on the scientific evidence provided by that original predicate to prove safety claims (Hines, Lurie, Yu, & Wolfe, 2010).

Given the increasing number of technologically complex medical devices entering the market, lack of scientific research into mechanisms of the approval process, and growing concern about

the safety of the established regulatory process, this thesis aims to explore the 510(k) Process through a case study of a Robotic Assisted Surgery (RAS) device, the Intuitive Surgical Da Vinci Surgical System. In particular, this thesis aims to:

1. Explore what information exists in publicly available FDA regarding device approval history via predicate relationships.
2. Develop a methodology for the identification and analysis of predicate relationships via publicly available data.
3. Assess whether predicate creep has occurred between predicates and identify any other patterns in the device approval history.
4. Identify implications of finding for the current approval process and other related medical device policies

2 BACKGROUND: THE FDA AND THE REGULATORY PATHWAY

The FDA was originally created after the passage of the Pure Food and Drug Act of 1906 in response to growing concerns about the safety of products marketed for human consumption. In 1938, the passage of the Food, Drug, and Cosmetic Act (FFDCA) gave the FDA jurisdiction over medical devices. However, that jurisdiction extended only to device which were considered "adulterated" or "misbranded". The FDA was not given premarket approval power over devices until Congress passed the Medical Device Amendments of 1976 (MDA), which established the current definition of a medical device and the risk-based device classification framework and approval process in use today.

The intention of the MDA was that the FDA would classify all existing devices into one of three risk categories, and that the level of regulatory rigor would be based on the category a device was placed in (90 Stat. 539). Any new device entering the market was automatically required to go through a strict pre-market approval process (PMA) intended for the highest risk devices, unless the device was shown to be substantially equivalent to an existing device with a low level of risk or was reclassified by the FDA into a lower-risk category. Lower risk categories did not have to meet the strict PMA requirements, but instead had to meet device based performance standards created by the FDA. New device manufacturers were required to give the FDA at least 90-days' notice of a new product to be brought to market, regardless of risk classification, to allow for the device to pass through FDA approval processes.

The 510(k) Process was developed from the MDA to reduce the amount of resources required for the FDA to meet the growing demand for device approvals. Rather than put each new device through the PMA process, the FDA developed a process based on the 90-day notification clause. The new process classified new devices as low(er) risk based on substantial equivalence to existing devices. However, even with the creation of the 510(k) Process, the FDA lacked sufficient resources to complete the tasks assigned in the MDA (IOM, 2011). As a result, the Safe Medical Devices Act (SMDA) of 1990 was passed to clarify and modify the guidelines set in the MDA in order to streamline the FDA's work.

The SMDA modified the definition of a Class II device to differentiate Class II devices from lower risk Class I devices. It also removed the previous requirement that all Class II devices have defined performance standards, replacing the mandatory standards with special controls for specific devices developed at the discretion of regulators. The SMDA formalized the 510(k) Process by creating a legal definition of substantial equivalence, although the only specifications provided for a "predicate device" was that it had to be legally approved for market. Additionally, the Act created a series of rules for post-market surveillance and adverse event reporting.

The Food and Drug Administration Modernization Act (FDAMA) of 1997 was passed to further simplify the approval process in response to concerns that regulations were creating backlogs at the FDA (Merrill, 1999). The FDAMA eliminated 510(k) notification requirements for most Class I and some Class II devices. It also created the De Novo approval process for new Class I or II devices that had no legally marketed predicate and would therefore had previously been required to undergo PMA as a Class III device by default. This process allows manufacturers to

seek approval for Class I or II medical devices using scientific evidence and existing regulatory guidelines without going through the full PMA process. Moreover, the FDAMA requires the FDA to take the "least burdensome approach" to demonstrating equivalence, which resulted in the creation of the Special and Abbreviated 510(k) Processes. The Act eliminated the FDA burden of creating performance standards for Class II devices by allowing for recognition of established standards created by a nationally or internationally recognized organization.

The current definitions of each device class originally established by the MDA of 1976 and subsequently modified, and the general approval process followed by devices in each class, are detailed below.

2.1 CLASS I DEVICES

Class I devices are low risk and not life sustaining, and therefore subject only to general regulatory controls (US Food and Drug Administration [FDA], 2006). Examples of Class I devices include dental floss, elastic bandages, and tongue depressors. Many Class I devices are considered exempt from premarket notification requirements, meaning they do not need FDA approval to enter the market. If a device is not classified as exempt, the manufacturer must submit a 510(k) identifying a predicate device and providing evidence that the new device is substantially equivalent.

2.2 CLASS II DEVICES

Class II medical devices pose a higher risk than those in Class I, but not life sustaining or supporting. The level of technical complexity of Class II devices varies widely, with examples ranging from plastic surgical drapes to infusion pumps. While the complexity of less technical Class II devices and Class I devices is often similar, the distinction between the two classifications is typically drawn based on the potential severity of device failure. Failure of dental floss, such as fraying or breakage, is merely an annoyance that poses little risk to the patient. However, failure of a plastic surgical drape, which is used to ensure equipment sterility in operating rooms, could potentially result in bacterial contamination of equipment that might cause life threatening infections in a patient. Class III devices that are considered to possess well-understood technical characteristics may be placed under Class II by exemption to expedite the approval process. Class II devices are subject to both general controls and more specialized performance controls based on the functionality and potential risk of the individual device (US Food and Drug Administration [FDA], 2006).

The approval pathway for a Class II device varies based on the intended use and level of potential risk inherent in the particular device design. Like many Class I devices, some low risk Class II devices have been exempted entirely from the premarket notification process. Other lower risk Class II devices are subject only to general controls and special controls well defined by official guidance documents or recognized standards, which allows manufacturers to file for approval using the Abbreviated 510(k) Process. If the manufacturer of a Class II device can utilize an existing device they marketed as a predicate for substantial equivalence, then the new device can be approved using a streamlined alternative process known as the Special 510(k).

This approach is typically only accepted by the FDA for generational product improvements, as it allows the manufacturer to declare conformity to design control requirements without providing data to support their claims.

If a Class II device does not meet any of the requirements for exemption or streamlined 510(k) approval, it must go through the traditional 510(k) Process. This process relies on the performance of similar devices currently on the market, known as predicates, to provide proof of safety for the new device, rather than independently evaluating the device through lengthy clinical trials. The process begins with the manufacturer submitting an application detailing the device description, intended use, intentions for use, identified predicate devices, and performance data supporting the claim of substantial equivalence. The FDA then has 90 calendar days to declare the device either substantially equivalent (SE) or not substantially equivalent (NSE) to the predicate (s) based on the material presented in the 510(k) application. If a device is declared SE by the FDA, the manufacturer receives clearance to place the device on the market after registering and officially listing the device (Center for Devices and Radiological Health, 2017b).

If the FDA finds a device NSE, it will automatically be reclassified as a Class III device unless the manufacturer submits a De Novo approval application. The De Novo process evaluates the scientific evidence presented by the manufacturer and allows the FDA to grant approval without a predicate device if the evidence provides sufficient proof of safety, effectivity, and minimal risk (Center for Devices and Radiological Health, n.d.).

2.3 CLASS III DEVICES

Class III medical devices are life sustaining or supporting, or present unreasonable potential risk to the user. These include most implantable devices, such as pacemakers, stents, and orthopedic prosthetics, as well as life supporting devices such as external defibrillators. The FDA has determined that general or special controls are insufficient to assess the safety and efficacy of these devices. Instead, the vast majority of Class III devices are approved via Premarket Approval (PMA) process, a rigorous scientific and regulatory review which requires device specific non-clinical and clinical testing to prove safety and effectiveness (US Food and Drug Administration [FDA], 2006). A limited number of Class III medical devices receive PMA exemptions, allowing them to be approved via the 510(k) Process instead.

3 A REVIEW OF THE LITERATURE ON THE 510(K) PROCESS

Existing research has identified a variety of potential gaps in the 510(k) Process, including concerns about the validity of "substantial equivalence" as an approval mechanism, lack of scientific evidence to support claims, predicate creep, Class III device exemptions, and insufficient post market surveillance among others. Some major studies also presented suggestions for improvements to the process, which resulted new guidance documentation issued by the FDA beginning in 2012.

3.1 GAPS IN THE 510(K) PROCESS

3.1.1 VALIDITY OF SUBSTANTIAL EQUIVALENCE

One major criticism of the 510(k) Approval Process commonly identified is the use of "substantial equivalence" as an approval mechanism for ensuring safety and efficacy of new devices. According to the current FDA definition a device is substantially equivalent if, in comparison to a predicate it:

1. has the same intended use as the predicate; and
2. has the same technological characteristics as the predicate;

Or

1. has the same intended use as the predicate; and
2. has different technological characteristics and does not raise different questions of safety and effectiveness; and
3. the information submitted to FDA demonstrates that the device is at least as safe and effective as the legally marketed device.

(Center for Devices and Radiological Health [CDRH], 2017b)

Although this definition was intended to clarify when the use of substantial equivalence was appropriate for medical device approval, some scholars have expressed concerns about the vagueness of the definition. A 2010 CDRH working group report identified confusion surrounding the definition of "intended use" for substantial equivalence determinations compared to the term "indications for use". The report defines "intended use", a requirement for substantial equivalence, as based on the objective intent expressed by the manufacturer. "Indications for use," a more general term often used in 510(k) applications but not required to be the same for substantial equivalence, describes the general disease or condition the device is designed to treat. However, among industry officials and in many official FDA documents the two terms are used interchangeably, creating a lack of clarity about the actual requirements of substantial equivalence (CDRH, 2010).

Another issue identified is that, due to the lack of a clear official definition for the key term "intended use", the FDA has allowed permissive interpretation of "intended use" by applicants. Since intended use is defined by the manufacturer rather than regulators, manufacturers are able to modify the wording of the stated intended use to make changes in device function appear minimal. Over time, this has resulted in the approval of significantly altered devices, or even novel devices, as substantially equivalent to established predicates (CDRH, 2010; Heneghan & Thompson, 2012; Hines et al., 2010).

One example of this provided by the CDRH Working Group (2010) was the gradual approval of cryosurgical devices as a treatment for prostate cancer, rather than a tool for removal of

unwanted tissue these devices were initially designated for. A new cryosurgical device that could more readily be used to access the prostate area was approved in 1990 with an indicated use for "tissue destruction." Manufacturers aggressively pushed to have the indicated use expanded to include "treatment of prostate cancer," but were refused on the grounds that a clinical application carried different risks and implications than the general use. Instead, manufacturers went around the FDA by gradually changing the intended use, first to "tissue destruction in urology," then including "removal of prostate tissue" and "prostate tumor – palliative." At this point in time, with an intended use specifically indicated for prostate tumors, a growing number of researchers began experimenting with the tool as a treatment for prostate cancer, despite the lack of official approval for this express purpose. Caving to pressure from manufacturers and the increasing prevalence of the device as a treatment in clinical settings, in 1997 the CDRH allowed cryosurgical devices to be cleared for an indicated use of "treatment of prostate cancer" without ever identifying a new "intended use" or requiring clinical data to support device approval. Ultimately, many problems arose following the widespread adoption of cryosurgery as a treatment for prostate cancer, an application of the device that the CDRH never specifically evaluated for safety or effectiveness (CDRH, 2010). Many issues may have been prevented had the device undergone a full review prior to being placed on the market for this application.

The example of cryosurgical devices as a treatment for prostate cancer shows the potential risk of permissive interpretation even in the case of a device which has already been on the market and proved safe for other applications. However, the potential risk of permissive interpretation increases drastically when combined with the provision within the definition of substantial equivalence that allows for approval of devices with different technological characteristics. This

provision expands the selection of predicates to include devices with different materials or mechanisms of action, if the new device has a similar safety profile to the predicate, which creates additional uncertainty about how a device will perform when placed on the market.

3.1.2 Outdated Predicates

One major concern identified by researchers is that the 510(k) Process makes the implicit assumptions that substantial equivalence means that a device is safe and effective, and that the predicates on which substantial equivalence determinations are based are safe. In his concurring opinion for the 1996 case of *Medtronic v. Lohr*, Supreme Court Justice O'Connor explained the court's interpretation that a finding of substantial equivalence proves only that the device introduces no new safety hazards and functions at least as effectively as the predicate device (Medtronic vs. Lohr, 1996, pg. 513). However, if the predicate device poses risk or is ineffective, then the new device may perpetuate these flaws. Thus, there are concerns that the 510(k) Process can create a cyclical approval pattern of unsafe devices. There is disagreement, however, as to whether the process is invalid entirely or only for specific types of high risk or technologically complex devices (Ardaugh, Graves, & Redburg, 2013; Lennox, 2014; Zuckerman, Brown, & Das, 2014).

3.1.3 Predicate Creep

Some literature pointed to the risks of using of multiple predicate devices for a single substantial equivalence determination. The CDRH working group report identified three types of 510(k) predicate submissions: single, multiple, and split (CDRH, 2010). While most academics agree

that single predicate submissions, which directly compare a new device to a single device on the market, provide significant assurance of safety and efficacy in most cases, many have raised questions about whether multiple and split predicates can provide the same level of assurance (Ardaugh, Graves, & Redburg, 2013; Zuckerman, Brown, & Das, 2014). For example, Ardaugh et. al examined the approval history of the DePuy ASR XL Acetabular Cup System, a metal-on-metal hip implant that caused life altering injuries to hundreds of patients due to metal particle shedding within the body. The ASR XL was approved using three different devices as predicates, each with a unique technological characteristic which was incorporated into the XL. Since all three devices were deemed safe based on market performance, and the XL simply combined parts of the devices, it was placed on the market without undergoing clinical testing. However, after the discovery of particle shedding, it was determined that the cause of the failure was the unique combination of the material (from one predicate) and geometry (from a different predicate) of the ASR XL (Ardaugh, Graves, & Redburg, 2013). Regulators had reasoned that if these characteristics were safe independently, then they should be safe when put together. However, without any evidence from previous devices with this combination of material and geometry or actual testing of the device over time, that reasoning was mere assumption, which in this case proved disastrous.

Another growing concern expressed in the literature is that, in many cases, the predicates on which evaluations of safety and efficacy are based were also approved via 510(k) (Hines et al., 2010). Substantial equivalence allows a device to "piggyback" on the reasonable assurance of safety from existing predicate devices without undergoing independent testing. (CDRH, 2010; Lennox, 2014). However, when the predicate was also approved via substantial equivalence, as

was its predicate and so on, a cycle is created in which there may be a significant gap between the current device and the most recent device for which scientific evidence of safety was provided (Fargen et al., 2012). This creates an iterative process through which, over multiple cycles of small device modifications and subsequent substantial equivalence findings, a new device may be approved which is significantly dissimilar to the original predicate for which scientific evidence exists (Hines et al., 2010). This process is known as predicate creep (Hines et al., 2010; Zuckerman, Brown, & Das, 2014). While the exact impact of predicate creep is difficult to identify, a few researchers have attempted to construct ancestral equivalence trees utilizing the 510(k) database maintained by the FDA, with mixed results (Ardaugh, Graves, & Redburg, 2013; Waetjen et al., 2015; Zuckerman, Brown, & Das, 2014).

Although there is very little evidence provided within the literature to prove the existence of predicate creep, two papers were found that used a technique constructing ancestral equivalence tree to identify information present in the predicate history of a specific device. Ardaugh et. al (2013) used documents obtained through the FDA 510(f) Database and Freedom of Information Act filings to trace the predicate history of the DePuy ASR XL Acetabular Cup System, a metal-on-metal hip implant, over five decades with the purpose of identifying the cause of safety flaws present in the design. Zuckerman et. al (2014) used the FDA 510(k) Database to trace the predicate history as far back as available for a random sample of 50 newly cleared devices, with the stated purpose of identifying the most recent predicate to present definitive scientific evidence of safety and effectiveness to support a claim of substantial equivalence. Neither article specified the exact methodology used to trace predicates. Examination of the database,

however, shows that in many cases the predicate device(s) is readily identified in the available paperwork.

The research performed by Zuckerman et al. (2014) focuses on identifying the most recent point in the predicate history when scientific evidence was presented to support a claim of substantial equivalence, as part of a larger argument the researchers present about a lack of publicly available scientific evidence to support the safety and effectiveness of implantable medical devices. This group's research focuses on whether evidence was provided to support claims of equivalence, and the type of evidence provided, rather than examining the technological relationship between the devices on which the claim was based. One notable finding presented in this research was the identification through an ancestral trace of predicate devices that have been recalled from the market due to safety concerns, which raises red flags about the safety of subsequent devices.

Ardaugh et al. (2013) studied the predicate history of the ASR XL with the express purpose of discovering how a device with major design flaws was able to enter the market through the 510(k) Approval Process. The researchers examined the technological relationship between predicates with the specific purpose of identifying when features which became "flaws" in the final device were introduced in predicates. However, the characterization of predicate relationships in this research was performed with the specific intention of locating technological characteristics present in the final device, rather than to understand and characterize predicate relationships in general.

3.1.4 Scientific Burden of Proof

Another flaw commonly identified in the literature is insufficient scientific evidence of safety and efficacy. The 510(k) Process requires only sufficient scientific evidence to prove substantial equivalence to a predicate and, in the case of new technological characteristics, mitigate any new concerns of safety and efficacy. This evidence is typically presented in the form of non-clinical data, which may range from descriptive device data, essentially physical characteristics, to more involved performance testing (Flaherty, 2008; Waetjen et al., 2015). While in some cases this evidence is clearly enough to demonstrate substantial equivalence and assure device safety, many worry that it is insufficient to ensure the safety of devices which are inherently higher risk, or which are declared equivalent to devices of questionable safety (Ardaugh, Graves, & Redburg, 2013; Heneghan & Thompson, 2012; Janetos, Ghobadi, Xu & Walter, 2017; Waetjen et al., 2015; Zuckerman, Brown, & Nissen, 2011). The lack of available scientific evidence supporting substantial equivalence claims may be partially due to inconsistently defined testing requirements dictated by the FDA. While the regulatory definition of a Class II device identifies "general and specialized performance controls" (FDA, 2006) as requirements for approval, what specifically defines those controls is not necessarily scientifically based and often unclear (Zuckerman, Brown, & Das, 2014).

3.1.5 Class III Device Exemptions

Along with a lack of required clinical testing, another flaw identified with the 510(k) Process in the literature is the approval of devices identified as Class III (high-risk) through the less

stringent 510(k) Process. While Congress mandated in the 1990 Safe Medical Devices Act that the FDA either reclassify these devices or establish a schedule for requiring PMAs (Hines et al., 2010), as of 2008, 20 of these device types could still be cleared via 510(k) (GAO, 2010). In fact, a GAO report found that between 2003 and 2007 more Class III devices were cleared for market via the 510(k) Process than the original PMA process (GAO, 2010). Many high profile failures of Class III devices approved via 510(k), including the DePuy ASR XL Acetabular Cup System and Poly Implant Prosthese (PIP) breast implants, have had increased calls for the removal of the Class III device exemption (Garber, 2010; Heneghan & Thompson, 2012; Kramer, Xu, & Kesselheim, 2012; Sorenson & Drummond, 2014).

3.1.6 Insufficient Post Market Surveillance

A comprehensive post market surveillance system is a necessary complement to premarket approval processes to mitigate potential patient exposure to harmful medical devices. The FDA maintains the Manufacturer and User Facility Device Experience (MAUDE) database, a centralized database for reporting data on device safety and efficacy (Dhruva & Redburg, 2012). Current post market surveillance rules require mandatory manufacturer reporting of serious adverse events or deaths associated with a device, although the decision of whether an event is associated with the device is left to the manufacturer (Sorenson & Drummond, 2014). Voluntary reporting by healthcare providers, fear of litigation, lack of causal association with a particular device, and several additional factors lead to severe underreporting of adverse events (Sorenson & Drummond, 2014). Druhva & Redburg (2012) found that only 5 -10% of all adverse events are reported to the FDA.

In addition to a lack of reporting, insufficient device traceability and a lack of formal review mechanisms make it difficult for the FDA to identify patterns in adverse events reports that may suggest serious safety risks (Dhruva & Redburg, 2012; Garber, 2010). This limited availability of data makes identification of hazardous devices difficult, and has led to calls for an improved post market surveillance system with more comprehensive data and traceability (Heneghan & Thompson, 2012; Hines et al., 2010; Janetos, Ghobadi, Xu & Walter, 2017).

3.2 PROPOSED 510(K) PROCESS MODIFICATIONS

3.2.1 CDRH WORKING GROUP REPORT (2010) RECOMMENDATIONS

The lack of consistent testing requirements and potential for high risk devices to enter the market without clinical data supporting safety claims led the CDRH working group to propose a modification to the existing device classification system in their 2010 report. To prevent a complete overhaul of the existing regulatory structure while still improving regulatory predictability and safety outcomes, the group suggested the creation of Class II subclasses, Class IIa and IIb. Class IIa would contain the majority of devices for which guidance documentation exists or safety and efficacy is well established by existing predicates. Class IIb would contain those devices which, due to new technological characteristics, technical complexity, or inherent risk to patients, require higher levels of device specific testing and evidentiary support to prove safety and efficacy. This may include devices such as implantables, in vitro diagnostic devices,

or reclassified Class III exemption devices which typically pose more risk. Devices in Class IIb would be typically require significant scientific data, including animal testing and clinical data, for approval (CDRH, 2010).

3.2.2 Institute of Medicine Report: The 510(k) Process at 35 Years (2011)

Following the publication of the 2010 Working Group Report identifying potential flaws within the 510(k) Process, and recognizing growing concerns within the industry, the Department of Health and Human Services tasked the Institute of Medicine with conducting a thorough review of the 510(k) Process (IOM, 2011). The report, published on October 25th, 2011, presented a comprehensive review of the 510(k) Process and considered a multitude of sources both internal and external to the regulatory process, including some found in this literature review (CDRH, 2010; Hines et al., 2010; Zuckerman, Brown, & Nissen, 2011).

The report ultimately concluded that the existing 510(k) Process was insufficient to adequately determining the safety and efficacy of new devices, and the committee recommended that the FDA design a new regulatory framework to replace the process entirely. However, the report specifically addressed the implications of that recommendation by stating that "The committee is not suggesting that all, many, or even any medical devices cleared through the 510(k) clearance process and currently on the market are unsafe or ineffective. Rather, the committee found that the available information is insufficient to support highly confident conclusions about the safety and effectiveness of 510(k)-cleared medical devices in clinical use" (IOM, 2011, pg. 193).

3.2.3 FDA Response

Although the FDA declined to implement either of the major recommendations from (name the two) for a restructuring of the classification and approval process made in these reports, the FDA has responded to the concerns identified. Based on the findings of these two major reports, the FDA began implementing a series of reforms and new regulations in early 2012 to improve the 510(k) Process. In 2014, the FDA issued new guidance documentation for evaluating substantial equivalence in 510(k) applications which addresses many of the concerns identified in the literature. The new documentation provides specific definitions for "intended use" and "intentions for use", clarifications on the use of multiple predicates, and more detailed guidelines for the use of scientific evidence in supporting substantial equivalence claims (United States Food and Drug Administration [FDA], 2014).

Additionally, in 2012 the FDA issued a strategy document detailing its approach to creating a comprehensive post market surveillance system. A key element of this strategy is the creation of a system of standardized Unique Device Identifiers (UDI) that can be incorporated into electronic health databases to increase device traceability and streamline the response to adverse events reports (Gross & Crowley, 2012).

3.3 SUMMARY OF LITERATURE REVIEW FINDINGS

The review of current literature on the 510(k) Process conducted above identified two primary areas of concern regarding the effectiveness of the current process. First, many critics expressed concerns about vague definitions, lack of clear guidance or requirements for evidentiary support of equivalence claims, and subjective equivalence determinations by FDA officials which affect the consistency and predictability of the regulatory process. Second, scholars and regulators determined that the use of predicate devices as an approval mechanism may have adverse impacts on the safety of new devices due to the use of inappropriate predicates or the presence of predicate creep over time. The implication of the various concerns identified within the literature is that the current approval process has gaps which may allow the approval of devices for market without ensuring they are safe for use.

Although the FDA has recently implemented changes the approval process to address some of the concerns identified within the literature, it has declined to implement any major changes to the overall approval process. Various reasons, including resource restrictions and approval time constraints, may have contributed to the approach the FDA chose to address the recommendations it received. However, another important factor the agency is obligated to consider is the balance of regulation versus innovation. While it is necessary to ensure that devices are safe and effective prior to placing them on the market, increasing regulatory requirements for new devices automatically makes it more difficult to bring innovative devices to market. Many device manufacturers already feel that the application process and approval times under current regulatory guidelines create barriers to innovation (California Healthcare Institute [CHI], 2011). Many medical device companies have begun launching initial product

offerings overseas where regulations are perceived as less stringent and more conducive to innovation, or relocating operations entirely (CHI,2011). As a result, any modifications made to the regulatory process within the United States must be carefully structured to allow for innovation without negatively impacting the safety of devices.

3.4 RESEARCH GOALS

The 510(k) Process was originally envisioned as a means to streamline the approval process and reduce the impact of regulatory requirements on devices which present minimal risk to patients. While scholars call into question whether the process effectively serves its intended purpose, there is a distinct lack of evidence to support the actual impact of many of the gaps identified by experts within the literature. Most of the articles included in this review simply discussed potential flaws in the existing process, providing only one or two anecdotal examples of highly publicized failures to support claims. The internal review conducted by the CDRH Working Group is the only study identified which compiled data from a large number of approval applications to identify trends and potential regulatory flaws (CDRH, 2010). The review conducted by the IOM Committee used a combination of public workshops, literature reviews, expert opinions, internal CDRH reports, and information contained in public FDA databases to draw conclusions about the regulatory process. However, the IOM Committee expressly stated that it was unable to fully assess the quality of 510(k) submissions, including the types of data submitted to support equivalence claims, due to FDA statutory requirements that prevented the committee from reviewing applications to protect proprietary information. (IOM, 2011, pg. 20)

The limited availability of data due to intellectual property protections, as encountered by the IOM during its review, is a major restriction for determining the impact of predicate creep within the approval process. Still, it is possible to trace portions of the predicate history of current medical devices using data available through FDA databases or via Freedom of Information Act (FOIA) requests. Despite this, only two articles identified within this literature review made any attempt to trace the predicate relationships of devices in order to determine whether a lack of scientific evidence or predicate creep occur within the 510(k) Process.

Given the overall lack of data presented within the literature to support concerns surrounding the 510(k) Process, especially regarding the use of predicates as an approval mechanism, the aim of this thesis is to develop a methodology for identifying predicate relationships of devices approved via the 510(k) Process and evaluating the potential impact of predicate creep and other trends observed within this data. In order to concentrate on the development of an effective analysis method, this research will be structured as a case study of the Da Vinci Surgical System, a robotic surgical platform. The following section discusses in depth the methods used to select this case study, gather data, and identify instances of predicate creep. The Data Analysis section illustrates the data gathering process and relationship comparisons. Findings discusses the conclusions drawn from the relationships identified within the Analysis section, and the Conclusions section discusses the implications of those findings for policy and future research.

4 METHOD

4.1 CASE STUDY SELECTION: THE INTUITIVE SURGICAL DA VINCI SURGICAL SYSTEM

The method I have chosen to analyze the effectiveness of the current regulatory structure for developing biomedical technologies, particularly in robotics, is a case study of the Intuitive Surgical Da Vinci robotic surgical system. I will conduct a comprehensive review of the approval process by tracing the predicate history of the Da Vinci. This methodology for analyzing the regulatory approval process of the Intuitive Da Vinci was selected based on the availability of data through public databases.

One of the first and only examples of a robotic medical device approved for market is the Intuitive Da Vinci Surgical Platform, a Robotic Assisted Surgery (RAS) device initially approved by the FDA in 2000 for laparoscopic surgery. While Intuitive has subsequently brought multiple iterations of the Da Vinci to market, 16 years later it remains the only full RAS platform on the market as competitors struggle to develop a viable competitor around Intuitive's strong patent foothold. While the Da Vinci served as a predicate device for subsequent models, as well as for RAS devices produced by competitors and potentially for other robotics technologies, the Da Vinci itself was initially approved under a 510(k) application. This approval was granted based on a complex web of component-level substantial equivalence, most likely supplemented by additional testing.

The Da Vinci Surgical System is a robotic-based laparoscopic surgical tool which replaces a surgeon's hands with robotic arms for more precise control and motion. It is comprised of three physical components. A "cart" onto which three robotic arms are mounted, a "tower" which houses the computer systems, and a "console" where the surgeon sits to control the arms and view the procedure. The system also includes a software component which allows the surgeon to control the arms and a 3D vision system, so the surgeon can view inside the patient during surgery. Typically, the device is configured so that two robotic arms are mounted with surgical tools, and the third arm acts as an endoscope (Intuitive Surgical, 2017). Use of a Da Vinci System requires extensive training, and the estimated cost of installation in $2 million.

The Da Vinci is an interesting case study for assessing the FDA approval process for several reasons. As stated, the Da Vinci is one of the only examples of robotics surgical devices on the market, and since it has been approved for over 15 years, its function is well documented. In fact, over 10,000 peer-reviewed articles have been published about the Da Vinci. Additionally, the Da Vinci is well documented legally, with over 800 patents registered to Intuitive Surgical and 3000 product liability claims filed. The uniqueness of the device as an emerging technology with no direct competitor on the market makes it representative of many of the challenges the FDA will face with other developing medical technologies currently in development. Many of these upcoming medical technologies, such as personalized 3D printed prosthetics, nanotechnologies, and other devices with high levels of software integration, possess unique functions and challenges which do not necessarily fit within the existing regulatory structure. The Da Vinci was one of the first major medical technologies to pose similar challenges regarding software integration, in addition to the technical complexity of the device, so it serves as a good case

study to use as a basis for identifying the general regulatory approach to these types of complex devices. The methodology described here for evaluating the Intuitive Da Vinci seeks to give a more complete view of how the FDA adapts the existing regulatory process for innovative medical devices with high levels of technical complexity and no clear predicate.

4.2 DATA GATHERING AND ANALYSIS

The main objective of this research is to identify publicly available data pertaining to approval of medical devices via the 510(k) Process, with a focus on RAS devices, and examine that data to draw conclusions about how that process has been implemented. Therefore, the first step to conducting my research was to develop a methodology for identifying and compiling pertinent publicly available data in FDA databases.

4.2.1 DATABASE EXPLORATION

The FDA maintains a number of different databases related to various aspects of medical device regulation, including post-market surveillance, incident reporting, device recalls, and device approvals. As illustrated in Figure 1, there are a variety of different methods and databases which can be used to identify information relevant to this research. As this research is focused on Class II medical devices, the database containing the most directly applicable data is the 510(k) approval database. This database was created in the early 1990's during the implementation of the Safe Medical Devices Act, which officially developed the 510(k) Process as a separate

approval process, to serve as a centralized location for all information pertaining to 510(k) approvals.

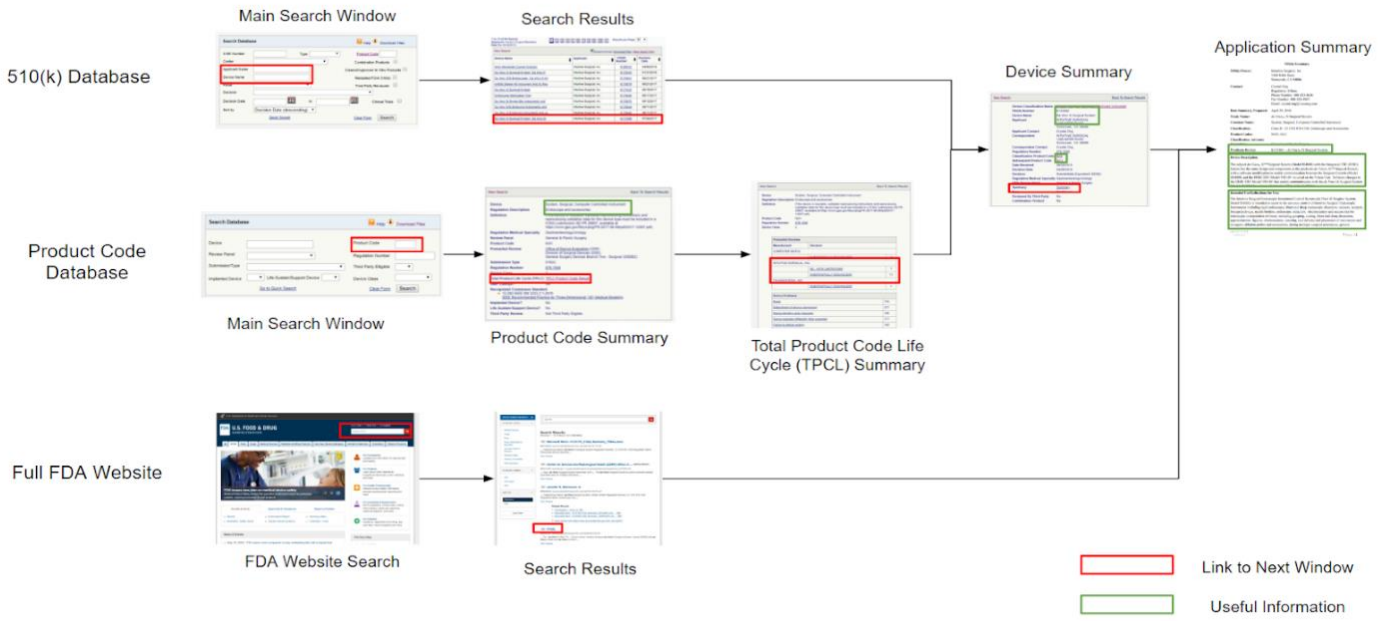

Figure 1: Overview of database structure and locations of useable information for three FDA database searches; the 510(k) Database, the Product Code Database, and the Full FDA Website

The existing search mechanisms allows for searches based on keywords, applicant, device name, decision date, approving panel, and 510(k) Number. The 510(k) Number (K#) is a unique identification number used to track approval applications. A K# corresponds to an approval application, which may be for a new device, a new functionality of an existing device, or a modification of an existing device. Inputting a search term into the database results in a list of relevant results, including the device name, applicant, K#, and decision date, which can be sorted alphanumerically based on a selected parameter. Clicking on either the device name or K# within the search results brings you to a standardized device-summary page containing information that pertains to that 510(k) application. This includes all the searchable parameters present on the

main search page, as well as additional information specific to the application filing, such as initial application date and applicant contact information, relevant regulations, the review information, and in some cases an attached PDF summarizing the information contained in the actual application. It is within the attached application summary, if one exists, that information required for determination of substantial equivalence, such as predicate devices, intended use, indications for use, and scientific evidence may be presented.

In addition to the application summary, another useful piece of information contained on the device summary page is the device product classification code. This product code identifies a more device-specific classification based on the technological characteristics and intended use of a device. (Stuart, J., n.d.) This can be used to identify potential predicate devices based on the substantial equivalence parameters for a new device. For this research, it may also be useful to identify devices which are predicated on a particular device, information which cannot be easily found in the 510(k) database due to the nature of the application summary formatting.

The FDA product classification database functions similarly to the 510(k) database, with a main page allowing for searches via parameters including device name, review panel, product code, and regulation number. As product classification codes are applied to all medical devices, not just Class II devices, the database also allows for specification of parameters based on medical device class.

A search via product code results in a code summary window identifying the device to which the code pertains, a regulatory description, and details about the regulatory process for devices under

this classification. The code summary also includes a link to the Total Product Life Cycle (TPLC) Report which summarizes all regulatory activity associated with the code, including information about all devices with approval applications filed under this code. This can be used to directly identify devices with related predicate histories.

If information about a Class II device cannot be found via the 510(k) or Product Code databases, a final option for investigating available public information is the "brute force" method. Rather than a targeted search through specialized databases, this method involves entering search terms in the general search bar on the FDA web page. This returns results from all FDA publications, including database information, conference presentations, regulations, and internal memos. Although this method returns significantly more results, the search function offers limited filtering options and requires manual sorting to determine whether results are relevant.

4.2.2 Data Compilation

Although data on Class II medical device approvals does exist, multiple databases and layers of search results presented in different formats within the databases prevents direct analysis of device information and predicate relationships. Instead, manual construction of a separate database containing general device information and available approval details was required before meaningful data analysis could be performed. Identification of devices for inclusion in a manual database was guided by a database construction parameters. The two major construction parameters considered for this research were product code classification and predicate relationship, meaning a device was either a predicate of or predicated on the device, such as the

Da Vinci, around which the database was constructed. Each newly constructed database included the K#, device name, manufacturer, approval date, product code, and any predicate or intended use information available for all devices relevant to the database construction parameter.

4.2.2.1 Da Vinci Initial Search

The initial focus of my research was tracing the approval history of the Intuitive Da Vinci Surgical System. Using the previously described methodology, I searched the 510(k) database for applications filed by Intuitive Surgical and identified an application for the Da Vinci Si Surgical system, the second iteration of the device family offered by Intuitive. Examination of the regulatory summary revealed that this device is classified under the product code NAY, which refers to devices classified with the keywords "System, Surgical, Computer Controlled Instrument" under a regulatory description of endoscope and accessories (FDA, Product Classification- System, Surgical).

As the Da Vinci was the first device of its kind, devices identified under the product classification code NAY are exclusively iterations of the Da Vinci itself, devices which serve as direct predicates, or devices that are directly predicated on the Da Vinci. Therefore, I was able to use the information contained in the Total Product Life Cycle report to construct a database of information about every 510(k) application Intuitive Surgical has ever filed directly related to the Da Vinci System. This new database includes the device name, 510(k) number, applicant, approval date, predicates identified, and the substantial equivalence determination (See Appendix 1).

4.2.3 Expansion to Related Devices

After observing the wide variety of technological characteristics present across a given predicate generation in the Da Vinci trace, I looked at how the technological characteristics of the Da Vinci compare to other devices in its own generation. While tracing backwards through equivalence identifies predicates with different characteristics ultimately present in a subject device, tracing forward from a given predicate to subsequent subject devices should reveal a group of devices which share the common characteristics of the initial predicate. Based on the definition of substantial equivalence, these devices should share a common intended use and similar technological characteristics. However, each device may incorporate different technological aspects of the identified predicate device(s) along with new technology to develop a device with unique benefits for users. As a result, it is possible that significant deviations in technological characteristics exist between two subject devices with the same predicate, even if the stated intended use is the same. When multiple predicate devices are identified in an approval application, the new device design may be composed of a combination of the technological characteristics of the predicates, including functions present only in one predicate device, potentially creating even more significant deviations in overall device function compared to the predicate.

I chose to start my investigation by searching for subject devices predicated on Computer Motion Inc.'s Automated Endoscopic System for Optimal Positioning (AESOP) System, rather than any devices within the first generation of the Da Vinci trace, for three reasons. The first reason was

that the devices contained within the first generation were all identified as components of the previous Da Vinci model ISI 1000, which makes it unlikely that any subsequent subject device would be predicated on a component rather than the system as a whole. Secondly, the AESOP is the first recorded device in the NAY product classification family to which the Da Vinci belongs. Although I was already aware through the TPLC Report that no additional devices within this product code family were predicated on AESOP, I felt that using this device as the starting point would return subject devices with functionality closest to that of the Da Vinci. Finally, AESOP is one of the oldest and most well-known devices to appear in the tree, so I felt it was the most likely of the devices in the trace to have multiple subject devices predicated on it.

Due to the construction of the 510(k) database, it is essentially impossible to search for a subject device, rather than a predicate, without knowing the product code of the device you are searching for. As I already knew no eligible devices were present in the NAY classification family, I was required to use the brute force approach to identify devices predicated on AESOP. This was done by searching the keywords “AESOP” and “Computer Motion” in the overall FDA search bar and manually sorting through the results to identify relevant devices.

4.2.4 PREDICATE TREE CONSTRUCTION

Using the data gathered in these newly created databases, I constructed predicate trees, structured similarly to an ancestry tree, to help identify instances of predicate creep and any patterns present in the regulatory history of the device(s). Creation of an equivalence tree is a technique that has been used by two other research groups working in the space of FDA regulations to identify information present in the predicate history of a specific device. Ardaugh et al (2013) used documents obtained through the FDA 510(f) Database and Freedom of Information Act filings to trace the predicate history of the DePuy ASR XL Acetabular Cup System, a metal-on-metal hip implant, over five decades with the purpose of identifying the cause of safety flaws present in this design. Zuckerman et. al (2014) used the FDA 510(k) Database to trace the predicate history as far back as available for a random sample of 50 newly cleared devices, with the stated purpose of identifying the most recent predicate to present definitive scientific evidence of safety and effectiveness to support a claim of substantial equivalence. Neither article specified the exact methodology used to trace predicates, however examination of the database shows that in many cases the predicate device(s) is readily identified in the publicly available paperwork.

Following a similar method as Ardaugh et al. (2013) and Zuckerman et al. (2014), I constructed an ancestral equivalence tree using the information gathered from the FDA databases as described in the previous section. An example structure for a resulting equivalence tree is shown in Figure 2 below.

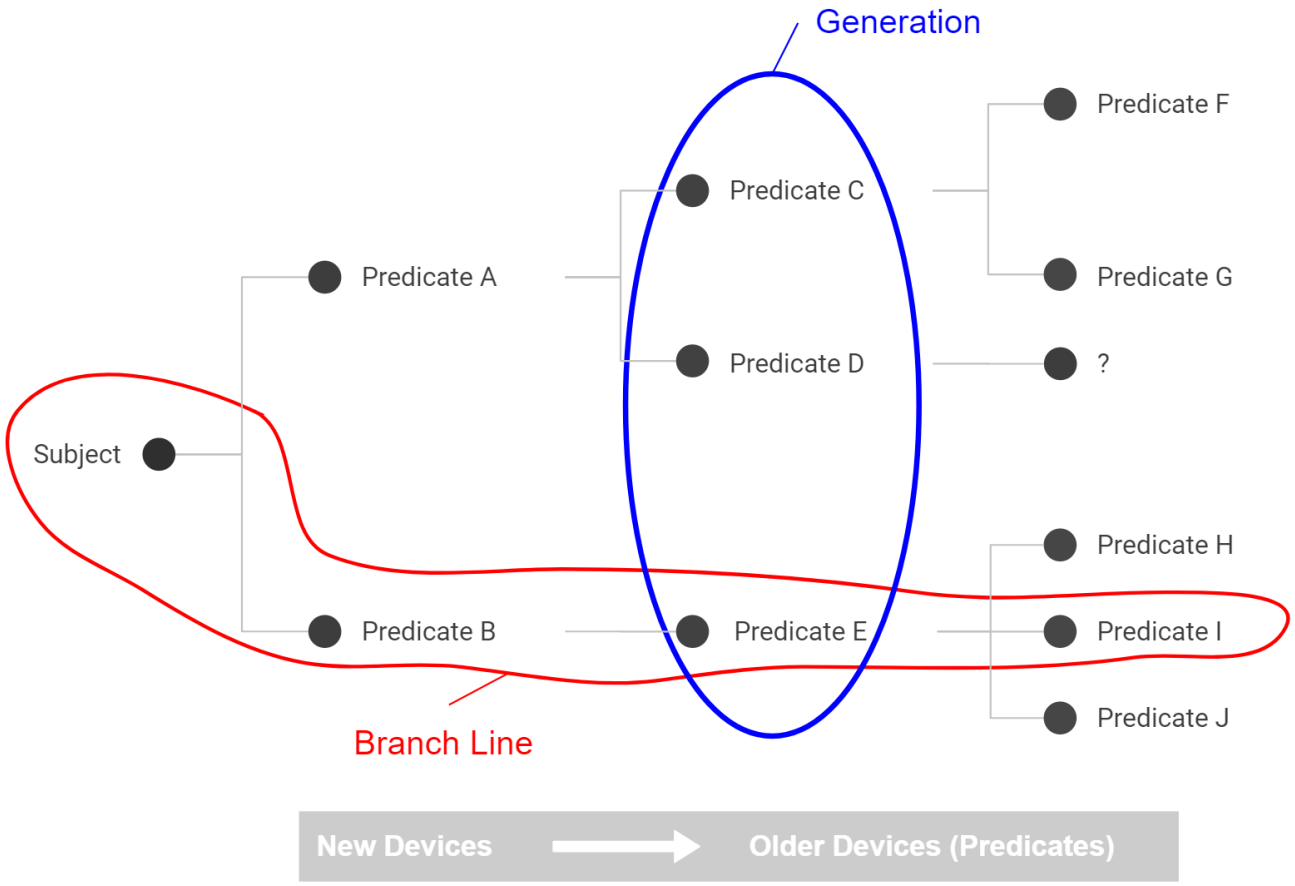

Figure 2: Sample predicate tree tracing the history of the "subject" device and illustrating major structural elements including a predicate generation (blue) and a predicate branch line (red).

As illustrated in the sample predicate tree above, the subject device is the device from which the predicate trace originates. A question mark in the trace indicates that the device was approved via the 510(k) Process, indicating that a predicate device does exist, but there is insufficient information available in the databases to identify that predicate. For this research, a predicate generation is identified as a group of predicates that are the same number of steps removed from the subject device. The generation number is the total number of steps between the predicate and main subject device. For example, the generation identified in blue in Figure 2 is the 2nd

generation and contains a total of 3 different devices, C, D, and E. A branch is defined as a group of devices whose relation can be traced directly through single-step substantial equivalence determinations. In this example devices E, H, I, and J all belong to the device B branch. A branch line is a more specific group of devices which belong to a single branch, with each device belonging to a different generation as shown in red in Figure 2. Ultimate or originating predicates are defined as the oldest devices to which a branch line(s) can be traced, such as Predicates J for the sample branch line shown above. For purposes of clarity when discussing findings, a device within an ancestral trace will be defined based on the presence of a unique K-number, even in cases where multiple K-numbers have been identified as part of a single device.

For devices where overlapping or increased numbers of predicates appear make traditional tree diagrams unwieldy, an alternate diagram structure known as a network map was used to display predicate relationships within the approval ancestry. A network map represents each unique device with a dot corresponding in size to the number of predicate relationships associated with that device. The dots are arranged from left to right in reverse chronological order beginning from the subject device, in a similar manner to that shown in Figure 2. Each predicate relationship is represented by an arrow between two dots, with the arrowhead pointing from the subject device towards the predicate. Unlike the traditional ancestry tree structure illustrated in Figure 2, predicate arrows within a network map can overlap, create a significantly more compact diagram.

4.3 IDENTIFICATION OF PREDICATE CREEP

Predicate creep is the introduction of technology creep into the 510(k) Process via the substantial equivalence relationship between devices. Researchers have theorized that accumulation of predicate creep may ultimately result in the approval of devices which possesses significantly different technological characteristics than earlier predicates with little assurance of safety, due to the minimal evidentiary requirements of the 510(k) Process. However, due to the nature of information contained within the public 510(k) databases, it is impossible to determine exactly what level of scientific evidence was provided to support each substantial equivalence claim. Therefore, this research focuses on identification of gradual changes in the technological characteristics of devices over multiple predicate generations based on small changes made within each predicate relationship.

For this research, predicate creep is identified using three primary methods: direct comparison of technological characteristics, comparison via regulatory structures, and presence of multiple predicate devices. Direct comparison of technological characteristics is the traditional method for identifying technology creep involving identification of the technological characteristics of two or more related devices and observation of changes in technical characteristics between them. For this research, devices will be compared along branch lines, using the identified predicate relationship as a basis for comparison, and within a predicate generation. This method can be used to identify specific instances of predicate creep and illustrate potential impacts it may have on device functionality and safety.

In addition to direct comparison of technological characteristics, a second method for identifying predicate creep is through the use of existing mechanisms or structures which identify characteristics of the technology from a regulatory perspective. FDA product codes are particularly useful for this purpose, as they are designed to identify groups of devices with the same intended use and technological characteristics. As possessing the same intended use is a requirement for approval via substantial equivalence, it follows that any device approved via 510(k) with a different product code that the predicate must either possess different technological characteristics, or be in violation of the requirements for substantial equivalence. Therefore, the introduction of new product codes in the predicate ancestry tree should be indicative of the introduction of new technological characteristics.

Another indicator of technological creep within the approval tree is the presence of multiple predicate devices. Although it is perfectly permissible to have multiple predicated with the same intended use and extremely similar technological characteristics present on a 510(k) application, the inclusion of both devices is redundant if the subject device also possesses the same characteristics. Instead, an application including multiple predicate devices is often used when a new device contains a unique combination of the different technological characteristics present in the predicate devices. Although the technological characteristics of the subject device did exist individually before, they are present in this device in a unique combination that did not exist previously, which is a form of predicate creep.

4.4 PATTERNS IN THE REGULATORY HISTORY

Patterns in the regulatory history will be identified using a combination of qualitative and quantitative observation to draw conclusions about how the general guidelines of the 510(k) Process have been implemented in practice by regulators and process users. As predicate creep, these patterns will be identified using the manually constructed databases and predicate approval trees developed from publicly available FDA data. Observations made during this portion of the analysis will include whether there is a common methodology used during the 510(k) application process for selection of predicate devices, the level of overlap between different predicate traces, comparison of the number of predicates identified in different traces, and other general observations.

In addition to general observations, data collected from the FDA Medical Device Recall Database will be used to identify devices with documented safety concerns. Although it is difficult to identify the scientific evidence presented to support claims of safety between predicates, a correlation between the presence of predicate creep and issued recalls would be indicative that concerns expressed by researchers surrounding the effects of predicate creep are founded.

5 DATA ANALYSIS

5.1 INITIAL PREDICATE TRACE DEVELOPMENT

Using the information in the newly constructed NAY Product Code database, I was able to identify the earliest iteration of the Da Vinci System known as the Da Vinci Surgical System Model ISI 1000, which was first approved on May 30th, 2001. However, the 510(k) database contained no application summary or information regarding the direct predicates used in the approval process. Further investigation via additional FDA databases and Intuitive Surgical's website revealed no additional information regarding the approval process for this model. In fact, Intuitive does not list or reference this model anywhere on its website (Intuitive Surgical, 2018).

Although this the lack of information on the first Da Vinci System poses a problem for this investigation, information is available for the next iteration of the device approved in June 2002, the Da Vinci Surgical System Model IS1200. Using the information obtained from the TPLC Report, I was able to obtain the 510(k) application number for this device, K021036, which in turn allowed me to obtain the application summary.

From the application summary I was able to identify the predicate of the Da Vinci Model IS1200 as the Da Vinci Surgical System Model ISI 1000. This application referenced four K-numbers associated with the predicate device, including K011002, the number previously identified and investigated without success. Using the information found in the 510(k) database for the remaining three K-numbers and subsequently identified predicates, I was able to construct an ancestral equivalence tree going back four generations on the longest branch.

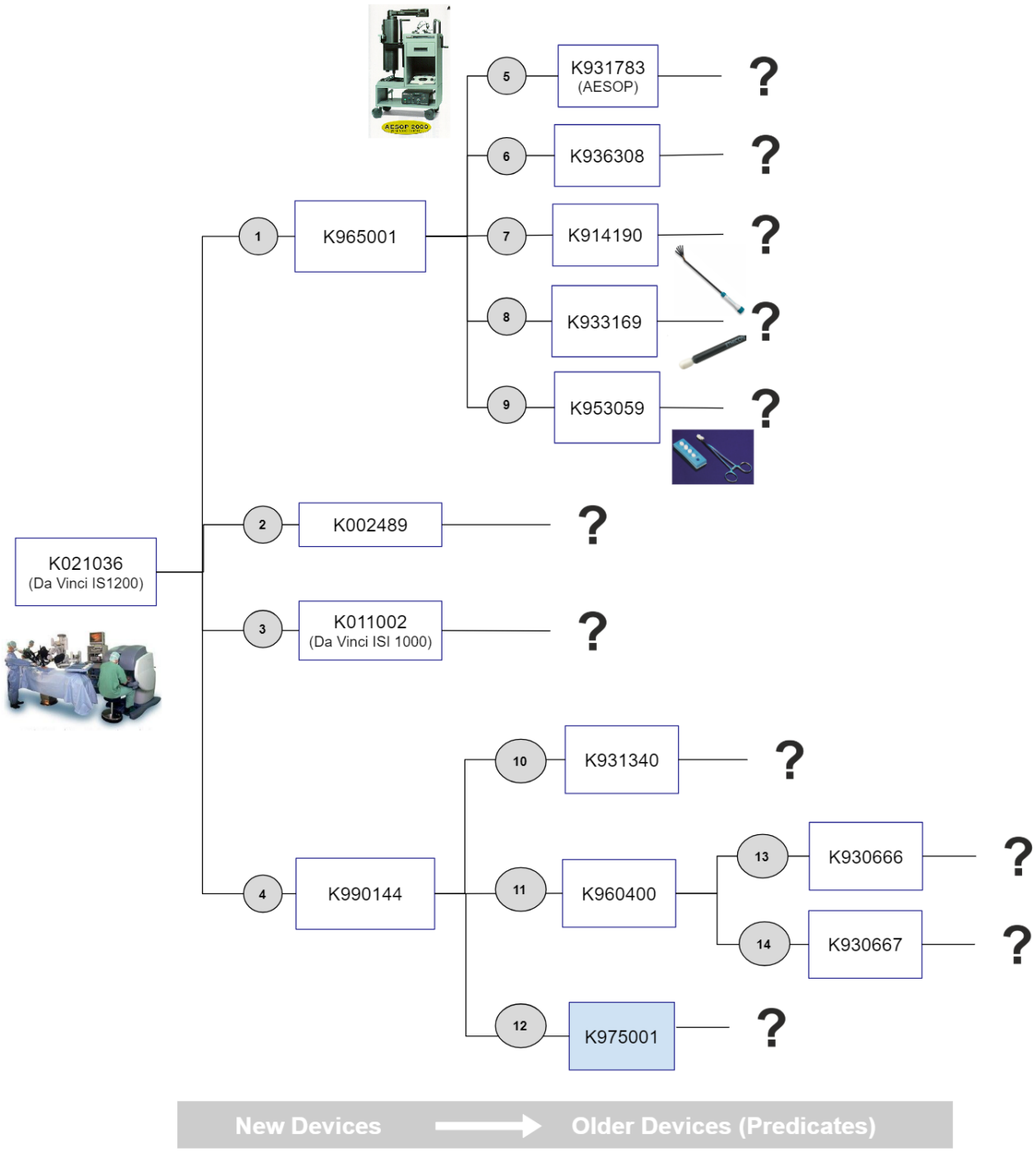

Figure 3: Intuitive Da Vinci Model IS1200 predicate ancestry tree, with predicates identified by K# (see Table 2 for device descriptions) and substantial equivalence relationships numerically identified in grey circles (see Table 3 for device characteristic comparisons).

There are a total 14 predicate devices listed in this tree, with four devices in the first generation, eight in the second, and two in the third. The tree contains 11 unique branch lines, but only two primary multi-generational branches. Unfortunately, the size of this trace is limited by the availability of information in the database, with the oldest identified predicate device receiving approval only ten years before the subject device, in May 1992. Additionally, one identified predicate device, K975001, was listed by K#, name, and manufacturer on the application summary for the Intuitive Surgical Reposable Endoscopic Instruments and Accessories, but no record of that K# or device exists in the 510(k) database. Further examination revealed that the identified device possessed the same name, Intuitive Surgical Endoscopic Instrument Control System and Select Instruments, as is identified by K002489 and within the application summary of K965001, which suggests that this may be an earlier model of the Intuitive Endoscopic Control System. However, the non-existence of the device within the 510(k) database and the extreme similarity between its identified K# K975001and the K# K965001, which was identified by the same name, leads me to believe that this may have been an error on the part of the summary writer, and that the correct predicate device may in fact be K965001. However, for purposes of this analysis I used the information as found in the database, regardless of suspected errors. Table 2 below contains a summary of the devices identified in this trace, including the stated intended use (if available), product code, and a brief device description.

Table 2: Summary of information for device contained within the Da Vinci IS1200 predicate history, including the intended use (if indicated) and a brief description of the technical characteristics of each device,

K-Number	Device Name	Manufacturer	Approval Date	Product Code	Intended Use*	Device Description
K021036	Da Vinci Surgical System, Model Is1200	Intuitive Surgical, Inc.	6/26/2002	NAY	Assist in accurate control of endoscopic instruments during laparoscopic surgical procedures	Three manipulator arms (8 DOF each) with attached endoscope and endoscopic instruments, controlled by a surgeon from a console with a 3D vision system, used to perform laparoscopic surgical procedures
K965001	Monarch Laparoscopic Manipulator **	Intuitive Surgical, Inc.	7/31/1997	GCJ	Precise and accurate control of instruments during thoracoscopic and laparoscopic surgical procedures	Multiple manipulator arms (8 DOF each) with attached endoscope and endoscopic instruments controlled from a surgeon console to view and perform surgical procedures
K002489	Da Vinci Endoscopic Control System	Intuitive Surgical, Inc.	3/2/2001	NAY		Multiple manipulator arms (8 DOF each) with attached endoscope and endoscopic instruments controlled from a surgeon console to view and perform surgical procedures
K011002	Da Vinci Surgical System, Model ISI 1000	Intuitive Surgical, Inc.	5/30/2001	NAY	Assist in accurate control of endoscopic instruments during laparoscopic surgical procedures	Two manipulator arms (8 DOF each) with attached endoscope and endoscopic instruments, controlled by a surgeon from a console with a 3D vision system, used to perform laparoscopic surgical procedures
K990144	Intuitive Surgical Reposable Endoscopic Instruments and Accessories	Intuitive Surgical, Inc.	7/11/2000	NAY	Assist in accurate control of endoscopic instruments during laparoscopic surgical procedures	Various endoscopic instruments with control interfaces designed for use with the Intuitive Endoscopic Control System
K931783	AESOP (Automated Endoscopic System for Optimal Positioning	Computer Motion, Inc	11/22/1993	GCJ		An endoscopic telemanipulator consisting of a motorized arm with 6 degrees of freedom, controlled by a foot pedal to manipulate and stabilize an endoscope
K936308	Endex Endoscopic Positioning System	Andronic Devices, Ltd.	3/31/1994	FQO		A jointed arm which can be manually positioned by a surgeon to position and stabilize an endoscope. A single motor-driven linear joint (1 DOF) controlled by a foot pedal is used to move the endoscope into and out of the body.
K914190	Auto Suture(R) Endoscopic Fan Retractor	United States Surgical, A Division of Tyco Healthcare	5/6/1992	GAD		An endoscopic instrument with multiple prongs which can be expanded inside the body using a cable-driven mechanism into a fan-like shape to keep tissue away from the operating area.
K933169	Endoscopic Blunt Dissector	Inman Medical Corp.	4/19/1994	GCJ		A manually controlled endoscopic instrument with a rounded tip used to manipulate tissue during laparoscopic surgical procedures

K-Number	Device Name	Manufacturer	Approval Date	Product Code	Intended Use*	Device Description
K953059	Kittner Dissector	Medical Perspectives Corp.	9/14/1995	GDY		A non-absorbable gauze sponge for use with an endoscopic blunt (rounded tip) dissector
K931340	Endoscopic Instruments	Baxter Healthcare Corp.	7/1/1993	GCS		Various manually positioned, motor driven endoscopic instruments including grasp forceps, scissors, dissectors, and a needle holder
K960400	Diamond-Touch And Micro Diamond-Touch Instruments/Diamond-Line Instruments/Diamond-Port (Access Parts)	Snowden-Pencer	3/12/1996	FBM GCJ GEI	Various endoscopic instruments for use in laparoscopic cardiac surgical procedures	Manual endoscopic instruments, including an access port, endoscopes, needle holders, graspers and clamps, scissors, probes, knife blade handles, clippers, and other instruments
K975001***	Intuitive Surgical Endoscopic Instrument Control System and Select Instruments	Intuitive Surgical, Inc.	N/A	N/A		Multiple manipulator arms (8 DOF each) with attached endoscope and endoscopic instruments controlled from a surgeon console to view and perform surgical procedures
K930666	Reusable Laparoscopic Instruments W/ Electrocautery	Snowden-Pencer	5/19/1994	GEI		Various laparoscopic instruments with reusable handles which incorporate wire electrodes to generate heat, which is used to burn away unwanted tissue and seal blood vessels during surgery
K930667	Reusable Laparoscopic Instruments	Snowden-Pencer	5/16/1994	GCJ		Various laparoscopic instruments with reusable handles which

**Intended use information only available for devices with approval application summaries present in the public 510(k) database*

*** The name for this device referenced in the approval application summary is the Intuitive Surgical Endoscopic Instrument Control System*

**** This device is referenced in the approval summary for K990144 by K# and Device Name. However, the K# listed does not appear in the FDA database, and the name corresponds with K965001*

The Da Vinci IS1200 trace includes devices from eight unique manufacturers, although Computer Motion later combined with Intuitive Surgical in 2003. Devices belong to eight unique device product code classifications. It is worth noting that in addition to the four K-Numbers marketed under the Da Vinci Model ISI 1000 (those in the first predicate generation), K-Numbers K930666 and K930667 are both associated with the Snowden-Pencer Reusable Laparoscopic Instruments. This means that this trace contains only 9 unique devices which were manufactured and introduced to the market, compared to 14 difference devices when referenced from a regulatory perspective. Since the successful performance of each predicate device on the market is part of the body of evidence to support the safety claims of the new device, a smaller number of unique devices with market performance data effectively reduces the level of assurance of safety for the subject device, in this case the Da Vinci IS1200.

To identify instances of predicate creep within the trace, I have compiled in Table 3 a list of the technological differences between each of the subject-predicate pairs present in this trace. The numbered predicate relationship corresponds to the numbers identified in grey in Figure 3.

Table 3: Differences in technological characteristics between the two devices in each predicate relationship (identified by number in Figure 3) within the Da Vinci IS1200 approval history

Predicate Relationship	Subject Device	Predicate Device	New Technological Characteristics in Subject Device
1	Da Vinci Surgical System, Model IS1200	Monarch Laparoscopic Manipulator	The IS1200 incorporates a 3D vision system and specialized endoscopic instruments designed to mimic the motion of a human wrist
2	Da Vinci Surgical System, Model IS1200	Da Vinci Endoscopic Control System	The IS1200 incorporates a 3D vision system and specialized endoscopic instruments designed to mimic the motion of a human wrist
3	Da Vinci Surgical System, Model IS1200	Da Vinci Surgical System, Model ISI 1000	The IS1200 includes updated software and a 3rd manipulator arm
4	Da Vinci Surgical System, Model IS1200	Intuitive Surgical Reposable Endoscopic Instruments and Accessories	The Da Vinci includes a surgeon console, 3D vision system and manipulator arms for control and positioning of existing endoscopic instruments
5	Monarch Laparoscopic Manipulator	AESOP (Automated Endoscopic System for Optimal Positioning	The Monarch includes multiple teleoperated arms with increased range of motion, is controlled from a surgeon console, and is used to perform surgical procedures using endoscopic instruments in addition to positioning and stabilization of an endoscope
6	Monarch Laparoscopic Manipulator	Endex Endoscopic Positioning System	The Monarch includes multiple teleoperated arms with increased range of motion, is controlled from a surgeon console, and is used to perform surgical procedures using endoscopic instruments in addition to positioning and stabilization of an endoscope
7	Monarch Laparoscopic Manipulator	Auto Suture(R) Endoscopic Fan Retractor	Monarch incorporates articulated instrument control arms and multiple instruments operated from a console
8	Monarch Laparoscopic Manipulator	Endoscopic Blunt Dissector	Monarch incorporates articulated instrument control arms and multiple instruments operated from a console
9	Monarch Laparoscopic Manipulator	Kittner Dissector	Monarch incorporates articulated instrument control arms and multiple instruments operated from a console
10	Intuitive Surgical Reposable Endoscopic Instruments and Accessories	Baxter Healthcare Endoscopic Instruments	The Intuitive instruments have a unique control interface which enables use with the Intuitive Endoscopic Control System
11	Intuitive Surgical Reposable Endoscopic Instruments and Accessories	Diamond-Touch And Micro Diamond-Touch Instruments/Diamond-Line Instruments/Diamond-Port (Access Parts)	The Intuitive instruments have a unique control interface which enables use with the Intuitive Endoscopic Control System
12	Intuitive Surgical Reposable Endoscopic Instruments and Accessories	Intuitive Surgical Endoscopic Instrument Control System and Select Instruments	No technological changes identified between instruments
13	Diamond-Touch And Micro Diamond-Touch Instruments/Diamond-Line Instruments/Diamond-Port (Access Parts)	Reusable Laparoscopic Instruments W/ Electrocautery	No technological changes identified
14	Diamond-Touch And Micro Diamond-Touch Instruments/Diamond-Line Instruments/Diamond-Port (Access Parts)	Reusable Laparoscopic Instruments	No technological changes identified

An initial overview of the technological differences identified in Table 3 reveals that almost every device present in the trace demonstrated some level of technological creep. In some cases, technology creep was limited to the introduction of a new mechanical control interface or the addition of an extra arm, but in other cases the degree of technological difference is striking. This is most conspicuous in the comparison of the various endoscopic instruments to the Monarch Laparoscopic Controller, which incorporates telemanipulator arms and a surgeon console to move the instruments and perform procedures. However, the Monarch is a system which incorporates versions of these instruments, so it appears that they are serving as predicates only for the endoscopic end effectors and are not intended to provide any assurance of safety or efficacy for the system as a whole. However, the technological gap between the AESOP and ENDEX Systems and the Monarch is still quite large. The Monarch not only incorporates additional degrees of freedom into the manipulator arm, but it also consists of multiple arms, is controlled by a surgeon sitting at a separate viewing console, and is used to perform actual surgical procedures without the surgeon directly contacting the patient. This is a huge change in technology within a single predicate relationship.

5.2 EXPANSION TO RELATED DEVICES

Examination of the wide variety of technological characteristics present across a given predicate generation in the Da Vinci IS1200 trace led me to wonder how the technological characteristics of the Da Vinci compare to other devices in its own generation. Therefore, I decided to identify other devices which share a common predicate with the Da Vinci IS1200, in order to identify the

degree of difference between different devices within the same technological generation and theoretically also the same device family. The predicate which I chose to base my trace off of was the AESOP system, both because it is the oldest device within the IS1200 trace which is not a basic surgical instrument, and because it is the ultimate predicate which is most similar to the Da Vinci in terms of technological characteristics, complexity, and function.

5.2.1 Device Identification

While tracing backwards through substantial equivalence relationships identifies predicates with different characteristics ultimately present in a subject device, tracing forward from a given predicate to subsequent subject devices should reveal a group of devices which share the common characteristics of the initial predicate. Based on the definition of substantial equivalence, these devices should share a common intended use and similar technological characteristics. However, this type of tracing is extremely difficult to do within FDA databases, as devices approved based on a specific device are not identified anywhere in that device's approval information. Therefore, I used the brute-force search methodology to identify a total of seven additional devices predicated on AESOP, including a newer model of the AESOP system. The ancestry of each device was then traced to construct a tree connected to the Da Vinci trace as shown in Figure 4. Rather than identify generations based on predicate distance, the number of predicates between the two devices, for this tree generations were grouped based on the number of subject devices between the two devices, known as subject device distance. As a result, while previous trees were constructed to trace the approval history of a device backwards in time

through predicate generations, this tree was used to trace forwards in time and identify generations of subject devices approved based on the AESOP System.

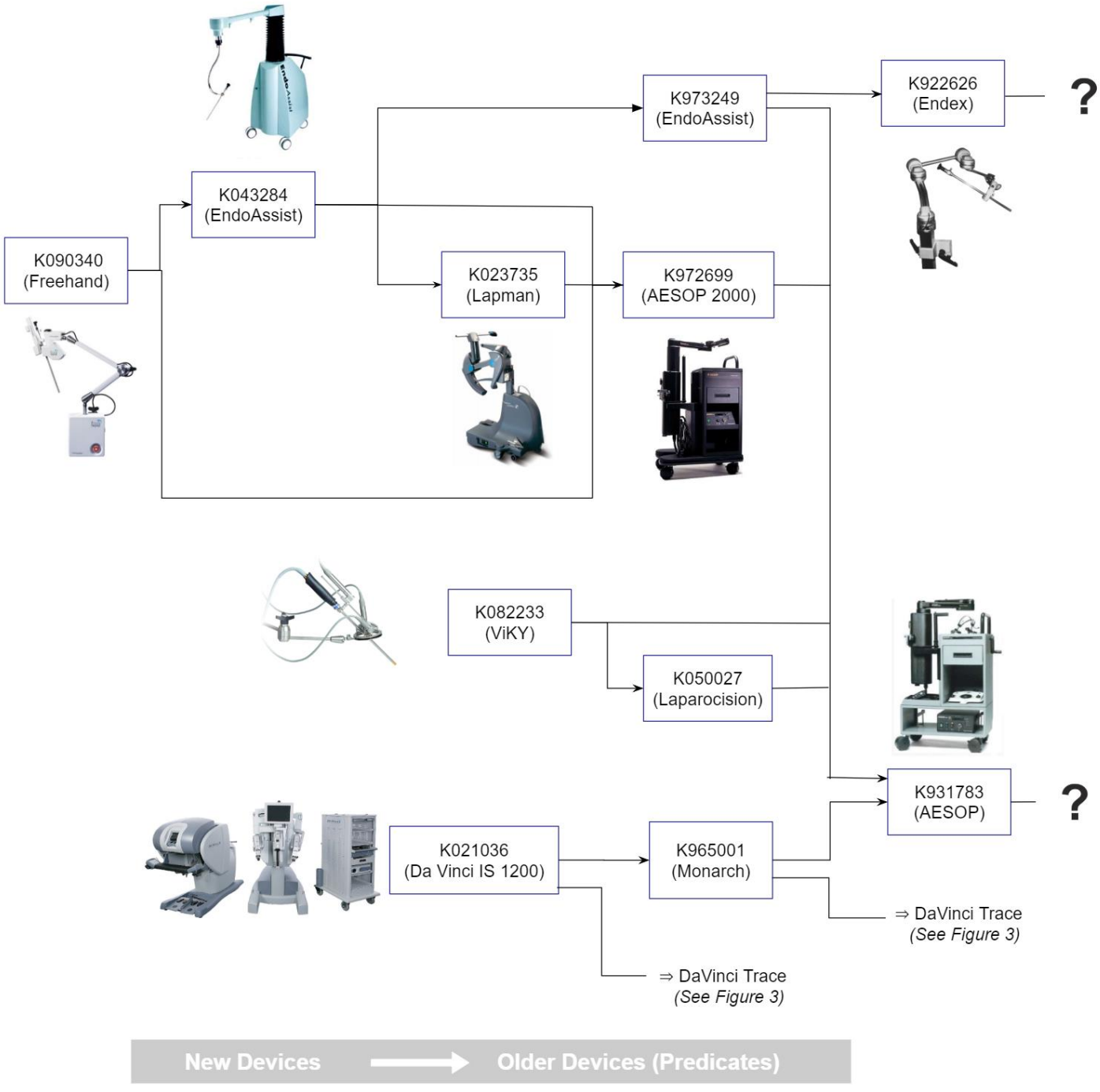

Figure 4: Ancestry tree illustrating devices predicated on the AESOP System. Arrows indicate a substantial equivalence relationship pointing from newer subject device to older predicate device, with "subject generation zero" including the oldest devices (far right).

The trace above illustrates the substantial equivalence relationships between the devices predicated on the AESOP system. To identify any safety issues identified while on the market, each device was run through the FDA recall database. Of the eleven devices included in this trace, only the Da Vinci model IS1200 had any recalls associated with it. The IS1200 has undergone a total of 18 Class II recalls, recalls of moderate severity, ranging from user manual mistakes to incorrect component installation which may cause power loss. Table 4 (below) provides additional information about the devices in this trace, along with a brief technical description of each device.

Table 4: Summary of Devices in Expanded AESOP Trace

510(k) Number	Device Name	Manufacturer	Approval Date	Product Code	Device Description	Generation (Subject)
K931783	AESOP Laparoscopic Positioning and Control System	Computer Motion	11/22/93	GCJ	An endoscopic telemanipulator consisting of a motorized arm with 6 degrees of freedom, controlled by a foot pedal to manipulate and stabilize an endoscope	0
K922626	Endex Endoscopy Instrument Positioning System / Adept Instrument Positioning System	Andronic Devices	10-19-92	GAD	A jointed arm which can be manually positioned by a surgeon to position and stabilize an endoscope. A single motor-driven linear joint (1 DOF) controlled by a foot pedal is used to move the endoscope into and out of the body.	0
K973249	EndoAssist	Armstrong Healthcare Limited	11/26/97	GCJ	A freestanding arm mounted on an extended boom with 2 DOF. It is controlled by a head-tracking system which tracks the head motion of the surgeons and is engaged using a foot pedal.	1
K972699	AESOP 3000	Computer Motion	12/19/97	GCJ	An endoscopic telemanipulator consisting of a motorized arm with 6 degrees of freedom, controlled by a foot pedal to manipulate and stabilize an endoscope	1
K050027	Laparocision Scope Controller System	GMP	1/25/05	GCJ	N/A	1
K965001	Monarch Laparoscopic Manipulator	INTUITIVE SURGICAL, INC.	7/31/1997	GCJ	Multiple manipulator arms (8 DOF each) with attached endoscope and endoscopic instruments controlled from a surgeon console to view and perform surgical procedures	1
K082233	ViKY	EndoControl	12/18/08	GCJ	An endoscope holder consisting of a jointed arm with three actuated degrees of freedom which can be attached directly to an operating table and a command from which the surgeon can control position using a footswitch or verbal commands	1, 2
K021036	Da Vinci Surgical System, Model IS1200	INTUITIVE SURGICAL, INC.	6/26/2002	NAY	Three manipulator arms (8 DOF each) with attached endoscope and endoscopic instruments, controlled by a surgeon from a console with a 3D vision system, used to perform laparoscopic surgical procedures	2
K023735	LapMan Laparoscopic Manipulator	Medsys	8/7/07	GCJ	An actuation arm composed of two parallel kinematic joints and one linear joint to provide 3 DOF, located on a moveable cart and controlled with a wireless joystick for use in gynecological surgery.	2
K043284	EndoAssist	Armstrong Healthcare Limited/Prosurgics	2/25/05	GCJ	A freestanding arm mounted on an extended boom with 2 DOF. It is controlled by a head-tracking system which tracks the head motion of the surgeons and is engaged using a foot pedal.	2, 3
K090340	Freehand	Prosurgics	5/22/09	GCJ	A portable arm mounted to the operating table with 3 DOF. It is controlled by a head-tracking system which tracks the head motion of the surgeons and is engaged using a foot pedal.	2, 4

Including the Da Vinci IS1200, this ancestry tree contains a total of eleven devices spanning four equivalence generations (plus the originating generation). These devices are classified under three different product codes; 1 device under code NAY, 1 device under code GAD, and the remaining 9 under GCJ. The common use of product code GCJ implies that the technological characteristics of the majority of devices contained in the trace should be extremely similar. The only devices not classified under product code GCJ, which refers to devices described as "endoscope and accessories" for laparoscopic and general surgery (FDA, 2018d), are the originating predicate devices and the Da Vinci itself.

Except for the Da Vinci, all the devices within this trace share two originating predicates, the Endex Instrument Positioning System and the AESOP system. The Endex System is classified under code GAD, which refers to a retractor with a regulatory description of "manual surgical instrument for general use" (FDA, 2018d). Code NAY, under which the Da Vinci is classified, refers specifically to computer controlled surgical devices with the base function of "endoscope and accessories" (FDA, 2018c). Code GCJ has a more general device description than code NAY, similar to code GAD, although devices classified under this code share similar technical characteristics to devices in code NAY, such as the inclusion of a manipulator arm. However, the addition of "computer controlled" to the device description for code NAY implies that the level of technical complexity in the control system of Da Vinci may be higher than in other devices in this trace classified under code GCJ, despite sharing the same regulatory description of "endoscope and accessories". This correlation between changes in product code classifications

and technical complexity is supported by the comparison of actual device technical characteristics as described in Table 4.

5.2.2 OBSERVATIONS

Inspection of the predicate relationships within the AESOP subject device trace reveals an interesting pattern. Although there were six additional subject devices introduced in this tree, tracing the branch lines of the devices creates a web where the subject device equivalence refers to earlier existing predicates multiple times. This results in an equivalence tree with only two ultimate predicates, AESOP and the Andronic Endex Instrument Positioning System. Only the Da Vinci refers to a different set of ultimate predicate devices. Although this interrelatedness is not entirely unexpected, as there are a limited number of devices available to serve as predicates for any given device function, it does make the width and variety of the Da Vinci trace appear unusual. Considering the technological characteristics of the devices, one possible implication of the size of the Da Vinci trace, which is primarily caused by the presence of multiple predicated for each 510(k) application, is that Intuitive Surgical used multiple predicate devices to justify the relatively large differences in technological characteristics when compared directly to each individual predicate.

Additionally, the appearance of one predicate device multiple times within the trace in different generations illustrates that the intermediary predicates serve as stepping stones, introducing slight changes in technological characteristics but ultimately referring back to a single set of ultimate predicates. This method introduces new technological characteristics incrementally into

the ultimate subject device, while keeping the majority of the dependence for evidentiary support of the safety of new characteristics on the ultimate predicate(s).

5.3 EXPANSION TO DA VINCI SI

Due to the age-based limitations of the 510(k) database, it proved to be impossible to expand the Da Vinci trace past three predicate generations using publicly available data. As a result, a lack of scientific evidence reduces the significance of observations made using the trace. However, one option to create a larger ancestral trace is to begin the trace using newer models of the Da Vinci. As new technological characteristics, and subsequently new predicate devices, were introduced into the Da Vinci S and Si models, the size of the traceable ancestry tree expanded. Patterns identified in this larger trace may be more indicative of the regulatory behavior on the part of both Intuitive Surgical and the FDA.

5.3.1 PREDICATE ANCESTRY TRACE

The predicate ancestry of the Da Vinci Si Model was traced using the same method described previously for the Da Vinci IS1200 predicate tree development. Unlike the previous trees, the number of devices and predicate relationships contained in this trace is too large to be easily illustrated with a traditional ancestry tree diagram, so an alternative diagram was constructed using network mapping techniques as shown in Figure 5.

Within this network mapping diagram each device is represented by a dot, with the dot size increasing based on the total number of substantial equivalence relationships that device is involved in. Substantial equivalence relationships (also known as predicate-subject device relationships) are represented by lines drawn between the two devices involved. Each dot is labeled with the K# of the device which it corresponds to. The trace begins with the main subject device (i.e. the Da Vinci) on the left side of the trace, and advances toward the left, with each line originating at a subject device and terminating at its respective predicate. Therefore, the oldest devices present in the trace are located on the right side, although vertical alignment does not correlate exactly to approval date, and the newest devices are to the left of the trace.

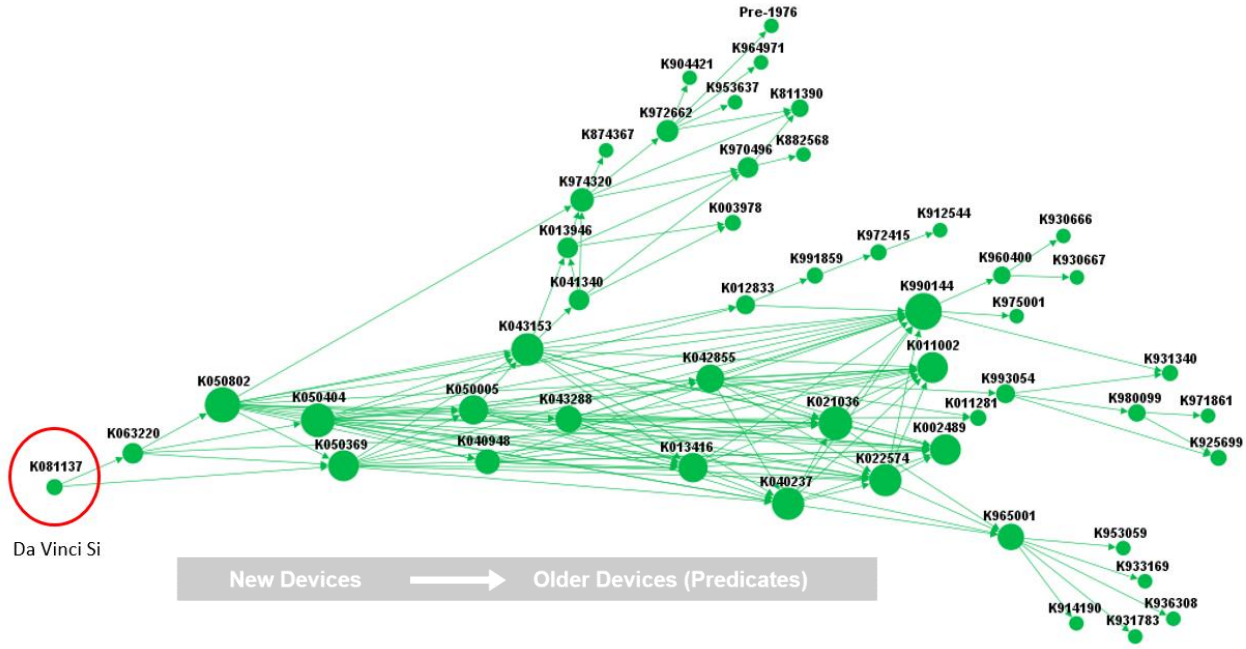

Figure 5: Expanded Da Vinci Si predicate trace originating from the Da Vinci Si (far left) with each predicate device represented by a dot and identified by K# (see Appendix 2). Trace lines indicate substantial equivalent relationships with the arrowhead pointing towards the predicate device and relative dot size indicating the number of substantial equivalence relationships associated with each device.

The expanded equivalence tree, which uses the Da Vinci Si as the subject device, includes 2618 device instances, with a total of 50 unique devices. The unique devices within this trace are classified under a total of 15 different product codes, with the majority of devices, including the various Da Vinci models, categorized under code NAY. Additional information about each device, including the manufacturer, approval date, and any recalls issued, can be found in Appendix 2.

Recall data from the FDA database, which tracks recalls issued by the manufacturer either due to an error identified internally or in response to a series of incidents traced directly to a problem with the device, was used to identify devices in the Da Vinci ancestry with significant safety issues. The FDA classifies recalls based on the severity of potential impact to the patient. Class III recalls are minor and not likely to cause any adverse health effects. Class II recalls occur when exposure may cause temporary or reversable adverse health effects, or where there is a low probability of serious adverse effects. Class I is the most severe type of recall, in which there is a reasonable probability that exposure will result in serious adverse effects or death. While a couple of Class II or III recalls will likely have minimal effect on overall device safety, repeated Class II recalls or any Class I recall is directly indicative of potential device issues.

Of the 50 devices included in the Da Vinci Si trace, 7 devices, all manufactured by Intuitive Surgical as part of a DaVinci system, had multiple recalls associated with the device. These recalls include 18 for the Da Vinci Model IS1200, 43 for the Da Vinci IS2000 (aka Da Vinci S), and 24 for the Da Vinci Si. All the recalls associated with these devices were Class II, which

means that although there was no immediate risk of patient death due to the issue, there was still significant risk of harm to the patient.

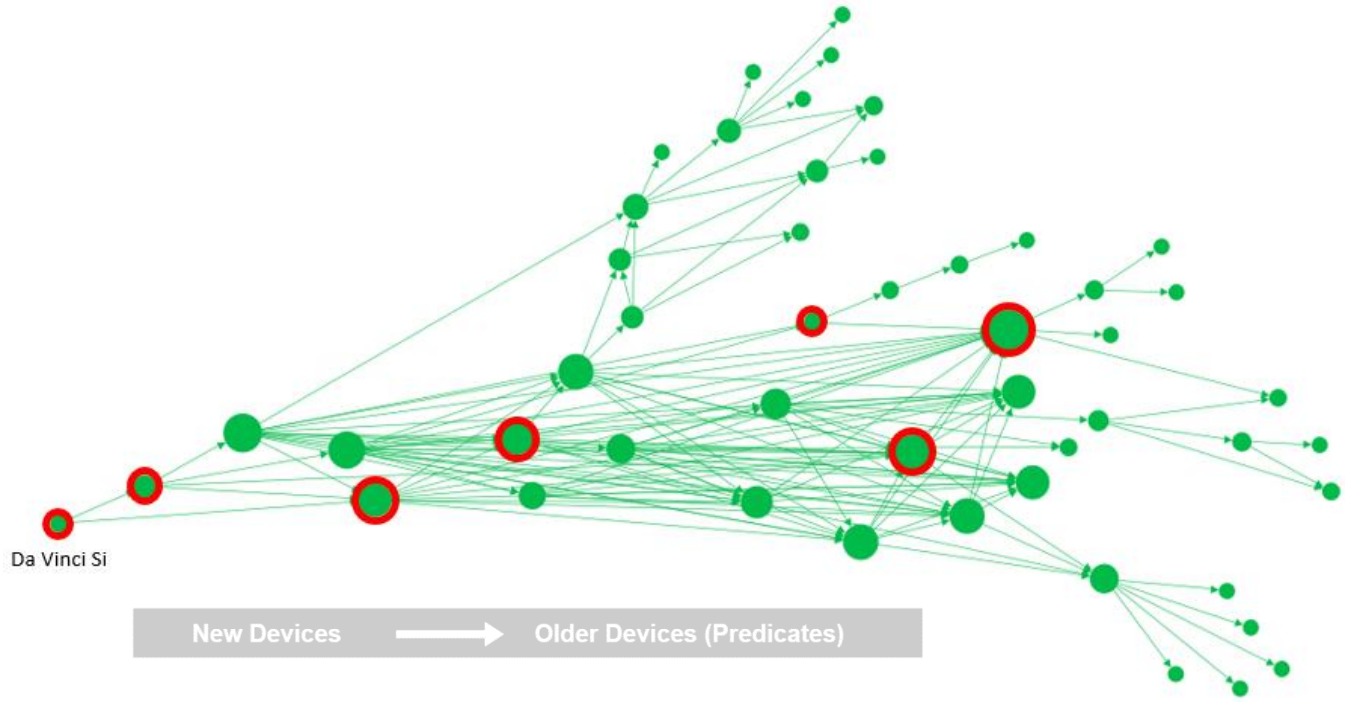

Figure 6: Da Vinci Si Trace with devices which have undergone 3 or more recalls highlighted in red.

When the devices with associated recalls are highlighted in the ancestry trace, it becomes clear that all of these devices are newer, complex devices which were approved relatively recently. Furthermore, despite the high numbers of recalls associated with early Da Vinci models, Intuitive continued to release subsequent Da Vinci models whose approval was directly reliant on the previous models.

Looking at the overall spread of the ancestry trace, certain patterns within the predicate structure begin to emerge. The initial central portion of the trace includes a number of devices with many

overlapping substantial equivalence lines. These devices are mostly developed by Intuitive Surgical, with the majority of identified as either sub-components or iterations of the Da Vinci Surgical System. However, as the trace expands the inter-related predicates are replaced with five distinct groups of predicate devices with no overlap between substantial equivalence lines. Each group appears to contain devices with similar characteristics, where each of the five groups representing diverse technological characteristics which were later combined together to form the more complex Da Vinci system.

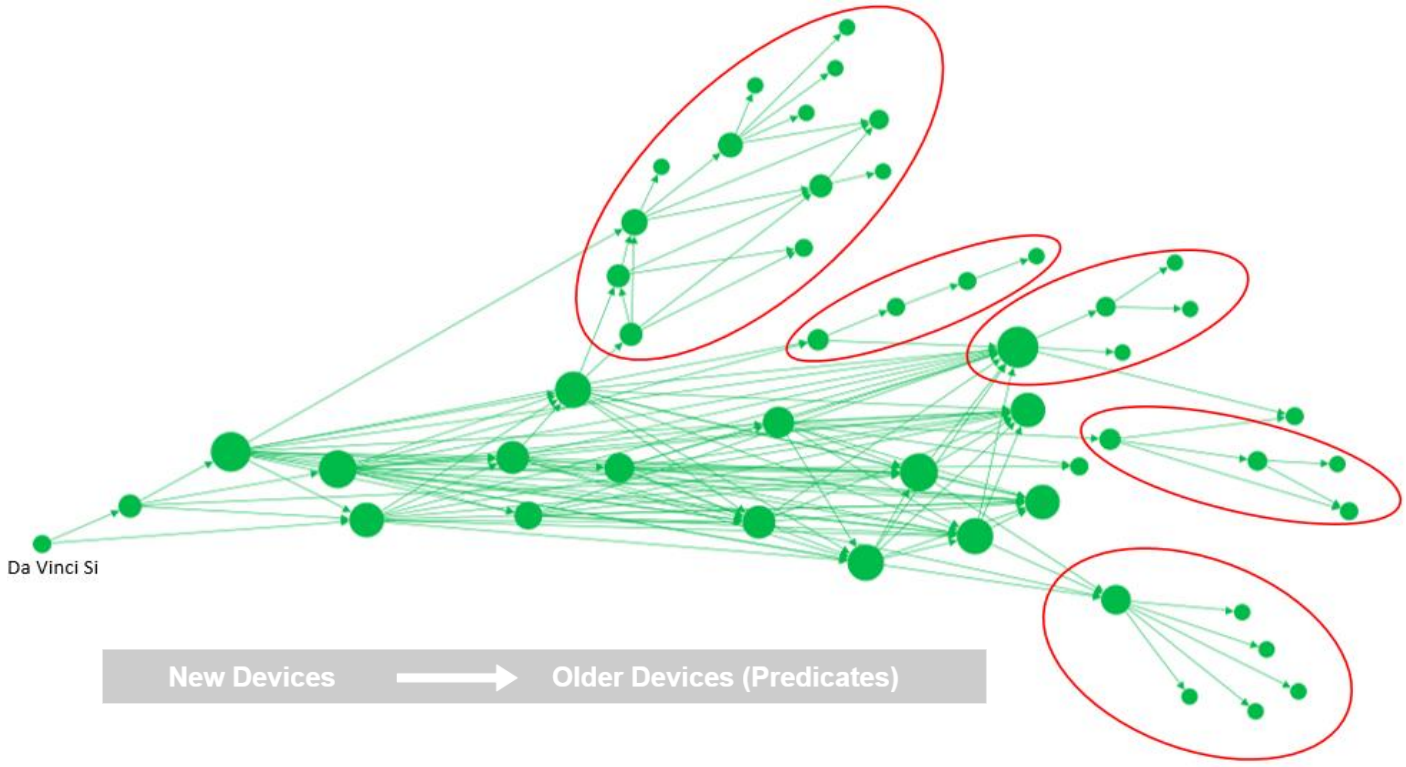

Figure 7: Da Vinci Si trace with the five distinct predicate branches highlighted.

5.3.2 Grouping via Regulatory Mechanisms

Considering the size of this data set, attempting to identify the exact technological characteristics of each device contained within to try to identify specific examples of predicate creep would be extremely difficult and time consuming. However, categorizing the devices in the trace by product code can help identify patterns within the trace using more general device characteristics to identify trends over time.

A list of the codes, the device identification key, and the regulatory description for each code is shown in the table below. The device identification key is a set of functions or characteristics which distinguish devices in that product classification, while the regulatory description is the primary function or intended use as identified by the FDA.

Table 5: Product Codes in Da Vinci Si Trace

Code	# Devices	Device Identification	Regulatory Description
FBM	1	Cannula and Trocar, Suprapubic, Non-Disposable	Suprapubic urological catheter and accessories
NEY	3	System, Ablation, Microwave and Accessories	Electrosurgical cutting and coagulation device and accessories
NAY	17	System, Surgical, Computer Controlled Instrument	Endoscope and accessories
HET	1	Laparoscope, Gynecologic (And Accessories)	Gynecologic laparoscope and accessories
GEI	5	Electrosurgical, Cutting & Coagulation & Accessories	Electrosurgical cutting and coagulation device and accessories
LFL	4	Instrument, Ultrasonic Surgical	N/A
OCL	5	Surgical Device, For Cutting, Coagulation, And/Or Ablation of Tissue, Including Cardiac Tissue	Electrosurgical cutting and coagulation device and accessories
GEH	6	Unit, Cryosurgical, Accessories	Cryosurgical unit and accessories
GCJ	6	Laparoscope, General & Plastic Surgery	Endoscope and accessories
GDY	1	Gauze/Sponge, Internal, X-Ray Detectable	Nonabsorbable gauze for internal use
FQO	1	Table, Operating-Room, Ac-Powered	Operating tables and accessories and operating chairs and accessories
GCS	1	Endoscope, Battery-Powered and Accessories	Endoscope and accessories
GAD	1	Retractor	Manual surgical instrument for general use
MAV	1	Syringe, Balloon Inflation	Angiographic injector and syringe
HQO	1	Unit, Cautery, Thermal, Ac-Powered	Thermal cautery unit

A breakdown of the devices present in the trace color-coded by product code is pictured in Figure 8 below. The most prevalent code is NAY for computer controlled surgical systems, as mentioned previously. The next two most prevalent codes are GEH for cryosurgical units and GCJ for general laparoscopic surgery. Color-coding devices by code highlights common device functions within the trace and allows for easy identification of technical characteristics as they evolve through predicate generations.

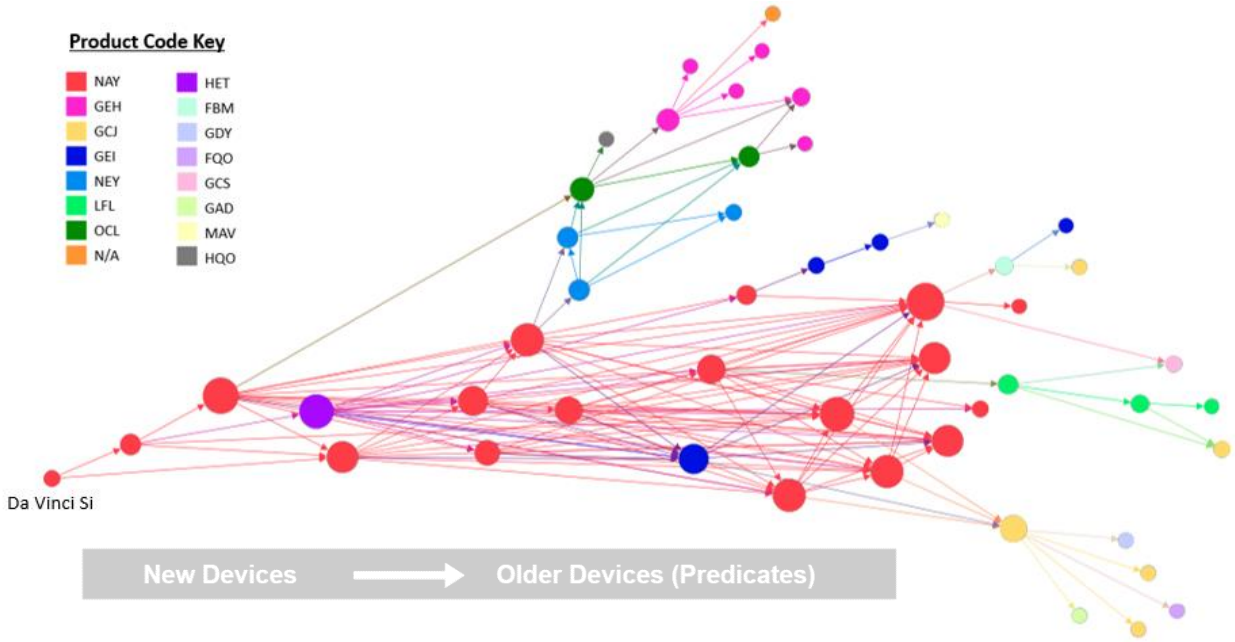

Figure 8: Da Vinci Si Trace with devices color-coded by product classification code (See Appendix 3 for full list of product code definitions).

Looking at the tree breakdown by product code in Figure 8, we can see the progressive evolution of devices from more general laparoscopic surgical tools (to the right) to the more technologically complex computer-controlled system of the Da Vinci. The five distinct branches identified earlier emerging from the intertwined trace center are each dominated by one or two distinct product codes, while the devices within the central web belong almost exclusively to the same product classification as the Da Vinci. This implies that the technological characteristics the FDA uses to identify devices belonging to code NAY are a combination of the characteristics present in each distinct predicate group. This illustrates how larger "jumps" in technological complexity of devices new devices can occur through the 510(k) Process, by combining the characteristics of multiple well-understood devices into a new type of device.

Another perspective to examine the technological evolution within the ancestral trace is based on the regulatory description rather than the product code. While the product code considers both the intended use and specific characteristics of a device, the regulatory description is a broader, more general description based on the function of the device as defined by the FDA. For example, the specific device description for product code GCJ is “laparoscope, general and plastic surgery,” which specifies both a particular type of device and use, while the regulatory description “endoscope and accessories” specifies only a general classification of devices. Because of these broader descriptions, there is often overlap between the regulatory descriptions of different product codes. In this trace, devices from 15 product codes can be placed into 11 groups based on regulatory descriptions, resulting in the formation of two larger groups which contain the majority of devices within the trace.

The regulatory definition breakdown reveals that approximately half of the devices (24) within the trace are classified from a regulatory perspective as endoscope and accessories. A further ~25% (13 total) are classified as electrosurgical cutting and coagulation devices, devices which use a high frequency electrical current to perform surgical operations. 6 of the devices are cryosurgical units, all classified under product code GEH, with the remaining devices representing a wide variety of functions and characteristics.

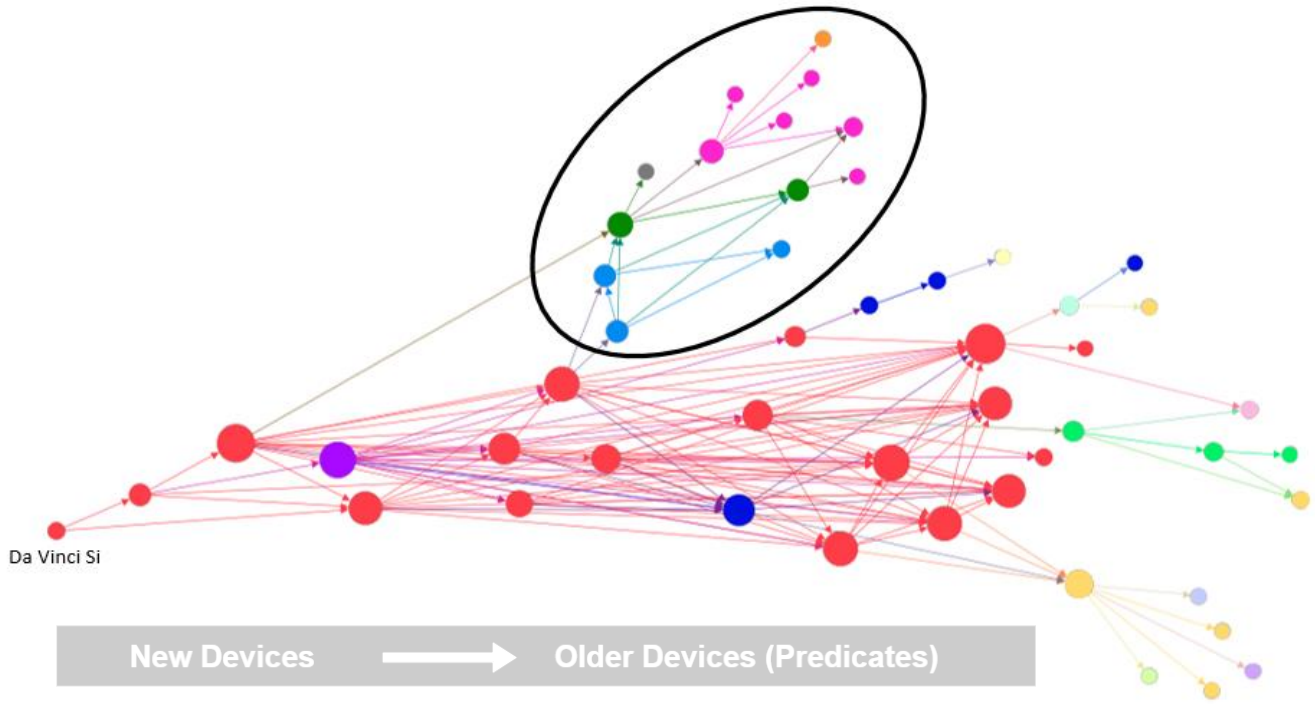

Figure 9: Da Vinci Si trace sorted by product classification code with the upper predicate branch highlighted for identification.

Unlike a grouping by product code, which highlights the evolution of specific technical characteristics over time as new codes are introduced to the trace, viewing the trace based on the regulatory description highlights groups of predicates based on general device functions. For example, in the product code trace the upper branch is comprised of four distinct product codes. However, when color-coded by regulatory description it becomes apparent that the originating predicate (branch tips) are all cryosurgical units with accessories, which serve as predicates to the electrosurgical cutting and coagulation devices the make up the middle of the branch, which in turn serve as predicated for the computer controlled surgical devices present in the web center. While color-coding by the product code specifically identifies groups of devices which the FDA considers similar enough to be substantially equivalent, devices with the same intended use and

technological characteristics, color-coding by regulatory description makes it easier to trace the general progression of technology over time based on the general function of these devices.

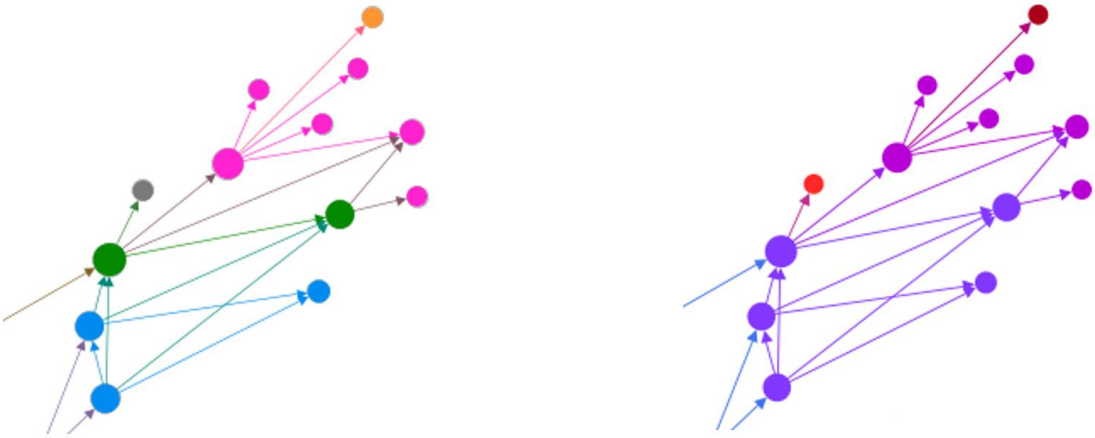

Figure 10: Direct comparison of devices in upper Da Vinci Si predicate branch (See Figure 9) color-coded by product code (left) and regulatory description (right). The new central group present in the regulatory description trace combines two product codes to create a more general device grouping.

Figure 11 shows the devices in the entire DaVinci Si Trace color-coded by regulatory description. The teal nodes and lines represent devices approved as “endoscopic instruments and control systems” under code NAY.

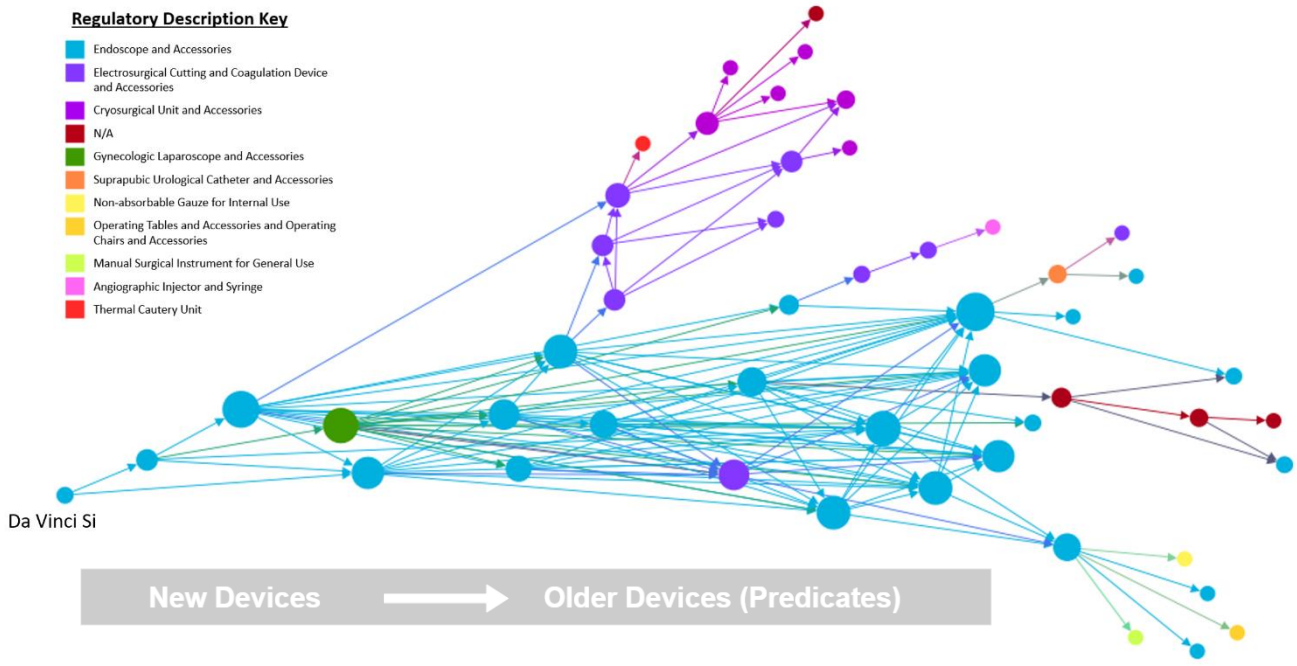

Figure 11: Da Vinci Si Trace with devices color-coded by regulatory description.

This style of coding based on regulatory description also draws attention to predicate devices with unusual functional characteristics that do not fit with the primary function of most devices within the trace. In some cases, this may be an indication of an unnecessary or ineffective predicate relationship, while in others it may be indicative of secondary device functions.

For example, in this trace there is a device identified as a non-absorbable gauze/sponge for internal use. This device, the Medical Perspectives Kittner Dissector, is a sponge used during surgical procedures to prevent bleeding. It was identified as a predicate of the Monarch Laparoscopic Manipulator system, which included customized versions of many basic surgical instruments such as gauze. Although there is a purpose for including this device as a predicate for a custom surgical tool, this part of the system is secondary to the main function of the Da Vinci as a computer controlled surgical system.

In fact, sorting predicates by regulatory description appears to allow for easy identification of both primary and secondary device functions, based on the prevalence and location of a given function in the trace. Primary device functions would be those identified directly by the regulatory description of the given device, while secondary functions would be functions present in predicate devices but absent in the regulatory description of the subject device. The more prevalent a function is in the predicate history, the more likely it is to be present in the subject device in at least a secondary capacity. Additionally, the significance of a particular secondary function to the overall function of the device appears to correspond to the number of predicates with that secondary function identified as a primary function. For example, the second most prevalent regulatory description in the Da Vinci trace is "electrosurgical cutting and coagulation device and accessories," which corresponds to the function of an essential component of the Da Vinci system. Although this is no longer listed as a primary function for the Da Vinci, it is an important component of the system.

However, this absorption of a primary predicate device function into a secondary system function draws attention to the increasing complexity of devices over time, where the Da Vinci represents a particularly large leap in complexity. While the five main predicate branch groupings each generally contain one or two primary device functions which evolve and become more complex over time, the Da Vinci suddenly combines all those functions together into a single device where none of the functions serve as the primary function. The listed primary function "endoscope and accessories," is a very generalized term which only identifies the device as one used for internal imaging, even though it includes all the other secondary functions

derived from the predicate devices, and is in fact used to directly perform surgeries. This indicates that the regulatory description for product code NAY, and possibly other product codes classified under this regulatory description, is much too broad to characterize the actual function of the devices it describes.

5.3.3 General Trace Observations

The overall dimensions of the expanded Da Vinci Si equivalence tree are somewhat unequal, with the longest branch-line (depth) among over 100 branches (width) encompassing only 8 generations. The reason for these uneven dimensions appears to be due to the choice of participants in the regulatory process to include inter-related predicates in approval applications. That is to say, the application for the Da Vinci Si is predicated on both the Da Vinci S V1.1 and the Da Vinci S, even though the Da Vinci S V1.1 is itself predicated on the Da Vinci S. This essentially creates a duplicate set of predicates in the ancestral history. This practice of using inter-related predicates appears often in the predicate history of the Da Vinci, resulting in an extremely wide tree with an extremely high instance of duplication. This is why, although there are over 2500 instances of predicates referenced in the trace, less than 2% of those device instances are unique. Of those unique devices, just over half of them have identifiable predicate device relationships. The remaining 24 ultimate predicates represent devices for which no further equivalence information is available, terminating the branch-line trace.

The intention of the current regulatory system is for all devices to be clearly traceable via substantial equivalence to a device legally marketed Pre-Amendment or post-amendment

through the PMA process. However, only one branch line was traced to an originating predicate classified as a Pre-Amendment device. Most ultimate predicates in the Da Vinci trace were approved via the 510(k) Process and therefore were declared equivalent to another previously cleared device, but the traceability of approval information for older devices is limited by the availability of data.

5.4 TRACE COMPARISON

Investigation into the approval history of the Da Vinci Surgical System revealed evidence of technological creep in predicate devices. However, the limited availability of data on older predicate devices makes it difficult to trace the origin of many significant technological characteristics present in the system, including the use of a computer-controlled manipulator arm. Expansion of the substantial equivalence tree to include subject devices in the same technological generation as the Da Vinci revealed that, although the devices did share similar technological characteristics, the functionality of the Da Vinci system was significantly more complex than other devices classified as endoscopic manipulators.

In an effort to determine whether patterns identified in the Da Vinci trace were unique to this device or common across the approval process, I made the decision to expand my research to other Class II devices. To directly compare the new device traces to that of the Da Vinci, I selected devices which the FDA designates as “robotic surgical devices.” Although these technologies do not have the exact same intended use as the Da Vinci, they do possess technological characteristics which are extremely similar to the Da Vinci. This allowed for direct comparison of predicate device relationships and other trace patterns, which in turn allowed me

to make broader observations about how the FDA regulates complex surgical technologies through the 510(k) Process.

The method used to identify robotic-based surgical systems with similar functions and levels of technological complexity as the Da Vinci, was a search of the 510(k) database using the keywords “robot” and “surgical system” in the device name category. The search was limited to the 510(k) database rather than the wider FDA database in order to identify systems approved through the 510(k) Process with a traceable predicate history. The term “robot” returned 62 results, and the term “surgical system” returned 173 results. Each of these results was then reviewed in order to identify systems with similar technological characteristics to the Da Vinci. After eliminating devices which did not meet this criteria, and duplicates of devices with multiple models on the market, this method resulted in the identification of ten devices for investigation (See Table 6).

Table 6: Identified Robotic Surgical Devices

510(k) Number	Approval Date	Manufacturer	Device Name	Product Code
K171120	10/13/2017	TransEnterix, Inc.	Senhance Surgical System	NAY, GCJ
K021152	09/24/2002	Computer Motion. Inc.	ZEUS' MicroWrist Surgical System	NAY
K072629	8/6/2008	Integrated Surgical Systems, Inc.	DigiMatch ROBODOC® Surgical System	OJP, HAW
K143420	10/30/15	IMRIS Inc	SYMBIS Surgical System	HAW
K101791	9/23/10	MedTech S.A.	ROSA Surgical Device	HAW
K172796	01/18/2018	Medrobotics Corporation	Medrobotics Flex® Robotic System and Flex® Transabdominal Drive	HET, GCJ
K162330	5/4/17	Medrobotics Corporation	Flex Robotic System and Flex Colorectal Drive	FDF
K093425	02/24/2010	MAKO Surgical Corp	(RIO) Robotic Arm Interactive Orthopedic System -THA	OLO
K003431	10/05/2001	Computer Motion. Inc.	Zeus Robotic Surgical System	GCJ
K003661	10/05/2001	Computer Motion. Inc.	Socrates Robotic Telemonitoring System	NEQ

Further investigation of these devices revealed some substantial equivalence relationships, where one device was predicated on another device identified for investigation, which resulted in the creation of four device groups which could each be used to construct a separate predicate tree. The Senhance Surgical System, ZEUS MicroWrist Surgical System, and DigiMatch ROBODOC were all predicated on an iteration of the Da Vinci System, and could be added to the existing Da Vinci Si trace. The SYMBIS Surgical System is predicated on the ROSA Surgical device, and the two Medrobotics systems are related to each other. The Zeus and Socrates systems had no available predicate information, so they were removed from consideration. Thus, I was able to identify a total of three additional systems to trace beginning from the SYMBIS Surgical System, MAKO RIO – THA Surgical System, and Medrobotics Flex Transabdominal System (Flex). The raw data and an overview of the findings from each trace can be found in Appendices 4, 5, and 6 respectively.

Using the data contained in the four predicate traces described above, it is possible to make comparisons between the devices to evaluate the regulatory process. Table 7 contains a summary of the information derived from each trace.

Table 7: Comparison of Robotic Surgical Device Traces

	Predicates Identified	Unique Devices	Number of Companies	Ultimate Predicates	Earliest Approval Date	Unique Codes	Most Prevalent Code	Unique Regulatory Descriptions	Most Prevalent Regulatory Description
Da Vinci Si	2618	50	18	24	Pre-1976	15	NAY	9	Endoscope and accessories
SYMBIS	43	26	13	10	6/2/1981	2	HAW	2	Stereotaxic instrument
RIO - THA	590	53	17	21	12/15/1986	7	HAW	6	Stereotaxic instrument
Flex	109	42	10	21	1/3/1985	23	GCJ, EOB	10	Endoscope and accessories

Comparison of the number of predicate relationships identified in each trace indicates that the Da Vinci Si trace is the largest by a significant margin. However, the number of unique devices present in each trace indicates that the Da Vinci trace is fact smaller than the RIO -THA trace. This discrepancy is due to redundancies in predicate identification, where Intuitive Surgical identified the same device as a predicate multiple times within the approval history. Although this redundancy is present to some extent within all of the traces, it is far more visible within the Da Vinci trace than any of the others.

Comparison of the number of companies present within each trace reveals an interesting pattern in the methodology used by companies to select predicate devices. Each trace contains a number of companies that is at most half the number of unique devices within the trace. As a limited

number of medical device manufacturers exists, and most specialize in a specific type of medical device, it is not unexpected that a manufacturer might show up multiple times in a predicate trace. However, the number of recurrences of companies listed within these four traces indicates this pattern was created by choice rather than coincidence. For example, 38 of the 42 unique devices identified within the trace of the Flex System were developed by the Olympus Corporation. The common repetition of this pattern across multiple traces indicates that manufacturers may be preferentially selecting their own devices to serve as predicates, rather than other devices on the market.

This theory is further supported by the lack of overlap between the traces constructed, all of which are classified as robotic surgical systems, and which share similar technological characteristics. In fact, the only overlap of predicates present in any combination of the four traces is a small group of 9 devices in the SYMBIS and RIO traces, all of which serve as ultimate predicates or originate ultimate predicate branches, and therefore lack significant connection to the core section of the trace. The lack of major overlap between the two traces, even though the shared dominant product code and regulatory description indicates that devices contained within the trace should be extremely similar, supports the idea that companies are preferentially choosing predicate devices with which they are familiar.

The only device identified through this expanded investigation which overlaps more than two traces is the DigiMatch ROBODOC, which is predicated on three (K043153, K991081, and K052851) present in the Da Vinci Si, SYMBIS, and RIO - THA traces respectively. In fact, the ROBODOC is directly predicated on the Da Vinci Model ISI 1000 and the MAKO Voyager

Linux with Tactical Guidance System, both important predicates in their respective traces. The ROBODOC system uses diagnostic images to assist in planning and performance of total hip arthroplasty (THA) procedures under direct control of a surgeon, incorporating additional technological components from the Voyager Linux guidance system, and the Da Vinci System, which performs surgeries using a robotic arm guided by a surgeon. Although the ROBODOC does not serve as a predicate device itself, and therefore cannot be used to make any major observations about predicate creep past the technological components it shares with predicates, its existence as a device predicated directly on components of multiple major traces investigated within this thesis validates the selection of devices for predicate history comparison.

A combined trace of all four RAS systems is shown in Figure 12 below to illustrate the relationships between the predicate ancestries. Unlike the diagrams for the individual traces, the combined trace originates from the newest devices located at the center of the trace, with older devices serving as ultimate predicates located at the outer edges of the combined trace. Each RAS System trace is color coded, with the overlap devices between the RIO and SYMBIS trace identified in yellow, and the DigiMatch ROBODOC identified in purple.

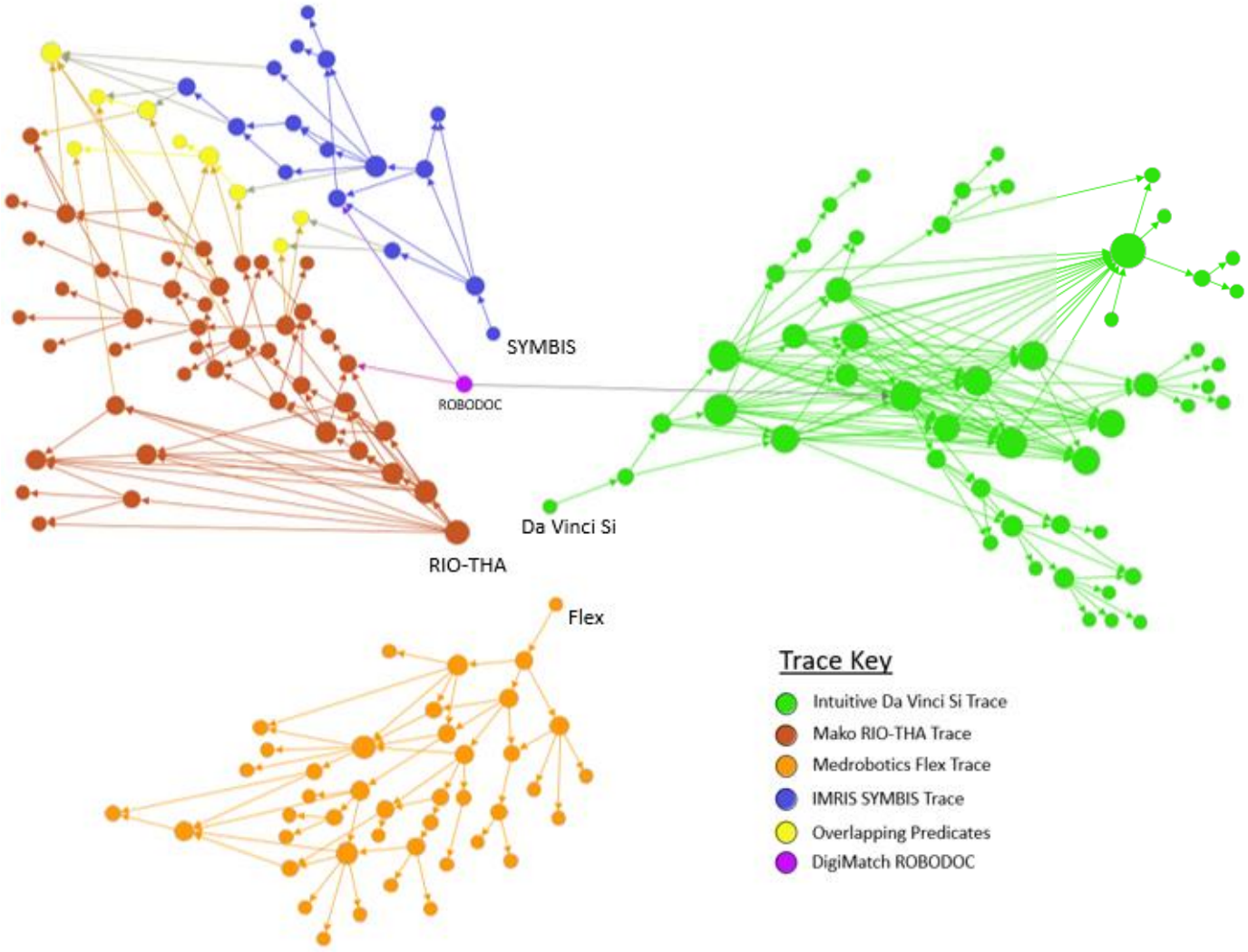

Figure 12: Combined predicate trace of the four robotic surgical systems analyzed, with the newest devices located closest to the center of the combined trace. The only overlap between the traces is highlighted in yellow between the RIO-THA and SYMBIS traces.

Although the Da Vinci Si and Flex Transabdominal System share a common regulatory description, if you exclude the ROBODOC, there is no overlap at all between the traces. Considering the different intended use and overall technological characteristics of the two devices, the lack of overlap is understandable, especially since there is also little overlap between

the product codes present in the trace. However, the amount of variation in intended use and technological characteristics between devices and traces with a common regulatory description does indicate that definitions assigned using the current method may be too broad. In fact, these broad regulatory definitions may be contributing to increased levels of technology creep present within the 510(k) approval system by allowing approval of devices based on predicates with significant technological differences due to the broad terms used in approval applications.

5.4.1 RECALLED PREDICATES

In Section 5.3.1, the devices contained within the predicate ancestry of the Da Vinci Si were analyzed through the FDA's Recall Database to identify potential safety flaws. The results included multiple Class II recalls for the Si and many of its immediate predicates, the majority of which were classified as robotic surgical devices. While a couple of Class II or III recalls will likely have minimal effect on overall device safety, repeated Class II recalls or any Class I recall is directly indicative of potential device issues. To determine whether this issue with repeated recalls was unique to the Da Vinci product line, or a more general issue with complex robotic devices, the devices contained within the SYMBIS, RIO-THA, and Flex Robotic System predicate traces were analyzed for comparison. Table 8 below summarizes each instance of repeated recalls identified within the traces, with a full overview of recall information included in Appendices 2, 4, 5, and 6.

Table 8: Summary of predicate devices with more than two registered recalls. Devices are sorted based on which device trace they belong to.

Trace	K Number	Device Name	Manufacturer	Approval Date	Recalls
Da Vinci Si	K081137	Intuitive Surgical Da Vinci Si Surgical System: Model IS3000	INTUITIVE SURGICAL, INC.	2/18/2009	24 – Class II
	K063220	Da Vinci S Surgical System-V1.1, Model IS2000	INTUITIVE SURGICAL, INC	12/1/2006	4 – Class II
	K050369	Intuitive Surgical Da Vinci Surgical System, Model IS2000	INTUITIVE SURGICAL, INC.	4/29/2005	43 – Class II
	K021036	Intuitive Surgical Da Vinci Surgical System, Model IS1200	INTUITIVE SURGICAL, INC.	6/26/2002	18 – Class II
	K012833	Intuitive Surgical Bipolar Forceps	INTUITIVE SURGICAL, INC	11/16/2001	4 – Class II
SYMBIS	K101791	ROSA SURGICAL DEVICE	MEDTECH SAS	9/23/2010	12 – Class II
	K092239	ROSA SURGICAL DEVICE, MODEL ROSA 1.1	MEDTECH S.A.	11/17/2009	9 – Class II
	K050438	STEALTHSTATION SYSTEM UPDATE	MEDTRONIC SURGICAL NAVIGATION TECHNOLOGIES	6/2/2005	11 – Class II
RIO – THA	K060336	NAVITRACK SYSTEM-OS KNEE UNIVERSAL, MODEL PRO-05002	ORTHOSOFT, INC.	4/28/2006	2 – Class II 1 – Class III
	K022365	STRYKER NAVIGATION SYSTEM - HIP MODULE	STRYKER INSTRUMENTS	1/22/2003	10 – Class II
	K001284	STEALTHSTATION SYSTEM GOLDENEYE MICRO-MAGNETIC TRACKING SYSTEM	MEDTRONIC SURGICAL NAVIGATION TECHNOLOGIES	6/12/2000	27 – Class II 1 – Class III
	K993239	STRYKER NAVIGATION SYSTEM - NEURO MODULE, MODEL 6000-XXX-XXX	STRYKER CORP.	1/18/2000	2 – Class I 4 – Class II
	K990214	FLUORONAV MODULE FOR THE STEALTHSTATION SYSTEM	SURGICAL NAVIGATION TECHNOLOGIES, INC.	4/22/1999	29 – Class II

Examination of the devices with multiple recalls identified through this research revealed a few key findings. First, while the Flex system had no instances of repeated recalls within its predicate ancestry, both the SYMBIS and RIO-THA had multiple instances with comparable levels of severity to the recalls issues for Da Vinci Si predicates. This indicates that the level of complexity of robotic surgical technology may be partially responsible for the repeated recalls, rather than a specific flaw with the Da Vinci System.

Second, two Class I recalls were issued for the Stryker Navigation System – Neuro Model, a device which serves as a predicate in the RIO – THA trace. These recalls were issued in

November of 2009, after the approval of multiple subsequent device generations, in response to a series of software problems which rendered the device unusable and unsafe. Although this is the only instance of a Class I recall, it does illustrate the potential for devices with serious safety flaws to be used as predicate devices, if those flaws are not discovered prior to approval of the subject device seeking approval.

6 DISCUSSION

6.1 PREDICATE CREEP

It is clear from the data gathered in this research that predicate creep, and technology creep in general, does indeed exist to some extent within the 510(k) Process. Due to the limited availability of detailed information on the technical characteristics and testing procedures of new devices presented in approval application summaries, it can be difficult to determine the amount of scientific evidence provided to mitigate predicate creep within a device's approval history. However, even without knowledge of the evidence provided to support substantial equivalence claims, correlations can be about the impact of predicate creep on the 510(k) Process.

The 510(k) Process uses a combination of predicate performance data and design validation testing data to determine if a device is both substantially equivalent to a predicate and safe to be placed on the market. However, unless the validation testing performed includes clinical trials, there is no way to ensure for certain that a device will perform as expected when it enters the market and is used on patients. Therefore, in the absence of clinical trials, the only data used to support device safety is the performance of predicate devices. As a result, if technology creep occurs between predicates, even if all the new aspects of a device are tested thoroughly in non-clinical settings, there is no way to 100% guarantee that the new device will perform as anticipated. However, it is extremely difficult to mitigate this small scale form of predicate creep without the use of mandatory clinical trials, which would defeat the purpose of the 510(k) Process entirely. Instead, requirements for non-clinical testing are used to mitigate much of the

risk associated with small scale predicate creep, which in most cases works effectively. However, there are two scenarios in which non-clinical evidence may be insufficient to adequately mitigate the risks associated with small scale predicate creep.

The first case is when the non-clinical evidence provided to support substantial equivalence claims is insufficient to ensure that new technological characteristics do not introduce new safety issues within a device design. Given the data available for analysis in this thesis, it was not possible to determine whether any instances of insufficient evidence were present within the Da Vinci or other device traces.

The second scenario in which non-clinical evidence is insufficient to support device safety is if multiple generations of devices approved via substantial equivalence each possess a degree of technology creep. This is the theory of predicate creep discussed in previous literature, where technology creep causes subtle changes in device form and function to build up over time, until eventually a device is introduced to market which bears no resemblance to the original device. Although each individual device characteristic is supported by some form of non-clinical evidence, the only clinical evidence supporting the approval of newer devices is based on a device which they are essentially unrelated to. A simple example of this type of creep is illustrated using shapes in Figure 13 below, where each change present in a new iteration of the shape is relatively small and well supported logically.

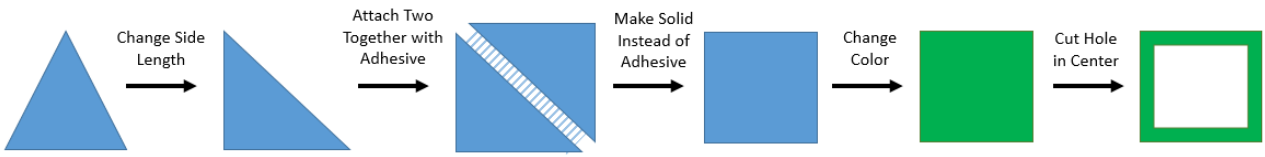

Figure 13: An example of the impact of small scale predicate creep over multiple device generations, where a solid blue triangular shape is transformed step-by-step into a hollow green rectangle which bears no resemblance to the original shape.

The final device (or shape in the example above) is essentially a totally different device than the original predicate upon which it is based. However, the original predicate is the only device that was actually tested pre-market for safety. This means that the cumulative effect of continuous technology creep over time is large scale predicate creep, where changes in device characteristics result in the creation of entirely new device types without any clinical evidence of safety and efficacy. Even if the effects of small scale predicate creep are mitigated by non-clinical testing, the effects magnified on a larger scale result in the development of entirely new device types without clinical evidence, essential circumventing the requirements of the PMA process over time.

This research was able to detect the presence and analyze the effects of large scale predicate creep (referenced simply as predicate creep) for the data sets using three different methods of predicate analysis; technological characteristic comparison, regulatory structure comparison, and predicate relationship analysis.

6.1.1 Technology Characteristics

The first method used to identify technology creep is the traditional method of direct characteristic comparison described in the methods section. Comparison of the technical capabilities of devices in a substantial equivalence relationship highlights the exact device component which represents a new technological innovation, thus making it easy to identify instances of technology creep. The severity of technology creep varies based on the degree of change between the technological characteristics of the device, from minor changes of a single components to major changes in device function.

An examination of the traces constructed in this research finds that, even without detailed technical descriptions, many instances of technology creep can be identified from the device descriptions provided in approval application summaries. For example, following one five generation branch line in the SYMBIS trace connects the SYMBIS system (K143420), which uses jointed mechanical arm guided from a surgeon console to position stereotactic instruments, to the Brown-Roberts-Wells Stereotaxic System (K811452), which uses a CT scanner and physical structure comprised of a series of rods and a curved metal frame to position stereotaxic instruments for neurosurgery (Apuzzo & Fredricks, 1988). Although both devices have the same core function, there are significant changes in the technological characteristics between the two devices. Even the device which the Brown-Roberts-Wells System serves as an immediate predicate for, the Neuromate Stereotactic System, incorporates significant new technological components, primarily the use of a jointed mechanical arm for positioning. Another major example of technology creep from the RIO-THA trace is the progression, within a single predicate generation, from a handheld flexible endoscope to a system incorporating a robotic arm for endoscope and tool positioning driven from a separate console as described in Appendix 5.

Other instances of technology creep include the progression from an intraoperative image guidance system with a handheld probe (K052213) to a guidance system with a robotic arm serving an "intelligent" tool holder to provide feedback (K072806) in the Mako RIO trace and the progression from individual manual surgical instruments to a robotic surgical system within the Da Vinci Si trace. In fact, even based on the limited information available through approval summaries, the majority of substantial equivalence relationships examined within this thesis appear to possess some degree of technology creep. Although it may be expected due to the nature of the regulatory process, these many examples confirm that technology creep is prevalent within the 510(k) Process.

The traces within the research where it is easiest to directly identify technological characteristics are the initial Da Vinci Model IS1200 trace and the AESOP System trace, due to the relatively small trace size and availability of technical device descriptions. An example of short-term, high impact technology creep is the branch line between the AESOP and Da Vinci Systems, which moves from an assistive endoscope positioning system to a system performing robotic surgeries in only two generations. Starting from AESOP, the line passes to the Monarch (a sub-component of Da Vinci Model ISI 1000) which incorporates multiple manipulator arms, a console for controlling the arms, and primary functionality of the arm(s) from scope positioning to actual surgery, then directly to the Da Vinci IS1200 which incorporates a 3D vision system and specialized instruments. This significant amount of change within just three generations is somewhat startling, as it implies that the level of similarity required between technological characteristics for substantial equivalence is extremely low.

The high degree of technology creep within the Da Vinci trace becomes even more apparent when compared to other devices in the AESOP trace, which share the same predicate device. Although there is also predicate creep present within these branch lines, the degree of technological change is significantly less. For example, all of the devices in the same generation as the Da Vinci within this trace share the same basic function as the AESOP system, to position and hold an endoscope during surgery. The major technological innovations present in these devices are changes in the number of movable joints in the manipulator arm, and the arm control interface. Comparatively, the Da Vinci incorporates many additional core device functions, such as manipulation of surgical tools, cutting and electrocautery, as well as the inclusion of multiple new manipulator arms and a new control platform. While the other second generation devices within the Da Vinci trace are examples of low-impact technology creep, where the resulting predicate creep is small scale and unlikely to introduce major safety concerns, the high-impact technology creep present in the Da Vinci branch is an example of large scale predicate creep. Although the stated intended use of these devices is the same, the Da Vinci represents a sudden "leap" in technology by effectively introducing a new intended use in addition to the prior intended use of endoscope positioning.

6.1.2 Multiple Predicates

One of the major indicators of technology creep is the use of multiple predicates in an approval application. If a device is approved based on a single predicate, then technological changes between the two predicates are easily identifiable and can be directly addressed through non-clinical testing. However, in an approval application with multiple predicate devices the characteristics of the subject device are typically a combination of characteristics from the predicate device. This new combination of technological characteristics, which have not previously been tested, make it more difficult to identify and test for potential device flaws, and subsequently increase the probability of device failure. This exact problem was responsible for the failure of the Dupuy ASR XL, which possessed a unique combination of material and geometry never before tested on patients (Ardaugh et al., 2013). Further, although these devices often represent significant leaps in technology, they are often approved without additional clinical testing, as was the case for the ASR XL. In these instances, non-clinical tests alone are insufficient to assure device safety and mitigate the effects of small scale predicate creep.

Examining the predicate relationships of the Da Vinci Si and other systems, the use of multiple predicate devices in approval applications appears to have changed over time. Older devices approved prior to the early 1990's, when predicates are traceable, typically use only one or two predicate devices. However, newer devices, especially those approved in the late 1990's - early 2000's, often use three or more predicate devices. Although other factors may also contribute, it appears that this change is mostly due to the increasing pace of technological innovation within medical device fields. Devices which use more than two predicates typically appear to represent more significant innovations and changes in technological characteristics compared to devices

with fewer predicates. For example, in the Da Vinci Si trace 15 of the 20 devices (75%) associated directly with the Da Vinci System (i.e. the system and components) have three or more predicate, while only 5 of the remaining 29 predicates (17%) have three or more predicates. The exception to this rule is when companies use one approval application to approve a group of devices, for example a line of surgical instruments, rather than a single device.

In addition to larger leaps in technical innovation, the use of multiple predicates as split predicates also contributes heavily to predicate creep. The FDA defines a split predicate as the use of one predicate device to validate equivalence of intended use, and different a predicate (or predicates) to support equivalence of technical characteristics (CDRH, 2010). Using this method, devices can be approved for new applications without ever undergoing testing to prove that the device is safe for that application. Further, if the device also combines characteristics of multiple technical predicates in addition to introducing a new intended use, it is nearly impossible to ensure that the new device is safe without clinical trials. Previously, companies validated the use of split predicates by claiming that the term "predicate" in the definition of substantial equivalence refers to the combination of all prior devices identified in an approval application, rather than each individual device. However, in the 2010 Working Group report and subsequent guidance documents issued by the CDRH, the term "predicate" in the definition of substantial equivalence is clearly interpreted to apply to a single device already on the market. Under this interpretation of the definition, the use of split predicates as defined by the FDA clearly violates the terms of substantial equivalence.

The FDA's interpretation of the definition of substantial equivalence means that every single device identified as a predicate is subject to the entirety of the definition of substantial equivalence, and therefore MUST possess the same intended use as the subject device. However, there are many instances within the predicate histories investigated in this research where predicates are identified for the purpose of validating technical characteristics of the subject device without possessing the same intended use as the subject device. For example, the Intuitive Monarch Laparoscopic Manipulator/Endoscopic Control System shares the same intended use and many technological characteristics of the AESOP system, one of its immediate predicate devices. However, the Monarch also cites three different types of manual surgical tools as direct predicates, none of which share the same intended use of "control of instruments during surgical procedures." By the FDA's interpretation of substantial equivalence, these surgical tools do not qualify as valid predicate devices. But without the inclusion of these surgical tools, Intuitive would not have been able to validate the use of the Monarch System for any surgical tasks other than endoscope positioning, which was an essential step to the subsequent approval of the Da Vinci System. These "partial predicates", which are used to validate technological characteristics of a device without possessing the same intended use, are often included on approval applications of "leap" devices, which contain major technological innovations in one or two predicate generations.

In 2012, to mitigate some of the risk introduced by split predicates while still allowing for larger technological innovations like those present in the Da Vinci trace, the FDA created a new regulatory mechanism called Reference Devices. Unlike a predicate device, which is required to possess the same intended use as the subject device, a reference device can be used to validate

the safety of technological characteristics without possessing the same intended use as the new device. However, a reference device can only be used in addition to a valid predicate device and cannot on its own serve as sufficient validation for device approval. One example of a device approved using reference devices was found in the Medrobotics Flex Transabdominal System, described in Appendix 6.

This new regulatory mechanism does address the issue of split predicates as they are defined by the FDA. However, instances of split predicates are extremely rare, to the point where no examples can be identified within any of the four traces constructed here. Instead within these traces there are many instances of partial predicates, which are often associated with the leap devices that contribute so heavily to technology and predicate creep. Rather than address potential safety issues with the approval of technology for untested use scenarios, the FDA has essentially given the green-light to continue using these partial predicates by giving them an official regulatory definition as Reference Devices. Although it is difficult to determine the potential impacts to the regulatory process of such a new mechanism, the effects of previous examples of partial predicates indicate that reference devices will be used to approve devices with significant new innovations for market without the use of clinical trials.

6.1.3 Product Codes and Regulatory Descriptions

Another interesting pattern is the evolution of product code classifications over time within the traces. The FDA designates product codes based on the intended use and technical characteristics of devices, combining those characteristics to identify a device type and basic regulatory description. If the FDA finds that a device does not fit into an existing product code, they will designate a new code, even if the device was approved via 510(k). As a result of technological creep and innovations over time, new product codes are often introduced into the device traces. For example, in the RIO trace the majority of the devices were classified under code HAW, while the originating predicates were classified under a variety of different product codes. Similarly, the devices in the Da Vinci Si trace were classified under a variety of product codes prior to the designation of code NAY, which subsequently included all of the newer devices in the trace. Looking at the characteristics of devices under the codes which existed in the trace prior to the introduction of the dominant code gives clues to the technological characteristics present in devices classified under the dominant code. Examining the differences between subject and predicate devices with different codes also gives insight into what level of technological change triggers the creation of a new product code.

6.2 Other Issues

6.2.1 Redundant Predicates

As discussed within the Research Expansion section, there is a large discrepancy between the number of identified predicate relationships and the number of unique devices present within each trace. This is caused by redundant predicates, where a subject device references a predicate device multiple times within its ancestral trace. This creates multiple ties to a single predicate device, which rapidly expands the size of the ancestral equivalence tree. Figure 14 illustrates the three types of predicate redundancies identified within the ancestral traces, with redundant predicate relationships highlighted in red.

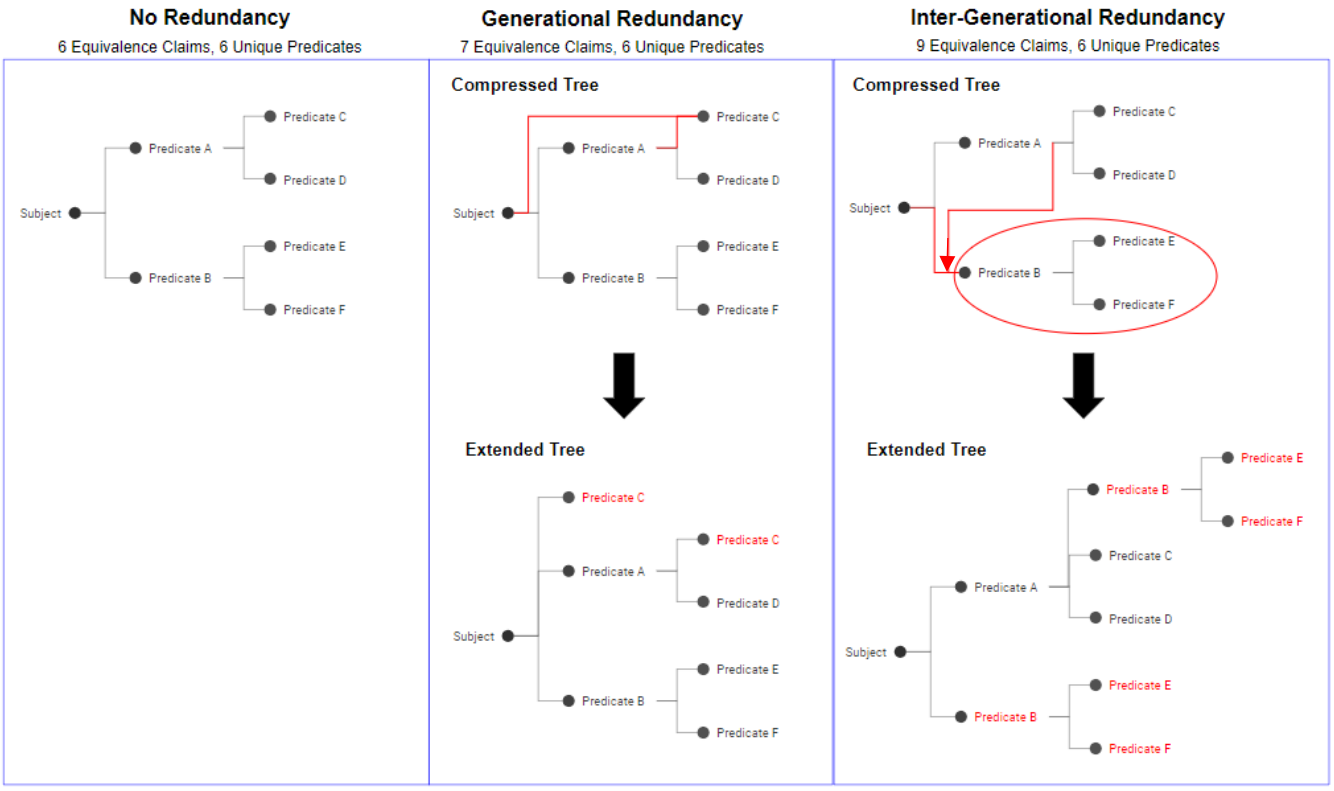

Figure 14: Sample illustration of the different types of predicate redundancy in both compressed and expanded tree forms, with the redundant predicates highlighted in red.

On the left is a basic predicate trace with no redundancy, which consists of the subject device and 6 predicate devices with a total of 6 substantial equivalence claims, one per unique device. In the center an example of generational redundancy, where the subject device directly references a predicate which also appears as a predicate device for another device in the same generation. This creates a single redundancy, with Predicate C now appearing twice in the trace. The effect of redundancies is magnified by inter-generational redundancy, where a predicate device present in the trace references another predicate device within the trace. As seen in the example shown above, the redundant relationship causes the entire branch originated by Predicate B, circle in red, to become redundant, which results in a total of 9 equivalence claims for a trace consisting of only 6 devices. The effects of inter-generational redundancy cause entire branches to be duplicated, creating a stacking effect that turns the relatively straight expanded trace into a web-like structure when condensed.

There are two major issues with the use of redundant predicate devices in the approval process. First, although redundancy increases the number of appearances of a particular predicate device within a trace, this number does not necessarily correlate to the degree of equivalence between the predicate and subject device. This is because the 510(k) Process makes no differentiation between predicates used to introduce a single technological characteristic and predicates which are nearly identical to the subject device. For example, in an expanded version of the Da Vinci Si trace where all redundant predicate instances are visible, the Baxter Healthcare Endoscopic Instruments (K931340) appear 170 times, while the AESOP System (K931783) appears only 143 times. Examining the actual technical characteristics of each device, it is apparent that the Baxter

Instruments are traditional handheld endoscopic surgical instruments used as predicates for the end effector instruments of the Da Vinci system, while the AESOP system serves as a predicate for many of the complex technological components of the Da Vinci System such as the manipulator arms and software control. Based on these technical descriptions, it is apparent that the AESOP system has a higher degree of technological similarity to the Da Vinci System, and is therefore more relevant for proving safety and efficacy from a regulatory standpoint. However, the number of appearances of each predicate device within the trace does not reflect the actual degree of technical similarity to the Da Vinci.

Because the natural tendency of an observer is to assume that devices which are cited more often have a higher level of significance within the trace, this lack of discussion on degree of equivalence may result in an undue amount of importance being placed on redundant predicates. This is particularly problematic when predicates which appear more often within the trace have few technical characteristics in common with the subject device, as the level of evidence for safety assurance provided by these predicates is significantly less than that provided by other, more technologically similar devices.

The second issue with redundant predicates is the use of repeated device citation to increase the number of devices on the market that a new device is being compared, and subsequently the amount of evidence supporting substantial equivalence claims, without increasing the size of the actual body of evidence present. For example, the Da Vinci Si trace has 2618 different instances of equivalence claims, where a device is cited as a predicate, but only 50 unique devices actually present within the trace due to the repeated use of inter-generational redundancy. This

redundancy is present when Intuitive cites both the previous model of the Da Vinci system and the devices which served as a predicate for that model. While such duplications may make sense at first glance, since a greater number of immediate predicates for a new device means more evidence to support its safety, these duplications are actually indicative of potential flaws within the previous Da Vinci model.

Since direct predicate device(s) are supposed to provide evidence of safety and efficacy via performance on the market, the fact that Intuitive felt the need to cite the predicates of the previous Da Vinci model, in addition to the model itself, indicates that they believe there is insufficient evidence to support approval of the new model based on the previous model alone. While this belief may or may not be true, it highlights the potential issues with highly complex devices introduced to market via the 510(k) Process without a direct predicate device which shares the same technological characteristics. As a result of the lack of safety evidence provided by the initial version of such a device, companies like Intuitive are forced to redundantly cite the predicates of that device in addition to the device itself when filing for approval of subsequent device models. However, since regulators typically only look at the evidence provided by direct predicates, and the additional devices already served as predicates to the original model, this effectively disguises the fact that the only additional evidence provided to support approval of the new model is the performance of the old model. The initial model of the device therefore served as a "step" device to incrementally introduce new technological characteristics into the marketplace before more significant innovations could be introduced in the second model.

Although incremental development is a common and necessary component of technological innovation, the use of redundant predicates as a regulatory mechanism to get these innovations to market can go too far. If a device with innovative components can stand on its own as a predicate from a safety and efficacy perspective, or with minimal redundancy, then it is valid to use it for incremental innovation. However, when a company repeatedly cites the same predicate devices for each incremental innovation of a device, it indicates that either the company habitually cites prior predicates without purpose, or duplication of earlier predicates is required to prove the safety of each incremental innovation. Requirement of redundant predicates for device approval indicates that the amount of innovations present in the new device may be too significant for the 510(k) Process to provide effective assurance of device safety.

6.2.2 Self-Citation

The trace maps constructed through this research illustrate the evolution process of technological characteristics in new medical devices over time. Comparison of four different robotic surgical device traces reveals an interesting pattern of independent branch line development. While logic would dictate that devices with similar technological characteristics should share common predicate devices, these traces reveal instead the development of parallel branch lines, where technological improvements in one line are made independently of other lines.

Of the four independently traced lines, only the Mako RIO and SYMBIS systems have any overlap, and that overlap consists of 4 devices contained in a single branch. The only device identified which truly overlaps multiple traces is the DigiMatch ROBODOC, which is predicated

on the Da Vinci (K043153), a direct predicate of the Mako RIO called the Mako Voyager Linux (K052851), and the Frameless Nueromate (K991081) by Integrated Surgical Systems, which appears in the SYMBIS Trace. Other than these devices, all the devices identified in the approval traces were unique. However, comparison of the product codes and regulatory descriptions associated with the traces reveal that many of the predicate devices share similar characteristics. The methodology for the selection of predicate devices by applicants must therefore be influenced by factors other than the particular technological characteristic of the device.

One of the most likely factors influencing the selection of predicates is based on the intellectual property and availability of technical information associated with device. When there are many similar devices available within the market to serve as predicates, a company will select a device which they believe they have best access to information about. Most often, this is a device previously released by the company or a subsidiary for which the company has full access to both the intellectual property and previous scientific evidence to support equivalence claims. This practice is evident within all four of the constructed traces, with each trace including a number of manufacturers less than half the number of unique devices.

Table 9: Trace Comparison

	Unique Devices	Number of Companies
SYMBIS	26	13
Da Vinci	50	18
Flex	42	10
RIO	48	15

This practice of using familiar predicate devices is advantageous to companies, as it reduces the number of unknown variables present in the approval process. However, it has created a pattern in which multiple companies often independently develop new technological innovations rather than piggybacking on existing technologies. This may ultimately slow the overall progress of technological innovation.

6.2.3 Lack of Information about Software Controls

One of the major components of the Da Vinci System and other similar robotic surgical devices is the software package developed to control the device. In fact, it can be argued that the software package for the Da Vinci system, capable of interpreting surgeon motions and directly controlling multiple manipulator arms while providing feedback in real time, was the major innovation of the device. However, the information available through the FDA databases and Intuitive Surgical's website focuses almost exclusively on the physical infrastructure and capabilities of the device, rather than the software that runs it. In fact, the only information related to the Da Vinci software infrastructure in the available 510(k) approval summaries was a statement saying that its exists and has been updated for each new Da Vinci Model.

At the time of the approval of the original Da Vinci Model ISI 1000 in 2001, the information regarding device software included in a 510(k) submission was regulated by a guidance document issued by the FDA in 1998. This document describes how to classify a device based on the "Level of Concern," or severity of potential failure implications, and then lays out requirements for software architecture design, traceability, and verification as well as international consensus standards which the software should meet (U.S. FDA, 1998). The document was subsequently updated in 2005 and again in 2016 to clarify when software changes necessitate resubmission of a 510(k) application.

Creation of standards for validation and testing of software-based device components is particularly essential given the growing level of software complexity present in newer medical devices. For a more traditional hardware-based device potential failures of major components such as motors or switches can be easily predicted and tested using physical methods. However, the structure of software programs, with thousands of lines of code requiring extremely specialized knowledge to create and interpret, makes potential software failures much more difficult to identify or predict. This is especially true of small glitches or "bugs" within the program, which don't affect the overall device functionality and appear only under a very specific set of conditions. Detection of these bugs requires a wide variety of rigorous testing procedures to ensure that nothing with the potential to harm patients slips through the cracks. However, although the FDA does require information about software testing to ensure device safety, specific requirements for testing procedures are covered only by general industry standards which may or may not be applicable to the medical device being tested.

Given the existing FDA regulations at the time, and the lack of major recalls or reports regarding problems with the Da Vinci software, it was presumably evaluated using various standards to ensure device safety. However, the lack of evidence surrounding this software testing and that of subsequent software iterations is somewhat concerning. Since the complexity of the Da Vinci software is relatively high compared to other devices on the market at the time of its approval, there is subsequently a higher likelihood of an existing flaw causing major safety issues. Although there have been no severe recalls on the Da Vinci system due to software malfunctions, another device in the predicate history of the RIO - THA, the Stryker Navigation System – Neuro Model, was the subject of two separate Class I Recalls in 2009 due to software flaws which had the potential to cause fatal injuries to patients.

While the Stryker system illustrates the potential for severe risk posed by software-based medical devices, the structure of the Da Vinci system, where software directly controls the motion of the device performing surgery, magnifies the potential risk posed by software malfunctions. In most other surgical devices at the time of the Da Vinci's approval, and even in many of the newer devices examined within this research, the surgeon is still in direct physical control of the motion of the tool manipulator. This means that, while a software flaw could potentially freeze the tool in place or provide inaccurate information, the surgeon is still ultimately in control of the tool motion. However, with the Da Vinci platform the software directly controls the tools performing surgery, which means a small software glitch could have catastrophic consequences. For example, if a small software bug causes the manipulator arm motor to reverse direction or move more than directed during surgery at the wrong time, it could

potentially sever a blood vessel and cause internal bleeding or worse before the surgeon has a change to notice or stop it. Although Intuitive has obviously performed software tests to prevent such occurrences from happening, the lack of information about the testing conducted makes it difficult to determine whether their success in prevention of such issues is due to intensive testing or luck.

6.2.4 Recalled Predicates

One of the notable findings identified in the previously reviewed study conducted by Zuckerman et al. was the presence of devices which had undergone major recalls within the predicate history of newly approved medical devices (Zuckerman et al., 2014). Similar instances of devices continuing to serve as predicates after undergoing major recalls or even being removed from the market were also identified as one of the issues which led to the failure of the DuPuy ASR XL (Ardaugh et al., 2013). A predicate which has undergone major recalls can be indicative of inherent safety issues with the technological basis of subsequent devices if they share major technological characteristics with that predicate. Even if a predicate has not undergone any major recalls, patterns of multiple minor recalls for similar recurring issues may still be indicative of an issue with the device design. Alternatively, patterns of multiple minor recalls may indicate that the associated technology was insufficiently developed or rushed to market without a strong technical foundation to support the functions it provides. To determine whether there was any impact from recalled predicates on the devices studied in this thesis, each of the predicates identified within the four major traces were run through the FDA Recall Database.

Based on the results of the Recall Database analysis discussed in section 5.3.1 and 5.4.1, there is a definitive pattern of related device technologies present among the devices with multiple Class II recalls. All the devices with multiple recalls present in the Da Vinci trace were either iterations or components of the Da Vinci system itself. Although none of the recalls were due to catastrophic failures, the repeated pattern of recalls for different, moderately severe issues indicates that the technology entered the market before it was perfected. This is reinforced by the fact that issues continued to arise even with subsequent models of the device. Additionally, the variety of issues which triggered recalls, ranging from overheating batteries to user manual updates and incompliant factory testing, is likely indicative of the complexity of the system both as a device to operate and a device to manufacture. It is notable that all the recalls within the Da Vinci trace were issued for devices manufactured by Intuitive Surgical, which may also point towards a level of inexperience with this type of device manufacturing as a relatively new company (it was founded in 1995 and exclusively manufactures the Da Vinci and accessories) in addition to issues created by the technical complexity of the Da Vinci. Like the Da Vinci system, the three iterations of the Stealthstation system present across the RIO – THA and SYMBIS traces have a combined 68 recalls between them. Yet despite the high number of recalls, the device continues to serve as not only a predicate, but also an active component of the SYMBIS Surgical System.

However, whether inexperience on the part of Intuitive Surgical contributes to the high number of recalls or not, the Da Vinci is not the only complex surgical system which experienced high rates of recalls. Both iterations of the ROSA surgical system, the direct predicate to the SYMBIS System, experienced a large number of Class II recalls within a relatively short period of time

during 2017. Similar to the Da Vinci, the reasons for these recalls varied, but the majority were directly associated with potentially faulty components used during the manufacturing process. This brings up one of the major issues with highly complex medical devices, which is that they often rely on third-party vendors for most of the component sourcing and manufacturing. As a result, even if the design is sound, the sheer number of components and manufacturers involved in the creation of such a device makes the probability of device failure significantly higher than less complex devices.

Finally, although not necessarily as prevalent within these traces as in previous research, there have been significant recalls on devices which continue to serve as predicates for new products. For example, in the case of the Stryker Navigation – Neuro Model the RIO-Total Hip Arthroplasty (THA) was approved based on devices predicated on the Neuro Model after the recall was issued without additional investigation of the intermediary device safety. Nowhere in any of the documentation presented for approval requests was reference made to any existing product recalls, and no subsequent evidence to reinforce device safety despite recalls was provided. Additionally, there was no record anywhere within the publicly available data of the FDA returning to previously cleared devices to reevaluate safety in light of a new product recall on a predicate device. This leads to the conclusion that the FDA currently does not possess a mechanism for evaluating the potential impact of device recalls on devices cleared through the 510(k) Process.

6.3 AVAILABILITY OF DATA

In the 510(k) database, information required for determination of substantial equivalence, such as predicate devices, intended use, indications for use, and scientific evidence, is located within the application summary attached to the main device summary page. However, the level of information contained within these summaries varies widely, and in many cases these summaries do not exist at all, due to the gradual evolution of requirements for 510(k) application submissions. Although the 510(k) Process was officially implemented via the 1990 Safe Medical Devices Act, official guidelines for the contents of submissions, including the creation of summaries detailing equivalence claims, were not issued by the FDA until 1994. (Medical devices; Substantial equivalence, 1994) Further, use of the standardized "Indications for Use" form was not implemented until 1996, (CDRH, 2010) and specific guidelines for the formatting of traditional and abbreviated 510(k) applications were not issued until 2005. (CDRH, 2005) As a result, the level of information available in the 510(k) database varied widely based on the date of approval. Devices approved prior to 1992 typically only include the basic information available on the device-summary page, and in some cases are not present in the database at all. Data available for devices approved between 1992 and 2005 is inconsistent, with some results containing full PDF summaries of approval applications, including identification of predicate devices and intended use, and others containing only a statement certifying equivalence claims or no information at all. Consistent inclusion of application summaries in the database does not begin until applications filed around 2005-06. Even within applications which include summaries, the level of information varies as 510(k) application guidelines were modified multiple times, most notable in 2007 and 2012.

The lack of consistent data is one of the major challenges to research which seeks to understand the impacts of the evolution of the 510(k) Process. In cases without an application summary, such as the device summary shown on the left, it is impossible to identify the predicate device(s) based on the available public information.

The difficulty of locating relevant data became evident almost immediately during this research process, as there is no information within wither the FDA database or Intuitive Surgical's own website about the approval process utilized with the first model of the Da Vinci Surgical System, Model IS1000. The lack of publicly available information about the approval process for the IS1000 model is troubling, as it obscures both the regulatory and technical origins of the device function. While Intuitive Surgical's website history section references several medical innovations created in the early 1990's with similar technological functions as the Da Vinci, including the Laparoscopic Assistant Robotic System (LARS) and the Stanford Research Institute's Telepresence Surgery System, there is no way to determine whether these devices served as predicates for the initial model of the Da Vinci.

Theoretically, a map of all of the predicate relationships for every device approved via 510(k) should resemble a web, where different spurs originating pre-1976 initiate groups of device based on a primary function which then evolves over time. The density of devices contained within the map should increase somewhat exponentially reflecting the pace of technological innovation moving through time away from the web origin. However, if the contents of the entire 510(k) database was mapped today, it would resemble a donut with a large hole in the center due to lack of information about older devices.

The impact of this lack of data varies depending on the intended use of the mapping structure. From a regulatory perspective, older devices are mostly obsolete, and have been replaced by newer devices. These new devices would still be visible grouped by device function, due to mutual originating Pre-Amendments devices, around the central ring. The impact of the lack of data about older devices is felt only when one attempts to trace technological characteristics to their origin device. While this type of trace is not performed often, it can be used to identify the level of scientific evidence supporting claims of device safety and efficacy, which can be useful when disasters occur.

7 CONCLUSIONS

7.1 SUMMARY OF FINDINGS

This thesis set out to explore the 510(k) Approval Process as it is applied to complex medical devices, with particular focus on robotic surgical systems such Intuitive Surgical's Da Vinci System. The goal of this research was to develop a methodology to identify predicate relationships using publicly available data and to determine the validity of concerns expressed by previous researchers surrounding the potential impact of predicate creep and other issues with the existing approval process. In this section I will summarize my findings on the impact and policy implication of predicate creep and other issues within the 510(k) Process.

7.1.1 TECHNOLOGY CREEP

Given the purpose of the 510(k) Process, to bring new medical devices to market, it should be expected that there is a level of technology creep inherent in the process. If manufacturers are limited to only submitting identical devices for approval through the 510(k) Process, there can be no innovation. Even in new versions of existing devices submitted by the same manufacturer, such as the Da Vinci Models IS1000 and IS1200, there can be somewhat significant technological changes. Removing all technology creep from the process would only hinder progress within the medical devices industry.

Inherent predicate creep in limited amounts, where the new device can be guaranteed safe based on available scientific evidence, appears to actually be beneficial to companies, patients, and regulators alike. However, there are instances, evidenced both within these traces and in other's

research, where technology creep goes too far. Devices are approved via 510(k) which bear little resemblance to predicates or possess a unique combination of predicate technological characteristics never before tested on a patient, making it impossible to assure the safety of the new device through predicate evidence alone.

In the case of devices which bear little resemblance to predicates, it appears from this data that approval through the 510(k) Process is accomplished by manipulating vague regulatory definitions using broad device descriptions and general intentions for use to make a device appear more closely related to a predicate than it actually is. This is especially evident in the case of the Da Vinci system.

The regulatory description of the Da Vinci as an endoscope, an instrument that is introduced into the body to view its internal parts, and accessories rather than as a device which directly performs surgeries offers an important clue into the inner workings of the regulatory process. A device which is performs a surgical procedure without direct physical control by a surgeon has significantly more inherent risk than a simple viewing device, and might therefore fall under Class III regulatory guidelines. Additionally, while endoscopes and accessories are considered to be well understood devices with clear predicates and a defined intended use, no device has ever been approved as a “robotic surgical system”. Therefore, any device seeking approval under this classification would be considered a new device and automatically placed into Class III. By identifying the Da Vinci as an endoscope with accessories, although the endoscope isn’t the only major function of the device, it allows the manufacturer and regulators to circumvent the more stringent and lengthy Class III regulatory requirements.

Whether devices approved through this method do in fact pose a safety hazard to the public is a question which cannot be answered without further study. However, it is apparent that the broad interpretation of regulatory descriptions combined with the discretionary manner in which special controls to mitigate safety issues are applied, leaves room for unsafe devices to potentially slip through the cracks and into the market.

7.1.2 Measuring Predicate Creep

The major contribution of this research to the discussion surrounding the 510(k) Approval Process for medical devices is the development of two novel methods for identifying predicate creep: through the use of product classification codes and by identifying instances of multiple predicates. While many scholars have identified predicate creep as a potential problem within the 510(k) Approval Process, existing literature on the topic is primarily limited to theoretical discussion. In the few instances where attempts were made to prove the existence of predicate creep, the methodology used was limited to identification of technological characteristics and scientific evidence present in each individual predicate within the approval history (Ardaugh et al., 2013; Zuckerman et al., 2014).

While identifying specific technological characteristics is an effective method for identifying instances of technology creep, especially for characterizing the nature and extent of the creep to determine potential impacts, it has many limitations including time, access to data, and knowledge to interpret data into meaningful results. In particular, this method requires not only identification of predicates, itself a time consuming process often limited by data availability, but also identification and understanding of specific technical properties for each predicate. The

amount of technical data available in FDA databases is extremely limited and often purposefully vague, most likely to protect proprietary rights, which means that technical details must be gleaned from other sources such as patent applications or manufacturer publications. However these publications are not always readily available for devices, such as in the case of the Da Vinci Model IS1000, and when they are available specialized technical knowledge is often required to interpret the information provided. As a result, although this method is effective for identifying predicate creep in specific instances where a particular technical characteristic is under investigation, it is unnecessarily complicated for identifying general instances of predicate creep.

Using information readily available in FDA databases, this research developed two methods to identify instances of predicate creep without requiring additional device information. Like the method described above, each new method begins by tracing the predicate history of the subject device. The first method then looks at the developed ancestry tree and identifies instances where a device has multiple predicates, particularly 3 or more, as predicate creep. This is because to be substantially equivalent, the subject device must share the same intended use and, most likely, some technological characteristics as each predicate device. In most of these cases, the subject device takes specific characteristics from each predicate device and combines them together into a unique device. This means that the device is not identical to any of the predicate devices, which is predicate creep. The only way predicate creep would not occur in this instance is if all of the predicates are essentially identical to each other, which is highly improbable due to intellectual property laws, especially in the case of more than two devices. Therefore, there must be some

degree of technological difference between and the subject device and at least one of its predicates, which is predicate creep.

The second method looks at product classification codes, a regulatory mechanism developed by the FDA to classify medical devices based on device characteristics. Specifically, a product code is supposed to identify a group of devices with the same intended use and similar technological characteristics that can serve as predicates for other similar devices. Since possessing the same intended use is a requirement for a substantial equivalence finding, it can be assumed that all devices within the predicate history of a given subject device have essentially the same intended use. Therefore, any time a device with a different product code than the subject is identified as a predicate, it must indicate the introduction of new technological characteristics in the subject which necessitated the new product code, and therefore indicates predicate creep. Although instances of predicates with different intended uses were identified within this research, which is a violation of the principle of substantial equivalence, even these instances can be considered a form of predicate creep, as a new use for a device was introduced without additional evidence to support safety or efficacy of that use.

7.2 LIMITATIONS

The depth of this study and significance of conclusions are limited by several factors. First, the investigations performed in this study were based solely on data available publicly through FDA databases. Predicate devices are identified within the database only when application summaries are provided, which was not required for inclusion until the mid 2000's. This significantly limits the number of devices with traceable predicate histories, and thus the scope of this investigation. Additionally, the information available through these databases is from general device summaries which are written to protect intellectual property rights, including minimal details about the specific technological characteristics of each device and the evidence provided to support equivalence claims. Since this information is essential to identifying the level of technology creep present using traditional comparison techniques, this thesis attempted to develop alternative methods to identify predicate creep. However, without the information to correlate findings to actual technological characteristics and the evidence used to support their existence, it is difficult to evaluate the significance of findings. Further, the lack of insider information regarding decision making of FDA officials during the review process creates a knowledge gap, where a given equivalence determination may appear strange on paper, but regulators may have had good reasons for making that determination.

Another limiting factor for this study was time, as the process for identifying predicate devices is rather arduous due to the current structure of the database. Application summaries, including information such as identification of predicates and intended device use upon which substantial equivalence determinations are based, are attached to device summary page in PDF documents. This information is not identified anywhere else within the searchable text of the database, and

these documents lack a standard format and may be typed, scanned, or hand written. This lack of standardized formatting makes a computer-automated search of summary information nearly impossible. As a result, tracing the predicate history of each device required manual construction of a database before any analysis could be performed. This is time consuming and significantly more prone to human error, requiring additional effort and making the overall process extremely time consuming.

Another limiting factor which may impact the significance of conclusions is the choice to limit the scope of this research to robotic surgical devices. Conclusions drawn from this research about patterns present in the larger regulatory picture may be biased by practices specific to the regulation of robotic surgical devices. In particular, the technical complexity of robotic surgical devices may lead to a higher number of predicate devices than would be present in less-complex devices. The high number of predicates per generation in this investigation was determined to be partially responsible for the high rate of predicate creep, so other types of devices may not have such significant predicate creep.

7.3 IMPLICATIONS OF FINDINGS

7.3.1 IMPLICATIONS FOR FUTURE RESEARCH

7.3.1.1 Non-public Data

Since the information available in the database is incomplete, particularly with respect to devices approved prior to 1994, I was unable to trace many of the predicate origins to the originating pre-amendment or Class III device. Further information about substantial equivalence applications of earlier devices could be obtained with the use of Freedom of Information Act (FOIA) requests.

Another limitation related to the availability of data is the lack of inside information about the process of substantial equivalence determinations. While the general process is outlined by regulatory guidelines, many of the decisions used to implement these regulations are made at the discretion of regulators. Conducting interviews with regulatory officials would provide additional perspectives not available through examination of predicate data, and may provide explanations for some of the common regulatory patterns identified by this investigation.

7.3.1.2 Expansion to Other Device Types

The choice to limit this investigation to robotic surgical devices allowed for an in-depth exploration of the predicate history and technological development of a particular device type. This investigation proved the presence of technological creep in predicate histories and made observations about common regulatory patterns and practices, which were then generalized to

the overall regulatory process. However, the choice to focus this investigation on robotic surgical systems, a device type known for its technical complexity, may have biased the resulting conclusions drawn. Exploring the predicate history of additional device types with primary functions unrelated to the devices observed for this investigation would allow for comparison of regulatory patterns across device types and validate the conclusions of this investigation.

Long-term, the creation of a map of the full 510(k) database could provide useful information to regulators and applicants about devices eligible to serve as predicates. A complete map would reveal common patterns in predicate relationships which could be used as a basis for identifying viable predicates for new technologies. For example, the Da Vinci trace revealed a strong equivalence connection between endoscope controllers and robotic surgical systems. The map might also be used for market research by companies, to identify areas of the medical device market which are developing or have space for development, or areas which are oversaturated.

Another potential use of this map would include the identification of devices predicated on recalled devices or devices with known regulatory problems, such as those identified by Zuckerman et al. (2014). The FDA currently does not have a mechanism for identifying these devices, which results in the devices remaining on the market and continuing to serve as predicates for future devices without additional scrutiny to determine whether safety concerns exist.

7.3.1.3 Balancing FDA Approval with Patent Requirements

While the 510(k) Process purports to identify predicate devices based on substantial equivalence in both functionality and technology, the patent process in the US requires proof that an idea is new and novel to secure a patent. For medical devices, the requirements of substantial equivalence and novelty appear to be in direct conflict. If a device is substantially equivalent, how can it then be novel enough to be granted a patent?

In the US, the most comprehensive database to track and identify new technologies is part of the patent system, which provides legal protection of innovative technologies in return for public disclosure. In the medical community it is common practice to apply for patent rights and FDA approval concurrently to ensure a first-to-market advantage. Examination of the patent literature for devices which appear in the ancestral equivalence tree constructed from the regulatory history might allow for identification of new technological characteristics introduced in each device. Theoretically, larger technological "leaps" present in substantial equivalence trees should correspond to a stronger patent presence for a given device.

For substantial equivalence, applicants are required to provide evidence that the technological characteristics of the device are similar to existing devices. Conversely, when applying for a patent companies are required to prove that new technological characteristics do not correspond to an existing device by referencing all existing devices upon which particular characteristics are based and defining how the new device is different. Considering the apparent conflict between the requirements of substantial equivalence and patent rights, it is also likely that some correlation exists between device relations in the patent and 510(k) databases.

7.3.2 Implications for Policy

Looking at the regulatory process from an outside perspective, it is clear that predicate creep exists inherent within the substantial equivalence process. When this technology creep occurs on a small scale, introducing a new technology feature or application which slightly alters the form or function of the device while preserving the overall function and technological characteristics of the predicate, there is little potential impact to the safety of the public. In fact, purposeful inclusion of small amounts of technology creep is necessary to allow for innovation and improvement in medical device design. However, the effects of predicate creep over time have allowed for the development and approval of entirely new devices without undergoing the stricter PMA approval process. Because this snowballing effect is directly dependent on small-scale predicate creep, it is difficult to address the problem without negatively impacting the ability of manufacturers to bring innovative devices to market. Therefore, rather than trying to prevent the snowballing effect in its entirety, my recommendation is for the FDA to develop a comprehensive, easily accessible database of predicate relationships which can be used to identify break points, where a new device is significantly different from the closest predicate with scientific evidence of safety. At these break points the FDA can then require additional scientific evidence of the overall device function, such as a small clinical trial, to ensure that no safety flaws have been introduced in the device due to predicate creep. This would allow for the continued use of small-scale predicate creep for technical innovation, while mitigating the introduction of untested technical characteristics and potential safety flaws over time.

However, the largest problem identified through this research is not the presence of predicate creep over time, but rather the sudden introduction of devices with high levels of technical

complexity into the market through the 510(k) Process. While a combination of various flawed elements within the approval process make this possible, it appears based on the evidence presented here that one way companies take advantage of the substantial equivalence process is by creating "step" devices, which are approved for the specific purpose of serving as a predicate for technical characteristics, rather than as a marketable medical device. These "step" devices serve as intermediate predicates to allow more innovative devices with larger technological "leaps" into the market. Although devices with larger technological leaps are not necessarily unsafe or ineffective, for example the Da Vinci has remained on the market for over 15 years without a major recall, they do inherently possess more potential risk due to the fast-paced introduction of less-understood technologies into the marketplace.

Although the FDA makes efforts to mitigate this risk through existing regulatory mechanisms, the lack of clearly defined substantial equivalence requirements makes it difficult to determine whether measures taken for a particular device are sufficient. For example, in their analysis Ardaugh et. al (2013) found that insufficient measures were taken during the approval process for the DuPuy ASR XL, which ultimately resulted in approval of a device with serious safety concerns without any significant new scientific or clinical evidence provided to support safety claims. The FDA possesses tools to mitigate this risk, including the ability to require clinical trials or additional scientific evidence for approval, but there are no clear guidelines to determine when this extra evidence might be required. Like the substantial equivalence determinations themselves, requirements for evidence are currently left to the discretion of FDA officials. This results in inconsistent regulatory requirements and creating cracks in the regulatory process through which potentially unsafe devices, such as the ASR XL, might slip.

In the future, the FDA should make efforts to identify the "leap" devices and create a more targeted approval process that addresses new questions raised by these technologies, perhaps through a hybridized version of the 510(k) and PMA processes that allows for substantial equivalence evidence while still requiring a level of clinical assurance. Defining clear guidelines for the amount scientific evidence required based on the significance of new technological characteristics for device approval would help reduce this inherent systematic risk.

Through the data and subsequent findings gathered in this research, I have identified three categories of medical devices within Class II based on the technological characteristics and intended application of the device which can be used to develop guidelines for evidentiary requirements to support substantial equivalence claims as follows:

1. If the new device is identical to an existing device but being used for a new application, or introduces a minor technological change, such as replacing one type of motor with another or using a new material, bench testing adhering to existing standards is sufficient for defining substantial equivalence.
2. If a device introduces a new technological component which does not exist in a previously approved device, such as a new software system, or utilizes a novel combination of technological characteristics from multiple previously approved devices, additional testing to verify the safety of the novel technological characteristics should be required.

3. If a device introduces multiple new technological components at once or possesses a novel use scenario, such as the Da Vinci System allowing a surgeon to remotely perform surgical procedures rather than requiring the surgeon to make contact with the patient, clinical trials should be required to ensure patient safety and identify possible failure modes within the design.

These guidelines are not intended to create any additional burden for regulators or manufacturers, and the testing requirements identified are all currently utilized at the discretion of the CDRH. Rather these guidelines are intended to standardize testing requirements across 510(k) approval applications and close some of the gaps which have allowed the approval of "leap" devices.

The FDA has recently begun taking steps to address the presence of extreme technology creep, so-called "leap" devices, in the regulatory process by creating more stringent guidelines for identification of predicate devices. These new guidelines reject the use of split predicates, where a device identifies one predicate for intended use and a separate predicate for technological characteristics. Although rarely utilized, this form of predicate identification is especially dangerous, as without additional scientific evidence it provides no assurance that a technology is safe for a particular use scenario. However, most "leap" devices identified in this research were not approved using split predicates, but rather multiple predicates comprised of "step" devices specifically designed to advance the desired use case for a particular technology. Although the FDA discourages the use of multiple predicates when possible, it is still considered a viable approval mechanism IF the intended use of the predicates and subject device are the same. Based

on the high number of multiple predicate relationships identified in the approval history of the Intuitive Da Vinci and other devices analyzed in this research, I would recommend that the FDA take steps to create specific guidelines limiting the number of predicates which can be identified in a single predicate generation.

7.4 CONCLUDING THOUGHTS

Given the number of new medical devices entering the market each year, and the increasing technical complexity of those devices, it is unsurprising that new regulatory challenges have also emerged. However, many scholars and experts agree that the regulatory challenges which have emerged from major device failures in recent years are not due solely to the introduction of new technologies, but rather are symptomatic of inherent flaws in the foundation of the regulatory process. In particular, researchers point to the use of substantial equivalence for determining device safety and efficacy in the 510(k) Approval Process as a mechanism by which many flaws, such as predicate creep and lack of scientific evidence, are introduced into the regulatory process.

This research focused specifically on examining the 510(k) Approval Process as it was applied to various Robotic Assisted Surgical systems, an emerging technology with a high degree of technical complexity, with specific focus on the Intuitive Da Vinci Surgical System. The objective of this research was to examine the predicate history of these devices in order to explore the level of information publicly available about the approval process, assess whether

significant predicate creep or other issues occurred within the regulatory process, and identify resulting implications for policy.

The primary method used to address these objectives was the development of multiple predicate ancestry trees using information available through FDA databases. Although the amount of available data is significantly limited due to database restrictions, particularly the lack of approval summaries for older devices, the predicate traces developed contained enough information to draw conclusions about the approval process. Through analysis of these traces, including the use of additional regulatory information such as product classification codes, I was able to conclude that there is indeed predicate creep present within the 510(k) Approval Process. In fact, upon examination of the relationship between the 510(k) Process and technological innovation in medical devices, I found that small amounts of technology creep must exist in predicate relationships for new medical devices to possess any level of innovation or value to the market. This small-scale predicate creep between one device and the next has minimal impact on the safety of new medical devices, if the guidelines laid out in the approval process are followed and adequate precautions are taken to ensure that new device characteristics are safe.

This research has found, however, that although small-scale predicate creep has a place in the approval process, inadequate measures have been taken to address the impact of large-scale predicate creep and other regulatory issues, such as multiple predicates, which have allowed for approval of entirely new devices via the 510(k) Process. Large-scale predicate creep occurs over time, as repeated small-scale innovations slowly change a device until it no longer resembles the original predicate. Although this process technically violates the intention of the 510(k) Process by ultimately approving new devices with minimal scientific evidence, there is some assurance

of device safety provided by the market success of existing predicates. If all the preceding predicate devices are safe, and precautions are taken to mitigate small-scale predicate creep, in many cases devices exhibiting large-scale predicate creep may still be safe. The potential problems with large scale predicate-creep arise when the lack of scientific evidence is combined with unsafe predicates or other regulatory issues.

Although predicate creep was identified by other researchers as one of the primary concerns with the regulatory process, this research found that the most pressing concern with the 510(k) Process is the presence of "leap" devices. While large-scale predicate creep occurs through a series of steps over a long period of time, allowing for some risk mitigation at each step, a "leap" device is one in which there is a sudden increase or change in the technological complexity and characteristics of a device. Combinations of vague regulatory definitions, broad device descriptions, and use of multiple predicates under the current regulatory process have allowed the approval of these "leap" devices, which display high levels of technology creep in a short period of time. The regulatory process as it currently exists is unable to consistently ensure the safety of such devices, as the powers to require additional evidentiary support are applied at the discretion of FDA officials, and few guidelines exist for when they should be applied. Therefore, my recommendation is to implement a modified version of the 510(k) Process, which provides definitive guidelines for the level of scientific evidence required to support safety and effectivity claims based on the degree of new technological characteristics or functions in a device.

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APPENDIX 1: PRODUCT CODE NAY DATABASE

K Number	Decision Date	Device Name	Company	Application Type	Determination
K965001	7/31/97	Intuitive Surgical Monarch Laparoscopic Manipulator	Intuitive Surgical	Traditional	SE
K990144	1/15/99	Endoscopic Instrument and Accessories	Intuitive Surgical	Traditional	SE
K002489	3/2/01	DaVinci Endoscopic Control System	Intuitive Surgical	Traditional	SE
K011002	5/30/01	DaVinci Surgical System Model ISI 1000	Intuitive Surgical	Traditional	SE
K011281	7/24/01	Intuitive Surgical Ultrasonic Shears	Intuitive Surgical	Traditional	SE
K012833	11/16/01	Intuitive Surgical Bipolar Forceps	Intuitive Surgical	Traditional	SE
K021036	6/26/02	Intuitive DaVinci Surgical System Model IS1200	Intuitive Surgical	Traditional	SE
K021152	09/24/02	ZEUS Microwrist Surgical System and Accessories	Computer Motion	Traditional	SE
K022574	11/12/02	Intuitive Surgical da Vinci Endoscopic Instrument Control System and Endoscopic Instruments or da Vinci Surgical System	Intuitive Surgical	Traditional	SE
K030578	6/24/03	Bipolar Grasper and Bipolar Scissors for the ZUES Microwrist Surgical System	Computer Motion	Traditional	SE
K040948	5/5/04		Intuitive Surgical	Special	SE
K040237	7/7/04		Intuitive Surgical	Traditional	SE
K042855	11/12/04		Intuitive Surgical	Special	SE
K043153	12/15/04		Intuitive Surgical	Special	SE
K050005	1/25/05		Intuitive Surgical	Special	SE
K043288	3/3/05		Intuitive Surgical	Traditional	SE
K050369	4/29/05		Intuitive Surgical	Traditional	SE
K050802	6/29/05		Intuitive Surgical	Traditional	SE
K060391	4/10/06		Intuitive Surgical	Special	SE
K061260	5/18/06		Intuitive Surgical	Special	SE
K063220	12/1/06		Intuitive Surgical	Traditional	SE
K072627	2/7/08		Intuitive Surgical	Traditional	SE
K070947	2/14/08		Intuitive Surgical	Traditional	SE
K080291	3/19/08		Intuitive Surgical	Traditional	SE
K081207	12/19/08		Intuitive Surgical	Traditional	SE
K081137	2/18/09		Intuitive Surgical	Traditional	SE

K Number	Decision Date	Device Name	Company	Application Type	Determination
K082497	5/7/09		Intuitive Surgical	Traditional	SE
K090993	12/16/09		Intuitive Surgical	Traditional	SE
K093217	1/21/10		Intuitive Surgical	Traditional	SE
K101743	2/4/11		Intuitive Surgical	Traditional	SE
K101581	4/8/11		Intuitive Surgical	Traditional	SE
K110451	8/26/11		Intuitive Surgical	Traditional	SE
K112584	9/29/11		Intuitive Surgical	Special	SE
K112263	10/7/11		Intuitive Surgical	Special	SE
K112208	12/8/11	Intuitive Surgical DaVinci Single-site Instruments and Accessories	Intuitive Surgical	Traditional	SE w/ limits
K110639	12/28/11		Intuitive Surgical	Traditional	SE
K120215	4/30/12	Intuitive Surgical da Vinci Single-Site Instruments and Accessories	Intuitive Surgical	Special	SE w/ limits
K113706	10/17/12		Intuitive Surgical	Traditional	SE
K121921	10/25/12		Intuitive Surgical	Traditional	SE
K123463	12/3/12		Intuitive Surgical	Special	SE
K123840	2/14/13		Intuitive Surgical	Special	SE
K122532	2/21/13	Intuitive Surgical da Vinci Single-Site Instruments and Accessories	Intuitive Surgical	Traditional	SE w/ limits
K130726	6/7/13	Da Vinci Single-Site Permanent Cautery Hook	Intuitive Surgical	Special	SE w/ limits
K130266	8/29/13		Intuitive Surgical	Traditional	SE
K131861	3/28/14		Intuitive Surgical	Traditional	SE
K131861	3/28/14		Intuitive Surgical	Traditional	SE
K131962	4/17/14	Da Vinci Sp Surgical System, Model 5P999, Endo Wrist Sp Instruments, and Accessories	Intuitive Surgical	Traditional	SE w/ limits
K140189	6/5/14		Intuitive Surgical	Traditional	SE
K140553	7/25/14		Intuitive Surgical	Traditional	SE
K141077	8/12/14		Intuitive Surgical	Traditional	SE
K123329	9/17/14	Intuitive Surgical da Vinci, da Vinci S and da Vinci Si Surgical Systems and EndoWrist Instruments and Accessories	Intuitive Surgical	Traditional	SE w/ limits
K141075	9/26/14	Single-Site Wristed Needle Driver	Intuitive Surgical	Traditional	SE w/ limits
K143217	12/3/14		Intuitive Surgical	Special	SE
K142683	12/10/14		Intuitive Surgical	Traditional	SE

K Number	Decision Date	Device Name	Company	Application Type	Determination
K150837	3/30/15		Intuitive Surgical	Special	SE
K143132	4/2/15		Intuitive Surgical	Traditional	SE
K150284	5/15/15		Intuitive Surgical	Special	SE
K151794	1/15/16		Intuitive Surgical	Traditional	SE
K152421	3/4/16		Intuitive Surgical	Traditional	SE
K152448	3/9/16		Intuitive Surgical	Traditional	SE
K152578	3/30/16		Intuitive Surgical	Traditional	SE
K152892	4/29/16		Intuitive Surgical	Traditional	SE
K161271	7/11/16		Intuitive Surgical	Special	SE
K153276	8/7/16		Intuitive Surgical	Traditional	SE
K162411	9/21/16		Intuitive Surgical	Special	SE
K161178	1/19/17		Intuitive Surgical	Traditional	SE
K162973	2/6/17		Intuitive Surgical	Traditional	SE
K170508	3/10/17		Intuitive Surgical	Traditional	SE
K170865	4/21/17		Intuitive Surgical	Traditional	SE
K171294	5/26/17		Intuitive Surgical	Special	SE
K171388	5/31/17		Intuitive Surgical	Special	SE
K170713	6/13/17		Intuitive Surgical	Traditional	SE
K171426	6/13/17		Intuitive Surgical	Special	SE
K171699	7/28/17		Intuitive Surgical	Traditional	SE
K170644	9/11/17		Intuitive Surgical	Traditional	SE
K170645	9/11/17		Intuitive Surgical	Traditional	SE
K170875	9/12/17		Intuitive Surgical	Traditional	SE
K171632	9/19/17		Intuitive Surgical	Traditional	SE
K170641	9/21/17		Intuitive Surgical	Traditional	SE
K170879	9/21/17		Intuitive Surgical	Traditional	SE

APPENDIX 2: DA VINCI SI PREDICATES

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K081137	Intuitive Surgical Da Vinci Si Surgical System: Model Is3000	INTUITIVE SURGICAL, INC.	2/18/2009	NAY	24 – Class II
K063220	Da Vinci S Surgical System-V1.1, Model Is2000	INTUITIVE SURGICAL, INC	12/1/2006	NAY	4 – Class II
K050802	Modification To Intuitive Surgical Da Vinci Surgical System And Endoscopic Instruments	INTUITIVE SURGICAL, INC.	6/29/2005	NAY	0
K050369	Intuitive Surgical Da Vinci Surgical System, Model Is2000	INTUITIVE SURGICAL, INC.	4/29/2005	NAY	43 – Class II
K050404	Intuitive Surgical Da Vinci Surgical System And Endoscopic Instruments	INTUITIVE SURGICAL, INC.	4/21/2005	HET	0
K043288	Modification To Intuitive Surgical Da Vinci Surgical System And Endoscopic Instruments	INTUITIVE SURGICAL, INC	3/3/2005	NAY	0
K050005	Intuitive Surgical Monopolar Curved Scissors, Model 400179; Tip Cover Accessory, Model 400180	INTUITIVE SURGICAL, INC.	1/25/2005	NAY	2 – Class II
K043153	Intuitive Surgical Da Vinci Surgical System And Endoscopic Instruments, Models Is1200 & Is1000	INTUITIVE SURGICAL, INC.	12/15/2004	NAY	0
K042855	Intuitive Surgical Harmonic Curved Shears Instrument	INTUITIVE SURGICAL, INC.	11/12/2004	NAY	0
K041340	Guidant Microwave Ablation System	GUIDANT CORPORATION, CARDIAC SURGERY	7/28/2004	NEY OCL	0
K040237	Intuitive Surgical Da Vinci Endoscopic Instrument Control System And Endoscopic Instruments	INTUITIVE SURGICAL, INC.	7/7/2004	NAY	0
K040948	Intuitive Surgical Endopass Endoscopic Delivery Instrument, Model P/N 400170	INTUITIVE SURGICAL, INC.	5/5/2004	NAY	0
K022574	Intuitive Surgical Endoscopic Instrument Control System & Endoscopic Instruments, Model Da Vinci ISI 1000/1200	INTUITIVE SURGICAL, INC.	11/12/2002	NAY	0
K021036	Intuitive Surgical Da Vinci Surgical System, Model IS1200	INTUITIVE SURGICAL, INC.	6/26/2002	NAY	18 – Class II
K013946	Flex 10 Accessory For The Afx Microwave Ablation System	AFX, INC.	2/27/2002	NEY OCL	0
K013416	Intuitive Surgical Endowrist Endoscopic Instrument Family	INTUITIVE SURGICAL, INC.	1/10/2002	GEI	0
K012833	Intuitive Surgical Bipolar Forceps	INTUITIVE SURGICAL, INC	11/16/2001	NAY	4 – Class II
K011281	Intuitive Surgical Ultrasonic Shears	INTUITIVE SURGICAL, INC.	7/24/2001	NAY LFL	0
K011002	Intuitive Surgical Da Vinci Surgical System, Model Isi 1000	INTUITIVE SURGICAL, INC.	5/30/2001	NAY	0
K003978	Afx Microwave Generator, Flex Ablation Wand, Lynx Ablation Wand, Model Series 1000, P/N 102006, P/N 102007	AFX, INC.	5/22/2001	NEY OCL	0
K002489	Intuitive Surgical Da Vinci Endoscopic Control System	INTUITIVE SURGICAL, INC.	3/2/2001	NAY	0
K990144	Intuitive Surgical Endoscopic Instruments, Intuitive Surgical Endoscopic Instrument Control System	INTUITIVE SURGICAL, INC.	7/11/2000	NAY	3 – Class II
K993054	Ultracision Harmonic Scalpel Coagulating Shears, Models Lcs-C5, Lcs-C1, Cs-23c, Cs-231, Cs-14c, Cs-141	ETHICON ENDO-SURGERY, INC.	12/9/1999	LFL	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K991859	Dexide Bipolar Forceps Ii ** Device	UNITED STATES SURGICAL, A DIVISION OF TYCO HEALTHC	6/23/1999	GEI	0
K980099	Ultracision Laparosonic Coagulating Shears (Lcs-5(Lcsk5 And Lcsb5))	ETHICON ENDO-SURGERY, INC.	4/9/1998	LFL	0
K974320	Cryogen Cardiac Cryosurgical System	CRYOGEN, INC.	2/3/1998	OCL	0
K972662	Cryogen Cryosurgical System	CRYOGEN, INC.	10/1/1997	GEH	0
K972415	Minisite*Bipolar Forceps** Device	UNITED STATES SURGICAL, A DIVISION OF TYCO HEALTHC	9/19/1997	GEI	0
K965001	Intuitive Surgical Monarch Laparoscopic Manipulator	INTUITIVE SURGICAL, INC.	7/31/1997	GCJ	0
K971861	Ultrasonic Hand Instruments	UNITED STATES SURGICAL, A DIVISION OF TYCO HEALTHC	7/1/1997	LFL	0
K970496	Heartport Maze System: Cryoprobe Set	HEARTPORT, INC.	5/9/1997	OCL	0
K964971	Cryogen Cryosurgical System	CRYOGEN, INC.	3/28/1997	GEH	0
K960400	Diamond-Touch And Micro Diamond-Touch Instruments/Diamond-Line Instruments/Diamond-Port (Access Parts)	SNOWDEN-PENCER	3/12/1996	FBM GCJ GEI	0
K953637	CMS Accuprobe 550/530	CRYOMEDICAL SCIENCES, INC.	12/4/1995	GEH	0
K953059	Kittner Dissector	MEDICAL PERSPECTIVES CORP.	9/14/1995	GDY	0
K930666	Reusable Laparoscopic Instruments W/ Electrocautery	SNOWDEN-PENCER	5/19/1994	GEI	0
K930667	Reusable Laparoscopic Instruments	SNOWDEN-PENCER	5/16/1994	GCJ	0
K933169	Inman Endoscopic Blunt Dissector	INMAN MEDICAL CORP.	4/19/1994	GCJ	0
K936308	Endex Endoscopic Positioning System	ANDRONIC DEVICES, LTD.	3/31/1994	FQO	0
K931783	AESOP (Automated Endoscopic System For Optimal Positioning)	COMPUTER MOTION, INC	11/22/1993	GCJ	0
K931340	Grasp Forceps/Scissors/Needle Holder/Dissector	BAXTER HEALTHCARE CORP.	7/1/1993	GCS	0
K925699	Harmonic Scalpel Laparosonic Clamp Coagulator Acc.	ULTRACISION, INC.	5/17/1993	GCJ	0
K914190	Auto Suture(R) Endoscopic Fan Retractor	UNITED STATES SURGICAL, A DIVISION OF TYCO HEALTHC	5/6/1992	GAD	0
K912544	Bipolar Forceps	EVEREST MEDICAL CORP.	6/24/1991	MAV	0
K904421	CMS Oncoprobe	CRYOMEDICAL SCIENCES, INC.	4/8/1991	GEH	0
K882568	130 Cryo Unit & Assoc. Cryoprobes & Spray	SPEMBLY MEDICAL LTD.	9/27/1988	GEH	0
K874367	Various Cardiac Cryoprobes Having Dia. & Cos. Diff	SPEMBLY MEDICAL LTD.	1/4/1988	HQO	0
K811390	Ccs100 Cryosurgical System	FRIGITRONICS OF CONNECTICUT, INC.	6/16/1981	GEH	0

APPENDIX 3: PRODUCT CODE DEFINITIONS

Product Code	Device	Regulation Description
FBM	Cannula And Trocar, Suprapubic, Non-Disposable	Suprapubic urological catheter and accessories
NEY	System, Ablation, Microwave And Accessories	Electrosurgical cutting and coagulation device and accessories
NAY	System, Surgical, Computer Controlled Instrument	Endoscope and accessories
HET	Laparoscope, Gynecologic (And Accessories)	Gynecologic laparoscope and accessories
GEI	Electrosurgical, Cutting & Coagulation & Accessories	Electrosurgical cutting and coagulation device and accessories
LFL	Instrument, Ultrasonic Surgical	
OCL	Surgical Device, For Cutting, Coagulation, And/Or Ablation Of Tissue, Including Cardiac Tissue	Electrosurgical cutting and coagulation device and accessories
GEH	Unit, Cryosurgical, Accessories	Cryosurgical unit and accessories
GCJ	Laparoscope, General & Plastic Surgery	Endoscope and accessories
GDY	Gauze/Sponge, Internal, X-Ray Detectable	Nonabsorbable gauze for internal use
GCS	Endoscope, Battery-Powered And Accessories	Endoscope and accessories
MAV	Syringe, Balloon Inflation	Angiographic injector and syringe
HQO	Unit, Cautery, Thermal, Ac-Powered	Thermal cautery unit
FAJ	Cystoscope And Accessories, Flexible/Rigid	Endoscope and accessories
OWB	Interventional Fluoroscopic X-Ray System	Image-intensified fluoroscopic x-ray system
EOQ	Bronchoscope (Flexible Or Rigid)	Bronchoscope (flexible or rigid) and accessories
DRF	Catheter, Electrode Recording, Or Probe, Electrode Recording	Electrode recording catheter or electrode recording probe
EOB	Nasopharyngoscope (Flexible Or Rigid)	Nasopharyngoscope (flexible or rigid) and accessories
NWB	Endoscope, Accessories, Narrow Band Spectrum	Endoscope and accessories
FAM	Sigmoidoscope And Accessories, Flexible/Rigid	Endoscope and accessories
FDF	Colonoscope And Accessories, Flexible/Rigid	Endoscope and accessories
HRX	Arthroscope	Arthroscope
FET	Endoscopic Video Imaging System/Component, Gastroenterology-Urology	Endoscope and accessories
FER	Anoscope And Accessories	Endoscope and accessories
FED	Endoscopic Access Overtube, Gastroenterology-Urology	Endoscope and accessories
GCF	Proctoscope	Endoscope and accessories
FCG	Biopsy Needle	Gastroenterology-urology biopsy instrument

Product Code	Device	Regulation Description
DXX	System, Catheter Control, Steerable	Steerable catheter control system
DYB	Introducer, Catheter	Catheter introducer
LZA	Polymer Patient Examination Glove	Non-powdered patient examination glove
FDS	Gastroscope And Accessories, Flexible/Rigid	Endoscope and accessories
GWG	Endoscope, Neurological	Neurological endoscope
ERL	Drill, Surgical, Ent (Electric Or Pneumatic) Including Handpiece	Ear, nose, and throat electric or pneumatic surgical drill
OXO	Image-Intensified Fluoroscopic X-Ray System, Mobile	Image-intensified fluoroscopic x-ray system
FDT	Duodenoscope And Accessories, Flexible/Rigid	Endoscope and accessories
MDA	Elastomer, Silicone, For Scar Management	Silicone sheeting
DZP	Instrument, Diamond, Dental	Dental diamond instrument
FJL	Resectoscope	Endoscope and accessories
FBN	Choledochoscope And Accessories, Flexible/Rigid	Endoscope and accessories
HTZ	Instrument, Cutting, Orthopedic	Manual surgical instrument for general use
CAL	Laryngoscope, Non-Rigid	Flexible laryngoscope
FBO	Cystourethroscope	Endoscope and accessories
HSZ	Instrument, Surgical, Orthopedic, Pneumatic Powered & Accessory/Attachment	Surgical instrument motors and accessories/attachments
KIJ	Instrument, Surgical, Orthopedic, Dc-Powered Motor And Accessory/Attachment	Surgical instrument motors and accessories/attachments
ODB	Endoscopic Contamination Prevention Sheath	Endoscope and accessories
JAB	System, X-Ray, Fluoroscopic, Non-Image-Intensified	Non-image-intensified fluoroscopic x-ray system
JAA	System, X-Ray, Fluoroscopic, Image-Intensified	Image-intensified fluoroscopic x-ray system
HWE	Instrument, Surgical, Orthopedic, Ac-Powered Motor And Accessory/Attachment	Surgical instrument motors and accessories/attachments
GCT	Light Source, Endoscope, Xenon Arc	Endoscope and accessories
FGA	Kit, Nephroscope	Endoscope and accessories
FAL	Panendoscope (Urethroscope)	Endoscope and accessories
EOX	Esophagoscope (Flexible Or Rigid)	Esophagoscope (flexible or rigid) and accessories
DRA	Catheter, Steerable	Steerable catheter
MQB	Solid State X-Ray Imager (Flat Panel/Digital Imager)	Stationary x-ray system
KGE	Forceps, Biopsy, Electric	Endoscopic electrosurgical unit and accessories
GCI	Laryngoscope, Endoscope	Endoscope and accessories
FGB	Ureteroscope And Accessories, Flexible/Rigid	Endoscope and accessories

Product Code	Device	Regulation Description
KNS	Unit, Electrosurgical, Endoscopic (With Or Without Accessories)	Endoscopic electrosurgical unit and accessories
HAW	Neurological Stereotaxic Instrument	Stereotaxic instrument.
LLZ	System, Image Processing, Radiological	Picture archiving and communications system
OLO	Orthopedic Stereotaxic Instrument	Stereotaxic instrument.
GAW	Suture, Nonabsorbable, Synthetic, Polypropylene	Nonabsorbable polypropylene surgical suture
EPT	Microscope, Surgical	Surgical microscope and accessories
LNH	System, Nuclear Magnetic Resonance Imaging	Magnetic resonance diagnostic device
IZH	System, X-Ray, Mammographic	Mammographic x-ray system

APPENDIX 4: ANALYSIS OF SYMBIS SURGICAL SYSTEM PREDICATES

Figure 15: SYMBIS Surgical System (T., 2015)

The IMRIS (now Deerfield Imaging) SYMBIS Surgical System was designed as a spatial positioning and orientation guide for instruments in needle based brain biopsies. The system is comprised of three components, a manipulator arm located on a mobile base, a surgeon workstation, and a robotic control rack containing electronic equipment. The trajectory of a stereotactic instrument is guided by the surgeon from the workstation, which includes haptic feedback and 3D imaging for position control, using a manipulator arm with six degrees of freedom. The positioning mechanism of the device uses a robotic manipulator controlled from a separate surgeon control station similar to the method used in the Da Vinci Surgical system. However in the SYMBIS System the surgeon is required to manually perform portions of the surgery, including final deployment of the biopsy needle (Pena, 2015). The design of the SYMBIS Surgical System relies heavily on the incorporation of previously approved third-party

technologies into the design for key functions, including specifying use of the Medtronic StealthStation (K133444) for navigation and the Medtronic Biopsy Needle Kit (K971247) for instrumentation (Pena, 2015).

The traceable predicate history of the SYMBIS Surgical System is comprised of 43 identified predicate relationships which includes 26 unique devices that can be traced to 10 ultimate predicate devices. The immediate predicate of the SYMBIS System is the ROSA Surgical Device (see Table 6), a computer-controlled electromechanical arm intended to aid in the spatial positioning and orientation of stereotaxic instruments (Eydelman, 2009). The intended use and technological characteristics of the ROSA System are very similar to those described for the SYMBIS System, with technological differences primarily associated with the incorporation of third-party positioning systems in the SYMBIS System (Pena, 2015). An overview of the predicate history for the SYMBIS Surgical System is shown in Figure 16 below.

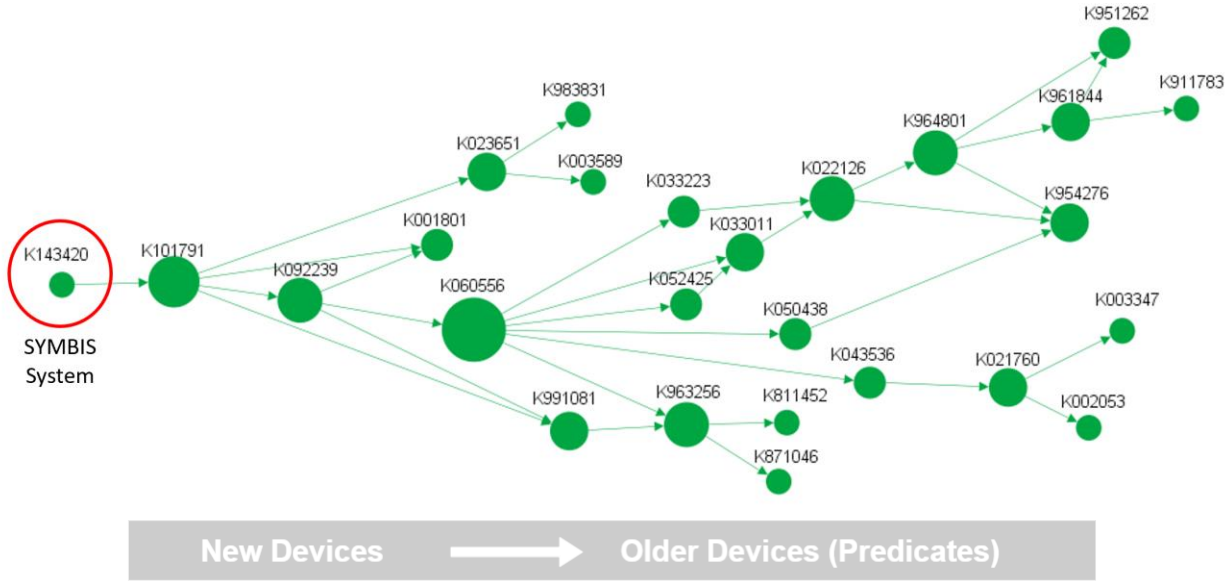

Figure 16: SYMBIS Surgical System predicate trace (see section A4.1 for additional device information).

Detailed approval information about the devices which appear in this predicate tree can be found in the SYMBIS Trace database in Section A4.1.

Additional information about the devices included in the predicate ancestry, particularly regarding predicate creep, can be gleaned from comparison of the product codes and regulatory descriptions associated with each device. The product code is an identifier designated by the FDA to group devices with the same intended use and similar technological characteristics. Each product code is assigned a regulatory description which describes the function and intended use based on the device type. The regulatory description is more general than the device description, which means that two product codes with slightly different device descriptions may possess the same regulatory description. For example, the SYMBIS was assigned product code HAW, which describes a neurological stereotaxic instrument with the regulatory description of stereotaxic instrument. The product code OLO describes orthopedic stereotaxic instruments, however it has the same regulatory description as code HAW, stereotaxic instrument. A percentage breakdown of the product codes and regulatory descriptions for the unique devices present in the SYMBIS trace is shown in Figure 17 below.

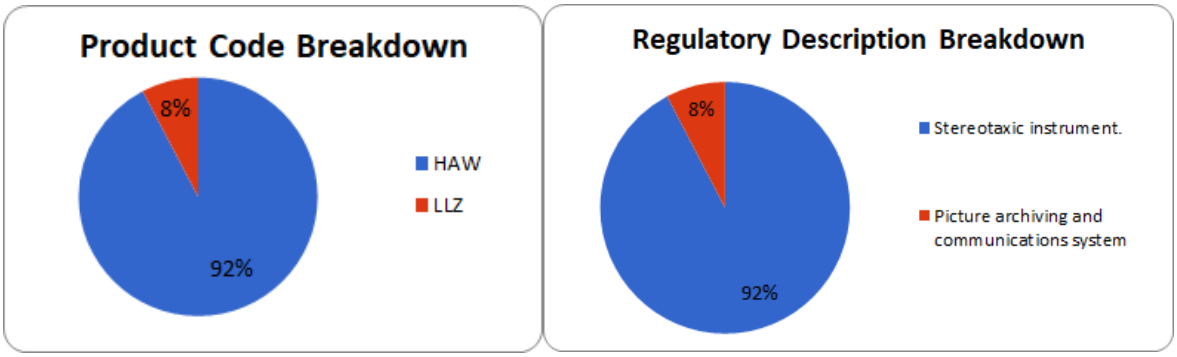

Figure 17: Breakdown of SYMBIS predicate devices by product code and regulatory description. Due to the nature of the devices in this trace, the two breakdowns are identical.

Unlike the devices in the Da Vinci trace, and the other robotic surgical system traces described below, the devices in the SYMBIS trace fall under only two product codes, HAW and LLZ. Code HAW, as described previously, pertains to neurological stereotaxic instruments, while code LLZ pertains to radiological imaging processing systems under the regulatory description "picture archiving and communications system". Because the two codes possess different regulatory description, the product code and regulatory description breakdowns for the SYMBIS System are identical. All but two devices contained in the trace fall under code HAW, making it the dominant device type in this trace. The two devices classified under code LLZ both serve as ultimate predicates along the branch originating from the Zimmer Knee Ortho Guidance Instruments (K033011), which incorporates CT scan modeling for surgical instrument guidance. Thus, these devices appear to be included in the trace to serve as predicates for the introduction of technological characteristics related to the imaging incorporated in later guidance systems.

A4.1 ADDITIONAL SYMBIS SYSTEM PREDICATE INFORMATION

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K143420	SYMBIS Surgical System	IMRIS, Inc.	10/30/2015	HAW	0
K101791	ROSA SURGICAL DEVICE	MEDTECH SAS	9/23/2010	HAW	12 – Class II
K092239	ROSA SURGICAL DEVICE, MODEL ROSA 1.1	MEDTECH S.A.	11/17/2009	HAW	9 – Class II
K060556	BRIGIT SURGICAL DEVICE	ZIMMER INC	7/31/2006	HAW	0
K052425	ZIMMER COMPUTER ASSISTED SOLUTIONS-ELECTROMAGNETIC AND IMAGELESS KNEE INSTRUMENTATION	ZIMMER, INC.	12/28/2005	HAW	0
K050438	STEALTHSTATION SYSTEM UPDATE	MEDTRONIC SURGICAL NAVIGATION TECHNOLOGIES	6/2/2005	HAW	11 – Class II
K043536	NAVITRACK SYSTEM - S&N IMAGE FREE KNEE	ORTHOSOFT, INC.	1/14/2005	HAW	0
K033223	ZIMMER ORTHO GUIDANCE SYSTEMS- HIP INSTRUMENTS	ZIMMER, INC.	2/18/2004	HAW	0
K023651	VECTORVISION CRANIAL/ENT	BRAINLAB AG	2/17/2004	HAW	1 – Class II
K033011	ZIMMER ORTHO GUIDANCE SYSTEMS- KNEE INSTRUMENTS	ZIMMER, INC.	2/12/2004	HAW	0
K022126	CATHETER INTRODUCER FOR THE STEALTHSTATION SYSTEM	MEDTRONIC SURGICAL NAVIGATION TECHNOLOGIES	1/3/2003	HAW	0
K021760	NAVITRACK SYSTEM-OPTICAL TKR CT-LESS, MODEL 900.120	ORTHOSOFT, INC	8/27/2002	HAW	0
K003589	VECTORVISION CRANIAL, VECTORVISION SPINAL, VECTORVISION ENT	BRAINLAB AG	5/21/2001	HAW	0
K003347	ORTHOPILOT	KINAMED, INC	2/23/2001	HAW	0
K002053	NAVITRAK SYSTEM-OPTICAL OPTION, MODEL 900.004	ORTHOSOFT, INC.	8/3/2000	HAW	0
K001801	STEATHSTATION TREATMENT GUIDANCE PLATFORM	MEDTRONIC SURGICAL NAVIGATION	6/30/2000	HAW	0
K991081	FRAMELESS NEUROMATE	INTEGRATED SURGICAL SYSTEMS, INC.	6/25/1999	HAW	0
K983831	VECTORVISION2	BRAINLAB, AG	5/19/1999	HAW	0
K964801	OPTICAL TRACKING SYSTEM (OTS)	RADIONICS SOFTWARE APPLICATIONS, INC.	6/2/1997	HAW	0
K963256	NEUROMATE STEREOTACTIC SYSTEM	INTEGRATED SURGICAL SYSTEMS, S. A	5/9/1997	HAW	0
K961844	OPERATING ARM SYSTEM (OAS) [WITH CT AND MR IMAGES]	RADIONICS SOFTWARE APPLICATIONS, INC.	10/23/1996	HAW	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K954276	STEALTHSTATION	SURGICAL NAVIGATION TECHNOLOGIES, INC.	1/24/1996	HAW	1 – Class II
K951262	OPERATING ARM SYSTEM (OAS)	RADIONICS SOFTWARE APPLICATIONS, INC.	11/13/1995	LLZ	0
K911783	ALLEGRO VIEWING WAND	I.S.G. TECHNOLOGIES, INC.	4/7/1994	LLZ	0
K871046	COMPASS STEREOTACTIC POSITIONING SYSTEM	STEREOTACTIC MEDICAL SYSTEMS, INC	5/8/1987	HAW	0
K811452	BROWN-ROBERTS-WELLS STEREOTAXIC SYTEM	TRENT WELLS, INC.	6/2/1981	HAW	0

APPENDIX 5: ANALYSIS OF MAKO RIO-THA SYSTEM PREDICATES

Figure 18: MAKO RIO-THA System

The MAKO (now Stryker Medical) Robotic Arm Interactive Surgical Operating System (RIO) is designed to provide stereotactic guidance during minimally invasive knee (K081867) and hip (K093425) procedures using patient CT scan data to assist a surgeon in pre-operative planning and intraoperative navigation. The system consists of three components, a computer station for inputting CT scan data and identifying markers, a viewing station, and the main RIO platform mounted on a moveable cart (Stryker, 2018). The main platform consists of a multi-jointed arm which uses sensors to provide real time visual, tactile, and auditory feedback as it is positioned manually by the surgeon during a procedure (Adventist Health Sonora, n.d.). The RIO arm aids in positioning and stabilization of tools to identify optimal locations for implant placement

during procedures to improve results and reduce complications. While the primary purpose of the Da Vinci system is to serve as a replacement for the surgeon's hands to increase surgeon dexterity and reduce error in traditional MIS procedures, the primary purpose of the RIO system is to assist in optimal positioning of implants for a manually performed surgery.

The traceable predicate history of the MAKO RIO-THA includes 590 predicate relationships between 53 unique devices, which can be traced to 21 ultimate predicate devices. The RIO system identified as the subject device for this trace is the RIO-THA, used in total hip arthroplasty procedures. Another version of the RIO System, used for applications in knee surgery serves, as a predicate device for the RIO-THA. An overview of the RIO System trace can be seen in Figure 19, with additional information about each device shown in the trace located in Section A5.1.

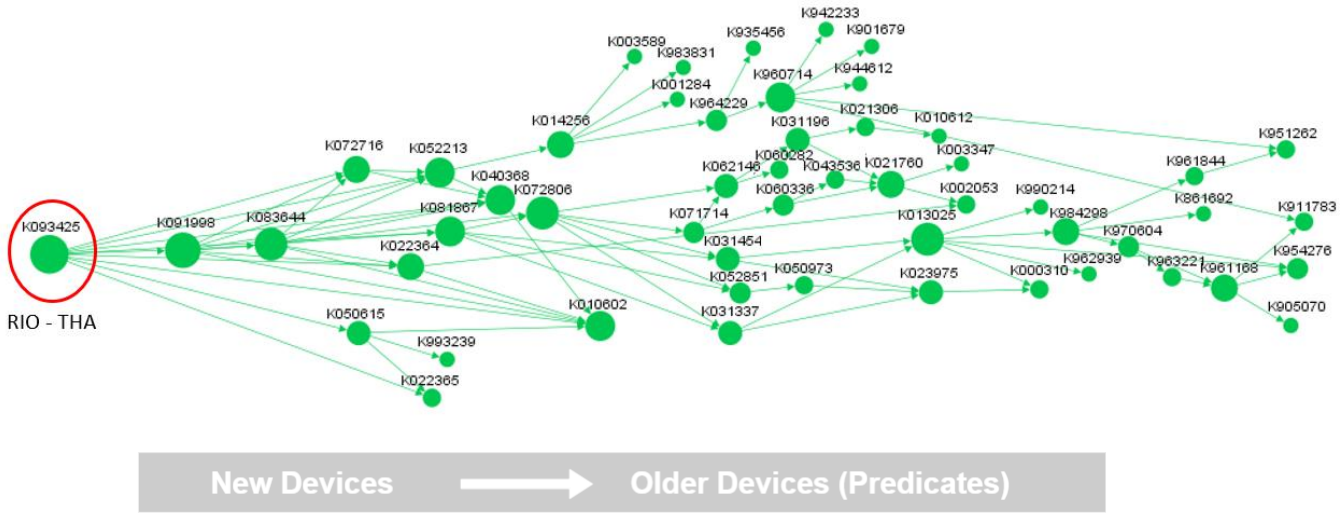

Figure 19: MAKO RIO – THA predicate tree (see section A5.1 for additional device information).

Examination of the RIO trace reveals patterns in the approval application process, including duplication of predicate devices between generations and within branches. This is evidenced by

the fact that there are only 53 unique devices identified among 590 substantial equivalence claims.

The 48 devices present in the RIO trace are grouped into 7 different product codes, with 42 of the devices under code HAW for stereotaxic instruments. Of the remaining devices, 3 are under code OLO, also for stereotaxic instruments, 4 are classified under code LLZ for radiological image processing, and the remaining 4 devices each have a unique product code. Examination of this breakdown, as seen in Figure 20, reveals that the RIO trace is dominated by stereotaxic instruments, primarily designated for neurological applications. It is only the two versions of the MAKO RIO and another associated product in the first predicate generation (closest to RIO) which are designated for orthopedic use under Code OLO.

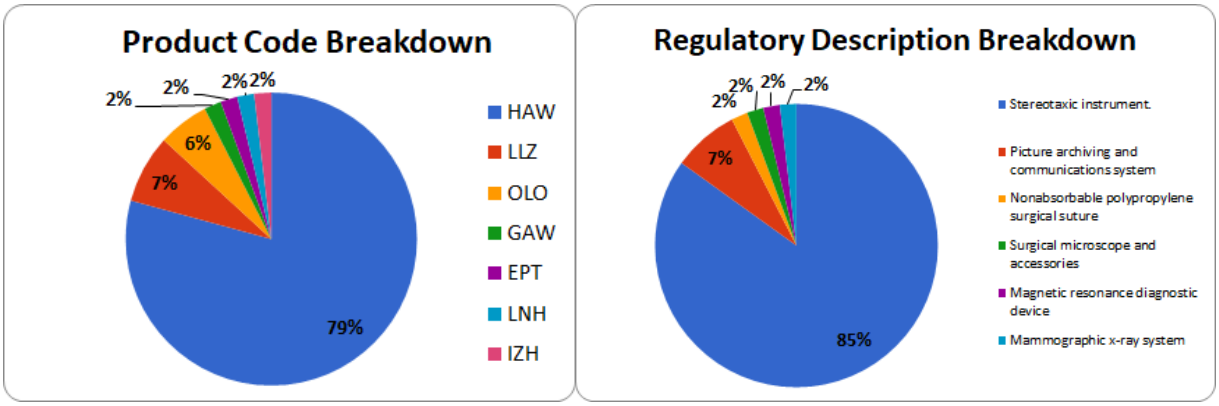

Figure 20: Breakdown of RIO-THA predicates by product code and regulatory description, The overall structures of the breakdowns are similar, with a single classification (HAW and Stereotaxic Instrument) containing most predicates. However, the largest regulatory description contains devices under product codes HAW and OLO, making the resulting group slightly larger.

A5.1 ADDITIONAL RIO-THA PREDICATE INFORMATION

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K093425	MAKO SURGICAL CORP ROBOTIC ARM INTERACTIVE ORTHOPEDIC SYSTEM-THA	MAKO SURGICAL CORP.	2/24/2010	OLO	1 – Class II
K091998	ROBOTIC ARM INTERACTIVE ORTHOPEDIC SYSTEM-HIP	MAKO SURGICAL CORP.	9/28/2009	OLO	0
K083644	MAKO SURGICAL TACTILE GUIDANCE SYSTEM-HIP	MAKO SURGICAL CORP.	6/19/2009	OLO	0
K081867	MAKO SURGICAL TACTILE GUIDANCE SYSTEM VERSION 2.0	MAKO SURGICAL CORP.	11/25/2008	HAW	2 – Class II
K072806	MAKO SURGICAL TACTILE GUIDANCE SYSTEM (TGS)	MAKO SURGICAL CORP.	1/24/2008	HAW	1 – Class II
K072716	VECTOR VISION HIP	BRAINLAB AG	10/12/2007	HAW	0
K071714	NAVITRACK SYSTEM - OS UNICONDYLAR KNEE UNIVERSAL, MODEL# PRO-06003	ORTHOSOFT, INC.	7/20/2007	HAW	2 – Class II
K062146	UNI KNEE SURGETICS NAVIGATION SYSTEM	PRAXIM S. A	8/21/2006	HAW	0
K060336	NAVITRACK SYSTEM-OS KNEE UNIVERSAL, MODEL PRO-05002	ORTHOSOFT, INC.	4/28/2006	HAW	2 – Class II 1 – Class III
K060282	TOTAL KNEE SURGETICS NAVIGATION SYSTEM	PRAXIM SA	4/10/2006	HAW	0
K052851	VOYAGER LINUX WITH TACTILE GUIDANCE SYSTEM (TGS)	MAKO SURGICAL CORP.	11/18/2005	HAW	0
K052213	NAVIGATION SW HIP 3.1 ON CI	BRAINLAB AG	11/2/2005	HAW	0
K031196	SURGETICS ORTHO KNEELOGICS NAVIGATION SYSTEM	PRAXIM	6/7/2005	HAW	0
K050973	MODIFICATION TO: VOYAGER LINUX	MAKO SURGICAL CORP.	5/17/2005	HAW	0
K050615	STRYKER NAVIGATION SYSTEM - CT-BASED HIP MODULE, MODEL 6007-621-000	STRYKER INSTRUMENTS	4/21/2005	HAW	0
K043536	NAVITRACK SYSTEM - S&N IMAGE FREE KNEE	ORTHOSOFT, INC.	1/14/2005	HAW	0
K040368	VECTORVISION HIP 3.0	BRAINLAB AG	8/23/2004	HAW	0
K031454	ACUMEN SURGICAL NAVIGATION SYSTEM	BIOMET, INC.	7/8/2004	HAW	0
K031337	ACUMEN SURGICAL NAVIGATION SYSTEM	BIOMET, INC.	9/15/2003	HAW	0
K022364	NAVITRACK SYSTEM TOTAL HIP REPLACEMENT, MODEL 900.200	ORTHOSOFT, INC.	2/4/2003	HAW	0
K022365	STRYKER NAVIGATION SYSTEM - HIP MODULE	STRYKER INSTRUMENTS	1/22/2003	HAW	10 – Class II
K023975	VOYAGER LINUX	Z-KAT, INC.	12/20/2002	HAW	0
K021306	VECTORVISION CT-FREE KNEE	BRAINLAB AG	10/25/2002	HAW	0
K021760	NAVITRACK SYSTEM-OPTICAL TKR CT-LESS, MODEL 900.120	ORTHOSOFT, INC.	8/27/2002	HAW	0

K014256	KOLIBRI IGS SYSTEMS	BRAINLAB AG	7/19/2002	HAW	0
K013025	MODIFICATION TO FLOUROLAB PLUS	Z-KAT, INC.	10/3/2001	HAW	0
K Number	**Device Name**	**Manufacturer**	**Approval Date**	**Product Code**	**Recalls**
K010602	VECTORVISION HIP	BRAINLAB, AG	9/12/2001	HAW	0
K010612	VECTORVISION KNEE	BRAINLAB, AG	9/6/2001	HAW	0
K003589	VECTORVISION CRANIAL, VECTORVISION SPINAL, VECTORVISION ENT	BRAINLAB AG	5/21/2001	HAW	0
K003347	ORTHOPILOT	KINAMED, INC.	2/23/2001	HAW	0
K002053	NAVITRAK SYSTEM-OPTICAL OPTION, MODEL 900.004	ORTHOSOFT, INC.	8/3/2000	HAW	0
K001284	STEALTHSTATION SYSTEM GOLDENEYE MICRO-MAGNETIC TRACKING SYSTEM	MEDTRONIC SURGICAL NAVIGATION TECHNOLOGIES	6/12/2000	HAW	27 – Class II 1 – Class III
K000310	VOYAGER 6.0 SOFTWARE OPTION	PHILIPS MEDICAL SYSTEMS(CLEVELAND), INC.	2/15/2000	HAW	0
K993239	STRYKER NAVIGATION SYSTEM - NEURO MODULE, MODEL 6000-XXX-XXX	STRYKER CORP.	1/18/2000	HAW	2 – Class I 4 – Class II
K984298	Z KAT FLUROTACTIC GUIDANCE SYSTEM MKI	Z-KAT, INC.	6/23/1999	HAW	0
K983831	VECTORVISION2	BRAINLAB, AG	5/19/1999	HAW	0
K990214	FLUORONAV MODULE FOR THE STEALTHSTATION SYSTEM	SURGICAL NAVIGATION TECHNOLOGIES, INC.	4/22/1999	HAW	29 – Class II
K964229	REGULUS NAVIGATOR	COMPASS INTL., INC	8/19/1997	HAW	0
K962939	VECTORVISION	BRAINLAB, INC.	5/22/1997	HAW	0
K970604	VIEWPOINT - 3.0 SOFTWARE	PHILIPS MEDICAL SYSTEMS(CLEVELAND), INC.	5/19/1997	HAW	0
K963221	OPTICAL DIGITIZER OPTION FOR VIEW POINT	PHILIPS MEDICAL SYSTEMS(CLEVELAND), INC.	1/10/1997	HAW	0
K961844	OPERATING ARM SYSTEM (OAS) [WITH CT AND MR IMAGES]	RADIONICS SOFTWARE APPLICATIONS, INC	10/23/1996	HAW	0
K960714	ISG VIEWING WAND	I.S.G. TECHNOLOGIES, INC	5/29/1996	HAW	0
K961168	VIEWPOINT	PHILIPS MEDICAL SYSTEMS(CLEVELAND), INC.	5/16/1996	GAW	0
K954276	STEALTHSTATION	SURGICAL NAVIGATION TECHNOLOGIES, INC.	1/24/1996	HAW	1 – Class II
K944612	ACUSTAR I ADVANCED SURGICAL NAVIGATION SYSTEM	Codman & Shurtleff, Inc.	12/11/1995	LLZ	0
K951262	OPERATING ARM SYSTEM (OAS)	RADIONICS SOFTWARE APPLICATIONS, INC.	11/13/1995	LLZ	0
K935456	REGULUS MEASUREMENT UNIT	COMPASS INTL., INC.	10/13/1995	HAW	0
K942233	MKM (MULTIPLE COORDINATE MANIPULATOR) SYSTEM	CARL ZEISS, INC.	7/1/1994	EPT	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K911783	ALLEGRO VIEWING WAND	I.S.G. TECHNOLOGIES, INC.	4/7/1994	LLZ	0
K905070	VISTAR	PHILIPS MEDICAL SYSTEMS(CLEVELAND), INC.	1/2/1991	LNH	0
K901679	RESUBMITTED ISG 3DMV WORKSTATION	I.S.G. TECHNOLOGIES, INC.	5/29/1990	LLZ	0
K861692	FISCHER PPS/MAMMOTEST MAMMOGRAPHY SYSTEM	FISCHER IMAGING CORP.	12/15/1986	IZH	1 – Class II

APPENDIX 6: ANALYSIS OF MEDROBOTICS FLEX ROBOTIC SYSTEM PREDICATES

Figure 21: Medrobotics Flex System

The primary function of the Medrobotics Flex Transabdominal Robotic System, as seen in Figure 21, is to serve as an assistive laparoscopic device for minimally invasive surgical (MIS) procedures in areas of the body which may be difficult to reach with traditional rigid scopes. The system is comprised of two main components, a moveable cart containing the jointed robotic arm and attached scope, and a surgical control station with an HD imaging display and a joystick for motion control. The primary innovation in the Flex System is the flexible, multi-jointed positioning mechanism within the scope and accompanying instruments that allow access to areas of the body that would traditionally be unreachable with MIS. This mechanism is structured similarly to a snake, with an external cable steered structure allowing for motion and an internal skeleton (see Figure 22), which allows the scope to be reliably placed in a stable position, and then used as a guide for positioning of the handheld Medrobotics Flex Instruments, which are used to perform the actual surgical procedure (Medrobotics, 2018). Unlike the Da Vinci System, where the system is controlled remotely to perform surgical procedures, the Flex System serves solely as an assistive device. Additionally, use of the Flex system is currently

limited to surgical procedures which can be performed via natural bodily orifices, specifically the mouth or anus, while the Da Vinci can be used to perform surgery via incisions.

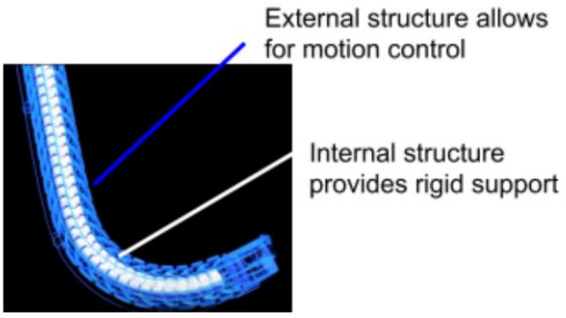

Figure 22: Medrobotics Flex System jointed scope structure (Medrobotics, 2018)

The traceable predicate history of the Medrobotics Flex Transabdominal System includes 109 substantial equivalence relationships between 42 unique devices, which can be traced to 21 ultimate predicates. An overview of the Flex System trace can be seen in Figure 23, with additional information about each device shown in the trace located in Section A6.1.

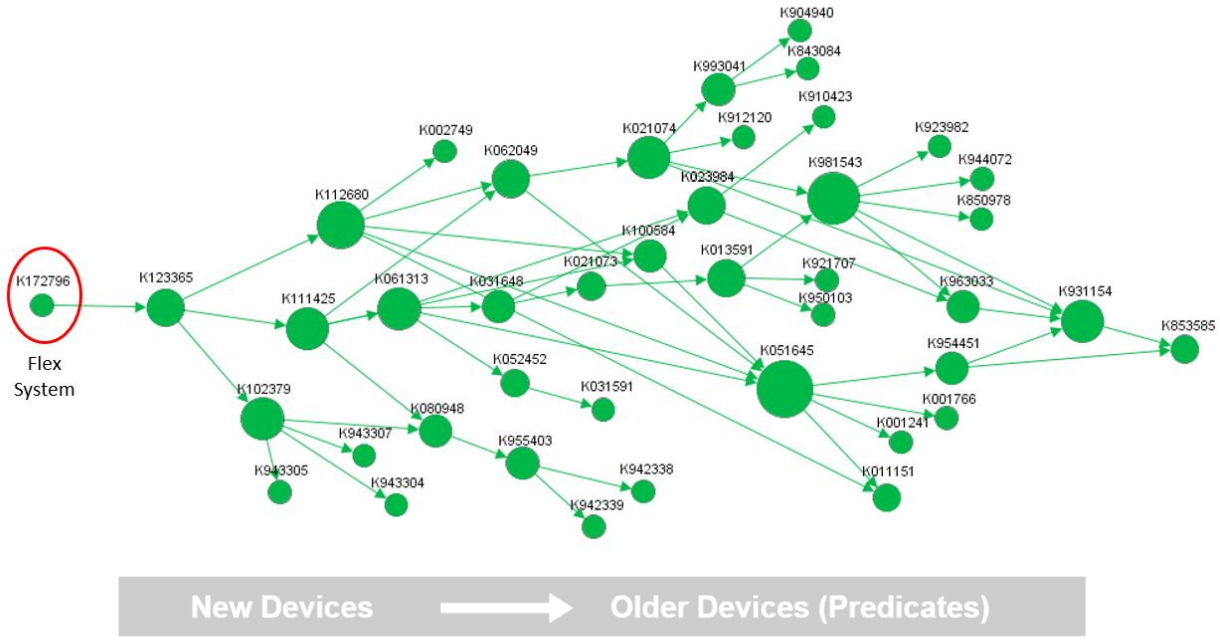

Figure 23: Medrobotics Flex System predicate trace (see section A6.2 for additional predicate information).

The 42 unique devices in the direct predicate trace for the Flex Transabdominal System are classified into 23 different product codes, with GCJ and EOB the most prevalent. Unlike the other three traces, which each possessed a clearly dominant product code, the Flex System has 5 codes each containing 7 or 8 predicate devices. However, although the devices described in these codes possess slightly different intended use cases, the majority share a common regulatory description as an endoscope with accessories. As a result, there are significant difference between the structure of the product code breakdown and regulatory description breakdown (see Figure 24).

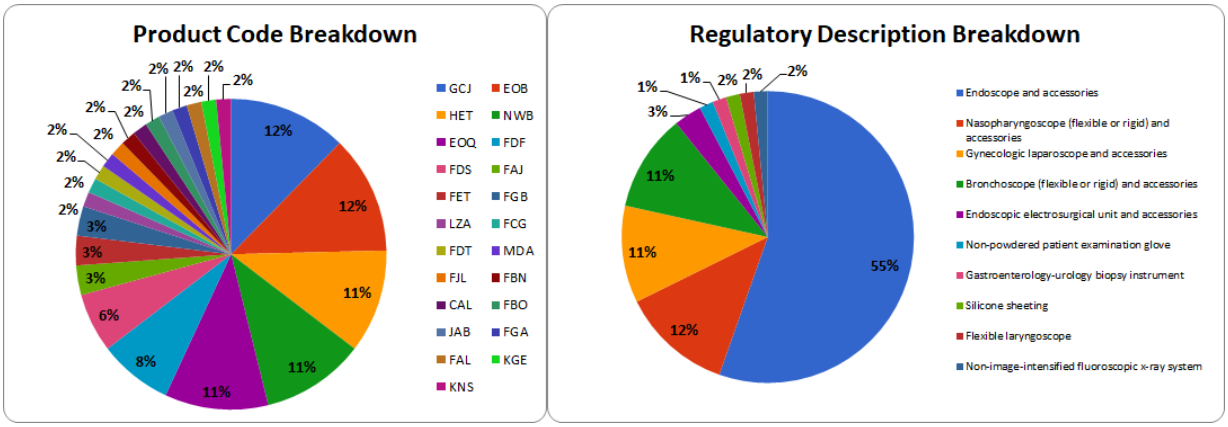

Figure 24: Breakdown of Flex System predicates grouped by product code and regulatory description. The product code classification breakdown shows a large number of product codes with no dominant code(s). However, many of these product codes share a common regulatory description as evidenced by the appearance of a dominant regulatory description in that breakdown.

A6.1 REFERENCE DEVICES IN THE TRACE

Unlike the subject devices analyzed in the other three traces, the sole direct predicate of the Medrobotics Flex Transabdominal System is not identified as a robotic surgical system. Instead this device, the Olympus EndoEye Flex 3D Deflectable Videoscope and associated system, is a

flexible video endoscope used for three-dimensional viewing of endoscopic instruments during surgery within the thoracic and abdominal cavities (Lerner, 2013). This device, shown in Figure 25, utilizes a similar cable-steered mechanism to make the scope flexible, however it does not include a powered arm for positioning and is controlled manually by the surgeon (Viviano, 2018).

Figure 25: Olympus EndoEye Flex 3D Deflectable Videoscope (Olympus Corp., 2018)

To mitigate some of the risk introduced with the inclusion of new technological characteristics, including the robotic arm and software driven positioning system, the 510(k) application for the Flex System includes two 510(k) applications associated with the Medrobotics Flex Colorectal System as reference devices. This system is classified under product code FDF as a colonoscopy and accessories with the regulatory description of endoscope and accessories. Although the Colorectal System is nearly identical to the Transabdominal System (Viviano, 2018), it was approved specifically as a device for colorectal surgery and is therefore ineligible to serve as a predicate for the Flex Transabdominal, which is indicated for a different intended use.

Inclusion of the reference devices and their subsequent predicates in the substantial equivalence tree significantly increases the size of the trace. With the reference devices included, there are 147 unique devices present in the trace classified under 48 different product codes (See Appendix 2). This trace expansion includes devices with a significantly wider array of technological characteristics, including the introduction of the robotic manipulator technology which is present in the subject device but missing in all the directly identified predicate devices. As reference devices are a relatively new regulatory mechanism, there is limited data available from this research to indicate whether reference devices could potentially impact the regulatory process. Since these devices are ineligible to serve as predicate devices, and therefore cannot directly contribute to predicate creep, analysis of the expanded trace was limited to the identification of reference devices and observation of introduced technological characteristics.

A6.2 ADDITIONAL FLEX SYSTEM PREDICATE INFORMATION

Note that this table includes devices classified as reference devices and subsequent reference predicates, identified with red text, in addition to direct predicate devices.

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K011782	Rectosight	SIGHTLINE TECHNOLOGIES LTD.	N/A (no record in database)		0
K172796	Flex Robotic System And Flex Transabdominal Drive	MEDROBOTICS CORPORATION	1/18/2018	HET GCJ	0
K172036	Medrobotics Flex Robotic System	Medrobotics Corporation	8/3/2017	FDF	0
K162330	Flex Robotic System And Flex Colorectal Drive	Medrobotics Corporation	5/4/2017	FDF	0
K150776	Medrobotics Flex System	MEDROBOTICS CORPORATION	7/17/2015	EOB EOX GCI	0
K123365	OLYMPUS LTF-190-10-3D, MAJ-Y0154, OLYMPUS CV-190	OLYMPUS MEDICAL SYSTEMS CORP.	3/1/2013	HET GCJ FGB NWB	0
K111004	HANSEN MEDICAL VASCULAR CATHETER CONTROL SYSTEM AND CATHETER	HANSEN MEDICAL, INC.	5/29/2012	DXX DRA	2 – Class II
K111425	OLYMPUS LTF-S190-10, OLUMPUS OTV-S190, OLYMPUS CLV-S190	OLYMPUS MEDICAL SYSTEMS CORP.	4/20/2012	HET EOB FGB GCJ NWB EOQ	
K112680	EVIS EXERA III VIDEO SYSTEM	OLYMPUS MEDICAL SYSTEMS CORPORATION	2/16/2012	FDF	0
K102733	VISION-SCIENCES ENT-5000 VIDEO ENT SCOPE WITH ENDOSHEATH TECHNOLOGY, VISION-SCIENCES DPU-5000/DPU-5050 VIDEO PROCESSOR	VISION-SCIENCES, INC.	5/18/2011	EOB GCJ HRX	0
K102379	LTF-Y0009; MAJ-YOO41; XOEV-3D1	OLYMPUS MEDICAL SYSTEMS CORPORATION	1/5/2011	GCJ	0
K102168	SENSEI X ROBOTIC CATHETER SYSTEM	HANSEN MEDICAL, INC.	10/22/2010	DXX	1 – Class II
K100584	EVIS EXERAII 180 SYSTEM	OLYMPUS MEDICAL SYSTEMS CORPORATION	7/2/2010	NWB FDF FDS	0
K093717	C-MOR VISUALIZATION DEVICE	AXIS SURGICAL TECHNOLOGIES, INC	3/2/2010	HRX	0
K091808	SENSEI ROBOTIC CATHETER SYSTEM, MODEL 02057	HANSEN MEDICAL, INC.	9/10/2009	DXX	1 – Class II
K090365	HANSEN MEDICAL ARTISAN S CONTROL CATHETER	HANSEN MEDICAL, INC.	5/7/2009	DXX DRA	1 – Class II

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K080948	HD ENDOEYE LAPARO-THORACO VIDEOSCOPE OLYMPUS LTF TYPE VH	OLYMPUS MEDICAL SYSTEMS CORPORATION	9/26/2008	HET GCJ NWB	0
K082293	SURGVIEW INTEGRATED VISUALIZATION SYSTEM	BIOVISION TECHNOLOGIES, LLC	9/9/2008	HRX GCJ	0
K081051	SPINEVU ENDOSCOPIC SPINE SYSTEM (SESS), SPINEVU MINISCOPE	SPINE VIEW, INC.	8/7/2008	HRX GEI	0
K073225	SENSEI CATHETER CONTROL SYSTEM	HANSEN MEDICAL, INC.	6/30/2008	DXX DRA	1 – Class II
K080415	DEVICE MODIFICATION TO PINNACLE DESTINATION PERIPHERAL GUIDING SHEATH	TERUMO MEDICAL CORP.	3/7/2008	DYB	0
K072879	INNERVUE DIAGNOSTIC SCOPE SYSTEM	BIOMET ORTHOPEDICS, INC.	1/14/2008	HRX	2 – Class II
K072073	VISION-SCIENCES ENT-5000 AND ENT-5100 VIDEO ENT SCOPE WITH ENDOSHEATH SYSTEM, DPU-5000/DPU-5050 VIDEO PROCESSOR	VISION-SCIENCES, INC.	8/29/2007	EOB	0
K070622	NEOGUIDE ENDOSCOPY SYSTEM	NEOGUIDE SYSTEMS, INC.	8/14/2007	FDF	0
K052480	HANSEN MEDICAL CATHETER CONTROL SYSTEM (CCS) AND ACCESSORIES, HANSEN MEDICAL STEERABLE GUIDE CATHETER (SGC) AND SHEATH	HANSEN MEDICAL, INC.	5/2/2007	DXX DRA	2 – Class II
K062049	EVIS EXERA II 180 SYSTEM	OLYMPUS MEDICAL SYSTEMS CORPORATION	9/22/2006	NWB	0
K061313	EVIS EXERA 180 SYSTEM	OLYMPUS MEDICAL SYSTEMS CORPORATION	8/31/2006	EOQ EOB NWB	0
K061246	ENDOSCOPIC SPINE SYSTEM	ARTHRO KINETICS INC.	8/23/2006	HRX	0
K061345	MODIFICATION TO ENDIUS ATAVI SYSTEM	ENDIUS, INC.	6/6/2006	HRX	1 – Class II
K052241	DISC-FX SYSTEM	ELLMAN INTERNATIONAL, INC.	2/24/2006	HRX GEI	0
K052930	NAVIGATOR ENDOSCOPY SYSTEM	NEOGUIDE SYSTEMS, INC.	1/31/2006	FDF	0
K053267	ENDIUS ATAVI SYSTEM	ENDIUS, INC.	1/13/2006	HRX	1 – Class II
K051645	EVIS EXERA 160A SYSTEM	OLYMPUS MEDICAL SYSTEMS CORPORATION	10/13/2005	NWB FDF FDS	0
K052452	VISERA RHINO-LARYNGOVIDEOSCOPE OLYMPUS ENF TYPE VT	OLYMPUS MEDICAL SYSTEMS CORPORATION	9/21/2005	EOB	0
K051827	JOIMAX ENDOSCOPE/MULTISCOPE, THESSYS FORAMINOSCOPE/MULTISCOPE, THESSYS LAMINOSCOPE/MULTISCOPE	JOIMAX GMBH	8/12/2005	HRX	0
K051601	PINNACLE DESTINATION PERIPHERAL GUIDING SHEATH	TERUMO MEDICAL CORP.	8/4/2005	DYB	0
K050972	VISION-SCIENCES ENT-3000 SCOPE	VISION-SCIENCES, INC.	4/29/2005	EOB	2 – Class II
K043395	SMITH & NEPHEW VIDEOARTHROSCOPE	SMITH & NEPHEW, INC.	1/12/2005	HRX EOB	0
K040604	INNERVUE DIAGNOSTIC SCOPE SYSTEM	ARTHROTEK, INC.	6/4/2004	GCJ	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K040984	VISION SCIENCES MODEL ENT-2000V FLEXIBLE NASOPHARYNGO-LARYNGOSCOPE	VISION-SCIENCES, INC	4/27/2004	EOB	0
K033954	SHAPE LOCKING ENDOSCOPIC OVERTUBE	USGI MEDICAL, INC.	3/19/2004	FED FDF	0
K032688	COLONOSIGHT MODEL 510B	SIGHTLINE TECHNOLOGIES LTD.	3/5/2004	FDF	0
K023902	SHAPE-LOCKABLE ENDOSCOPIC OVERTUBE	USGI MEDICAL, INC.	8/20/2003	FED FDF	0
K031648	VISERA RHINO-LARYNGOVIDEOSCOPE OLYMPUS ENF TYPE V	OLYMPUS OPTICAL CO., LTD.	7/24/2003	EOB	0
K031591	POWDER-FREE NITRILE PATIENT EXAMINATION GLOVE, WHITE (NON-COLORED), BLUE AND GREEN COLORED	PERUSAHAAN GETAH ASAS SDN BHD	6/26/2003	LZA	0
K030096	VIDEO ARTHROSCOPE, MODELS AR-3050-30, AR-3050T-30, AR-3050-70, AR-3051-30, AR-3052-30, AR3030AN, AR-3030AS, AR3030AW	ARTHREX, INC.	3/18/2003	HRX	0
K023984	MODIFICATION TO OLYMPUS BRONCHOSCOPES BF-40 SERIES, BF-240 SERIES, AND BF-160 SERIES	THE OLYMPUS OPTICAL CO.	1/31/2003	EOQ	0
K021555	STEREOTAXIS NIOBE MAGNETIC NAVIGATION SYSTEM	STEREOTAXIS, INC.	1/15/2003	DXX	0
K024095	MODIFICATION TO VISION SCIENCES ENDOSHEATH SYSTEM	VISION-SCIENCES, INC	1/9/2003	EOB	0
K022199	ENDIUS ATAVI SYSTEM	ENDIUS, INC.	10/2/2002	HRX	0
K012543	VISION SCIENCES ENDOSHEATH SYSTEM	VISION-SCIENCES, INC.	7/15/2002	EOB	0
K021748	ENDIUS ATAVI SYSTEM	ENDIUS, INC.	6/26/2002	HRX	0
K021344	B-F200 BRONCHOSCOPE WITH BSS-F21 ENDOSHEATH SYSTEM	VISION-SCIENCES, INC.	5/24/2002	EOQ	0
K021074	VISERA CYSTOVIDEOSCOPE OLYMPUS CYF TYPE V/VA	OLYMPUS AMERICA, INC.	5/2/2002	FAJ	0
K013484	TELSTAR MAGNETIC NAVIGATION SYSTEMS [MNS}, TELSTAR BI-PLANE DIGITAL IMAGING SYSTEM, NIOBE ELECTROPHYSIOLOGY MAPPING CATH	STEREOTAXIS, INC.	5/2/2002	DRF DXX MQB	0
K021073	VISERA RHINLARYNGOVIDEOSCOPE OLYMPUS ENF TYPE V	OLYMPUS AMERICA, INC.	5/1/2002	EOB	0
K020310	DAVLITE MICROENDOSCOPE & ACCESSORIES	DAVLITE TECHNOLOGIES	3/20/2002	GCJ	0
K013591	XENF-TP RHINO-LARYNGOFIBERSCOPE, ITS ACESSORIES AND ANCILLARY EQUIPMENT	OLYMPUS OPTICAL CO., LTD.	12/26/2001	EOB	0
K012812	CAROTID GUIDING SHEATH	TERUMO MEDICAL CORP.	11/14/2001	DYB	1 – Class II
K011189	VIADUCT MICROENDOSCOPE AND ACCESSORIES	ACUEITY, INC.	7/16/2001	GCJ	0
K010811	PERC-D SPINEWAND	ARTHROCARE CORP.	5/30/2001	HRX	0
K011151	EVIS EXERA GASTROINTESTINAL VIDEOSCOPE GIF-Q160Z	THE OLYMPUS OPTICAL CO.	5/15/2001	FDS	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K002749	ENDOSCOPE CONTOUR DETECTION DEVICE, MODEL 3DX45 AND COLONOSCOPE, MODEL XCF-Q140L/13D	THE OLYMPUS OPTICAL CO.	12/4/2000	FDF JAB	0
K002931	METRX SYSTEM	MEDTRONIC SOFAMOR DANEK, INC.	11/24/2000	HRX	0
K002437	ENDIUS ENDOSCOPIC ACCESS SYSTEM	ENDIUS, INC.	10/2/2000	HRX	0
K001766	OLYMPUS XGIF-N200H GASTROINTESTINAL VIDEOSCOPE	OLYMPUS OPTICAL CO., LTD.	9/8/2000	FDS	0
K002018	NDO SURGICAL SURGICAL OVERTUBE	SURGICAL, INC.	8/17/2000	FED	0
K994130	RECTOSIGHT RS 300-04	SIGHTLINE TECHNOLOGIES LTD.	6/30/2000	FER GCF	0
K001241	EVIS EXERA COLONOVIDEOSCOPE CF-Q160 AL/I AND PCF-160 AL/I	THE OLYMPUS OPTICAL CO.	5/9/2000	FDF	0
K993041	OLYMPUS XCYF-1T3 OES CYSTOFIBERSCOPE/NEPHROFIBERSCOPE ACCESSORIES AND ANCILLARY EQUIPMENT	THE OLYMPUS OPTICAL CO.	3/30/2000	FAJ FGA KGE KNS	0
K000046	KNIGHT ENDOSCOPIC SPINE SYSTEM (KESS)	RICHARD WOLF MEDICAL INSTRUMENTS CORP	3/30/2000	HRX	0
K994425	MODIFICATION TO ENDOSCOPIC SPINAL ACCESS SYSTEM	ENDIUS, INC.	2/16/2000	HRX	0
K991794	ENDOSCOPIC SPINAL ACCESS SYSTEM	ENDIUS, INC.	8/13/1999	HRX	0
K990354	ENDOSHEATH	VISION-SCIENCES, INC.	3/31/1999	EOB	0
K982819	ENDIUS SPINE ENDOSCOPE	ENDIUS, INC.	1/27/1999	GWG	0
K981543	OLYMPUS LF-TP AND LF-DP TRACHEAL INTUBATION FIBERSCOPES, ACCESSORIES AND ANCILLARY EQUIPMENT	THE OLYMPUS OPTICAL CO.	6/8/1998	EOQ	0
K973405	YEUNG ENDOSCOPIC SPINE SYSTEM	RICHARD WOLF MEDICAL INSTRUMENTS CORP.	3/13/1998	HRX	0
K974355	INTERVENTIONAL MOBILE DIGITAL IMAGING SYSTEM (HEREIN CALLED IMDIS)	GE DEC MEDICAL SYSTEMS	2/17/1998	OWB JAA OXO	1 – Class II
K973500	BARD ENDOSCOPIC OVERTUBE (#000307)	C.R. BARD, INC.	10/16/1997	FED	0
K971253	VARIOUS ARTHROSCOPES, ENDOSCOPIC BLADES, MANUAL INSTRUMENTS	SMITH & NEPHEW, INC.	6/13/1997	HRX	0
K963795	VISION-SCIENCES MODEL B-F100 BRONCHOSCOPE WITH MODEL BS-F21 DISPOSABLE ENDOSHEATH	VISION-SCIENCES, INC.	12/23/1996	EOQ	0
K961228	KARL STORZ MAGNIFYING ARTHROSOCPES	KARL STORZ ENDOSCOPY-AMERICA, INC	10/10/1996	HRX	0
K963033	BF 240/P240/IT240 BRONCHOVIDEOSCOPE & ACCESSORIES	OLYMPUS AMERICA, INC.	9/9/1996	EOQ	0
K950809	VISION-SCIENCES DISPOSABLE ENDOSHEATH FOR FLEXIBLE NASOPHARYNGO-LARYNGOSCOPES	VISION-SCIENCES, INC.	8/5/1996	EOB	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K961591	DISPOSABLE ENDOSHEATH FOR E-F100 FLEXIBLE NASOPHARYNGOSCOPE	VISION-SCIENCES, INC	7/2/1996	EOB	0
K961570	KEC-3840L/F, VIDEO COLONOSCOPE (*L OR F IN MODEL NUMBER DENOTES LENGTH)	PENTAX PRECISION INSTRUMENT CORP.	6/24/1996	FDF	1 – Class II
K961563	EC-384OTL, VIDEO COLONSCOPE	PENTAX PRECISION INSTRUMENT CORP.	6/19/1996	FDF	0
K954451	EVIS 140 SYSTEM	OLYMPUS AMERICA, INC.	3/29/1996	FET	0
K951579	EC-3800TL, VIDEO COLONOSCOPE	PENTAX PRECISION INSTRUMENT CORP.	3/21/1996	FDF	1 – Class II
K951574	EC-3800L, VIDEO COLONOSCOPE	PENTAX PRECISION INSTRUMENT CORP.	3/21/1996	FDF	3 – Class II
K955403	OES LAPARO-THORACO VIDEOSCOPE TYPE V	OLYMPUS AMERICA, INC.	3/11/1996	HET GCJ	0
K942265	FLEXIBLE NASOPHARYNGO-LARYNGOSCOPE AND ENDOSHEATH	VISION-SCIENCES, INC.	12/22/1995	EOB	0
K943307	3D SURGICAL ENDOSCOPY SYSTEM FOR GENERAL SURGERY	OLYMPUS AMERICA, INC.	12/20/1995	GCJ	0
K943304	3D SURGICAL ENDOSCOPY SYSTEM FOR UROLOGY	OLYMPUS AMERICA, INC.	12/20/1995	FCG FAL	0
K954989	DYONICS DISPOSABLE ENDOSCOPIC SURGERY BLADES	SMITH & NEPHEW DYONICS, INC.	11/27/1995	ERL	0
K943305	OLYMPUS 3D SURGICAL ENDOSCOPY SYSTEM	OLYMPUS AMERICA, INC.	11/17/1995	HET	0
K953910	PHILIPS BV 300 SERIES	PHILIPS MEDICAL SYSTEMS NORTH AMERICA, INC.	10/18/1995	OXO	1 – Class II
K930191	DANEK(TM) SPINAL EPIDURAL ENDOSCOPIC SY	SOFAMOR DANEK MFG., INC.	9/26/1995	HRX	0
K953695	DYONICS DISPOSABLE ARTHROSCOPIC BLADES	SMITH & NEPHEW DYONICS, INC	9/15/1995	HRX	0
K953484	POLLUX OA/POLLUX 30A/POLLUX 70A	POLLUX ENDOSCOPY, INC.	9/1/1995	HRX	0
K945209	PROCTOSCOPEA & ACCESSORIES, SIGMOIDOSCOPES & ACCESSORIES, PROCTOLOGY INSTRUMENTS	KARL STORZ ENDOSCOPY-AMERICA, INC.	3/6/1995	GCF FAM	0
K950103	LAPAROSCOPE, HAND INSTRUMENTS	OLYMPUS AMERICA, INC.	3/6/1995	GCJ	0
K943895	VISION SYSTEM COLONSCOPE	VISION-SCIENCES, INC.	2/3/1995	FDF	0
K944072	OLYMPUS NASAL AND SINUS ENDOSCOPES	OLYMPUS AMERICA, INC.	1/11/1995	EOB	0
K942338	OLYMPUS PF-8P OES PANCREATO FIBERSCOPE AND ACCESSORIES	OLYMPUS CORP.	11/30/1994	FDT	0
K942339	SKIN NEUVEAU SCAR TREATMENT	PURITAS HEALTH CARE, INC.	11/28/1994	MDA	0
K941036	CURVED ROTATABLE DISPOSABLE ARTHROSCOPIC SURGERY BLADES	SMITH & NEPHEW, INC	9/28/1994	HRX	0
K941919	OKTAS ENDOSCOPY VIDEO CAMERA SYSTEM	OKTAS	6/17/1994	FET	0
K942044	BARD ENDOSCOPIC OVERTUBE	C.R. BARD, INC.	6/10/1994	FED	0
K941967	HSW LAPAROSCOPE AND ACCESSORIES	HENKE-SASS WOLF, GMBH.	5/16/1994	GCJ	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K932987	BIRTCHER LAPAROSCOPE AND ACCESSORIES	BIRTCHER MEDICAL SYSTEMS, INC	4/25/1994	GCJ	0
K922519	MOD. PERCUTANEOUS ARTHROSCOPIC MICRO DISCECTOMY	SMITH & NEPHEW, INC.	3/29/1994	HRX	0
K932843	FLEXIBLE VIDEO SIGMOIDOSCOPE SYSTEM W/DISP. SHEATH	VISION-SCIENCES, INC.	2/14/1994	FAM FET	0
K934299	DYONICS DISPOSABLE ARTHROSCOPIC SURGERY BLADES MODIFICATION	SMITH & NEPHEW DYONICS, INC	2/14/1994	HRX HWE	0
K934918	EPM-3300 VIDEO PROCESSOR	PENTAX PRECISION INSTRUMENT CORP.	2/7/1994	FET GCT	0
K934981	DENTAL DRILL	EARE CONSULTING SERVICE	2/3/1994	DZP	0
K934920	VB-1830/VB-1530, VIDEO BRONCHOSCOPE	PENTAX PRECISION INSTRUMENT CORP.	1/26/1994	EOQ	0
K933247	PROTECTIVE SHEATH FOR FLEXIBLE NASOPHARY/LARYGNOS	VISION-SCIENCES, INC.	11/22/1993	EOB	0
K931154	EVIS 200 SYSTEM	OLYMPUS CORP.	10/7/1993	EOQ	0
K924125	CRI ELECTRONIC CONTROL SYSTEM	CATHETER RESEARCH C/O BURDITT, BOWLES & RADZIUS	5/26/1993	DXX	0
K924607	ARROW FISCHELL KINK RESIST PERCUT SHEATH INTRO SET	ARROW INTL., INC.	4/22/1993	DYB	2 – Class II 1 – Class III
K923982	OLYMPUS OES LAPAROSCOPY SYSTEM	OLYMPUS CORP.	3/15/1993	GCJ	1 – Class II
K926056	9600 FLUOROSCOPIC IMAGING SYSTEM	OEC-DIASONICS, INC.	1/21/1993	OXO	0
K925421	ENDOSHEATH	VISION-SCIENCES, INC.	1/15/1993	EOB	0
K921690	FLEXIBLE FIBEROPTIC SIGMOIDOSCOPE SYSTEM	VISION-SCIENCES, INC.	10/28/1992	FAM ODB	0
K921244	DISPOSABLE PROTECTIVE SHEATH	VISION-SCIENCES, INC.	10/6/1992	EOB	0
K921707	PENTAX NASO-PHARYNGO-LARYNGOSCOPE FNL-15P2/15RP2	PENTAX PRECISION INSTRUMENT CORP.	7/1/1992	EOB	1 – Class II
K920800	INTEGRATED ENDOSCOPY SYSTEM 1000	BIOMET, INC.	6/30/1992	HRX	1 – Class II
K914559	SMALL JOINT SYSTEM	SMITH & NEPHEW DYONICS, INC.	2/18/1992	HRX	0
K904940	OLYMPUS INFANT RESECTOSCOPE AND ACCESSORIES	OLYMPUS CORP.	1/13/1992	FJL	0
K912453	INTELIJET TM FLUID MANAGEMENT SYSTEM	SMITH & NEPHEW DYONICS, INC.	8/26/1991	HRX	0
K912120	URF-P2 URETERORENOFIBERSCOPE/CHOLEDOCHOFIBERSCOPE	OLYMPUS CORP.	8/7/1991	FBN	1 – Class II
K910423	BRONCHOSCOPE BF-N20	OLYMPUS CORP.	4/29/1991	EOQ	0
K903842	ST-E1 OVERTUBE	OLYMPUS CORP.	1/23/1991	FED	0
K904284	ARTHROSCOPIC SURGICAL BLADE	SMITH & NEPHEW DYONICS, INC.	12/5/1990	HRX	0
K900765	STEEROCATH(TM)	EP TECHNOLOGIES, INC.	5/7/1990	DRF	0

K Number	Device Name	Manufacturer	Approval Date	Product Code	Recalls
K900070	MODIFIED USES OF THE ARTHROSCOPIC SURGICAL SYSTEM	DYONICS, INC.	2/16/1990	HRX	0
K880518	MOBILE C-ARM OMNI 325	FISCHER IMAGING CORP.	3/9/1988	OXO	0
K853585	OLYMPUS EVS-ENDOSCOPIC VIDEO IMAGE & DATA SYS	OLYMPUS CORP.	1/21/1986	FET	0
K853678	KAMBIN SPINAL INSTRUMENT SET	PILLING CO.	9/24/1985	HTZ	0
K850978	OLYMPUS LF-1 INTUBATION SCOPE	OLYMPUS CORP.	5/23/1985	CAL	0
K843084	OLYMPUS CHP-P10 NEPHROSCOPE/CYSTOSCOPE	OLYMPUS CORP.	1/3/1985	FBO	0
K844131	NUCLEOTOME	MEDICAL INSTRUMENT DEVELOPMENT LABORATORIES, INC.	11/29/1984	HSZ	0
K833587	DISPOSABLE ARTHROSCOPY BLADE	DYONICS, INC.	11/14/1983	HRX	0
K822846	PENTAX FC-38LA & FC-38SA COLONOFIBER	PENTAX PRECISION INSTRUMENT CORP.	10/22/1982	FDF	0
K820367	INTRA-ARTICULAR SURGICAL SYSTEM	DYONICS, INC.	5/7/1982	KIJ	0
K771218	INTRA-ARTICULAR SHAVER	DYONICS, INC	2/1/1978	KIJ	0