

Written Statement

Ralph F. Hall

Distinguished Professor and Practitioner

University of Minnesota Law School

U.S. House of Representatives Energy and Commerce Subcommittee on Health

Hearing on “Impact of Medical Device Regulation on Jobs and Patients.”

February 17, 2011

Good morning, my name is Ralph F. Hall. I appreciate this opportunity to speak to this committee on these important medical device matters affecting patients, physicians, innovation and jobs. I am here to discuss research I have done into the safety of 510(k) products. I am here speaking in my personal capacity and not on behalf of the University of Minnesota or any other entity.

Background and disclosures:

To start, I serve as Distinguished Professor and Practitioner at the University of Minnesota Law School where I concentrate my teaching, research and writing in the area of FDA law and compliance matters. In addition, I am part time Counsel at the law firm of Baker & Daniels where I work with clients on a variety of FDA matters and also provide counsel to a national 510(k) coalition. Finally, I serve as CEO at MR3 Medical LLC. – a four person start up medical device company working on a new technology for cardiac rhythm devices generally regulated under the PMA process.

The research that is the focus of my comments was funded by the Ewing Marion Kauffman Foundation, a private nonpartisan foundation based in Kansas City, MO. Their generous support made this research possible. The Kauffman Foundation has given me complete academic freedom to pursue this research.¹

Summary:

The study I focus my comments on assessed the overall safety profile of medical devices approved or cleared by FDA from 2005-2009 by using Class I safety recall data. This study² evaluated Class I (or high risk) recalls of all medical devices, regardless of whether they were approved through the PMA system, cleared through the 510(k) process or were otherwise exempt.

The key conclusions from my research are as follows:

1. Overall, 510(k) regulated medical devices have an excellent safety profile. Over 99.5% of 510(k) submissions assessed during this study period did not result in a Class I safety recall. More relevant to this hearing, over 99.7% of 510(k) submissions did not result in a Class I recall for any reason relevant to the 510(k) premarket system.
2. Very few (less than 9%), Class I recalls during the study period involve possible undiscovered clinical risks. As such, increased preapproval clinical testing would not have any meaningful impact on reducing the number of Class I recalls.

¹ I want to thank Amanda Maccoux, Mark Jones, Chris Walker and Ron Song - the research assistants at the University of Minnesota Law School who spent long hours doing the detailed data collection and coding required for this study. Their talents, hard work and dedication are vital to this research and I appreciate all that they did.

² This research was presented to the Institute of Medicine committee reviewing the 510(k) system, reviewed with FDA and is being prepared for submission to a major peer reviewed journal.

3. The majority (approximately 55%) of all Class I recalls involve problems or issues that arose after market release and could not be affected by premarket approval systems or requirements. For example, a manufacturing mistake made three years after FDA approval or clearance may trigger a Class I recall. However, any premarket requirements such as clinical testing are irrelevant to preventing such a recall.
4. A very significant majority (over 90%) of all Class I recalls (including both premarket and post market issues) are directly related to quality system issues (so-called QSR systems). Improved QSR systems will have the greatest effect in reducing the number of Class I recalls.
5. My study did identify a bolus of Class I recalls in two device types – automatic external defibrillators (AEDs) and infusion pumps. Any changes to the 510(k) process should be targeted to demonstrated problems rather than applied in some random, shotgun way.
6. Finally, one should not confuse classification for premarket review processes with recall classification. These are very different things and serve very different purposes.

Study Background:

The need for the research that I will describe goes back several years when a number of stakeholders started to question the 510(k) system. I was and am familiar with the numerous issues relating to delays in submission reviews and changing data requirements. I was, however, struck by the belief among some that the 510(k) system didn't assess or consider product safety in making clearance decisions and that there was some major issue with the safety of products being cleared by the 510(k). First, it is critical to note that FDA does consider safety when deciding whether to clear a 510(k) submission. A number of commentators seemed not to be aware of this. Second, some stakeholders were advocating making major changes in the 510(k)

system to address presumed safety problems. I was then particularly struck by the fact that there was not good, objective data to support or refute the assertion that the 510(k) system needed to be changed because of these presumed safety issues.

In fact, at an early public meeting held by FDA to discuss making major changes to the 510(k) system, I commented that this was a “ready, fire, aim” exercise in which various interest groups were advocating major changes without any understanding of the actual performance of the system and any issues with the system. It struck me then and now that data not opinion should drive policy changes.

Some commentators were simply looking at the number of 510(k) recalls compared to PMA recalls. While not directly comparable, one must remember that there are around 3,500 510(k) submissions per year compared to 20-40 PMA applications (and some additional number of sPMA submissions). Given these disparate numbers, the fact that more recalls are for 510(k) products than PMA products is not meaningful or even a useful comparison. A more systematic study was needed.

Given my concerns over the lack of hard data, I commenced a study (with the able assistance of four research assistants) assessing the safety performance of FDA approval processes. To my knowledge, this was the first study designed to systemically assess the safety performance of the 510(k) system. This study was funded by the private, nonpartisan Kauffman Foundation. I am solely responsible for the study and its results.

Study Methodology:

This study assessed the overall safety profile of medical devices approved or cleared by FDA from 2005-2009 by using Class I safety recall data.

Class I safety recalls were chosen as the measure of safety as these recalls involve any medical device problem posing any significant risk of serious health consequences to patients and also correctly exclude risks considered as part of the approval or review process. Class II recalls involve generally remote risks to patients and Class III recalls involve minimal or no risk to patients. FDA, not industry, is responsible for assigning the recall classification. Note that the class of recall assigned by FDA is independent of the product's device classification. For example, no one would argue that a tongue depressor is a high risk device or needs a clinical trial. For premarket purposes it is classified as a low risk, exempt device. However, if the tongue depressor gets contaminated with deadly bacteria because of product tampering or some manufacturing problem there is a significant risk to patients. This would be a high risk or Class I recall even though for premarket review purposes it is a low risk device.

Using FDA data bases, we identified all Class I recalls posted by FDA on public databases during 2005-2009. We first combined all duplicate recalls into one data set of unique or stand alone recalls. (FDA may have several recall announcements and thus there may be multiple data entries for the same issue because of different package configurations, brand names or product sizes).

118 unique recalls were identified. We then coded each recall for a number of factors including regulatory pathway, medical specialty, whether implantable, and three letter product code. We also coded each recall with one of thirteen reasons for recalls. Generally speaking, these thirteen recall reasons can be combined into three broad grouping of premarket issues (i.e. something that could, at least theoretically, have been discovered during a premarket review process), post market issues and miscellaneous (counterfeit and "quack" products). We used FDA websites and publicly available information for this coding.

All data was entered into a standard Excel spreadsheet following quality control.

This study must be assessed in light of the following factors:

- First, we relied entirely upon publicly available data. We assume that the information in the FDA data bases is correct. We did not identify any meaningful errors in this data but did not conduct any structured assessment of the accuracy of FDA's data.
- Second, while companies are obligated to report recalls, there may be situations in which the company failed to meet this obligation. We believe that any such missing recalls would tend to be small and not common because of the penalties for non-compliance and the variety of information sources that would disclose any such recall. Importantly, there is no reason to believe that the distribution of the causes of such recalls would be different than the data we had.
- Third, we reviewed Class I recalls and not Class II recalls. [FDA defines a Class II recall as a situation in which the problem “might cause a temporary health problem, or pose only a slight threat of a serious nature. We believe that Class I recalls represent all recalls with any meaningful risk to patients and so represent a valid safety picture. Remember that Class II recalls are for remote risks or low impact problems. Class I recalls represent the majority of actual patient risk and tend to err in the direction of higher rather than lower classification. Risks as low as 1/20,000 have been classified as Class I recalls thus demonstrating the breadth of risks captured by Class I recall.
- Anecdotal review of some Class II recalls indicate (but do not establish) the same general pattern of reasons for recalls between Class I and Class II recalls.

- Finally we did not assess any effects of various regulatory systems or actions on patient access to new products, innovation or the economy in general.

In designing this study, we considered other methodologies; including reviewing adverse event reports (generally referred to as Medical Device Reports or MDR reports) and also tried to assess number of products involved in each recall. In these cases, the data is hopelessly inaccurate and incomplete, inaccurately counts actual events as compared to the risk of a malfunction or is not related to the binary decision to approve or not approve the submission.

We also determined the percentage of 510(k) submissions that resulted in a subsequent Class I recall. The numerator for this calculation is the number of recalls. The denominator is the number of submissions. The denominator for this calculation is a close estimate as there is no direct connection between the date of the submission and the subsequent recall. For example, a recall for a design defect might occur within a month after market release while a recall for a manufacturing error or packaging mistake could occur literally years after approval or clearance.

We determined an annualized number of submissions by taking the average number of submissions for a 10 year period (2000-2009) and annualizing that number. We used this number for all percentage calculations. Those percentages, however, are approximations due to this data challenge.

Study results and data:

Initially, we looked at the reasons for recalls for these 118 Class I recalls. It must be remembered that all devices carry risk and that Congress has balanced patient access to new technology with premarket processes by creating the standard that there must be "reasonable assurance" of product safety before the product should be marketed. We determined the reason for the recall by

examining FDA's public data bases and also reviewing publically available information including physician notification letters and SEC filings. I was responsible for all decisions relating to the reason for recall. I blindly recoded 10% of the recalls and had a complete match with the initial determination of the reason for the recall.

The following table shows the number of recalls by regulatory pathway and the reason for recall.

Reasons for recall in blue are those related, at least potentially, to premarket review processes.

The others are recall reasons that are completely unrelated to any premarket process.

Primary Reason for Recall	PMA	510K	Class 1	Other or Unknown	TOTAL
Manufacturing	6	31	2	1	40
Labeling Error	0	4	0	0	4
Design Issue	6	25	1	0	32
Software Design	1	9	0	0	10
Software Manuf. Failure	0	2	0	0	2
Supplier Issue	2	5	0	0	7
Failure to Identify Clinical Risk	0	0	0	0	0
Failure to Warn/Inadequate Instructions	0	8	0	0	8
Missing Parts	0	0	0	0	0
Sterilization	1	4	2	0	7
Regulatory Violation	0	1	1	0	2
Packaging/Handling	0	0	0	0	0
Other (Counterfeit, Sham)	0	6	0	0	6

As shown below, the majority of all recalls (approximately 55%) are for post market issues. For these recalls, no change in the premarket 510(k) or PMA process would affect the recall occurrence or frequency.

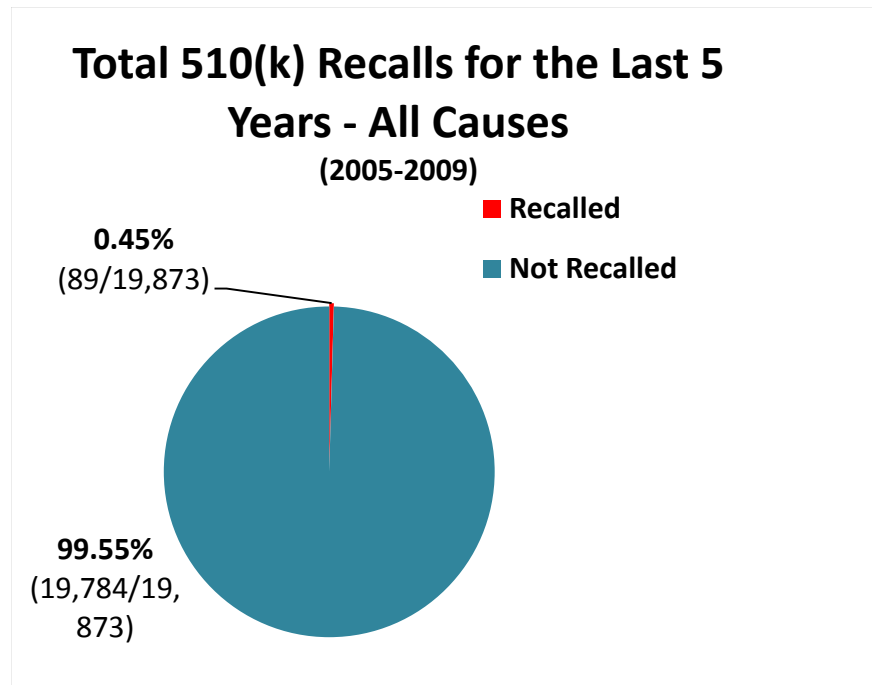
	Total Recalls	Recalls for Pre- Market Issues	Recalled for Post- Market Issues	Recalled for Other Issues	Percent of Recalls to Total Recalls
Class I or u/k	7	1 (14.2%)	6 (85.7%)	0 (0%)	5.9%
510(k)	95	43 (45.3%)	46 (48.4%)	6 (6.3%)	80.5%
PMA	16	7 (43.8%)	9 (56.3%)	0 (0%)	13.56%
TOTAL	118	51	61	6	118

As seen below, a very small percentage of 510(k) submissions led to a Class I recall during our study period. The first chart shows the ratio of 510(k) submissions to all Class I recalls and the second chart shows the ratio of 510(k) submissions to Class I recalls related to any theoretical premarket issue.

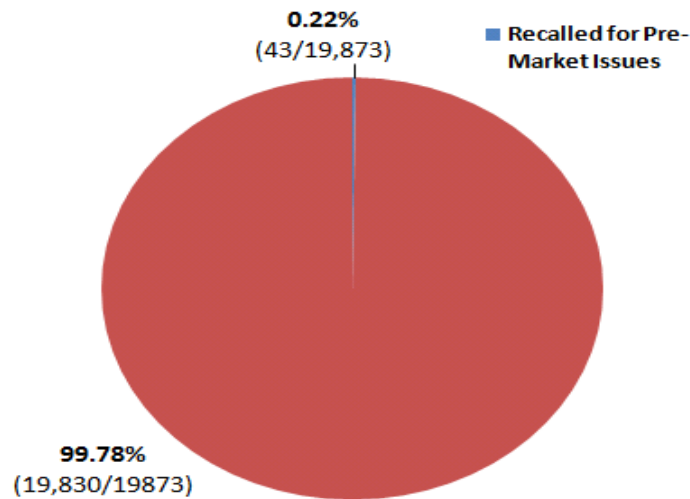
This data shows that CDRH and the submission sponsors have done an admirable job in identifying potential device risks, particularly clinical risks, prior to the approval or clearance decision. These risks can then be explicitly balanced against benefits as part of that premarket decision. Very few, if any, recalls in the device world are related to undiscovered clinical issues.

Based on this data, approximately 99.55% of all 510(k) submissions did not result in a Class I recall for any issue during the study period. More importantly for assessing the 510(k) process, approximately 99.78% of all 510(k) submissions did not result in a Class I recall for any reason

related to the premarket process. Stated differently, the maximum theoretical impact of any change in the 510(k) system would be on 0.22% of all 510(k) submissions. This data also demonstrates that additional premarket clinical testing would be ineffective in reducing Class I safety recalls.



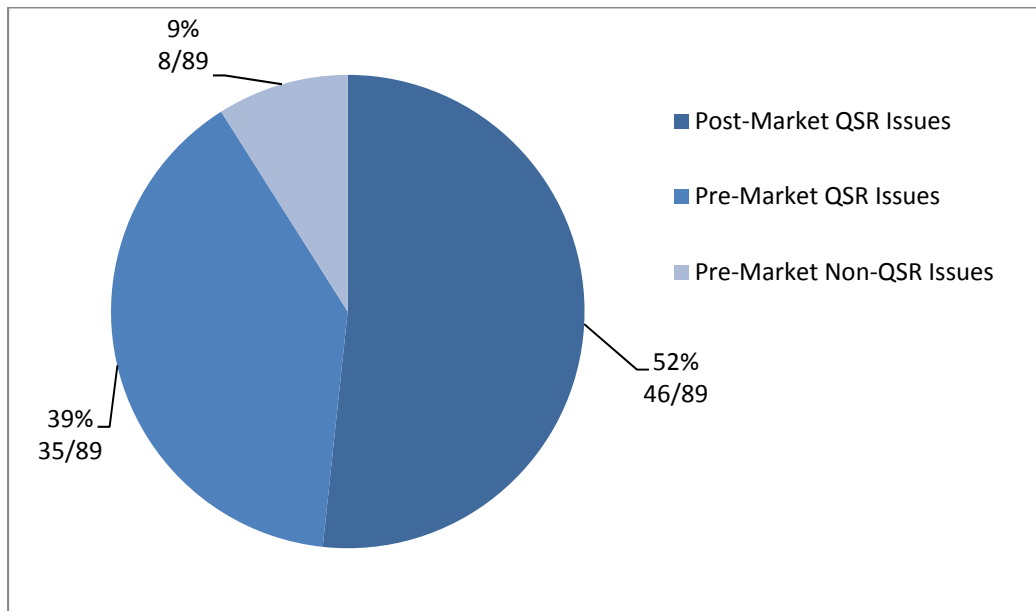
Total 510(k) Recalls for the Last 5 years – Premarket issues



Total 510(k) Submissions in 10 years	39,747
Average Submissions in 5 year time period	19,873
Total 510(k) Recalls for 2005-2009	89
Total 510(k) Recalls for Pre-Market Issues for 2005-2009	43

The number of recalls related to premarket issues is most relevant in assessing whether the 510(k) system is adequately addressing patient safety during the review process. This data demonstrates that post market issues, not premarket processes, should be the focus to improve patient safety.

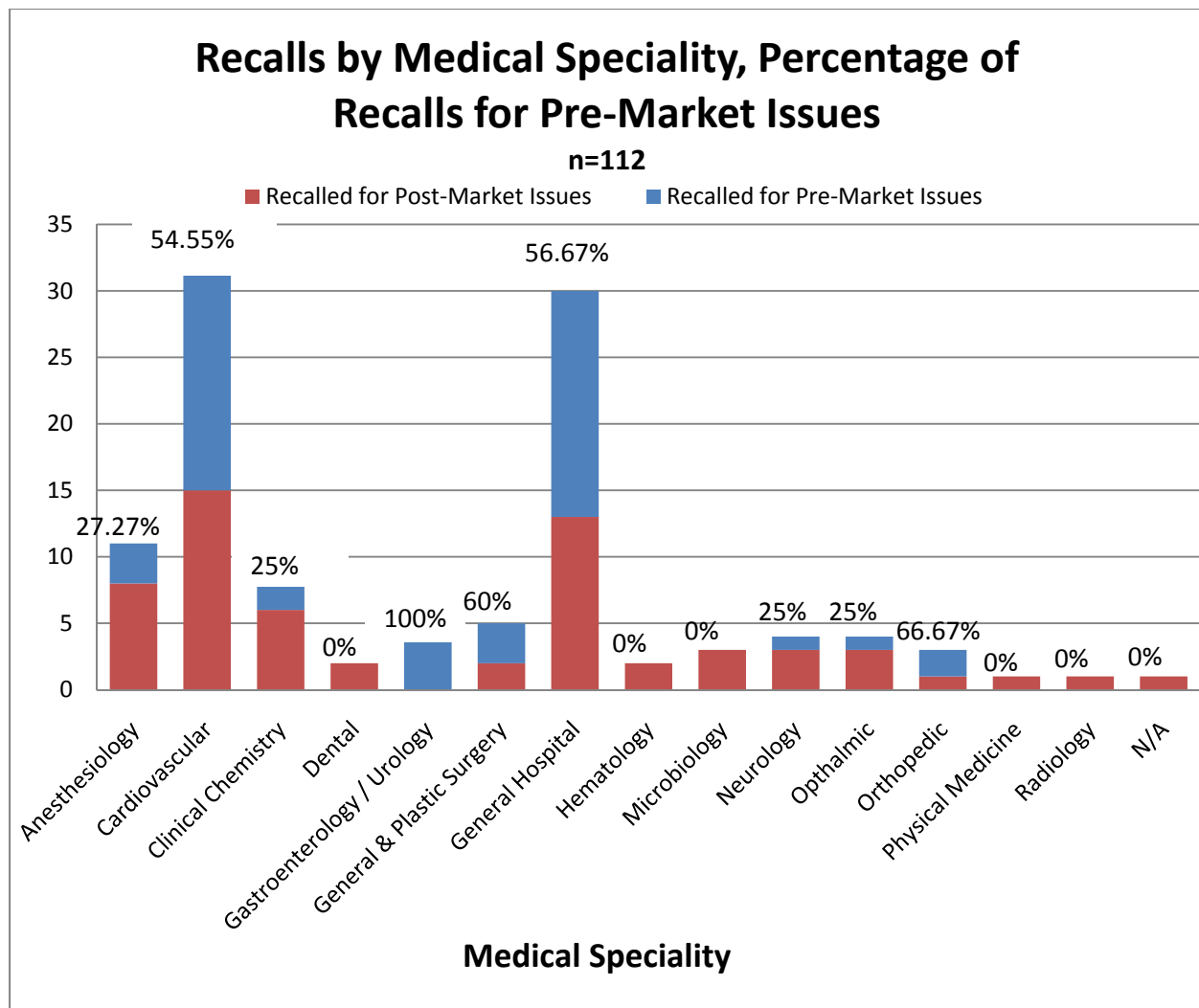
This conclusion is reinforced when we reviewed the role of quality systems in recalls. As shown below, over 90% of all Class I safety recalls are related to quality system issues and not to other factors such as a lack of clinical trials.



Clearly, this data demonstrates that all stakeholders should concentrate on QSR issues -- not the 510(k) system in its entirety -- as the most effective way to provide greater patient safety.

Making the 510(k) system more burdensome will have a negative impact on patient access to new technology without any corresponding patient benefit.

We also did sub analysis by product type and medical specialty. Such analysis can be used to identify concentrations of issues for further investigation by FDA, industry and other stakeholders. As seen below, Class I recalls are concentrated in several product types.



Further analysis indicated that automatic external defibrillators (AEDs) and infusion pumps accounted for 28% of all Class I recalls and accounted for a substantial part of the bolus or recalls seen in the cardiovascular and general hospital categories. Within the past 9 months, FDA has triggered new regulatory initiatives for both AEDs and infusion pumps.

This data also shows remarkably few Class I recalls for a number of product areas, including some product types that have been recently agued demonstrating flaws with the 510(k) system, such as orthopedics, radiology, and OB/GYN.

We also assessed the data to see whether implantable products or submissions that went through the third party review process had any concentration of Class I recalls. Our analysis showed that Class I recalls for implantable devices almost exactly matched the expected percentage of recalls and that there were fewer recalls for submissions reviewed under the 510(k) third party review system than might be expected.

Our confidence in our study design and results has been bolstered by subsequent studies by third parties finding very similar numbers and reasons for Class I recalls.

Conclusion:

This study demonstrates that very few 510(k) medical device submissions – less than 0.5% – become the subject of a Class I safety recall. Even in this small number of Class I recalls, the majority of Class I recalls involve post market issues such as manufacturing mistakes, and are focused around two product categories (cardiovascular and general hospital). These recalls involve quality system issues, not premarket issues. Overall, in excess of 90% of all recalls appear to involve quality system issues.

Our study shows that FDA has a very positive safety record in its 510(k) clearance decisions.

Thank you for your time and attention. I would be happy to answer any questions you might have.