A PROJECT REPORT ON

Can the Reasons for Class-I Device Recall Be Predicted Prior to Regulatory Approval?

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ABSTRACT:

The FDA recalls many medical devices every year, most of them being the class-I recalls, which are serious and life threating. This prevailing phenomenon affects the medical device industries and more importantly the health of the patients. This situation can be handled either by making the pre-approval process more efficient or by trying to understand the reason devices were withdrawn. This analysis may be helpful in preventing the further device failures. The project focusses on identifying the pre-approval data which were crucial for assessment of the risk factors associated with the device that was later withdrawn. The research was carried out on 41 devices, which were withdrawn in the year 2011.

INTRODUCTION:

WHAT IS A RECALL?

A firm's removal or correction of a marketed product that FDA considers to be in violation of the law it administers and against which the Agency would initiate legal action (i.e., seizure). *[21 CFR Part 7.3 (g), 2011]*[1]

WHY A MEDICAL DEVICE IS RECALLED?

The medical device recall doesn't necessarily mean the product usage must be stopped. The device may be recalled for a defect, checked, corrected and released back into the market. During a recall a patient must be informed about the risks of using the product versus the risk caused by discontinuing it. The device recall can also happen for other reasons including re-labeling, notifying patients of a problem, monitoring patients for health issues,

adjusting setting on the device and even to destroy the device. *(Recalls, Corrections and Removals, 2011)*[2]

The recall may end up in correction or market removal based on the severity of the issue,

- Correction – The repair, modification, adjustment, relabeling, destruction or inspection (including patient monitoring) of a product and/or promotional literature which causes the product to be violated, without its physical removal to some other location. *[21 CFR 7.3 (h) ,2011]*[3]
- **Removal** means the physical removal of a device from its point of use to some other location for repair, modification, adjustment, relabeling, destruction, or inspection. *[21 CFR 806.2,2011]*[4]

RECALLING RESPONSIBILITY AND FOLLOW-UP:

The recall of a medical device in most cases is done voluntarily by the manufacturer. According to 21 CFR 806[5,] Medical Device Correction and Removals, it is the responsibility of the manufacturer or importer to report the FDA why the recall was done, either if it is to reduce the possible risk to the health or if it had violated the Act caused by the device which may cause risk to the health. If the device continues to involve risk, the manufacturer must report a correction or removal of the device to the FDA within 10 working days from the time the firm initiated the recall. If the device no longer involves any risk then it must be kept off the record of the recall. . *(Recalls, Corrections and Removals, 2011)* [2]

But, if the manufacturer or importer fails to voluntarily recall the product then it will be the responsibility of Medical Device Recall Authority, FDA. The procedures to be followed for a device recall are described in 21 CFR 810[4] under section 518(e) of the Federal Food, Drug, and Cosmetic Act (Act). *(Recalls, Corrections and Removals, 2011)* [2]

In both the cases FDA publishes all the recalls, in a weekly FDA Enforcement Report. These reports in addition to listing the device being recalled also include field corrections, seizures and injunctions. *(Recalls, Corrections and Removals, 2011)* [2]

MEDICAL DEVICE RECALL CLASSIFICATION:

*The FDA classifies the recall after it is issued by the company depending on the extent of potential risk to the health of the patient. This classification will be helpful in knowing the severity of the recall and also determines several other factors like number of checks the company should do, number of audits FDA should go through so as to ensure the effectiveness of the recall action. (*What Happens in a Medical Device Recall, 2011)[5]

The classification is as follows: [5]

CLASS-I – The devices under this class fall in to high risk category, as there is a reasonable chance for the device to cause serious health problems or even death. ***(****What Happens in a Medical Device Recall, 2011)* [5]

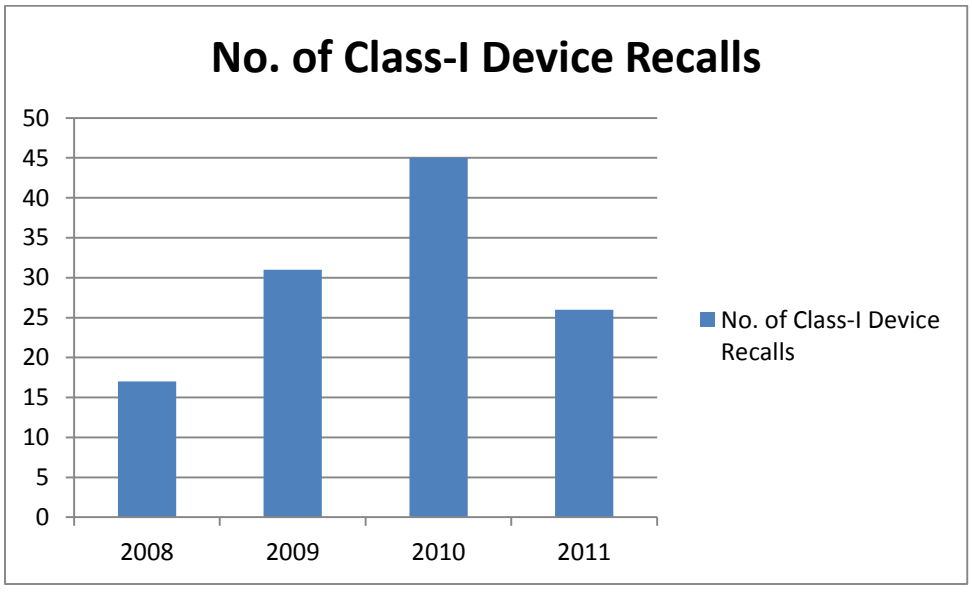
CLASS-II – The devices cause less serious risk than the above class. The device has the possibility of temporary or reversible health issues or sometimes these have a remote chance of causing serious health problems. *(What Happens in a Medical Device Recall, 2011)* [5]

CLASS-III – The devices under this category can cause less serious risk than a class II, the chance of risk caused is low. But however as the product violates the FDA law, an action needs to be taken to address the issue. *(What Happens in a Medical Device Recall, 2011)* [5]

BACKGROUND INFORMATION:

The Class-I device comprised about 95% of the device recalls made, from 2008 to 2011. The numbers of devices recalled during the period of 2008-2011 were 129. *(List of Device Recalls, 2011)* [6]

Graph showing the number of Class-I Device Recalls from 2008-2011:



Included in the class-I device recalls were Balloon Catheter Recall, Complications with surgical stents and Physio-Control Launches Class I Recall For LIFEPAK® 20/20e Defibrillators. [7]

The complications from all the above recalls are life threatening. For example the Balloon Catheter has the problem of retention of the device fragments in the arteries leading to fatal arterial injuries. *(Balloon Catheter Recall, 2011)* [8]

Below are statements made by some experts, which shows the class-I device recall as a potential problem:

"We're concerned because we have seen a substantial increase in the number of recalls over the last few years," Steve Silverman, senior advisor to the CDRH director, said May 5,2011 at the MedCon medical device conference in Cincinnati. "Perhaps even more troubling is that there has been a major jump in Class I recalls," he added. "Since the beginning of this fiscal year [which began Oct. 1, 2009], we have designated almost 30 recalls as Class I. That is nearly as many Class I recalls as we saw in all of fiscal year 2009." *(Shawn, 2011)* [9]

GOAL:

The goal of the project is to understand the reasons for Class-I device recall, and see if the reason for which the device was recalled could have been predicted prior to approval going through the pre-marketing submissions made to the FDA.

METHODS:

The methodology for the analysis uses data available from the FDA website. Information about Type-I device recall was obtained from FDA enforcement reports. Other online searchable FDA databases were be used to collect additional information. The overview of information related to FDA's approval to market the devices that are recalled was obtained from the FDA's Device Approvals and Clearances. The summary of safety and effectiveness from the FDA website was studied for individual medical devices from the list to see if the reason for recall could have been predicted prior to the device approval. In developing the project every 5^{th}class1 recall from January 2009 – September 2011 was to have been selected for analysis. If sufficient data were not available for the 5^{th} recall, then the very next recall (6^{th} one) was to have been considered, still maintaining the 5^{th} device interval as before.

RESULTS:

Below is the table showing the list of medical devices withdrawn in the year 2011, approval of the device whether it is a 510k or PMA and if the pre-approval data was available in the FDA website or any other publications.

Table1: Medical Devices withdrawn, 2011

Medical Device	PMA or 510 K	Pre-approval Data
Care Fusion AVEA Ventilator	510 k	Available
St.Jude Medical,Riata and Riata ST Silicone Endocardial Defibrillation Leads	PMA	Supplement
Cooper Vision AVAIRA Toric and Sphere Soft Contact Lenses	N/A	N/A
Draeger Medical Inc., Infinity Acute Care System Monitoring Solution (M540)	510 k	Available
King International, LLC., Shoulder Flex Deep-Kneading Shiatsu Massager	510 k	Not Available
Mizuho OSI Modular Table Systems	N/A	Not Available
Care Fusion EnVe Ventilator	510 k	Not Available
Lee Medical International Inc.,Custom Dialysis Trays/Kits	N/A	Not Available
Lee Medical International Inc.,Custom Dialysis Trays/Kits	N/A	Not Available
Medtronic Model 8637 SynchroMed II Implantable Infusion Pump	PMA	N/A
GE Healthcare Vital Signs Hygroscopic Condenser Humidifier Passive	N/A	Not Available

Arrow International, Inc. Arrow NextStep Antegrade Chronic Hemodialysis Catheter	510k	Available
GEM Premier 4000 PAK Cartridges for Use on the GEM Premier 4000 System	510 k	Available
Global Focus Marketing & Distribution, Ltd.,Silencer S2200 Centrifuge	N/A	Not Available
Roche Diagnostics Operations,ACCU CHEK Performa Strip	510 k	Available
Boston Scientific Innova Self-Expanding Stent System	PMA	Supplement
Churchill Medical Systems, a Vygon Company, Skin-Prep Wipes Used in Convenience Kits and Tray	N/A	N/A
Maquet Datascope Corp. Intra-Aortic Balloon Pumps	510 k	Available
Terumo Coronary Ostia Cannula 10, 12, 14 Fr	N/A	N/A
Boston Scientific iCross and Atlantis SR Pro 2 Coronary Imaging Catheters	510k	Available
Oridion Medical and Philips Healthcare Microstream CO2 Filterline (FilterLine H Set Infant/Neonate, VitaLine H Set Infant/Neonate)	510k	Available
Beckman Coulter, Inc., Synchron LX Clinical Systems Ion Selective Electrolyte (ISE) Flow Cell	PMA(LXI 725 only)	Supplement
Defibtech LLC, Lifeline and ReviveR AEDs: Software Defect May Cancel Shock	510k	Not Available
bioMérieux, Inc., VITEK® 2 Gram Negative Susceptibility Cards Containing Piperacillin/Tazobactam (TZP2) – Expanded Recall	510 k	Available
	510k	Available

Penumbra Inc., Penumbra Coil 400		
iCAD (formerly Xoft Inc.), Axxent® FlexiShield Mini, Model F5300	510k	Available
Millar Instruments Inc., Mikro-Tip Angiographic Catheter, Model SPC-454D and SPC-454F	510k	Available
Maquet Cardiovascular, LLC, Heartstring II Proximal Seal System (HS-1045)	510 k	Not Available
Roche Insulin Delivery Systems, ACCU-CHEK FlexLink Plus Infusion Sets	510 k	Available
Gen-Probe Inc., AccuProbe Group B Streptococcus Culture Identification Test, AccuProbe Mycobacterium Tuberculosis Complex Culture Identification Test, and AccuProbe Mycobacterium Avium Complex Culture Identification Test	510k	Available
Davol Inc., XenMatrix Surgical Graft	510k	Not Available
Cook Inc., Single, Double, Triple and Five-Lumen Central Venous Catheter Trays AND Single and Double Lumen PICC Peripheral Inserted Central Venous Catheter Trays	510k	Available
Medtronic SynchroMed II and SynchroMed EL Implantable = Infusion Pump and Refill Kits	PMA	Not Available
Abbott Glucose Test Strips	510 k	Available
Triad Group, Triad Sterile Lubricating Jelly	510k	Not Available
Arstasis One Access System	510k	Available
Merit Medical Systems Prelude Short Sheath Catheter Introducer	510k	Available

B. Braun, Outlook 400ES Safety Infusion System, Model Number 621-400ES	510k	Not Available
Arrow Ultra 8 Intra-Aortic Balloon Catheters (IABS) 8 FR 30CC and 40CC Universal and Arrow Intra-Aortic Balloon (IAB) Catheter with a Fiber Optic Sensor and Measurement System: UPDATE 01/26/2011	510 k	Available
Fresenius Medical Care North America, CombiSet True Flow Series Hemodialysis Blood Tubing Set with Priming Set and Transducer Protectors for Use with the Blood Volume Monitor	510k	Available
AngioScore Inc., AngioSculpt Percutaneous Transluminal Angioplasty (PTA) Scoring Balloon CatheterOTW 0.018" Platform (multiple sizes)	PMA	Available
Total	**41**	

According to list of medical device recalls in FDA website there a total of 41 class-I recalls for the year 2011. Twenty six devices were approved as 510k, 6 devices as PMA, most of which are supplements and not original approvals and 9 devices had no information available to know the type of approval. Twenty devices had no pre-approval data available.

Pre-marketing notification (510k) information was found for twenty devices and PMA for four devices. Below is the description of the information of the devices which had pre-approval data available and their reason for recall

Description of Medical Devices with pre-approval data available

Medical Device	Pre-approval data predicts the withdrawal of the Device
Care Fusion AVEA Ventilator **Reason For Recall:** Failure when the ventilator activates a false Extended High P peak alarm, opens the safety valve and stops ventilating.	X
St.Jude Medical,Riata and Riata ST Silicone Endocardial Defibrillation Leads **Reason For Recall:** Failures with the leads causes the conductors to be externalized which causes serious consequences including death	X
Draeger Medical Inc., Infinity Acute Care System Monitoring Solution (M540) **Reason For Recall:** The weight-based calculation of the drug dosage may be incorrect	X
Arrow International, Inc. Arrow NextStep Antegrade Chronic Hemodialysis Catheter **Reason For Recall:** Large number of complaints about the breakage/separation of the stylet part of the catheter	X
Roche Diagnostics Operations,ACCU CHEK Performa Strip **Reason For Recall:** Showing errors in the blood glucose test results	√
Boston Scientific Innova Self-Expanding Stent System **Reason For Recall:** Internal failure of the device may result in vessel wall injury and increased procedure time	X
Maquet Datascope Corp. Intra-Aortic Balloon Pumps **Reason For Recall:** Due to defective fan the device may overheat and shutdown without alarm causing unanticipated interruption of the therapy	X

Boston Scientific iCross and Atlantis SR Pro 2 Coronary Imaging Catheters **Reason For Recall:** Heart attack/blood vessel injury may be caused due to breakage of the tip of the catheter inside the patient	X
Oridion Medical and Philips Healthcare Microstream CO2 Filterline (FilterLine H Set Infant/Neonate, VitaLine H Set Infant/Neonate) **Reason For Recall:** The plastic strands on the inner surface of the adapter may become dislodged which may be inhaled and cause respiratory problems	X
Beckman Coulter, Inc., Synchron LX Clinical Systems Ion Selective Electrolyte (ISE) Flow Cell **Reason For Recall:** Due to ratio pump wear there may be microbial contamination resulting in problem of maintenance and ISE hardware causing incorrect electrolyte results	X
GEM Premier 4000 PAK Cartridges for Use on the GEM Premier 4000 System **Reason for Recall:** The potassium test results were incorrectly detected resulting in altered patient treatment	√
bioMérieux, Inc., VITEK® 2 Gram Negative Susceptibility Cards Containing Piperacillin/Tazobactam (TZP2) – Expanded Recall **Reason For Recall:** The susceptibility cards are showing incorrect susceptibility and resistance results causing the patients to be treated in appropriately	X
Penumbra Inc., Penumbra Coil 400 **Reason For Recall:** Due to some factors the coil may prematurely detach inside the body , migrate and cause unintentional clots.	X
iCAD (formerly Xoft Inc.), Axxent® FlexiShield Mini, Model F5300 **Reason For Recall:** The device leaves particles of tungsten in the body , which may become toxic in high levels	X
Millar Instruments Inc., Mikro-Tip Angiographic Catheter, Model SPC-454D and SPC-454F **Reason For Recall:** The particles from the catheter may travel to tissues and	X

blood vessels resulting in decreased blood supply	
Gen-Probe Inc., AccuProbe Group B Streptococcus Culture Identification Test, AccuProbe Mycobacterium Tuberculosis Complex Culture Identification Test, and AccuProbe Mycobacterium Avium Complex Culture Identification Test **Reason For Recall:** The tube components of the affected devices may not contain/partially contain the solution producing false negative results	X
Cook Inc., Single, Double, Triple and Five-Lumen Central Venous Catheter Trays AND Single and Double Lumen PICC Peripheral Inserted Central Venous Catheter Trays **Reason For Recall:** Leaks were detected from the plunger of the syringe which compromises the sterility of the solution delivered	X
Abbott Glucose Test Strips **Reason For Recall:** Leaks were detected from the plunger of the syringe which compromises the sterility of the solution delivered	X
Arstasis One Access System **Reason For Recall:** The device components may fracture and separator causing harm to the patient	X
Merit Medical Systems Prelude Short Sheath Catheter Introducer **Reason For Recall:** The introducer tips may detach during use and may causing arterial injury and hemorrhage	X
Arrow Ultra 8 Intra-Aortic Balloon Catheters (IABS) 8 FR 30CC and 40CC Universal and Arrow Intra-Aortic Balloon (IAB) Catheter with a Fiber Optic Sensor and Measurement System: UPDATE 01/26/2011 **Reason For Recall:** The sheath of the catheter may get stuck making the user unable to move to the IAB thereby delaying the therapy	X
Fresenius Medical Care North America, CombiSet True Flow Series Hemodialysis Blood Tubing Set with Priming Set and Transducer Protectors for Use with the Blood Volume Monitor **Reason For Recall:** The tubing set may cause kinking of arterial line , which leads to the destruction of RBC	X

AngioScore Inc., AngioSculpt Percutaneous Transluminal Angioplasty (PTA) Scoring Balloon CatheterOTW 0.018" Platform (multiple sizes) **Reason For Recall:** The defects in the design causes arterial injury due to peeling and detachment of the scoring element	X

X – Denotes the pre-approval data was not useful in predicting the reasons for device approval

√ –Denotes the pre-approval data was helpful in predicting the reasons for device approval

For two devices the pre-approval data was actually useful to predict the withdrawal of the device prior to the approval. The description of the two devices and predictions drawn from the pre-approval data were provided below. Detailed information could not be presented as both of the devices are 510k approvals which only had information about bio-equivalence which is very limited and doesn't show the summary of safety and effectiveness of the device.

Medical Device Recall description:

Name: GEM Premier 4000 PAK Cartridges for Use on the GEM Premier 4000 System

Recall Class: Class I

Use:

The cartridges which provide portable critical care are used for analyzing the whole blood samples at the time of delivery of health care in a laboratory or a clinical setting

Reason for Recall: The device was recalled on March 31, 2011 as the results of Potassium test of GEM Premier 4000 are very low when they are compared to the analyzer. The biases is 2.0 mmol/L which is more than the permissible limit of the standard error claim of plus or minus 0.5 mmol/L. So considering this factor the patient treatment would be altered and

inappropriate leading to serious consequences on the patient health including death. *(Medical Device recall Recall*, *2011*)[10]

Prediction drawn from the pre-approval data:

The 510k summary provides information about the device, its intended use and comparisons of GEM Premier 4000 to ABL 735 analyzer which is the standard. The device is intended for providing quantitative measurements of different parameters like pH, PCO2, *P02,* sodium, chloride, ionized calcium, potassium, , glucose etc. Using spectroscopic methods the GEM Premier 4000 is compared to the ABL 735 analyzer for the measurement of the parameter total bilirubin in adults and neonates and the results are found to be same. But there is no evidence of performing comparative tests with the standard for other parameters like sodium, chloride, potassium etc. So, if the device was tested for all the parameters is had to estimate then the deviation of the device from the permissible limit of the standard error claim would have been identified before prior to the approval of the device and the withdrawal have been prevented

Name: Roche Insulin Delivery Systems, ACCU-CHEK FlexLink Plus Infusion Sets

Recall Class: I

Use: This device is used for delivering Insulin to diabetic patients

Reason for Recall: Serious health problems including death may be caused due to use of the device because of the malfunctioning of the delivery tube which is connected to the ACCU CHEK flexlink infusion set. This results in the elevation of the level of glucose in the blood because of the under delivery of insulin *(Medical Device recall Recall*, *2011*)[11]

Prediction drawn from the pre-approval data:

Both the ACCU-CHEK flex link plus infusion set and the ACCUcomparisions CHEK Ultraflex infusion set are proved to be substantially equivalent in terms of the purpose of use, storage and operating conditions and in all aspects being tested. The accu check insertion device which is compared to ACCU-CH-EK insertion device substantially equivalent in every aspect like use, storage and operating conditions but except the dimensions of ACCU CHECK flex link device are longer and wider than the ACCU-CH-EK which is already in the market and being used successfully.

As far as the information available on 510k the only reason that could be predicted for the malfunctioning of ACCU CHEK flex link plus infusion set is due to the differences in dimensions with the device with which it should to be equivalent. If extensive studies were conducted to check the functionality of device with the new dimensions, the withdrawal could have been prevented.

DISCUSSION:

For the project every fifth device from the year 2009-2011 September must be considered. But due to limited availability of the data all the devices from the year 2011 are being presented for the study. The number of devices recalled in 2011 are 41, of which 26 are 510k approvals, which accounts for about 66%. This data shows 26 devices do not have a detailed summary of safety and efficacy but only have the bio-equivalence information. Because of this reason most of the devices could not be explored in detail because of the limited pre-approval data.

The data helps indicates that if the device would have been approved under PMA, then the recall might have been prevented because only four of the PMA-approved devices were withdrawn in the particular year and all the rest are 510k approvals.

The process of 510k approvals is putting the patients' health at risk, and it also affects the economy of various pharmaceutical and biotechnology industries, which focus on design and development of the medical devices. The approval process of the devices must be made more efficient. Time has to be invested by the FDA before the approval of the device rather than withdrawing the devices after a failure. If the same situation continues, then public loses faith in the FDA looking at the tremendous number of 510k approved medical devices being withdrawn from the market. The pre-approval data should be made available by the FDA for all devices approved, be they a 510k or a PMA. Because of the limited availability of the data the approvals of many devices could not be reviewed. This lack of transparency in the review process opens the FDA to criticism. More fully revealing the data upon which devices are approved would allow both Congress and the public to decide if a better approval process is required.

CONCLUSION:

The pre-approval data was not available for all 41 devices. For most of the devices with the pre-data are 510k approval, which do not have a detailed description of summary and efficacy of the device. From the pre-approval data available, the withdrawal of 2 devices would have been predicted prior to the approval which means the withdrawal of the devices cannot be predicted

prior to the approval. Hence the 510k process may be inefficient in protecting the US population adequately.

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