Predicate Data Availability in the Ventilator 510(K) Network

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Executive Summary: Past research has substantiated concerns over transparency in medical device clearance and approval by the Food and Drug Administration (FDA), including a lack of publicly available data. Transparency in this process is necessary for patients and researchers to understand why products are granted or denied clearance for public use, allowing them to make informed decisions ranging from the innovation of future products to personal healthcare judgements. This insight is important for the premarket notification process known as the "510(k) pathway," the regulatory process through which most medical devices are cleared for commercial distribution in the United States. This process relies on demonstrations that a new product is substantially equivalent to an existing product on the market, referred to as a predicate device.

One metric of transparency of the 510(k) pathway is the public availability of 510(k) submission summaries and the data they contain on substantially equivalent predicate devices. We analyze predicate data availability for medical ventilation devices cleared through the 510(k) pathway across a range of time intervals and product codes using one-way analysis of variance testing and Tukey's method of multiple comparison. Out of all cleared medical ventilation devices whose submissions were received from January 1990 through October 2020, 65.64% list publicly available predicate information, primarily through summary documents in the FDA 510(k) Premarket Notification database. There is a statistically significant increase in the percentage of device submissions with available predicate data over time, with predicate data available for 93.17% of all devices submitted in the fifteen-year-period between the beginning of 2005 and the end of 2019.

I. Introduction

Due to the human health impacts of medical devices, transparency is particularly important in the process of device clearance and market approval. There are numerous benefits to improving FDA transparency, including higher-quality information for use in educational settings and clinical practice, increased innovation rates, and improved public trust in the FDA (Sharfstein et al. 2017). An increase in information transparency in the FDA's public database for device submissions that have been cleared for market would allow providers and patients to select the most appropriate products for their specific needs, informing and personalizing patient care (Gottlieb 2018). Transparency in clinical testing may offer critical information on treating conditions that impact sub-populations differently. Research and development teams in other firms can learn from medical devices that failed to be cleared for market, improving innovation and performance in the medical device industry (Sharfstein et al. 2017).

The FDA categorizes medical devices into three classes, based on ascending risk. Class I devices (such as a tongue depressor) pose the lowest risk to

the patient, while Class III devices (such as an implantable pacemaker) pose the highest risk to the patient. Most Class III and some Class II devices are approved for market through the premarket approval (PMA) pathway. The PMA pathway requires extensive data from clinical and laboratory studies, along with clinical investigation documentation, to be submitted to the FDA (U.S. Food and Drug Administration 2019b). The clinical investigation documentation details information including study protocols, evidence of safety and effectiveness, adverse reactions, device failures, patient data and complaints, and statistical analysis results. Devices that are not required to undergo PMA are often submitted through the premarket notification pathway, also called the 510(k) pathway.

This pathway is intended to support innovation by offering an efficient alternative to PMA for new products that expand on previously existing products. A 510(k) submission requires a device to be substantially equivalent to at least one existing device on the market, known as a predicate device. A device is considered substantially equivalent to its predicate(s) if it has the same intended use and either shares the same technological characteristics as the predicate, or if its differing technological characteristics do not raise unique questions of safety and effectiveness (U.S. Food and Drug Administration 2022a). The 510(k) pathway is less time-consuming, less expensive, and less rigorous in comparison to the stringent clinical trials of a PMA submission.

Complete transparency of the FDA approval and clearance process is expected to promote innovation and increase the percentage of device submissions that are cleared for market (Muehlematter et al. 2021). Reviewing the flaws of rejected devices allows researchers and engineers to adjust their product to better conform with FDA standards, potentially reducing the likelihood of future rejections and allowing for faster device clearance, and as a result of this, more rapid innovation (Pietzsch et al. 2013; Grennan and Town, 2016). Some have suggested that increasing the transparency of 510(k) decision making would allow for public review on FDA assessment of a device, improving the safety and efficacy of clinical research as regulators and researchers alike learn from the successes and failures of previous medical devices (Shapiro 2014; Wizemann 2011; Muehlematter et al. 2021).

The Safe Medical Devices Act of 1990 (SMDA) required the inclusion of a statement or summary with all premarket notification submissions from the year 1995 onwards (Safe Medical Devices Act of 1990). Currently, one of the most direct ways for the public to analyze the assessment of safety and effectiveness of a product submitted through the 510(k) pathway is through these 510(k) summaries provided to the FDA by the companies. However, a statement of substantial equivalence can be provided instead, which offers no details beyond confirming substantial equivalence was proven (see Appendix). The information provided in the 510(k) summaries from the FDA database is limited and the content varies between products.

The importance of transparency and data availability was recognized by the FDA in 2009 with the introduction of a three-phase Transparency Initiative (U.S. Food and Drug Administration 2017). The first phase was launched in early 2010 and introduced FDA Basics, a digital resource offering information about the FDA to the general public. Phase two was launched mid-2010 and concentrated on releasing information pertinent to regulated products and firms. This was later improved in January of 2011 through the third phase, which increased the FDA's transparency regarding operations and decision making. Recognizing that issues with transparency and data availability persisted, the FDA improved the Medical Device Reporting Program in 2019. The Medical Device Reporting Program is responsible for monitoring device performance, detecting potential device-related safety concerns, and contributing to risk-benefit analyses (Shuren 2019).

Steps the FDA took to improve transparency include ending the Alternative Summary Reporting Program, requiring device manufacturers to submit what is referred to as a "companion" medical device report, and implementing the Voluntary Malfunction Summary Reporting Program, which allows manufacturers to submit quarterly reports on certain device malfunctions for eligible device types rather than on an individual basis (Shuren 2019). These changes allow the FDA to focus on the most significant risks that are associated with medical

devices, though despite these efforts, concerns remain about the lack of publicly available information.

Our research analyzes the availability of 510(k) submission summaries/statements of all medical ventilation devices classified as ventilators that have been cleared for market through this pathway. Medical ventilation devices were selected as a specific area of focus because of their recent rise in prominence during the COVID-19 pandemic and their potential as an area of future study on medical device evolution and innovation over time, as many ventilation devices are of a size and basic functionality to allow for mechanical deconstruction and design comparison. Understanding the predicate data available in the realm of medical ventilators may provide future researchers with a better foundation for examining patterns in ventilator predicate history and their relationship to device safety, whether in the context of ventilators developed through the traditional regulatory pathways or on devices cleared by Emergency Use Authorizations during the COVID-19 pandemic.

II. Literature Review

i. Safety and the 510(k) Process

The 510(k) pathway is the source of FDA market clearance for the majority of new medical devices, with 99% of all medical devices from 2008 through 2017 cleared through the 510(k) pathway and the remaining 1% of devices approved through the PMA pathway (Dubin et al. 2021). Recalled devices serve as a common metric of device safety in these pathways. Recalls are defined in this context as a manufacturer's removal or correction of a marketed product in order to address an issue in violation of FDA laws; this occurs when a device is either defective or poses a potential risk to user health (U.S. Food and Drug Administration, 2020). Multiple recall events may be associated with a single device; similarly, multiple devices may be associated with a single recall event.

Prior analysis of recalled devices initially cleared through the 510(k) pathway suggests that the pathway does not address all safety issues, as 97% of recalled devices were cleared through the 510(k) pathway (Dubin et al. 2021). A high percentage of recalled devices is expected given that most medical devices are cleared through this pathway, but for certain distinct products or device types, 510(k) devices are disproportionately recalled compared to other approval processes. An analysis of orthopedic devices found that for the devices assessed, 510(k)-cleared devices were 11.5 times more likely to be recalled than PMA-approved devices (Day et al 2016). A second study confirmed this, finding that knee arthroplasty devices cleared through 510(k) process were recalled 11.5 times more often than those approved through PMA, although their findings were not significant enough to state that devices cleared through the 510(k) pathway were more likely to experience a recall (Pellerin et al. 2020).

A total of 3,132 distinct 510(k)-cleared devices were recalled between 2003 and 2009, and of these devices, 26.1% were recalled more than once (Maisel 2011). The majority of 510(k) recalls from this study were the result of a few set causes: manufacturing process errors (28.8% of recalls), device design issues (28.4% of recalls), materials and component issues (16.3% of recalls), and change control processes (11.9% of recalls). These data show that recalls of devices cleared through the 510(k) pathway during this time period were not just due to manufacturing errors, but also the result of errors in product and material design. In comparison to non-recalled 510(k) submissions, recalled devices were more likely to have undergone third party review or been submitted under a Special 510(k) application (Maisel, 2011). A more focused analysis on the predicate ancestry network of surgical meshes cleared through the 510(k) process between 2013 and 2015 found that 16% of recently cleared meshes were connected to three predicate meshes that had been recalled for design/material-related flaws that caused serious adverse events, raising concerns over the ability of the 510(k) pathway to ensure patient safety (Zargar and Carr, 2018).

ii. Transparency and the FDA

There are a small number of studies that look at transparency of the 510(k) process. One study found that out of 50 implants cleared through the 510(k) pathway, only eight implants offer publicly available clinical support for substantial equivalence, despite legal requirements to provide the public with scientific evidence of equivalence, safety, and effectiveness (Zuckerman et al. 2014). More recent

research traces the predicate ancestry of robotic surgical systems, showing that 92.7% 510(k) clearances did not submit clinical data and 27.9% did not submit any supporting data (Liebeskind et al. 2022). This suggests current regulations may not be sufficient to ensure companies provide information to support their claims of equivalence. This could result from a lack of clarity in the guidelines, or from a lack of enforcement by the FDA. Studies analyzing networked predicate data tend to focus on specific devices or product codes, commonly limiting research to lower sample sizes (Ardaugh et al. 2013; Zargar and Carr 2018; Zuckerman et al. 2014). No prior studies were found on the predicate histories of ventilation devices or how data availability in the 510(k) pathway has changed over time.

There are additional issues of transparency and information availability within the FDA itself. A Department of Health and Human Services report found that the FDA did not consistently document their device reviews for the 510(k) process; at least one document was missing from most of the electronic files and many of the documents were not signed and dated, although exact numbers were not provided (Levinson 2013). The 510(k) pathway reduces the amount of information used to assess safety to make the market clearance process quicker and cheaper; by not releasing data when expected, the FDA contributes to a dearth of publicly available information (Hines et al. 2010; Sharfstein et al. 2017).

III. Methods

i. Data Sources

The specific requirements for a 510(k) submission vary depending on what type of submission is being made: traditional, special, or abbreviated. Certain information is required by all submission types, including a 510(k) summary or statement. A 510(k) summary demonstrates the basis of substantial equivalence and is required to list information such as contact details, the device name and classification, the predicate device(s), a device description, and a summary of technological characteristics in comparison to the predicate device(s); whereas a 510(k) statement does not contain any information on substantial equivalence but is intended to certify that such information will be provided to any person within 30 days of a written request (U.S. Food and Drug Administration 2019a). For this study, data were collected on medical ventilation devices, defined as those falling under one or more of the following 14 product codes: BSZ, BTL, BTM, BYT, BZD, CBI, CBK, MNS, MNT, NFB, NHJ, NHK, NOU, and ONZ (see Appendix, Table 5). Although 510(k) summaries/statements were not required until 1995, some device submissions from the period of 1990 through 1994 offered summaries. Devices from this time are still included in the sample.

ii. Data Collection and Treatment

A record of medical ventilation devices was created by filtering all 510(k) submissions from January 1990 through October 2020 for relevant product classes (U.S. Food and Drug Administration 2021). All ventilation devices were then searched in the FDA 510(k) Premarket Notification database to find available submission summaries (U.S. Food and Drug Administration 2022b). Information was also included for five devices with predicate data made available through the Freedom of Information Act (see Appendix). Additional information including device product classification codes, device names, and the company that submitted the application was recorded and used in tracking down "error" predicates that could not be found in the database. This category included devices with a missing or incorrectly listed k-number, the unique six-digit identifier for devices cleared through the 510(k) pathway.

iii. Data Analysis

Once the data were compiled, a combination of Python code (for larger selections of data) and filtered Excel tables (for smaller selections of data) quantified the number and percentage of devices with available predicate data. For the purposes of this report, data quality was assessed solely through the metric of predicate data availability. Device submissions without available predicate data were categorized according to whether they included statements, summaries that held no predicate data, or ones with neither summaries nor statements available, as well as devices with unresolvable errors. The percentages of devices in each of these categories were assessed across all 14 medical ventilation device product codes, with particular focus given to the five product codes with the most devices. Further examination of predicate data

availability was conducted across time, to show the distribution of available data in five-year intervals from January 1990 through December 2019. The percentages of available and unavailable data for each period were determined in the same manner used to analyze data across product codes. One-way analysis of variance (ANOVA) and Tukey testing was then performed through Minitab, a statistical software package, on the six time intervals to determine whether a significant difference in data availability existed between them. For this testing, a 95% confidence interval was used. Product code analysis was then repeated for the period from 2005 through 2019. One-way ANOVA and Tukey testing was conducted across the categories of the five most common product codes in this time period.

IV. Results

Over 65% of all 1237 medical ventilation devices from 1990 onwards listed publicly available predicate information, primarily given through summary documents in the FDA 510(k) Premarket Notification database (Table 1). Devices with no available predicate information fell into several categories: those with statements available in the database instead of a summary made up 7.60% of the network; those with no summary or statement attached made up 25.55% (denoted as "Blank"); those listed as having summary documents but the attached document did not include predicate information made up 1.05%; and those with errors that made predicate history impossible to trace made up 0.08% (such as devices which listed an incorrect k-number that could not be resolved). It should be noted that a small percentage of devices did not fall into any of these categories. Predicate devices that were listed by name only, and not by k-number (including pre-1976 devices) were not classified under any of these categories. Cases where the summed percentage of categories do not equal 100% were the result of this phenomenon.

Product Class	**Total Number of Devices Post-1990**	**% With Available Predicate Data**	**% With Blanks**	**% With Statements**	**% With Summaries Containing No Predicate Data**	**% With Unresolved Errors**
All Medical Ventilation Devices	1237	65.64%	25.55%	7.60%	1.05%	0.08%
NOU	6	100.00%	0.00%	0.00%	0.00%	0.00%
ONZ	6	100.00%	0.00%	0.00%	0.00%	0.00%
MNS	41	90.24%	4.88%	4.88%	0.00%	0.00%
MNT	19	84.21%	10.53%	5.26%	0.00%	0.00%
CBI	24	79.17%	20.83%	0.00%	0.00%	0.00%
BZD	407	78.13%	14.99%	6.39%	0.49%	0.00%
NHJ	19	68.42%	21.05%	10.53%	0.00%	0.00%
CBK	311	68.17%	26.05%	3.22%	2.25%	0.32%
BSZ	129	65.89%	28.68%	4.65%	0.78%	0.00%
NFB	49	51.02%	22.45%	24.49%	2.04%	0.00%
BTL	78	47.44%	38.46%	12.82%	1.28%	0.00%
BTM	132	26.52%	56.06%	16.67%	0.76%	0.00%
BYT	8	25.00%	75.00%	0.00%	0.00%	0.00%
NHK	8	12.50%	50.00%	37.50%	0.00%	0.00%

Table 1: Summary of predicate data availability for ventilation devices from January 1990 to October 2020.

During the period from 1990 through 1994 when the SMDA summary/statement requirement had been announced but was not yet in effect, 204 medical ventilation devices were cleared. The majority of submissions had neither a statement nor a summary listed in the 510(k) database for this period. There were four exceptions spread across three product codes: BSZ, where one device had available predicate data; CBK, where one device had available predicate data and a second device had a summary document listed in the database but no actual predicate information detailed; and BZD, where one device showed a listed summary document but contained no actual predicate data (Table 2). Due to the low level of predicate data availability of submissions in this period, it was beneficial to look more specifically at the data submitted from 1995 onwards.

A total of 1033 medical ventilation devices were cleared through the 510(k) pathway from 1995 through October of 2020, 78.41% of which offered publicly available predicate history information. 9.10% offered statements instead of summaries, while 11.33% offered neither a statement nor a summary. 1.06% of devices were listed with summaries but no predicate history information was available in the given documents, and 0.10% had unresolved errors (Table 3).

K-Number	Product Code	Predicate Data Available in Summary
K922102	CBK	yes
K924930	CBK	no
K925920	BZD	no
K946127	BSZ	yes

Table 2: Devices submitted prior to 1995 with summaries listed in the 510(k) database.

Product Class	Total Number of Devices Post-1995	% With Available Predicate Data	% With Blanks	% With Statements	% With Summaries Containing No Predicate Data	% With Unresolved Errors
All Medical Ventilation Devices	1033	78.41%	11.33 %	9.10%	1.06%	0.00%
BYT	2	100.00%	0.00%	0.00%	0.00%	0.00%
NOU	6	100.00%	0.00%	0.00%	0.00%	0.00%
ONZ	6	100.00%	0.00%	0.00%	0.00%	0.00%
MNS	40	92.50%	2.50%	5.00%	0.00%	0.00%
CBK	249	84.74%	8.43%	4.02%	2.41%	0.40%
MNT	19	84.21%	10.53 %	5.26%	0.00%	0.00%
BZD	380	83.68%	9.21%	6.84%	0.26%	0.00%
CBI	23	82.61%	17.39 %	0.00%	0.00%	0.00%
BSZ	104	80.77%	12.50 %	5.77%	0.96%	0.00%
NHJ	17	76.47%	11.76 %	11.76%	0.00%	0.00%
BTL	57	64.91%	15.79 %	17.54%	1.75%	0.00%

Product Class	Total Number of Devices Post-1995	% With Available Predicate Data	% With Blanks	% With Statements	% With Summaries Containing No Predicate Data	% With Unresolved Errors
All Medical Ventilation Devices	1033	78.41%	11.33 %	9.10%	1.06%	0.00%
BYT	2	100.00%	0.00%	0.00%	0.00%	0.00%
NOU	6	100.00%	0.00%	0.00%	0.00%	0.00%
ONZ	6	100.00%	0.00%	0.00%	0.00%	0.00%
NFB	47	53.19%	19.15 %	25.53%	2.13%	0.00%
BTM	77	45.45%	24.68 %	28.57%	1.30%	0.00%
NHK	6	16.67%	33.33 %	50.00%	0.00%	0.00%

Table 3: Summary of predicate data availability for ventilation devices from 1995 onwards. Note that shading has been added to help visualize percent of devices with available data, with darker blue indicating greater availability and white indicating less availability

The mean available data across all product codes from 1995 onwards was 78.41%, as indicated by the "all medical ventilation devices" category, with a standard deviation of 41.16%. Three classes (BYT, ONZ, and NOU) demonstrated 100% available data from 1995 onwards, meaning every device in those classes had a summary listing predicate information. There were two devices in the BYT product code and six devices each in the ONZ and NOU product classes. Excluding these classes, the highest percentage of available data from 1995 onwards was from the MNS product class; 92.50% of 40 devices had publicly available predicate information. The lowest rate of available data post-1995 was seen in NHK, with 16.67% of data available from a total of six devices. The next lowest rate of available data was BTM, with 45.45% of the 77 devices post-1995 offering publicly available predicate information. Devices with available data make up the majority of product classes overall, followed by devices with blanks and with statements. Only one product class, CBK, contained a post-1995 unresolved error (Table 3).

Many of the product classes under the medical ventilation devices category contained relatively few devices. With analysis restricted to the five largest product code sample sizes, the highest rate of available data post-1995 was found to be 84.74% for the CBK class, out of a total of 249 devices. It should be noted that although the CBK product code was the largest ventilation class overall, BZD was the largest class when considering devices from 1995 onwards (Table 3). The lowest rate was seen in the BTM class, with 45.45% of 77 total devices showing available predicate data (Figure 1).

An examination of predicate data availability was conducted across time to explore the distribution of available data in five-year periods from the beginning of 1990 through the end of 2019. To keep time intervals consistent, this limited the data to 1223 medical ventilation devices, removing 14 devices from 2020. One-way ANOVA testing comparing the mean data availability across the six interval groups returned a p-value of less than 0.05, indicating that there is statistically significant variance in data availability over time (Figure 2). Tukey's method for multiple comparison was then applied to determine more specifically which interval groups' means were significantly different when compared to each other (Table 4).

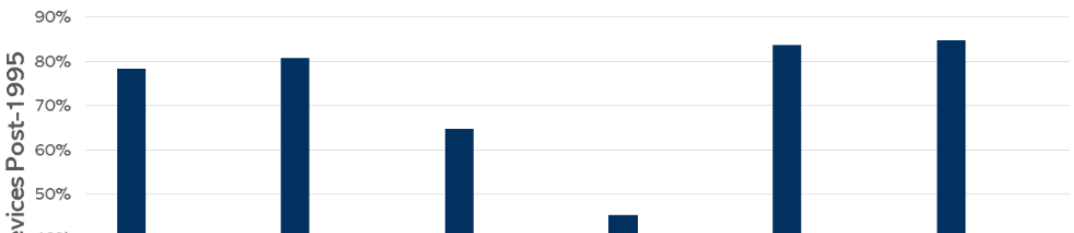

Figure 1: Percent of devices with available predicate data, as well as percentage of blanks and statements, for each of the five largest ventilator product classes and for the full network of medical ventilation devices post-1995. Note that unresolved errors and percentages of devices classified as having a summary but no available predicate information are not shown.

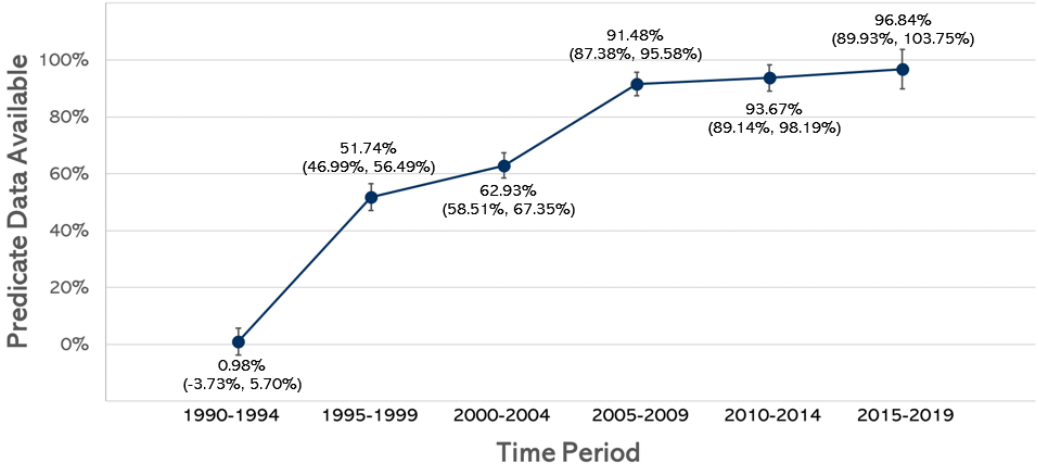

Figure 2: Interval plot of the mean percentage of predicate data availability across different time periods, with pooled standard deviation from ANOVA testing used to calculate 96% confidence intervals. The p-value for the associated ANOVA was less than 0.05

The five-year interval from the beginning of 1990 through the end of 1994 showed significantly lower data availability than all other time intervals, with 0.98% of predicate data available (Figure 2, Table 4). There was a drastic increase in the percentage of available predicate data moving to the next interval of 1995 through 1999 (with 51.74% available predicate data), as would be expected with the SMDA requirement for statements or summaries coming into effect (Table 4). However, data availability during this time period was still lower than future intervals. This pattern continued with an increase in data availability in the 2000 through 2004 period (62.93%), and another increase in available data occurs when moving to the 2005 through 2009 period (91.48%). The Tukey testing did not show a significant difference in data availability between the 2005 through 2009 period and the two intervals that followed (Table 4); analysis of variance for just these three intervals gave a p-value of 0.192. There was still a slight increase in mean percentage of available predicate data in 2010 through 2014 (93.67%) and again in 2015 through 2019 (96.84%) (Table 4). The total number of device submissions remained in the 200s for all time periods except the last, when it decreased to 95 devices from 2015 through 2019. The highest number of device submissions was 270 from 2005 through 2009 (Table 4).

Time Period	Total Number of Devices	% With Available Predicate Data	Tukey Method Grouping			
2015 through 2019	95	96.84	A			
2010 through 2014	221	93.67	A			
2005 through 2009	270	91.48	A			
2000 through 2004	232	62.93		B		
1995 through 1999	201	51.74			C	
1990 through 1994	204	0.98				D

Table 4: Summary of grouping information for ventilator predicate data availability from the beginning of 1990 through the end of 2019, using the Tukey method with a 95% confidence interval. Time intervals that do not share grouping letters have a significantly different percentage of available data.

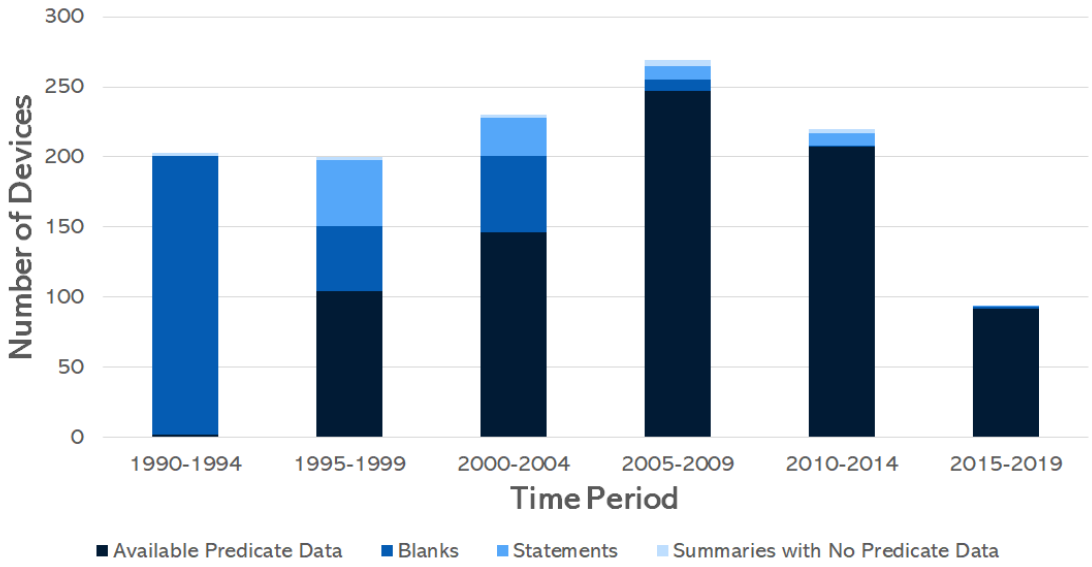

Figure 3: Number of devices and predicate availability classifications across time periods. Note that unresolved errors have been removed from this plot, as only one occurs during this time span (in the 2000 through 2004 time period).

Because the time intervals of 2005 through 2009, 2010 through 2014, and 2015 through 2019 did not demonstrate a statistical difference in data availability, the 2005 through 2019 time frame offered a period of particular use for analyzing differences across product classes. The earlier analysis of the five largest product classes from all of 1995 onwards was repeated for devices from the period 2005 through 2019. Overall, 93.17% of the 586 medical ventilation devices from this period have available predicate data. During this period, four of the largest product codes remained the same categories as in all post-1995 devices, although their percentages of available data changed: BZD (with 95.18% available predicate data), CBK (95.39%), BSZ (98.21%), and BTL (62.16%). However, MNS overtook BTM as the fifth largest product class when narrowing the time interval, with 96.77% available data (see Figure 4, as compared to Figure 1). ANOVA testing across these five product codes returned a p-value of less than 0.05, indicating that not all five of the means were equal. Tukey's method for multiple comparison found more specifically that the mean predicate data availability for BTL submissions was significantly lower than the other product codes (Table 5). No significant variance was shown between product codes BZD, CBK, BSZ, and MNS; one-way ANOVA testing across just these four product codes returned a p-value of 0.770.

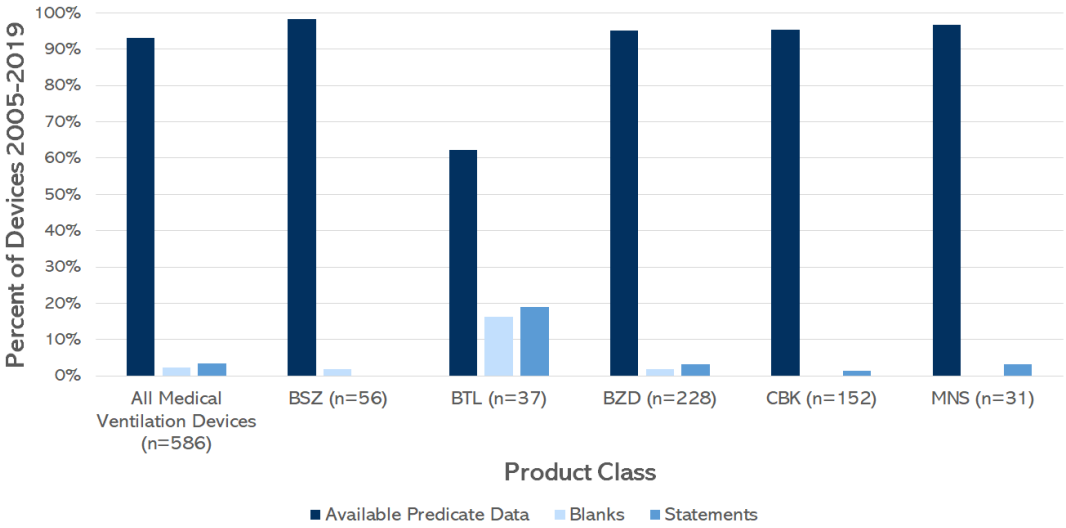

Figure 4: Percent of devices with available predicate data, as well as percentage of blanks and statements, for each of the five largest ventilator product classes and for the full network of medical ventilation devices from 2005 through 2019. Note that the percentages of devices classified as having a summary but no available predicate information are not shown. There were no unresolved errors for this period.

Product Code	Total Number of Devices	% With Available Predicate Data	Tukey Method Grouping	
BSZ	56	98.21	A	
MNS	201	96.77	A	
CBK	232	95.39	A	
BZD	270	95.18	A	
BTL	221	62.16		B

Table 5: Summary of grouping information for ventilator predicate data availability across the five largest product classes from the beginning of 2005 through the end of 2019, using the Tukey method with a 95% confidence interval. Time intervals that do not share grouping letters have a significantly different percentage of available data.

V. Discussion

These results build on prior critiques of data quality, availability, and transparency of the FDA 501(k) premarket notification pathway by offering an analysis of data availability in one specific area over time: predicate histories of medical ventilation devices from 1990 through 2019. Predicate history availability makes it possible for researchers and other members of the public to analyze connections between devices by elucidating the networks of substantial equivalence that support new device submissions (Ardaugh et al. 2013; Zargar and Carr 2018). In the same way, innovation could be tracked by analyzing how device designs have changed as they pass through these networks. Our research could be expanded by analyzing device predicates beyond an assessment of data availability.

Our data shows an 11.33% rate of noncompliance with FDA requirements to offer either a summary or statement for market-cleared ventilation devices whose submissions were received between January 1995 and October 2020. This may be the result of an improper submission by the applicant, or the result of the FDA failing to include the data publicly. Of these two options, there is evidence to suggest the latter may be the more common cause. Some of the devices that do not show statements or summaries in the 510(k) premarket notification database are listed as having been submitted with one in the downloadable 510(k) submission records files used to generate the initial list of medical ventilation devices for this data set, suggesting that these records may exist somewhere despite not being visible in the public database (U.S. Food and Drug Administration 2021). This is further supported by one anomaly noted in this research, a surge of "blanks" in the year 2000. It seems more likely that some policy or issue within the FDA led to a halt in data being added to the database, rather than a wide variety of companies all failing to include a necessary component of the 510(k) submission in the same year. Whatever the source of this information failure, the data shows that data availability and compliance with the SMDA requirement is increasing over time. Unresolvable errors and documents listed as summaries but containing no predicate information were minimal throughout the dataset, suggesting that these categories have little impact on overall predicate data quality and availability.

These findings also demonstrate that predicate data availability can vary significantly across product codes. In some cases, variance across product code may be confounded by the time period in which the majority of a product code's devices were submitted. This seems likely to be the case for BTM, which has a less than 50% rate of predicate data availability post-1995 (Table 3) but the majority of its devices were submitted prior to 2005, when the overall availability of predicate data increased above 90%. In other cases, variance across product code may be the result of factors not accounted for in this study. There is no statistical difference shown in data availability between the intervals of 2005 through 2009, 2010 through 2014, and 2015 through 2019, indicating that the lower rate of predicate data availability for BTL submissions when compared to other product codes during this period does not result from the time of submission (Table 5). Further research is recommended to pursue inquiry into other possible sources of variance, such as domination of the class by a particular company or innovative technology that discourages company transparency. Further research might explore whether the decreasing percentage over time of companies opting to submit statements for ventilation devices is indicative of a larger trend within the industry.

While the increase in availability of predicate information over time is encouraging, the lack of historical data, particularly in the first decade after 1995 (when data should be available), is still of significant note. From 1995 through 1999, only 51.74% of medical ventilation devices offer available predicate histories; from 2000 through 2004, this increases to just 62.93% of devices (Table 4). This historical predicate data is necessary to develop a greater understanding of patterns of substantial equivalence, in research on areas such as predicate creep; incremental versus radical innovation; medical technology analysis; public data quality and availability; and more. Understanding the evolution of products through the 510(k) system also offers some feedback on the efficiency of the system, which has been a point of contention through much of the literature mentioned earlier in this paper. The 510(k) system is by its nature a networked system, and availability of new data is not sufficient to offer a

complete view of products while access to prior data is still hampered.

i. Limitations

Because only medical ventilation devices are analyzed, caution is recommended in extrapolating these findings of predicate data availability within the overall premarket notification database, as well as the level of compliance with summary and statement submissions. Analysis was not conducted on reference devices, which are additional devices sometimes used to support the content of a 510(k) submission without being considered predicate devices. The sole metric for data quality was predicate history availability, with no further assessment of the quality or content of other data included in summary documents. Devices that include predicate history may fail to meet the Safe Medical Devices Act of 1990 requirement that, "an adequate summary of any information respecting safety and effectiveness or state that such information will be made available upon request by any person," or that summaries, "shall contain detailed information regarding data concerning adverse health effects and shall be made available to the public by the Secretary within 30 days of the issuance of a determination that such device is substantially equivalent to another device" (Safe Medical Devices Act of 1990). Additional submission data quality analysis is necessary to determine if these standards are being met.

ii. Implications for Research and Policy

With these limitations in mind, this study offers many directions for future analyses. Assessing predicate networks earlier than 1990 may prove difficult, misleading, or ultimately uninformative, as submission summaries will not be available. Further research is suggested to explore the reason that predicate data availability varies across product classes. One variable that was not accounted for in this study is the companies responsible for submitting device applications. Company policies and predispositions may contribute significantly to the choice to submit a summary or a statement. For larger companies that produce a significant number of different devices within a specific product class, this may influence the predicate history data availability statistics of the entire class. This factor is complicated by the fact that many medical devices companies change names or ownership over the years, making it difficult to account for when considering a network spanning multiple decades. As such, it was determined beyond the scope of this study, but is highly recommended as a subject for future research.

Several suggestions for premarket notification policy reform have been put forth. An Institute of Medicine report on a workshop entitled "Public Health Effectiveness of the FDA 510(k) Clearance Process" summarizes the recommendations of individuals and interest groups concerned with the 510(k) pathway, many of whom advocate for revisions to the process; among these recommendations were calls to create additional guidance for industry, involve more stakeholders in the process, increase transparency, adopt a risk-based classification system, and directly address the question of what factors in the process contribute to error (Wizemann 2010). One paper calls for the elimination of predicates and substantial equivalence, with a regulatory movement towards safety and performance-based metrics in extension of the 2019 Safety and Performance Based Pathway (Redberg and Dhruva 2019). One proponent of the current system suggested database reform as a tactic for addressing public concerns without fully overhauling the system (Shapiro 2014). All these recommendations indicate that some level of reform to the 510(k) pathway may be necessary to ensure safety, transparency, and effectiveness.

While an increase in transparency in the FDA review, analysis, and decision-making process could create more work for FDA officials, it would also provide a tremendous increase in knowledge to benefit a range of stakeholders (Gottlieb 2018). However, there are potential risks associated with significant increases in transparency. The information revealed is highly dependent on what the company chooses to disclose, and exploitation of loopholes could lead to a rise in misleading or partial information. Exposure of irrelevant data obscures pertinent information that could be readily incorporated into decision-making processes, and there is a risk of technical data being used or interpreted incorrectly when removed from context (Sharfstein et al., 2017). Several factors impact whether or not transparency regulation will appropriately address a policy problem, including the ease with which new information can be embedded into user routines and whether or not there is incongruence between the intended

objectives of increasing transparency and the goals of the people who use that information (Weil et al. 2006).

Calls for transparency in the form of increased availability of raw data submitted to the FDA during the 510(k) process might raise additional issues. The majority of the general public lacks the expertise in conducting clinical studies that is often necessary to interpret raw data (Amin et al. 2017). This can lead to incorrect assumptions and perceptions of submitted devices, which may decrease trust of scientific authority. There is some tradeoff, as improved transparency can serve to increase trust in other ways (Richardson, 2022). Raw data from FDA submissions can also be so extensive they become unwieldy to use; in order to gain a short list of predicate numbers, this research team submitted a request under the FOIA that led to the release of 1,832 pages of documentation (see Appendix). It might be advisable to limit calls for information release to targeted, relevant, critical data. Public release of raw data may also fail to provide the information companies need to better understand the FDA review system, such as the FDA's approach to those submissions, which sections fit their expectations and requirements, which were found lacking, and other details beneficial to companies preparing to submit a product. A combination of information availability and opportunities to engage and interact openly with regulatory entities are necessary to ensure that accurate and comprehensible information is disclosed (Weil et al. 2006). Transparency requires collaboration in addition to documentation.

The need for transparent, high-quality data is emphasized throughout this report, and the premarket notification pathway is a critical component in this process that may be indicative of a wider need for transparency. Beyond policies updating the 510(k) procedure, change may take a variety of broad forms: improving information on and accessibility of the mechanisms through which medical device submitters can request feedback from the FDA; improving transparency and quality of data with regards to clinical evidence, with special care being paid to combat historical establishment of medical racism; and ensuring that transparency is offered with regards to device data and labeling alike. While there are potential drawbacks to broad transparency, there is an expected standard of beneficial public information which is not currently being met, and predicate histories fall within this category. Our study suggests that with regard to predicate information the availability of data has improved over time. The results found in this study demonstrate a lack of compliance with providing summaries and statements from 1995 through 2004. Current policies may be sufficient to ensure availability of predicate data moving forwards if current trends continue. Further exploration is called for to determine if the quality of this data is actually sufficient to prove device safety and efficacy.

Appendix

i. Medical Ventilation Product Codes

Medical ventilation devices were here defined as any devices falling within one of 14 product codes (Table 6).

ii. Additional Sources of Predicate Information

To increase the availability of predicate data, a preliminary effort was made to attain more information in cases where predicate histories were not already publicly listed. This was done by contacting companies directly and submitting a request to the FDA under the Freedom of Information Act. In accordance with the Safe Medical Devices Act, "As part of a submission under section 510(k) respecting a device, the person required to file a premarket notification under such section shall provide an adequate summary of any information respecting safety and effectiveness or state that such information will be made available upon request by any person" (Safe Medical Devices Act of 1990, 1990). Any company that submitted a device with a statement after 1995 is required to respond to public requests for premarket notification data; the FDA states that, "The 510(k) Statement is a certification that the 510(k) owner **will provide** safety and effectiveness information supporting the FDA finding of substantial equivalence to ANY person within 30 days of a written request" (emphasis original) (U.S. Food and Drug Administration 2019a). The listed contacts for 23 post-1995 devices were emailed to request this summary, and the nature of their response was recorded. A request was also sent to the FDA under the Freedom of Information Act to release data for a random sample of five devices. These strategies were intended as preliminary methods of exploring how predicate data might be acquired; neither is intended as a complete overview of how to acquire predicate data on a device, or the statistical likelihood of hearing a response.

Product Code	Preferred Name
BSZ	Gas-machine, Anesthesia
BTL	Ventilator, Emergency, Powered (Resuscitator)
BTM	Ventilator, Emergency, Manual (Resuscitator)
BYT	Ventilator, External Body, Negative Pressure, Adult (Cuirass)
BZD	Ventilator, Non-continuous (Respirator)
CBK	Ventilator, Continuous, Facility Use
CBI	Tube, Tracheal/Bronchial, Differential Ventilation (W/Wo Connector)
MNS	Ventilator, Continuous, Non-life-supporting
MNT	Ventilator, Continuous, Minimal Ventilatory Support, Facility Use
NFB	Conserver, Oxygen
NHJ	Device, Positive Pressure Breathing, Intermittent
NHK	Resuscitator, Manual, Non Self-inflating
NOU	Continuous, Ventilator, Home Use
ONZ	Mechanical Ventilator

Table 6: Medical ventilation device product code descriptions (U.S. Food and Drug Administration 2022c).

Applicant companies for each of the 23 devices submitted after 1995 were contacted through email with a request for an adequate summary of this information, citing the applicable regulatory requirement. This sample of 23 included 10 devices with statement documents and 13 devices with no summary or statement attached. One company responded for their device: K991972. The research team was directed to look at the public summary for a later version of the device, K031745, which was available through the FDA website. However, the nature of this research intentionally differentiates devices by 510(k) submission, which typically means that new iterations of devices are still considered distinct devices. Without being able to assess the predicate history of K991972, we cannot confirm that it actually matches the predicate history of K031745, even if they are related designs. Although 510(k) submission forms do contain contact names, in many cases further contact information could not be located for these individuals. In some cases, the contact listed may no longer have worked for the company. In these cases, inquiries were directed to companies themselves.

K-Number	Statement or Blank	Company/Applicant Listed	Method/Recipient of Contact	Request Sent	Response
K991972	Statement	SENSORMEDICS CORP.	Person no longer works for company	6/15/21	Yes (company directed us to summary posted for later submission, K031745)
K001430, K003684	Blank	VORTRAN MEDICAL TECHNOLOGY 1, INC.	Individual listed on statement for K973975, K981726 and K982016	9/16/21	None
K973975, K981726, K982016	Statement	VORTRAN MEDICAL TECHNOLOGY 1, INC.	Individual listed on statement	9/16/21	None
K092148	Statement	HAMILTON MEDICAL AG	Hamilton Medical website contact page (email form)	4/22/21	None
K093905,	Statement	RESPIRONICS, INC.	Individual listed on statement	6/15/21	None
K132168	Statement	RESPIRONICS, INC.	Individual listed on statement	9/17/21	None
K140268	Statement	RESPIRONICS, INC.	Individual listed on statement	9/17/21	None
K000994, K002465, K010263, K953341, K953930, K000705, K001208, K954207, K962203	Blank	RESPIRONICS, INC.	Individual listed on statement for K093905	9/17/21	None
K112783	Statement	VBM MEDIZINTECHNIK GMBH	Individual listed on statement	6/15/21	None
K990949	Statement	INTERSURGICAL, INC.	Note: contact no longer works for the company	6/15/21	None
K003068, K010093	Blank	DRAGER MEDIZINTECHNIK GMBH	Company website contact form	4/7/21	None

Table 7: Overview of data requests sent to medical device companies for predicate histories of post-1995 devices, as well as the nature of the response. Note that "none" in the response column is indicative of not having heard a response by 2/22/2022.

A request was filed under the Freedom of Information Act to release information on a small subset of devices, as described previously. Over seven months later, the FDA released redacted premarket notification submissions for all five of these devices, which contained predicate histories among other information (see Table 8). The length of the individual submission documents varied from 19 to 721 pages.

K-Number	Statement or Blank	Company/Applicant Listed	Request Sent	Response
K073707	Blank	DATEX-OHMEDA, INC.	6/4/21	1/27/22
K032226	Statement	PULMONETIC SYSTEMS, INC.	6/4/21	1/27/22
K951046	Blank	RUSCH INTL.	6/4/21	1/27/22
K902114	Blank (Pre-1990)	DIEMOLDING CORP.	6/4/21	1/27/22
K912723	Blank (Pre-1990)	POSEY CO.	6/4/21	1/27/22

Table 8: Summary of FOIA request results.

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