Complaints Handling and Vigilance Reporting for Stryker Neurovascular Products

A Thesis submitted in the fulfillment of the requirement for the award of the degree of

Master of Technology

in

Biotechnology

By

Hinan U Nisa

Registration No.: 602004010

At

Stryker Global Technology Center

Under the Supervision of

Madan Unde

Manager (Quality)

Sagrika Sharma

Post Market Surveillance Analyst

THAPAR INSTITUTE
OF ENGINEERING & TECHNOLOGY
(Deemed to be University)

BIOTECHNOLOGY DEPARTMENT

THAPAR INSTITUTE OF ENGINEERING &

TECHNOLOGY, PATIALA

DECLARATION

I hereby declare that the work being presented in the dissertation report entitled "Complaints Handling and Vigilance Reporting for Stryker Neurovascular Products" submitted by me for the award of the degree of Master of Technology in Department of Biotechnology, TIET University, Patiala is true and original record of my own independent and original research work carried out under the joint supervision of Madan Unde and Sagrika Sharma. Further, I declare that no part of this dissertation has been submitted to any other University/Institute for the award of any degree in India or abroad.

Dated: 24-Jun-22 Hinan U Nisa

CERTIFICATE

This is to certify that the dissertation work entitled "Complaints Handling and Vigilance Reporting for Stryker Neurovascular Products" submitted by Hinan U Nisa (Roll No. 602004010) in partial fulfillment for the award of degree of Master of Technology in Biotechnology from Thapar Institute of Engineering and Technology, Patiala Punjab is the record of the candidates own independent and original research work carried out under our supervision and guidance. The matter embodied in this dissertation has not been submitted in part to any other University/Institute for the award of any degree or diploma in India or Abroad.

Madan Unde 26/06/2022

Mr. Madan Unde

Manager Quality

Stryker Neurovascular (SGTC)

Gurugram, India

Sagrika

Ms. Sagrika Sharma

PMS Analyst

Stryker Neurovascular (SGTC)

Gurugram, India

ACKNOWLEDGEMENT

First and foremost, I wish to thank my mentors **Madan Unde** (Manager-Quality NV) and **Sagrika Sharma** (Post Market Surveillance Analyst: CMC). It was my great pleasure and privilege to work under their guidance, who has been motivating and encouraging throughout the project and put in every possible effort to make the project a success.

I would like to thank NV SGTC team members for their valuable support and guidance. I am thankful for the suggestions, and meticulous guidance of my divisional mentors who helped me to understand things in a better way and being so supportive and motivating every time.

My special thanks to Stryker Global Technology Center and Thapar Institute of Engineering and Technology for giving me an opportunity to undertake this internship.

I would like to extend my sincere gratitude towards **Dr. M.S. Reddy**, HOD, Biotechnology department, for being cooperative to the students of the department and providing relevant guidance in their endeavors.

I thank my family and friends for encouraging me throughout my internship and being with me throughout as a support system.

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ABBREVIATIONS

1.	AIMDD	Active Implantable Medical Device Directive
2.	AIS	Acute Ischemic Stroke
3.	BGC	Balloon Guide Catheter
4.	CAPA	Correction action and preventive actions
5.	CE	Customer Excellence
6.	CFR	Code of Federal Regulations
7.	CHS	Complaint Handling System
8.	CIC	Complaint Intake Center
9.	CMC	Complaint Management system
10.	CNS	Central nervous system
11.	DAC	Distal Access Catheter
12.	DFU	Direction for Use
13.	DMR	Device Master Record
14.	DoC	Declaration of conformity
15.	DQA	Design Quality Assurance
16.	DR	Design Review
17.	ELT	Executive Leadership Team
18.	EUMDR	European Union Medical Device Regulation
19.	FDA	Food & Drug Administration
20.	GFE	Good Faith Effort
21.	HCP	Healthcare Professional
22.	HEM	Hemorrhagic
23.	ICAD	Intracranial Atherosclerotic Disease
24.	IFU	Instructions for Use
25.	ISO	International standard of organization
26.	LS	Long Sheath

27.	MDD	Medical Device Directive
28.	MDR	Medical Device Reporting
29.	MGT	Management
30.	NC	Nonconformance
31.	NV	Neurovascular
32.	OEM	Original Equipment Manufacturer
33.	PAC	Product Assessment Center
34.	PI	Product Inquiry
35.	PMS	Post Market Surveillance
36.	PR	Product Record
37.	PSUR	Periodic Safety Update Report
38.	QFM	Quality Form
39.	QMS	Quality Management System
40.	QPR	Quality Procedure
41.	QSIT	Quality System Inspection Technique
42.	RAQA	Regulatory Affairs and Quality Assurance
43.	RBA	Risk Benefit Analysis
44.	R&D	Research and Development
45.	RHV	Rotating Hemostasis Valve
46.	SNV	Stryker Neurovascular
47.	SOP	Standard of operations
48.	SGTC	Stryker Global Technology Center
49.	SRN	Single Registration Number
50.	SYK	Stryker
51.	TIA	Transient Ischemic Attack
52.	UPN	Unique Product Number
53.	US	United States
54.	USA	United States of America
55.	WHO	World Health Organization
56.	WI	Work Instruction

TERMINOLOGY

1. **Adverse Event:** Any event where the use of the medical device is suspected to have resulted in an adverse outcome for a patient.
2. **Approver:** A person responsible for verifying all requirements have been met before moving a Trackwise record to the next state.
3. **Awareness Date:** The date that the first person in Stryker becomes aware of an event.
4. **Becomes Aware:** Any Stryker employee or agent of Stryker has become aware of a MDR reportable event that is required to be reported to FDA within 30 calendar days or an event that is required to be reported within 5 working days pursuant to an FDA written request, or Any Stryker employee, who manages or supervises persons with regulatory, scientific, or technical responsibilities, or whose duties relate to the collection and reporting of adverse events, has become aware of an MDR reportable event from any information, including any trend analysis, and the event necessitates remedial action to prevent an unreasonable risk of substantial harm to the public health.
5. **Business Day:** A 24-hour weekday which excludes weekends and holidays.
6. **Cause:** Reason for the activation of the hazard.
7. **Caused or contributed:** A death or serious injury was or may have been attributed, directly or indirectly, to a Stryker device, or that a Stryker device was or may have been a factor in a death or a serious injury.
8. **Complaint:** Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a Stryker device after it is released for distribution by a manufacturing site.
9. **Complainant:** Person notifying Stryker of the complaint.
10. **Component:** Means any raw material, substance, piece, part, software, firmware, labelling, or assembly which is intended to be included as part of the finished, packaged, and labelled device.
11. **Complaint Handling Team:** People under the following the Division or Business Unit (Complaint Intake Center, Complaint Management Center, Product Assessment Center and CMC Regulatory Representative) in charge of the complaint process.

12. **Complaint Intake Center (CIC):** CIC is the Stryker entity or location that intakes event information into CHS.
13. **Complaint Management Center (CMC**): CMC is the Division or Business Unit associated with the product reported in the event.
14. **Complaint Project Record:** A CHS record that contains the complaint evaluation and the information required to determine if the complaint is a reportable event.
15. **Corrective Action:** Action taken to eliminate the cause of a nonconformance which has occurred to prevent its recurrence or reduce the occurrence to an acceptable threshold.
16. **Corrective and Preventive Action (CAPA):** The purpose of the corrective and preventive action subsystem is to collect information, analyze information, identify and investigate product and quality problems, and take appropriate and effective corrective and/or preventive action to prevent their recurrence. Verifying or validating corrective and preventive actions, communicating corrective and preventive action activities to responsible people, providing relevant information for management review, and documenting these activities are essential in dealing effectively with product and quality problems, preventing their recurrence, and preventing or minimizing device failures.
17. **Customer:** Anyone who is affected by the product, process or by the services performed by SGTC. Customers may be external or internal, however internal customers (or divisional partners) are defined as contracting Stryker divisions using resources for R&D Projects/Services. External customers are defined as health professionals who are the end users of Stryker's product in the field.
18. **Indications for Use (IFU):** A general description of the disease or condition the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended.
19. **Initial Reporter:** The person who initially reported the event to the manufacturer or company representative.
20. **Intended Use:** Use for which a product, process, or service is intended according to the specifications, instructions, and information provided by the manufacturer.
21. **Investigator:** The person responsible for conducting the complaint investigation and entering all the details into the Complaint Project Record.

22. **Labeling:** Information that serves to properly identify a device and its manufacturer and to communicate safety and performance related information to the user or other person, as appropriate.
23. **Malfunction:** The failure of a device to meet its performance specifications or otherwise to perform as intended.
24. **Manufacturer:** Natural or legal person with responsibility for the design, manufacture, packaging, or labeling of a medical device, assembling a system, or adapting a medical device before it is placed on the market or put into service, regardless of whether these operations are carried out by that person or on that person's behalf by a third party.
25. **Medical Device Reporting (MDR) Reportable Event:** An event about which Stryker has received or become aware of information reasonably suggesting that:
    - A Stryker device may have caused or contributed to death or serious injury, or
    - A Stryker device has malfunctioned, and the device or a similar Stryker device would be likely to cause or contribute to a death or serious injury if the malfunction were to happen again.
26. **Nonconformance**: An event that is contrary to a standard or requirement whether intended or specified.
27. **Occurrence Date:** The date a problem, or nonconformance, took place.
28. **Originator:** The originator is responsible for entering all new Product Inquiries into the System.
29. **PER (Product Experience Report) File:** The customer complaint, and its associated investigation, and any associated adverse incident reports to regulatory authorities (such as MDR or MDV reports) and miscellaneous supporting documents.
30. **Post-market surveillance:** Systematic process to collect and analyze experience gained from medical devices that have been placed on the market.
31. **Preventive Action:** Action taken to eliminate the cause of a potential nonconformance to prevent or reduce its potential occurrence.
32. **Product Assessment Center (PAC):** PAC is the site that performed the investigation regardless of the Stryker entity type it is (Division, Business Unit, etc.)
33. **Product Inquiry (PI):** The CHS record that contains the initial event information and is the root parent record.

34. **Project Record:** CHS project records include Product Inquiry, Complaint, eMDR, eMDV, Country Submission, and Product Return.
35. **Quality system:** The organizational structure, responsibilities, procedures, processes, and resources for implementing quality management.
36. **Query:** One of the two Components used to determine which Records are displayed in Trackwise. Query determines the search criteria based on any data field in the system.
37. **Record:** Document or electronic media stating results achieved or providing evidence of activities performed.
38. **Reprocess:** The act of preparing a reusable medical device for its next use. This process typically involves cleaning, disinfection and sterilization.
39. **Serious Injury:** Means an injury or illness that is:
    - Life-threatening (even if temporary in nature),
    - Results in permanent impairment of a body function or permanent damage to a body structure,
    - Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure. (Includes an additional medical or surgical intervention when the initial attempt was interrupted/discontinued due to the performance of a Stryker device.)
40. **Severity:** Measure of the possible consequences of a hazard.
41. **Scope:** One of the two Components used to determine which Records are displayed in Trackwise. Scope determines which Record types are displayed.
42. **Trackwise:** The validated database used by Stryker to manage complaints ("Product Inquiries"), Medical Vigilance Reports ("MDVs"), and Medical Device Reports ("MDRs") entered on or after January 1, 2013 (January 5, 2015, for Recon Robotics).
43. **Technical File (TF):** Collection of documents to support CE marking of Class I, Class IIa and Class IIb products. Instruments and some other devices fall into these categories.
44. **Unique Device Identifier:** An identifier that adequately identifies a device through distribution and use by meeting the requirements of 21 CFR 801 and 830. A unique device identifier is composed of:
    - **Device identifier** – a mandatory, fixed portion of the UDI that identifies the specific version or model of a device and the labeler of that device; and

- **Production identifier** – a conditional, variable portion of a UDI that identifies one or more of the following when included on the label of the device:
  a) The lot or batch within which a device was manufactured.
  b) The serial number of a specific device.
  c) The expiration date of a specific device.
  d) The date a specific device was manufactured.

ABSTRACT

The main goal of the company is to offer its customers the best quality products possible. One of the best ways to monitor the quality of product and provide feedback to the design, manufacturing, technical support, sales, and marketing teams is a well-designed Complaint Handling System. Medical device companies can continuously enhance user safety, regulatory compliance, and customer satisfaction by using an efficient complaint handling system. There are comprehensive quality management system software's available to automate functions such as recording customer complaints, investigations, and adverse event reporting according to regulatory standards. Trackwise is one such software which is used by Stryker for the Complaints Handling process. Medical device companies are required by the FDA to report incidents involving medical equipment in order to detect and address problems in a timely manner. Despite the best planning of medical devices, sometimes adverse events occur. These events may include medical device malfunctions, serious injuries, and deaths. Similar way events are captured by other medical device industries and reported to FDA. The data is readily available in public database forum. The data is extracted for market analysis and is documented in periodic safety update report (PSUR) along with other requirements. Furthermore, this project also focuses on the establishment of an automated statistical tool for estimating the product usage in the field.

Stryker's complaint handling system, Trackwise, serves as a central location for all complaints and supporting data. In the complaint handling team various roles are allocated to manage complaints, such as CIC (Complaint Intake Center), CMC (Complaint Management Center), and PAC (Product Assessment Center). This project focuses on CMC. After the CIC intake, CMC manages the complaint and uploads it to Trackwise. Additional event information is received via the RAQA or Sales Representative. Files an eMDR for Reportable Complaints, submit Complaints, approve Complaints after PAC investigation, and closes Complaints.

The Periodic Safety Update Report is a periodic report that medical device manufacturers are required to maintain and submit to their Notified Body (NB) on a regular basis. The PSUR is a summary of the findings of Post Market Surveillance activities, as well as the conclusions reached by manufacturers for Class IIa, IIb and III devices. A description and justification for any corrective or preventative actions (CAPAs) made by the manufacturer must also be included in

this report. Present study encompasses the retrieval, collection and analysis of data for periodic safety update report of medical device Catheter.

Stryker Neurovascular does not have an established statistical method to estimate product consumption in the market, when a product change has been made and a mixture of new and old product are in circulation. This project focuses on establishing a tool for estimating product usage in the field based on available data that eliminates the need for ad-hoc, manual analyses.

CHAPTER 1: INTRODUCTION

This project of "Complaints Handling and Vigilance Reporting" is conducted under the supervision of the Quality team at Stryker Global Technology Centre and Stryker Neurovascular. The project involved a cross-functional strategy and stakeholder management, as well as practical application of regulatory and business requirements.

Stryker is headquartered in Kalamazoo, Michigan, and has branches in North and South America, Europe, the Middle East, Africa, and Asia. Stryker has built a technology development center in India that focus on Stryker product design, development, and manufacturing support for the global market. Stryker's processes are fully connected with the ISO 13485:2016 standard for medical devices, and they've been consistently enhanced through audits throughout decades. Furthermore, the processes meet the standards of 21CFR820 as set forth by the US FDA and other regulatory organizations in countries where Stryker conducts business.

Stryker employs around 40,000 people worldwide. Stryker has 30 manufacturing and R&D centers across the world and sells its products in over 100 countries. Stryker develops and manufactures new and innovative products and services in the areas of orthopedics, medical, surgical, neurotechnology, and spine to significantly improve patient and hospital outcomes. The field of neurotechnology is divided into two divisions: cranial and neurovascular.

In January 2011, Stryker procured Boston Scientific's Neurovascular Division. "Stryker Neurovascular products are “A Complete Stroke Care Solution”. Stryker's innovative ischemic and hemorrhagic stroke devices and services are helping to advance the practice of less intrusive therapies.

Stroke is a medical disorder that occurs when a blood artery carrying oxygen and nutrients to the brain becomes clogged or bursts (or ruptures). When this happens, a section of the brain lacks the blood (and oxygen) it requires, and it, as well as brain cells, perish. In addition, there are two types of strokes: ischemic and hemorrhagic. An ischemic stroke occurs when the blood flow to a portion of the brain is cut off, causing the brain tissue in that area to deteriorate. Thrombosis, embolism, systemic hypoperfusion, and cerebral venous sinus thrombosis are the main causes of ischemic stroke. Hemorrhagic Stroke is caused by bleeding in the brain and results in brain dysfunction. There are two types of hemorrhagic stroke. Intracerebral hemorrhage (bleeding within the brain) and Subarachnoid hemorrhage (bleeding within the skull but outside the brain tissue).

According to the World Health Organization, 15 million individuals worldwide suffer from a stroke each year. Five million of them die, and another five million are completely disabled. More than 12.7 million strokes occur each year due to high blood pressure. Stryker NV offers a diverse, well-balanced, and effective product portfolio in the fields of HEM, AIS, ICAD therapy, and access products to reach the damaged location.

They are classified as follows:

1.1 Access: These products are used to approach the site, as the word access implies "a way to approach". Since the insertion site for these endovascular operations is the femoral artery, we require these access devices to get our implant to the target site in the brain. It consists of:

1.1.1 Catheters: These are the variety of the Catheters that assist and support the devices in gaining quick access to the target areas. AXS Catalyst 5, AXS Catalyst 6, AXS Catalyst 7, AXS Infinity LS, AXS Infinity plus, and AXS Offset are the different models of catheters. Some microcatheters are specifically designed to provide high and diverse performance. It also allows for a smooth tracking and stable delivery. Excelsior 1018, Excelsior SL-10, Excelsior XT-17, and Excelsior XT-27 are the models available.

Figure 1: AXS Catalyst

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/access.html

Figure 2: Excelsior SL-10

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/access.html

1.1.2 Guidewires: Synchro guidewires have a microfabricated exterior structure that improves torque distribution, while Transend provides control and responsiveness. Their coating makes it easier to move through a microcatheter. They serve as a guide for the catheters as they navigate to the intended site. Physicians track these guidewires using fluoroscopy, then move the catheters behind them, pulling the guidewire back from the catheter's lumen when it reaches the desired position.

Figure 3: Synchro

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/access.html

Figure 4: Transend

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/access.html

1.1.3 Balloon Catheters: They're engineered to track high, protect well, and provide quick access and reliable proximal flow control, such as Flow gate 2. Merci balloon guiding catheter is also available for support and protection.

Figure 5: FlowGate2

Source: https://stryker.highspot.com/items/5d93a577c247913e77a0a5a1?lfrm=srp.2

1.2 Angioplasty & Stenting: Angioplasty is a minimally invasive endovascular technique for widening restricted or blocked arteries, which is mostly used to treat arterial atherosclerosis. A deflated balloon catheter is inserted into the constricted vessel through a guidewire and then inflated to a specific size. This balloon aids in the widening of the blood vessel as well as the surrounding muscle wall, resulting in increased blood flow. A stent is implanted to guarantee that the vessel remains open during ballooning, and the balloon is subsequently deflated and extracted. Angioplasty refers to a variety of vascular procedures that are usually done transcutaneous. It consists of:

1.2.1 Stents: The stent system is intended to improve conformability, stability, and usability. It is self-expanding nitinol stent with the flexible design. The hybrid cell structure is designed to enhance stent opening, wall apposition and conformability. For example, Neuroform Atlas and Neuroform EZ (preloaded on the delivery wire).

Figure 6: Neuroform Atlas

Source: https://stryker.highspot.com/items/5d93a75fc71433076ca39f4d?lfrm=srp.13

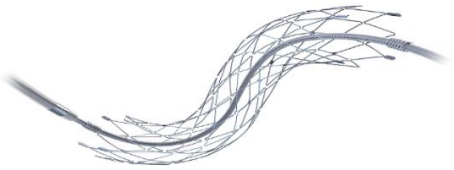


Figure 7: Neuroform EZ

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/angioplasty-and-stenting.html

1.2.2 Flow Diverters: The technology utilized to divert blood flow in order to prevent aneurysms in the vessels from rupturing. They're designed to enable optimal flow diversion, for example. Surpass Streamline, Surpass Evolve.

Figure 8: Surpass Evolve

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/angioplasty-and-stenting.html

1.2.3 ICAD Stent: Wingspan is developed for intracranial atherosclerotic disease. This stent system includes a gateway PTA balloon catheter that allows access to complex neurovascular anatomy. The Wingspan Stent System with Gateway PTA Balloon Catheter is designed to improve patient's cerebral artery diameter.

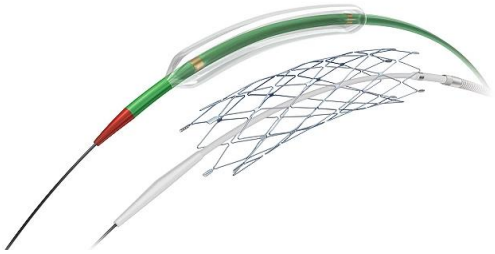


Figure 9: Wingspan Stent

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/angioplasty-and-stenting.html

1.3 Embolization: It is a procedure that involves cutting off the blood supply to a tumour or abnormal mass. The blood flow is blocked using coils and a balloon catheter in this procedure. Target 360, Target 3D, Target Nano, Target XL, Target XXL are some of the coils we use to fill aneurysms, depending on their size and structure. Transform, a balloon catheter used to obstruct blood flow, is also used in this treatment.

Figure 10: Target Detachable

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/embolization.html

Figure 11: Transform

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/embolization.html

1.4 Thrombectomy: When a clot or thrombus blocks a brain vessel, an interventional treatment is used. The clot is surgically removed from the veins in this technique. So, for thrombectomy, we have a retriever (Trevo XP) specially created for the removal of thrombus in Ischemic stroke patients. We also have an aspiration system (AXS Universal and AXS Vecta 71) that has extra power and uses next-generation vacuum technology to help with thrombus aspiration in the neurovasculature.

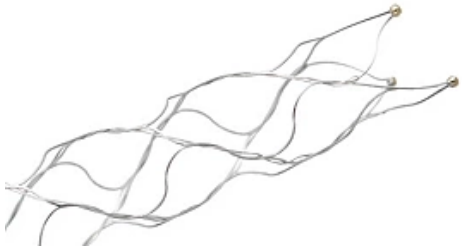


Figure 12: Trevo XP

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/thrombectomy.html

Figure 13: AXS Universal

Source: https://www.stryker.com/us/en/portfolios/neurotechnology-spine/neurovascular/thrombectomy.html

First part of the project focuses on the Stryker Neurovascular division's complaint handling process. The process follows the corporate quality protocol to assure that complaints are received, documented, reviewed, analyzed, and investigated by a formally designated unit in a consistent and timely manner. Medical device manufacturers must develop a customer complaint handling method to gather feedback on probable adverse events that must be reported to the FDA. To meet with regulatory quality standards, medical device businesses that market their equipment in Europe or the United States must build a customer complaint management process. It also assists in the identification of risks that the manufacturer is unaware of or those are not addressed in the product design Risk Table, which are then updated as necessary.

Second part of this project highlights the importance of creating the technical document Periodic Safety Update Report (PSUR) for Stryker Neurovascular products. The PSUR is an

obligatory report by the Medical Device Regulation for all Class IIa and higher devices. It gathers data about the device's security and performance that was discovered during the Post Market Surveillance process. The PSUR is completed at the end of the PMS period, which lasts two years in class IIa and one year in class IIb, and it transcribes your current knowledge of your device and its application in the current context. The PSUR is reported to the Notified Body (NB) via EUDAMED for Class III MDs and implanted devices, and it is taken into account during your NB's evaluations in all circumstances.

This project also focuses on development of an automated statistical tool for estimating the product usage in the field. This project was initiated to make the assessment of both progress as well as the effectiveness of change to products easier, as the current analyses for such assessment are highly manual and time consuming.

CHAPTER 2: REVIEW OF LITERATURE

2.1 Complaint Handling System

All organizations are actively interested in customer-focused quality, which includes addressing complaints when customers' wants and expectations are not met, and these complaints typically imply concerns, including potentially serious safety issues, with a product's use, design, and/or manufacture. Maintaining customer confidence and limiting exposure to the issue, as well as complying with FDA rules, requires an effective process for receiving and assessing complaints and rapidly executing relevant corrective actions. The Quality System Regulation (Title 21 Code of Federal Regulations [CFR] Part 820) specifies how medical device manufacturers should handle complaints. According to 21 CFR 820.3(b), a complaint is "any written, electronic, or oral communication that alleges issues pertaining to the identity, quality, durability, reliability, safety, efficacy, or performance of a device after it is released for distribution." Any sign that a device has failed to fulfil performance criteria, as well as any indication that the device has failed to satisfy consumer expectations, is considered a complaint. As a result, a product may fulfil all of the manufacturer's criteria but fall short of the intended usage and needs of the user (i.e., the specifications are inaccurate or inadequate). Under the Medical Device Reporting Regulation, device manufacturers are required to report certain concerns (adverse occurrences) to the FDA (21 CFR 803). Deaths, serious injuries, and device malfunctions that are likely to cause or contribute to a death or serious injury if they occur again are all examples of adverse incidents. The company must submit most reports to the FDA within 30 days after becoming aware of the event; however, there are specific requirements for five-day reporting. User facilities must also report serious injuries to device manufacturers and deaths to both the device manufacturer and the FDA within 10 days of becoming aware of the event, as per the Medical Device Reporting Regulation. Under the Quality System Inspection Technique (QSIT) Corrective and Preventive Action (CAPA) subsystem, FDA investigators examine a manufacturer's complaint handling system as part of their inspections of device manufacturing facilities. One of the most significant quality system elements, according to the QSIT guidelines, is the manufacturer's CAPA system.

The processing of complaints is an important part of a medical device manufacturer's overall quality system. Product complaints are simply claims that the manufacturer's quality control system failed to detect and rectify an issue prior to the device's distribution and use. Both the FDA and medical device companies are clearly interested in an effective complaint processing mechanism, not only to assure compliance with the Regulation, but also to ensure fast action in response to device quality issues [17]. Complaint handling system of a company utilizes many user roles in the complaint investigating process. As a result, to complete the tasks and functions, the following are required:

2.1.1 Complaint Intake Center (CIC):

- They initiate the complaint, and they examine it after an investigation and closes a complaint by approving it.
- They receive data regarding the complaint, enters it into complaint handling system, and asks quality screening questions to get clear information on the first interaction.
- They also assist complaint management system and product assessment center in getting the additional information required for the complaint assessment.[18]
- Finally, reviews the complaint after the investigation and submits it for the closure.

2.2.1 Complaint management system (CMC):

- After CIC, the complaint is taken by CMC, and they review the complaint.
- From receiving to closure, they manage the complaint handling process, maintains complaint-related files, evaluates complaints, ensures appropriate action is taken for specified products/product families, and assesses issues for adverse event reporting.
- They determine whether the complaint is reportable or not and prepares the necessary regulatory submission forms.
- They make sure that all other complaint records are closed for the product inquiry to be ready for final approval by complaint intake center.
- Based on the investigations done by the PAC they approve the complaint or reject it if it requires re-evaluation.

- CMC is the division or business unit associated with the product reported in the event. The international distribution division may be considered the CMC when it is identified as the legal manufacturer of an OEM product. [18]

2.3.1 Product assessment Centre (PAC):

- They conduct the investigation of the complaint and document it.
- They inspect the returned devices.
- They assess the risk associated with the event.
- Once the investigation is done, they send the complaint for approval of CMC.[18]

2.2 Periodic Safety Update Report:

The European Union Medical Device Regulation (EU MDR) represents a comprehensive reform of EU medical device legislation. The addition of more stringent post market surveillance (PMS) and vigilance requirements, which indicate a more prominent role for medical device manufacturers once a device has reached the market, is one of the most significant changes in the new guidelines. The PSUR is a report that summarizes the findings of post market surveillance activities as well as the conclusions reached by manufacturers. A description and justification for any corrective or preventative actions (CAPAs) made by the manufacturer must also be included in this report.[10]

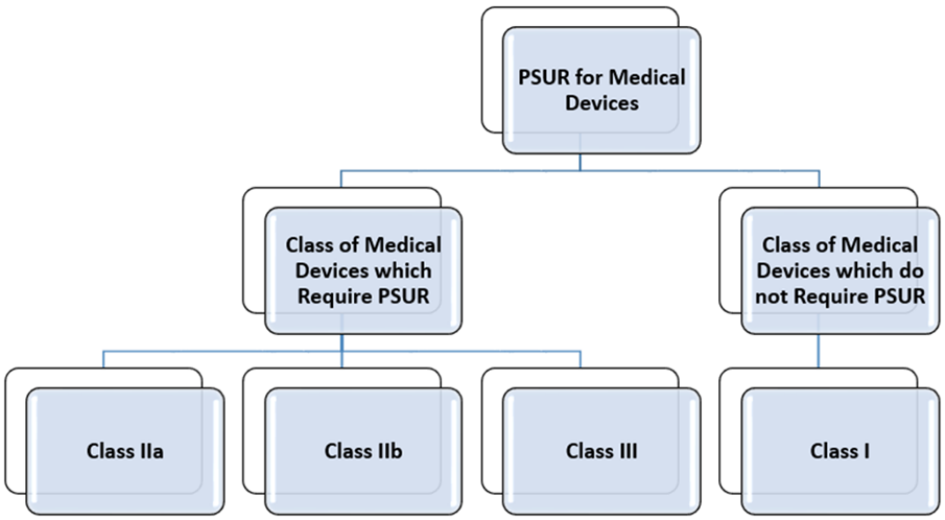


Figure 14: Showing classes of medical device requiring PSUR

The Periodic Safety Update Report is part of the technical documentation for a device, and it must be updated during its lifetime. The PSUR is first reported to a Notified Body during the device's conformity assessment audit, but it must then be updated annually or biennially thereafter. For moderate and high-risk devices, the PSUR is required. Medical devices designated as IIa, IIb, and III under MDR, as well as implanted devices, are included. The PSUR is required every two years for Class IIa medical devices. The PSUR must be submitted annually for Class IIb and III medical devices. EUDAMED is required to submit the PSUR for Class III and implantable medical devices. Article 86(2) of the MDR and Article 81(2) of the IVDR both contain this requirement. Both papers mention "an electronic system," which should be considered as EUDAMED.[10]

PSURs can vary depending on how much specific data the vendor chooses to include, but they should always include the following:

1.	Post Market Surveillance data
2.	The conclusions of benefit-risk analysis
3.	A description of any CAPAs and the rationale behind them
4.	The findings of Post Market Clinical Follow ups
5.	The device’s sales volume and an estimate of the user population
6.	An analysis and summary of all the information listed above

The PSUR format is made up of two parts: a PSUR form and a PSUR report. For class III devices and implantable devices, the PSUR report is a PDF file that the manufacturer must upload to EUDAMED. The PSUR form is an electronic form that the manufacturer will fill out in EUDAMED once they've performed the "completeness" check. The PSUR form includes all important administrative information as well as data that allows to identify and differentiate between different PSURs for the same device. It should include information needed to register the PSUR with EUDAMED.

The PSUR should be self-supporting, containing all the information needed to comprehend the situation:

- The manufacturer's/authorized representative's identity and contact information.

- ❖ Device identification and general information, including indications and patient profiles, regarding the device (or group, or category) and its intended use.
- ❖ Data on the number of devices sold and in use, the number of users, and the frequency with which they are used. This is necessary in order to determine the likelihood of risks occurring.
- ❖ Information on the monitoring period that has elapsed, including the start and end dates, as well as the reason for the surveillance period (longer or shorter depending on the risks and uncertainties).[3]

2.2.1 Surveillance results (including clinical follow-up):

The PSUR expands on the PMS plan's (Post Market Surveillance plan) major objectives, describing how they were met, and the outcomes reached. PMS plan outlines the methods and processes to collect and assess post- market surveillance data in order to monitor the safety, performance and risk-benefit information of the medical device. The Post-Market Clinical Follow-up (PMCF) plan and the clinical development plan are also considered. The PMCF plan and the clinical development plan outline the outcomes and status of current clinical trials. The data that confirms (or disproves) the claimed benefits is detailed in it. The actions (CAPAs) that had an impact on security or performance during the PMS period are summarized, justified, and the outcomes are also described. Alerts, major and non-serious incidents, adverse reactions, withdrawals, and other events are summarized and estimated (number, frequency of occurrence, health impacts), and the actions (including FSCAs) taken are described. The impact on the risk analysis is reported, with details on previously identified hazards as well as new risks discovered during occurrences. Any patterns discovered in PMS or vigilance are described, along with the conclusions reached and measures taken. When residual risks occur frequently enough to allow this study, the trends primarily concern the likelihood of occurrence and severity of residual hazards. The objective is to detect a potential increase and take appropriate preventive action, or a drop, which indicates the effectiveness of risk control. Trends can also be regional, particularly if there are regulatory differences between the EU and other regulatory areas. As a result, discovering and validating the relevance of new information or patterns (event unfolding) discovered in the field and likely to influence the benefit/risk ratio is a must. New risks are found, and quantified, existing risks and benefits are re-evaluated, and the benefit/risk ratio's acceptability is analyzed again. [16]

The PSUR conclusion outlines the implications for estimating important risks and benefits (which affect the benefit/risk ratio), as well as any new dangers and changes in the setting, particularly in connection to device use.

The data used to make PSUR is retrieved from various public database such as:

2.2.2 MAUDE:

The Manufacturer and User Facility Device Experience (MAUDE) database is a Post Market Surveillance reporting system established by the FDA.

It covers reports of medical device-related adverse events that occur after the device has been approved. It enables approved products to be monitored for safety after they have been placed on the market. The FDA can issue warnings or recalls if a device is faulty or poses a health concern. MAUDE has been turned into a searchable database on the internet. It covers all reported incidents in which medical devices have failed and resulted in death or serious harm. MAUDE is updated on a quarterly basis, and the date of the most recent update is displayed on the search page. The database is maintained by an FDA division and is open to the public under the Freedom of Information Act. It is available at the following URL: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.cfm.

All voluntary reports dating back to June 1993, user facility reports since to 1991, distributor reports from to 1993, and manufacturer reports dating back to August 1996 are included in the MAUDE database. Within 30 days after becoming aware of a device-related death, serious injury, or malfunction, manufacturers must report it to the FDA. The FDA also requires reports from user facilities (hospitals, outpatient diagnostic or treatment facilities, nursing homes, and ambulatory surgical facilities) within 10 working days. 8 Individual doctors can report occurrences to the designated person in their user facility, or they can submit a voluntary report to FDA via FDA's "MedWatch" program at http://www.fda.gov/medwatch/ index.html or by phone at 1–800-FDA1088.[23]

2.2.3 TPLC:

The Total Product Life Cycle (TPLC) is a framework for analyzing any product or service (medical or otherwise). For the manufacturer, TPLC refers to the market-driven evolution of a device or drug from conception to pre-market development, extensive market use, obsolescence, and eventual replacement by successive generations of products. From a pre-market standpoint, the producer compiles a lot of evidence to the point where it is convinced that submitting a product for FDA review is a good idea. Following that, the company gathers clinical data and submits a formal prospectus for review, which can be thought of as an application to market. Product labelling and device surveillance, as well as the absorption of data into subsequent quality improvement and product development, are the most visible aspects of the post-market side. In the best-case scenario, the company produces its own substitute product through internal research and development. The traditional practice of viewing pre-market review and post-market surveillance as separate and dichotomous aspects of regulatory obligation has been replaced with an integrated approach from the regulatory standpoint.[15]

The TPLC database incorporates data from several data sources to create a comprehensive record of medical device premarket and post market activity. The TPLC database organizes information by procode, a three-letter code that corresponds to a certain type of medical device. In the TPLC database, only datasets with a procode are included. Because not all of the entries in the data sources have procodes linked with them, the TPLC database excludes them. Counts of database information are included in the TPLC reports (i.e., number of recalls, number of premarket submissions). Links on the pages provide further information on the occurrences that were counted. These counts may change when the various data sources are updated or refreshed. Based on MAUDE medical device adverse event reports, the TPLC reports provide adverse event information as device problem counts.[15]

2.2.4 TPLC Data Sources:

Title	Description
Premarket Approvals (PMA)	Premarket approval by FDA is the required process of scientific review to ensure the safety and effectiveness of all devices classified as Class III devices. An approved Premarket Approval Application (PMA) is, in effect, a private license granted to the applicant for marketing a particular medical device. This database is updated on a monthly basis.
Premarket Notifications (510(k)s)	Medical device manufacturers are required to submit a premarket notification or 510(k) if they intend to introduce a device into commercial distribution for the first time or reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected. Some firm names may not be the current 510(k) owner. The Premarket Notification database is not updated when 510(k) ownership transfers from the original sponsor to other firm. The database is updated monthly.
MAUDE (Manufacturer and User Facility Device Experience)	MAUDE data represents reports of adverse events involving medical devices. The data consists of all voluntary reports since June, 1993, user facility reports since 1991, distributor reports since 1993, and manufacturer reports since August, 1996. MAUDE data is reported by patients, physicians, facilities and the device manufacturers. Preliminary, supplemental and duplicate reports exist.
Manufacturer Name Consolidation	Applicant/Sponsor/Manufacturer Firm names are not provided with consistent spelling or abbreviations in the MAUDE database. To aggregate the information all firm names have been simplified and consolidated. As data in MAUDE improves, firm names will become the firm name in the registration database.

Table 1: TPLC data sources

2.3 Statistical tools:

Statistical analysis is a scientific technique that assists in the collection and analysis of vast volumes of data in order to identify common patterns and trends and convert them into useful data. Briefly stated, statistical analysis is a data analysis method that supports in the extraction of useful conclusions from unstructured and raw data. The results are obtained through statistical analysis, which helps decision-making and allows companies to forecast future trends based on previous trends. It is a science that involves collecting and processing data in order to find and illustrate trends and patterns. Statistical analysis entails working with numbers and is used by corporations and other organizations to generate useful information from data.[12] Statistical analysis can be done using various tools, one such tool is Minitab.

2.3.1 **Minitab**:

It is a statistical software application that allows you to import and export statistical data, as well as analyses it to come up with constructive results. Minitab's statistical data analysis assists quality management professionals in analyzing huge amounts of data that would be difficult to evaluate otherwise. The analysis' findings can be used to improve the company's operations. It is used to develop process predictions and to make adjustments when necessary. Through data analysis, it aids in the evaluation of previous and current trends. It facilitates data visualization through graphs and charts, making understanding the link between multiple variables easier and faster.[7] As a result, understanding statistical analysis tools such as Minitab can assist companies in improving their business operations. It has more benefits than any other traditional statistical analysis tool. As a result, it has become the most widely used statistical data analysis tool in businesses and educational institutions to assist students comprehend statistics. It provides better and faster answers to extremely complex evaluations. Minitab is a versatile program that uses very little disc space and takes very little time to compute. Minitab, which was first employed in the manufacturing business, quickly gained popularity as a result of its significant advantages in statistical data analysis. It's employed in quality control and development in a variety of industries, including service, logistics and packaging, pharmaceuticals, and healthcare, etc. [21]

Statistical analysis is efficient but manual so to decrease the time consumption and labor put into operating these tools, automation is the key to unlocking the comfort and higher efficiency.

Data automation is the process of using automated systems to upload, handle, and process data instead of completing these processes manually. Data Automation is a great way for a company can save expense. It is a cost-effective and productive solution for a business because it increases work efficiency while lowering costs. Furthermore, automation benefits employees by allowing them to focus on more demanding and engaging activities rather than repetitive tasks. Furthermore, consistency is ensured by automatic data management. Manual methods could jeopardize work quality, which is critical for organizations. There are various tools for automating the statistical models such as Power BI.

2.3.2 Power BI:

It is a set of software services, apps, and connectors that work together to transform multiple data sources into logical, visually engaging, and interactive insights.

The data could be in the form of an Excel spreadsheet or a collection of hybrid data warehouses that are both cloud-based and on-premises. Power BI makes it simple to connect to the data sources, visualize and identify what matters, and share your findings with whomever you choose. It creates interactive dashboards and Business Intelligence reports by converting data from many sources. Power BI Dashboard is a single page visualization to explain the whole scenario. A dashboard's visualizations are built from reports, and each report is based on a single dataset. Canvas is the name for a single-page dashboard. Power BI Desktop allows you to build a variety of reports. The Power BI service can be used to publish these reports to the Power BI dashboard. By clicking the Publish button, a Power BI report prepared on Power BI Desktop can be published to Power BI Service.[11]

OBJECTIVES

1. Complaints Handling and Vigilance Reporting for Stryker Neurovascular Products
2. Data retrieval and data analysis for the Periodic Safety Update Report of Stryker Neurovascular Catheters.
3. To develop Automated statistical tool for the estimation of product usage in the field.

CHAPTER 3: MATERIAL AND METHOD

3.1 Complaint Handling System:

3.1.1 Trackwise:

It is a software platform for the Quality Management System (QMS) that is used by a wide range of industries to enhance product quality, achieve regulatory compliance, and decrease risk related with the company's medical devices. It is utilized to centralize operations and automate reporting within their organization as well as amongst worldwide supply chain partners. Complaint handling in the Trackwise QMS aids in regulatory compliance. It serves as a repository for complaints and other associated documentations. It's the system for resolving a customer's complaint. The CIC, CMC, and PAC are the three primary teams that deal with complaints and have different duties and responsibilities. The CMC is the focus of this project.

3.1.2 Complaint Management System:

3.1.2.1 Product Inquiry:

After the PI is submitted by the CIC, depending upon the number of products mentioned in the PI, PR is generated accordingly.

i. The PI are assigned to CMC every day in the form of daily assignments. PIs when assigned are in opened state and cannot be kept in the same state for more than 2 days, so they should be investigated and pushed to next state.

A	B	C	D	E	F	G	H	I
PR ID	Parent ID	Product Long Description	Product Available to Stryker	CMC Coordinator	Awareness Date	Event Description	Country of Event	Comments

Figure 15: The format in which PIs are assigned to the coordinators

ii. After logging in to the Trackwise software, the CMC owner enters the PI number that is assigned to the CMC in the search field.

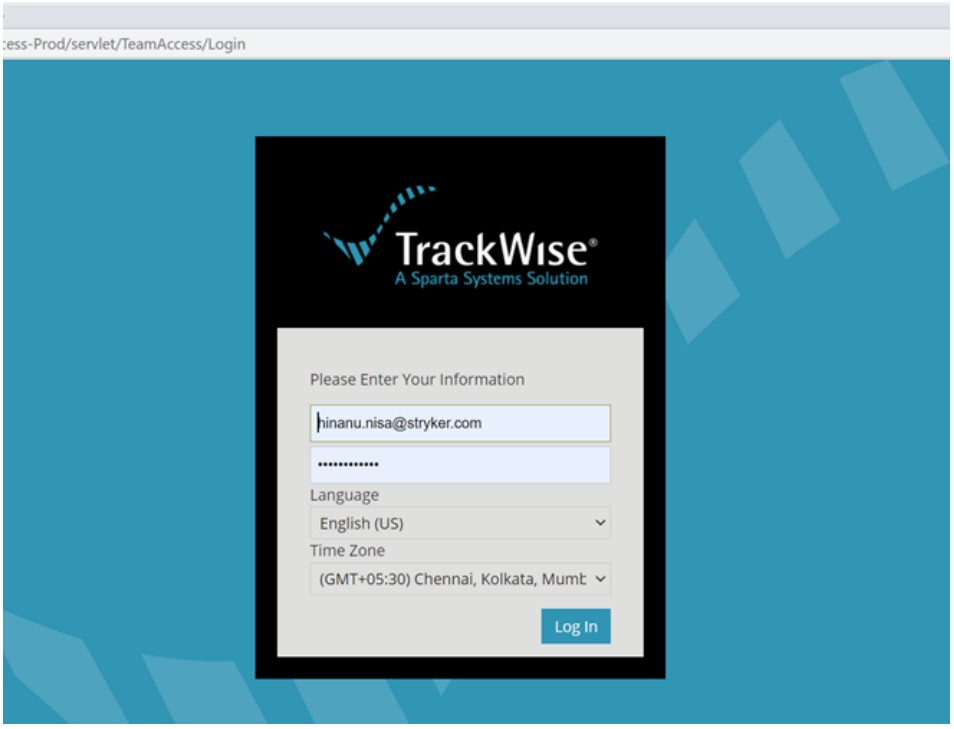


Figure 16: Login Page of Trackwise

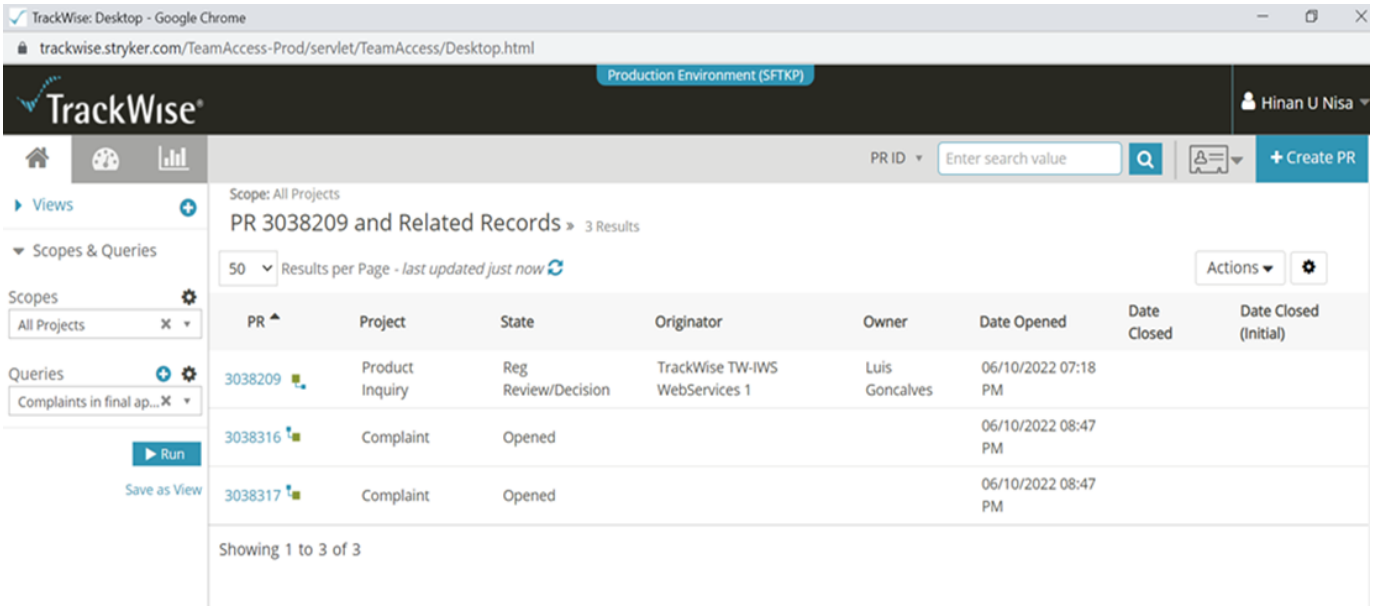


Figure 17: Search field in Trackwise

iii. **Intake Tab**: After opening the PI, intake tab is the first tab. The complaint should be opened within 1 business day after the awareness.

Date Opened	Generated by the system
Originator	Generated by the system
Country of the event	Indicates the country in which the event has taken place
CIC	Indicates the CIC responsible for the reported event
Intake Source	The media by which the event was been reported
Intake Source - Other	If the media is not specified in the dropdown menu
Awareness Date	Date on which the Stryker employee becomes aware of the event
Reason for Delay	It is filled if the Complaint is not opened in 1 business day after the opening of the complaint
Attachment – Intake	Supporting documents such as the PIF is attached here
Duplicate PI Search	It helps in searching if duplicate PI available
Communication Log	Additional Information in the report provided by the user

Table 2: Intake Tab

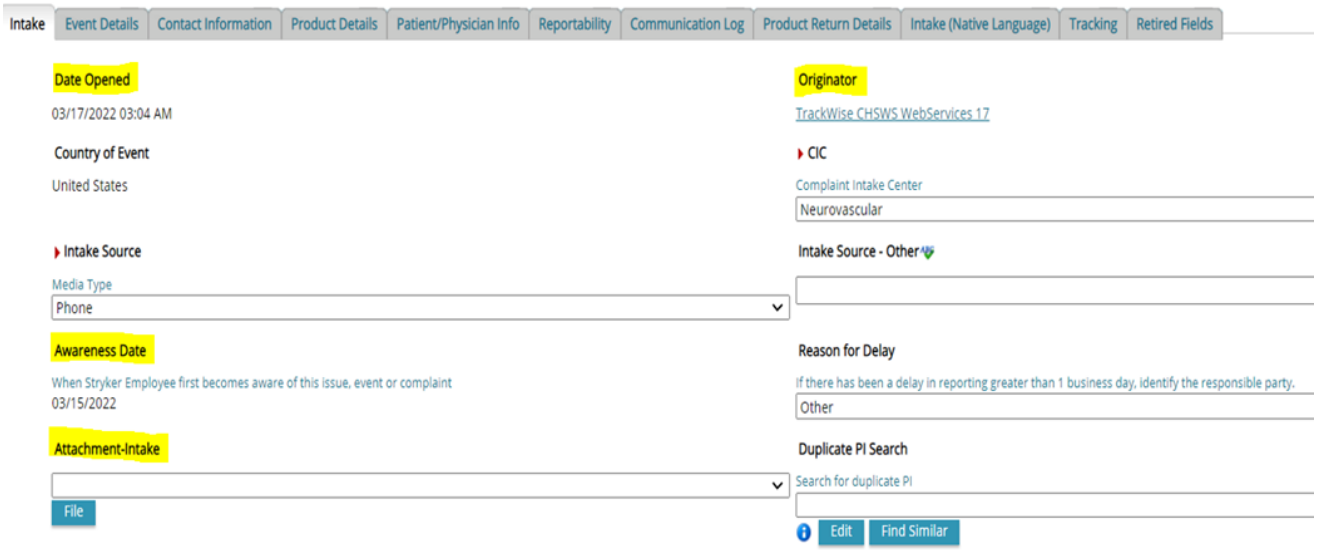


Figure 18: Intake Tab

iv. Event Details Tab:

Event Date	Date of the Reported event
Approx.	Only Chosen Yes if the Event date is unknown
Event Description	Details provided by the physician while reporting the event
How was issue noticed	When did the event occur Prior, during or after the procedure
Procedure Completed Successfully	Associated Procedure completed successfully
Patient Involvement	Was the patient impacted by the event and was he involved during the event
Medical Intervention	Unanticipated medical procedures, treatments or therapies were administered as a result of the alleged device malfunction
Surgical Delay	Procedure delayed due to the product malfunction or the event
Adverse Consequences	Were any Adverse consequences related to the product
Adverse Consequences Details	If any of the field like medical intervention, Surgical delay or Adverse consequences are marked “yes” So, the details of that must be included part.
Death Date	If the patient died the Death date must be mentioned
Notify Legal	Has the event notified to the legal bodies

Table 3: Fields of Event Details

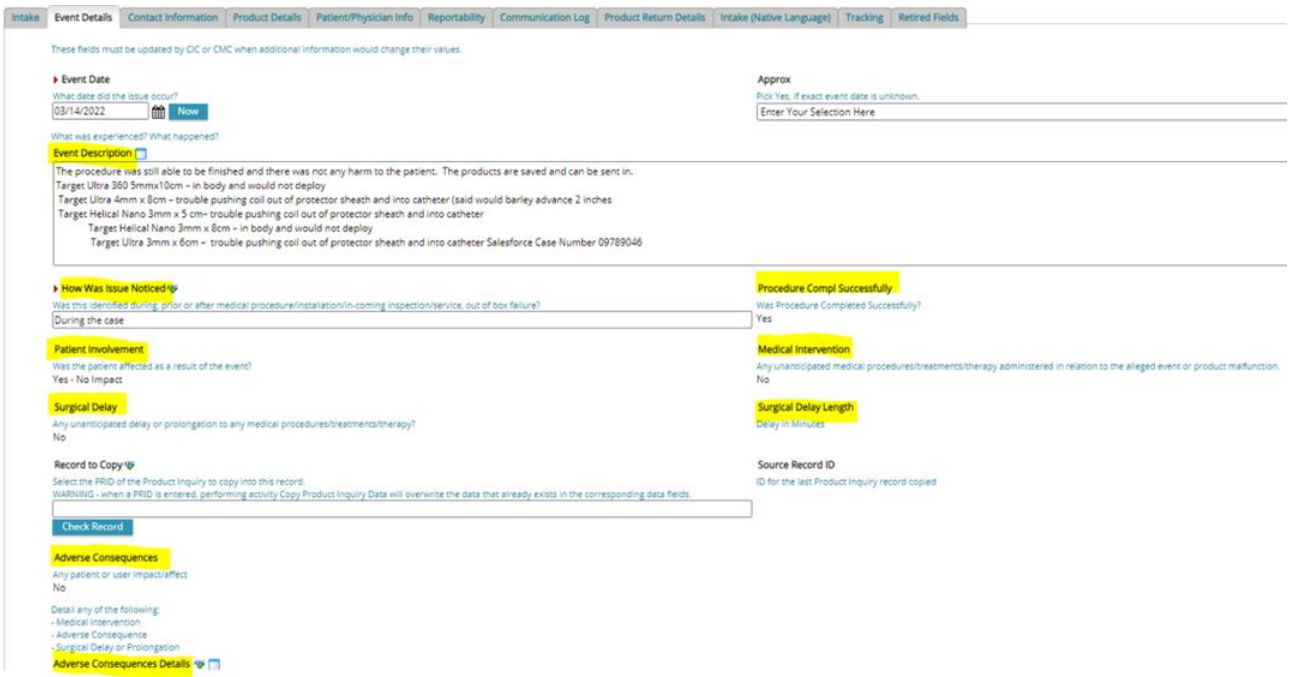


Figure 19: Event Details

v. Contact Information Tab:

Initial Reporter Facility	Name of the Reporting facility
Facility city	The city in which the facility lies
Initial Reporter Name and Address	Name of the reporter and the address for follow up
Initial Reporter Phone	Contact details of the reporter it must be added in the format +011(123)456789 for countries other than US and for US it must be +1(123)456-789
Initial Reporter Type	How is the Initial reporter i.e. Distributor or Health Professional etc.
Initial Reporter Type – Other	Initial Reporter other than already mentioned in the dropdown menu
Health Professional Occupation	If the Initial Reporter Type is as health professional so his occupation must be mentioned whether a physician or surgeon or others mentioned in the drop-down menu
HP Occupation – Other	The health professional not already entered in the system
Sales Rep	The company's sales rep for the Reported device

Table 4: Contact Information Fields

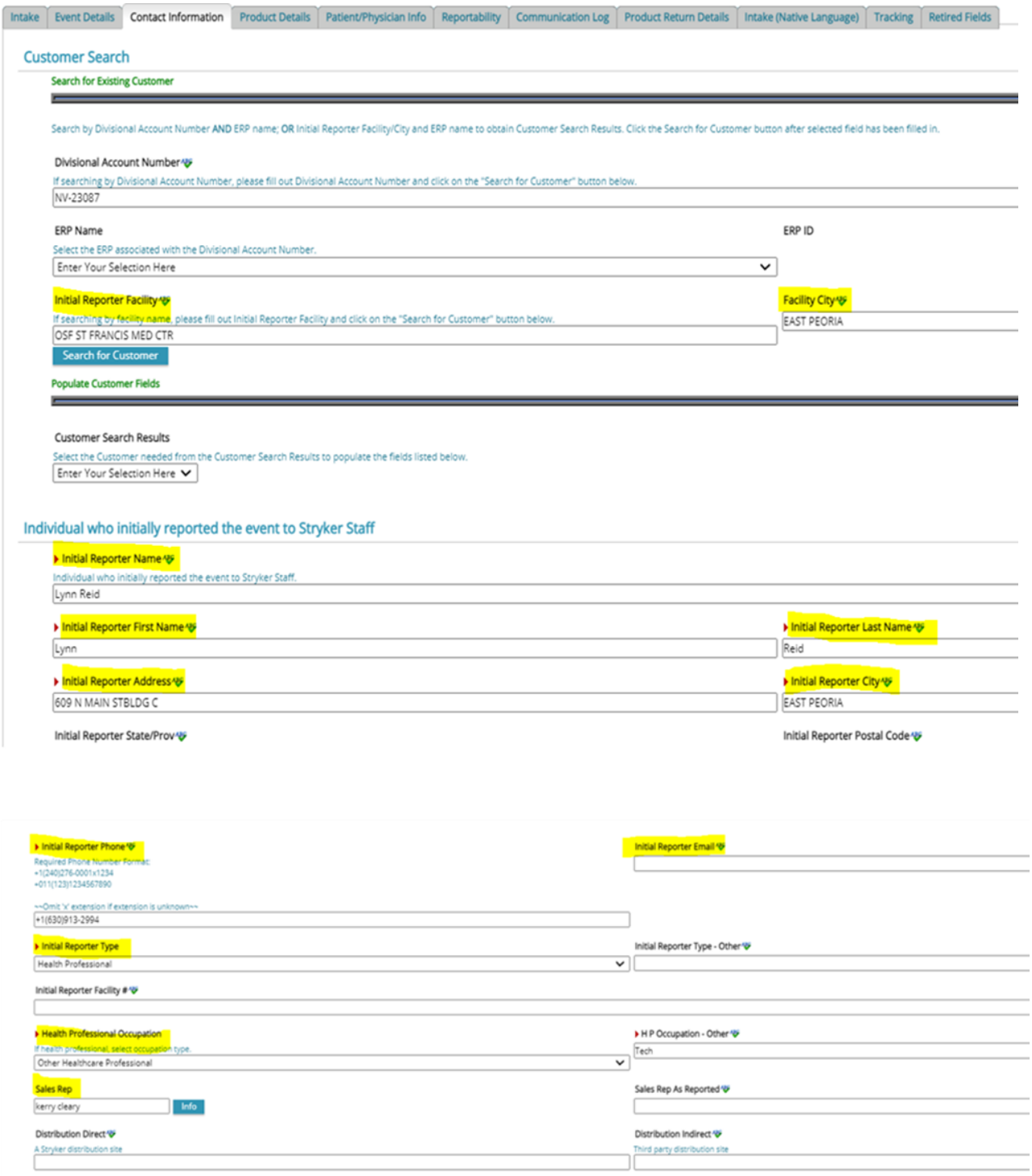


Figure 20: Contact Information

vi. Product Details tab:

Product Grid	The Product(s) involved in the event with their details such as Catalog No., Lot No., etc.
Complainant Acknowledgment Required	If the complainant has requested the notification of the receiving of the event
Acknowledgement Type	Which type of acknowledgement is requested by the complainant
Complainant Require Results	Complainant Requests the results of the Investigation
Complainant Result Type	In which format the results are requested by the complainant
Product Available to Stryker	Is the Product being send back for investigation
Product Not Available, Why Not	If the product is not coming back, then they must specify the reason for not returning the Malfunctioned product

Table 5: Product Details fields

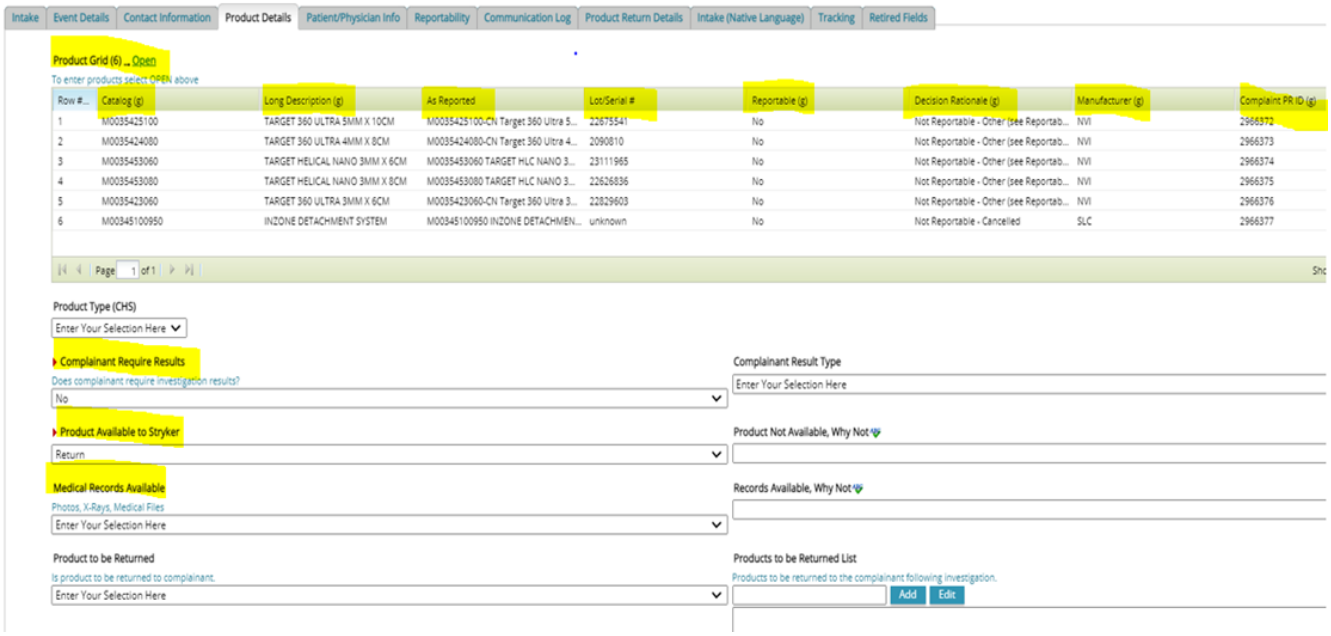


Figure 21: Product Details

vii. Patient/Physician Info Tab:

Patient Identifier	Identification of the Patient apart from using the patient name
Patient Information	It includes the Basic information of the Patient such as: Gender Age Weight Height
Physician Name	-
Physician Contact Information	-

Table 6: Patient/Physician Info fields

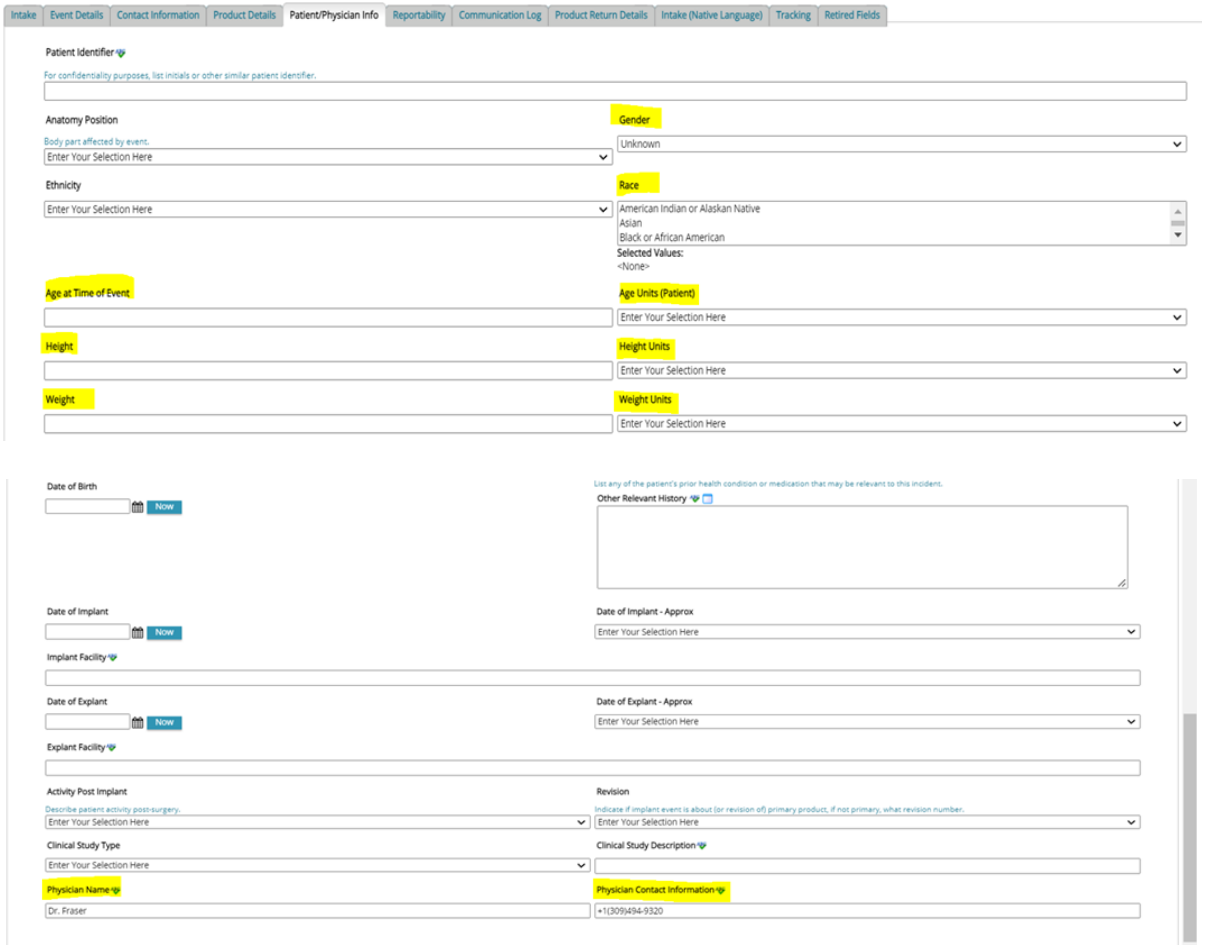


Figure 22: Patient / Physician Information Tab

viii. Reportability tab:

Reportability Owner MDR	The CMC assigned with the PI is the owner for the MDR
Reportability Owner MIR	The CMC assigned with the PI is the owner for the MIR
Commercially available in US	Check the availability of the Product in Us using the product approval matrix and select yes or No accordingly. If selected No, then the US tree closes, and you don't have to fill information as it becomes N/A. But if selected Yes then the Further questions are to be answered
5-day Report required	If the issue requires to be reported in 5-days as per FDA select Yes, otherwise No
Serious Injury or Death	Has the event lead to any kind of serious injury or death of the patient Choose Yes / No
Reportable Malfunction	Has anything happened to the product due to which the event becomes reportable according to the guidance document choose Yes/ No
Other Reportable Reason	Any other Reason making the event reportable
Event in EU country	If the event took place in any European country Choose Yes, otherwise No. If No is chosen, then the tree itself become N/A but if Yes CMC need to fill the tree
Device Contribute to event	Choose Yes/ No depending on the contribution of the device in the event (mostly Yes because event has taken place that is why we have complaint)
Ser Public health threat	Choose Yes/ No depending on if there were any health issues to the patient
Expected Side effect	Depending on the surgery if there was any side effect due to the surgery
Agreement for PSR	Does the event lie within scope of Periodic summary report
Death or Unant Ser Det	Has the product caused the death of the patient
May have led to death or death Ser det	Depending if there was possibility of death of the patient
Reportability Type - MIR	Is the event reportable and need to file MIR
Reportability Rational	In rational the event is explained Both reportable and non-reportable have different format or rational. In reportable only the relevant information is added to the point.

Table 7: Reportability tab fields

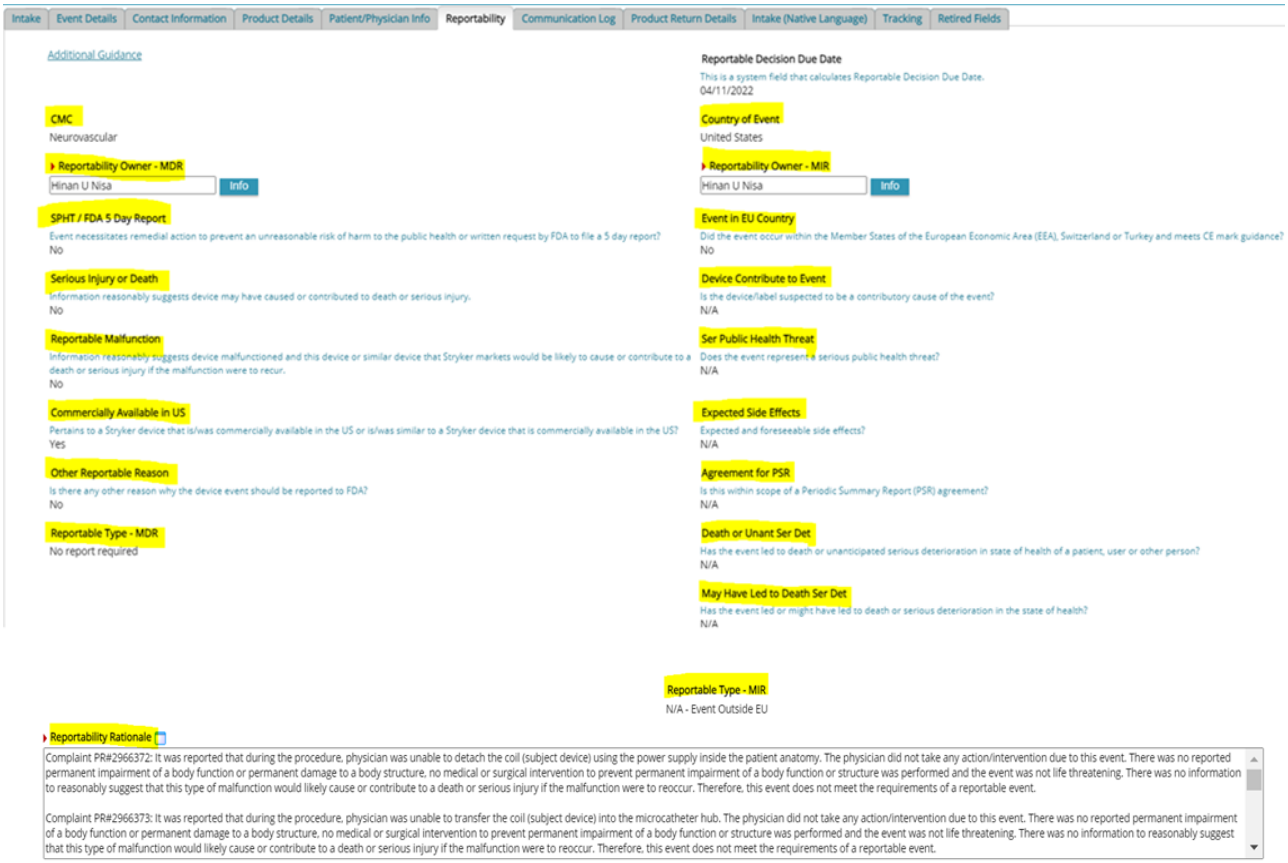


Figure 23: Reportability Tab

ix. Communication Log tab:

Customer Contact 1, 2 and 3	When the customer was contacted to get the additional information regarding the
Customer Contact Method 1, 2 and 3	Which methods were taken to contact the Customer e.g., e-mail or call.
Communication Details	This field once saved can't be edited. So, need to be filled carefully. Here the external communication regarding the event such as requests for additional information from customer, sales rep, or CIC
Attachment – Communication	Here the documents associated with the communications, Investigational material, or patient /customer information such as medical records.
Customer Response Date	When were the Result of the investigation were provided to the complainant or the sales rep as per asked per the Product grid Tab.
Customer Contact Status	How many contacts has been made to obtain additional information or the customer contact is complete
Owner	The person primarily responsible for customer communications

Table 8: Communication Log fields

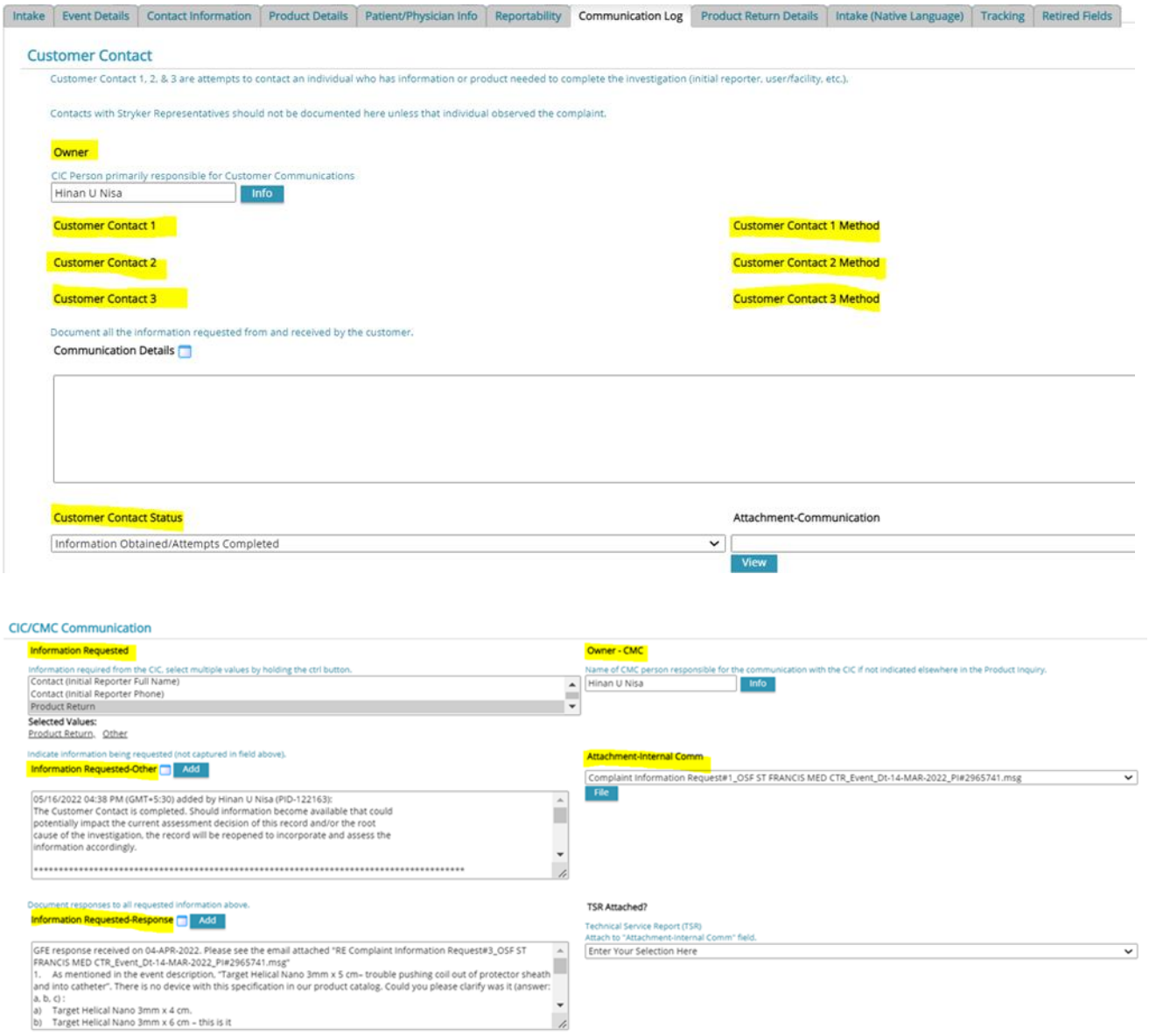


Figure 24: Communication

x. After completing all the tab, the PI will be submitted by CMC. Then further moved to PR.

3.1.1.2 Product Record

xi. Complaint Detail Tab:

PAC	The Manufacturing site of the product this helps in assigning the complaints to the investigators accordingly
Patient Involvement	Was the patient impacted by the event and was he involved during the event. Match with PI
AR	Unanticipated medical procedures, treatments or therapies were administered as a result of the alleged device malfunction. Match with PI
Surgical Delay	Procedure delayed due to the product malfunction or the event. Match with PI
Adverse Consequences	Were any Adverse consequences related to the product. Match with PI
Adverse Consequences Details	If any of the field like medical intervention, Surgical delay or Adverse consequences are marked "yes" So, the details of that must be included in this part. Match with PI
Adverse Consequences Event code	N/A if no consequences to the patient
AR contribute to event	Always Yes as the product was involved in the event causing failure
Packaging Issue	Was there any issue related to the packaging of the product causing failure
Labelling issues	Was there a labelling defect due to which the event was reported
Complaint Notes	This section is filled when we have more than 1 product related to the event
AR Product problem codes	The codes related to the product failure AR code 1 – The broad term for the failure AR code 2 – The is related to the Code 1 AR code 3 – The code which defines the failure They are chosen from the Code guidelines that suites the situation well AR code 4 – Filled by the PAC after investigation

Table 9: Complaint Details fields

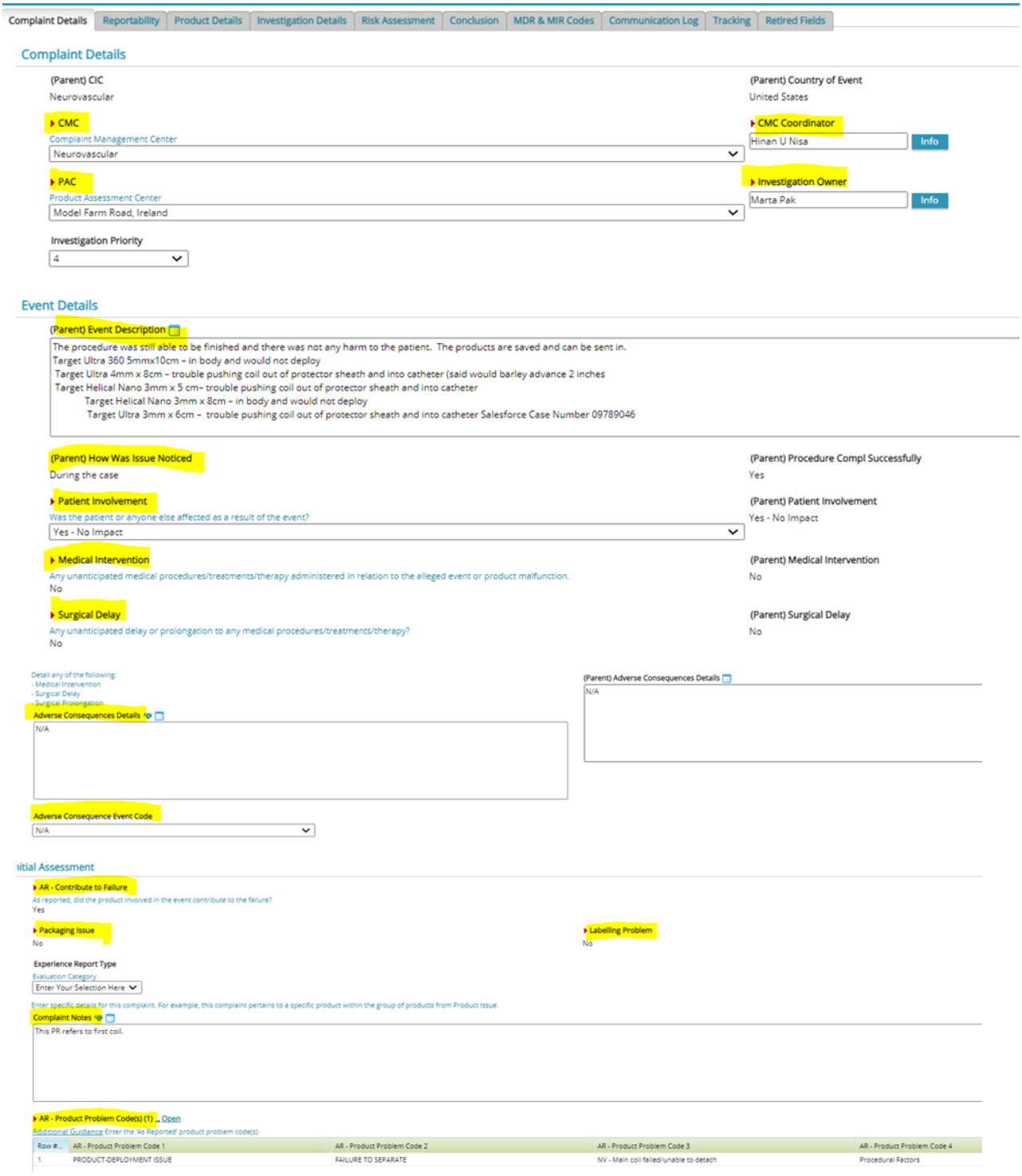


Figure 25: Complaint Details

xii. **Product details tab:** The product and system generated details associated to that product are checked by CMC and the Product Family field is filled accordingly.

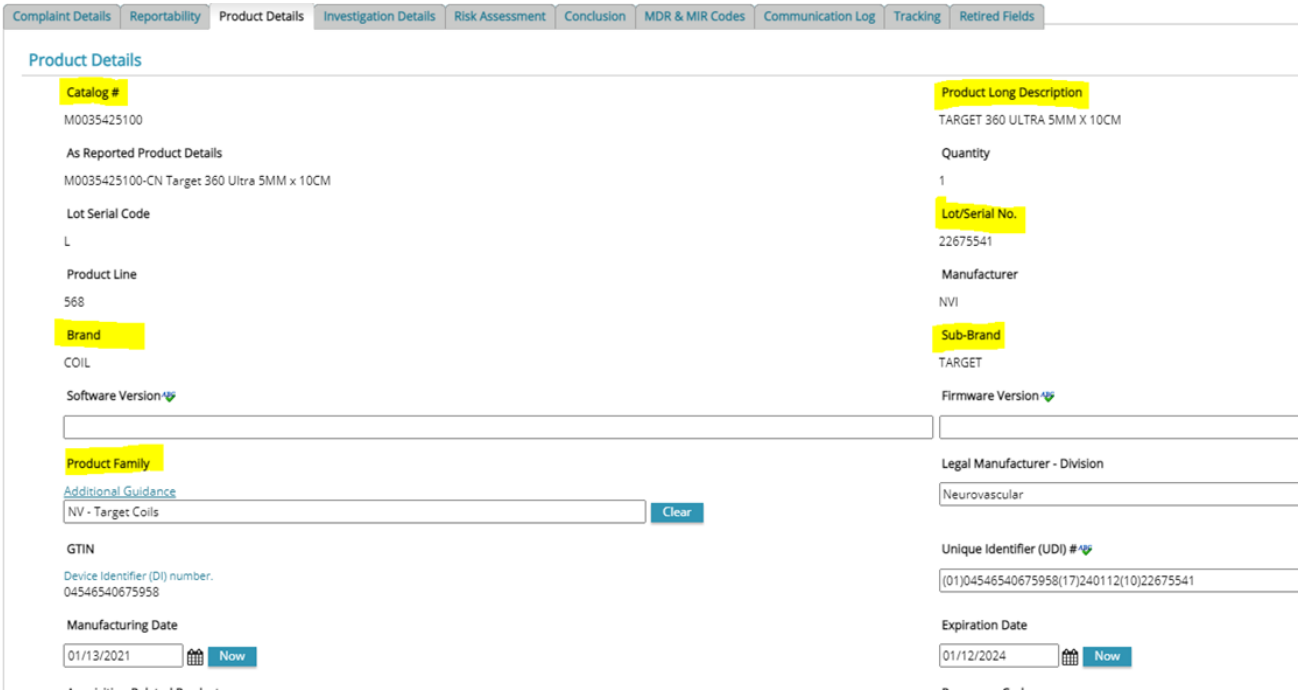


Figure 26: Product Details tab

xiii. **MDR & MIR codes tab:**

Device Code Grid	The code which explains the problem associates with the product for this there is a reference document to fill the
Patient Code Grid	Code includes the consequences to the patient if none use the code No consequences to the patient
Clinical signs Code grid	If there are any clinical signs and symptoms to the patient. There is a refence document to choose a perfect sign if none use the code no clinical signs or symptoms
Health Impact code grid	The code which tells about the health effects to the patient similar as the above code for the patient.

Table 10: MDR and MIR Codes fields

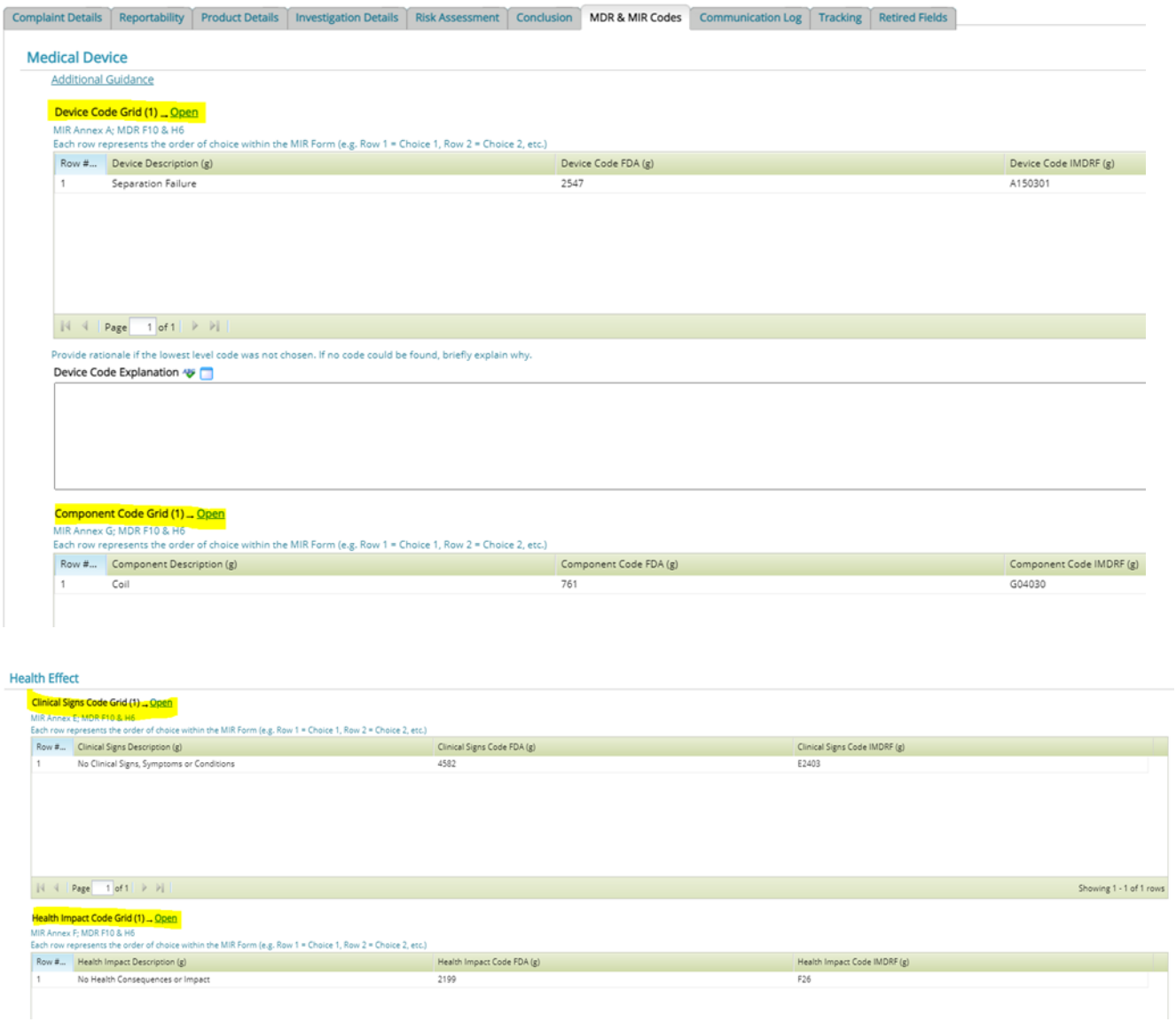


Figure 27: MDR & MIR Codes

xiv. In the activity type select submit and save and exit.

xv. Then open the PI again and in activity type select Determine reportability and then press save and exit.

xvi. Then the PI goes to approver for the approval and after that it goes to PAC for further investigation.

xvii. After PAC investigation is completed then it comes back to CMC for final approval and then the complaint.

In case the complaint is reportable then MDR must be filled. Open child record for countries depending upon the availability of the product in the country.

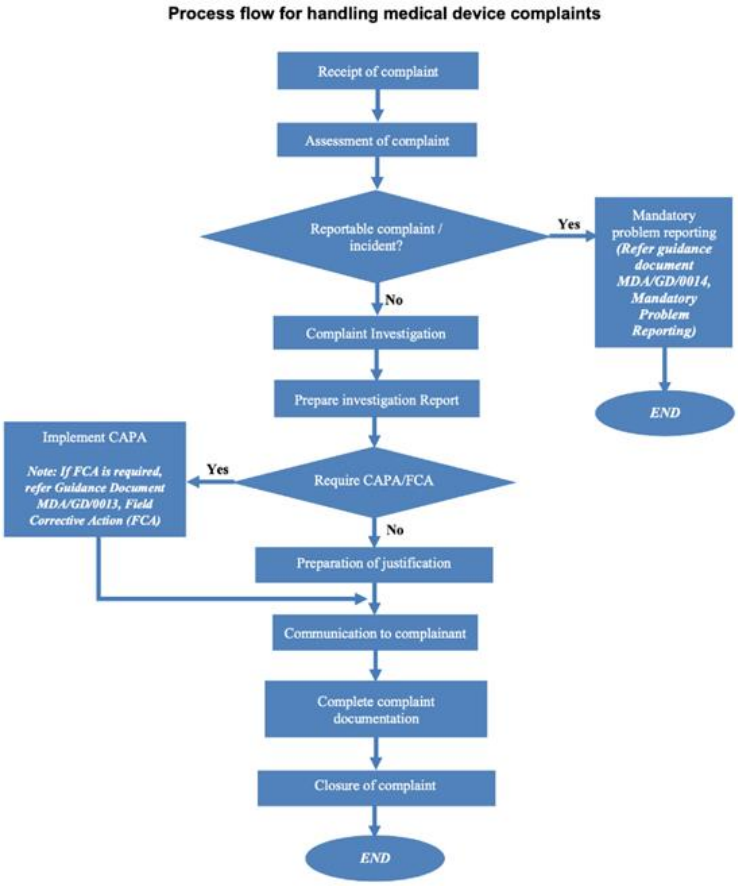


Figure 28: Process flow for handling medical device complaints

3.1.2.3 Initial MDR

When PI is turned reportable, it generates PR for MDR containing various tab to be filled and the MDR is submitted within 30 days.

- MDR is submitted within 20 days by CMC to give time to approver to review it and approving it.
- In the Conclusion Code field of PR, "Conclusion Not Available" should be added. If the device has not yet been investigated.
- After this the MDR needs to be filled as follows:

FDA reg#	The PAC location for the product Manufacturing
File attachment	This field is for attaching the files such as FDA documents or the MedWatch etc.
B1	Is the event related to product problem or the Adverse event or both
B2	Adverse Event type if any and the Date when event occurred
B5	This is related to the event detail we tell everything about the event including the additional information provided by the customer
Catalog Search	Here copy the catalog no of the product grid of the PI and search for the product and choose the Product
D2	Product code from the PMK# document select the product and check for 3letter code and Common device name
D3	Manufacturer of the Product obtained from the PAC list
D4	GTIN Number it will auto populate from the catalog
D5	Initial reporter to the company rep. i.e. the Health Professional
D6	If the product was an implant and contributed to the event add the date of implant
D8	Was the product reprocessed always no as the products are single use products
D10/H3	Select if the product is returned for evaluation
D11	For mentioning other devices used with the product during the procedure
Physician contact Information	Like the PI's Patient and Physician's Tab similar information can be filled
G1	MDR contact i.e. the site which can be approached by the FDA Manufacturing site Is the PAC associated with the Product Reporting contact for the FDA from Stryker
G3	Initial Reporter to the company i.e. The health professional
G4	Awareness date when Stryker employee becomes aware of the event
G5	PMA/510(k) section: Put the 510(k) from the PMK# rev.2 document
G7	Reportability of the event i.e. 5 days or 30 days initial

Table 11: Initial MDR fields

3.2 Periodic safety update report:

The PSUR (periodic safety update report) was created to be a stand-alone document that provides for a periodic but thorough examination of a marketed medical device's worldwide safety data. The PSUR can be a valuable resource for identifying new safety signals, determining changes in the benefit-risk profile, communicating risk effectively to regulatory authorities, and determining the need for risk management initiatives, as well as a tracking mechanism for monitoring their effectiveness.

This project focused on the data retrieval, data collection and data analysis of medical device Catheter. The code for Catheter is DQY.

The PSUR process entails a number of processes, including the collection of adverse event data, data retrieval, data analysis, and medical evaluation and risk assessment.

3.2.1 Data retrieval:

Data retrieval is the first step in the process of making PSUR. Data was retrieved from various public data bases. Public database contains huge amount of data and to get the desired data sets, user has to apply multiple search criteria.

3.2.1.2 **MAUDE** (Manufacturer and User Facility Device Experience):

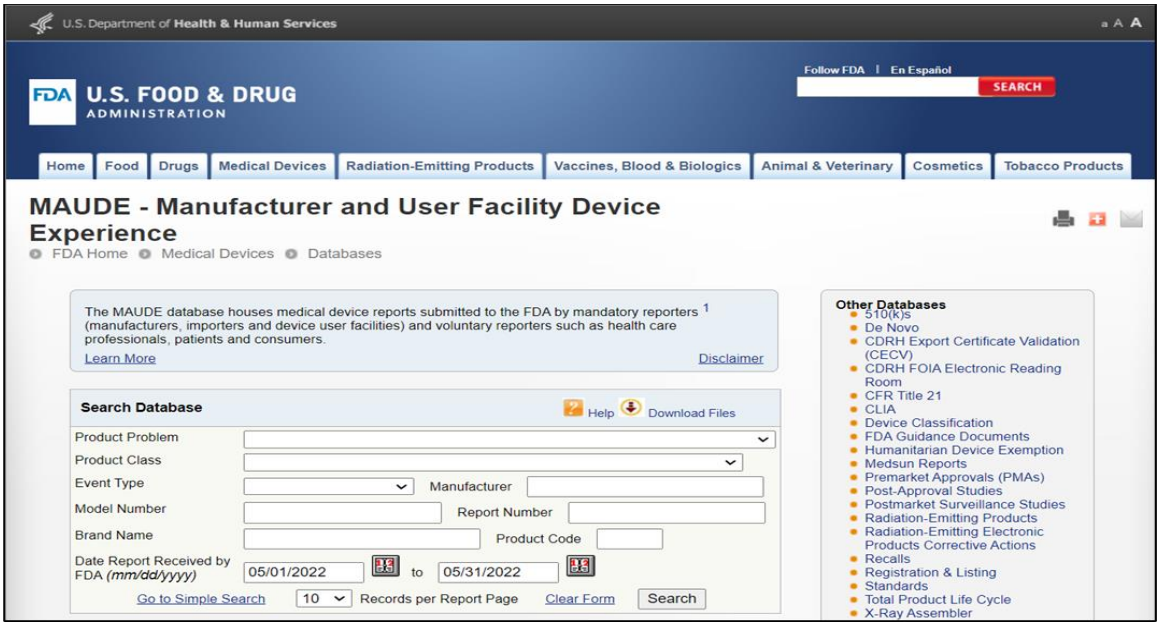


Figure 29: Homepage of MAUDE

i. For the data retrieval, the unique product code for catheter (DQY) was entered in the given tab.

ii. For this PSUR, the time frame was selected of 5 years i.e., from August 2016 – July 2021.

iii. The time frame was entered in the field Date Report Received by FDA.

iv. Then clicked on search to get the results.

Figure 30: Showing search criteria

v. Once the results are displayed, the data can be directly exported to the excel by clicking on the Export to Excel.

vi. The whole data set was retrieved in the excel file.

vii. Depending upon the number of records in search we had to narrow down the search criteria if the number of records exceeded 500. Then the query was repeated for the rest of the search criteria.

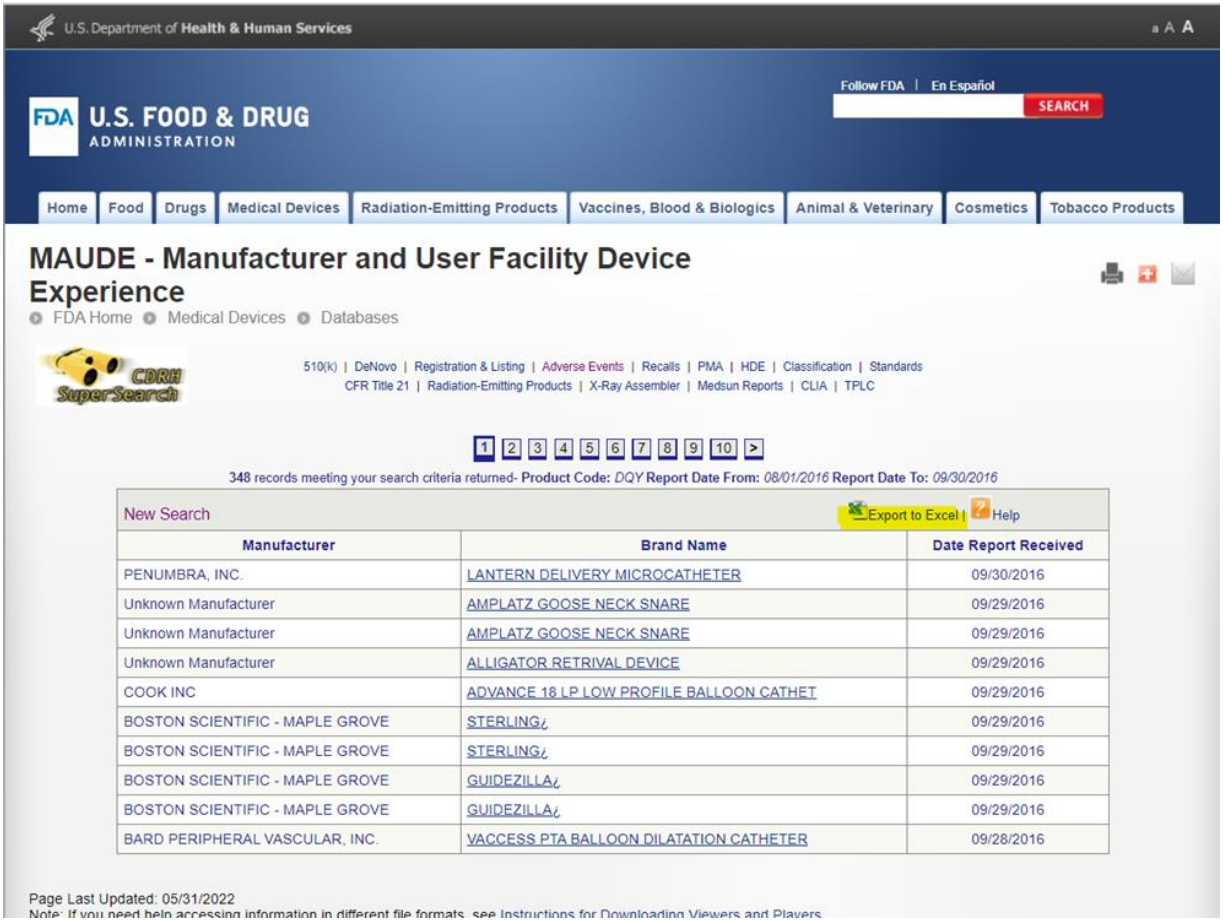


Figure 31: Showing the search results of MAUDE

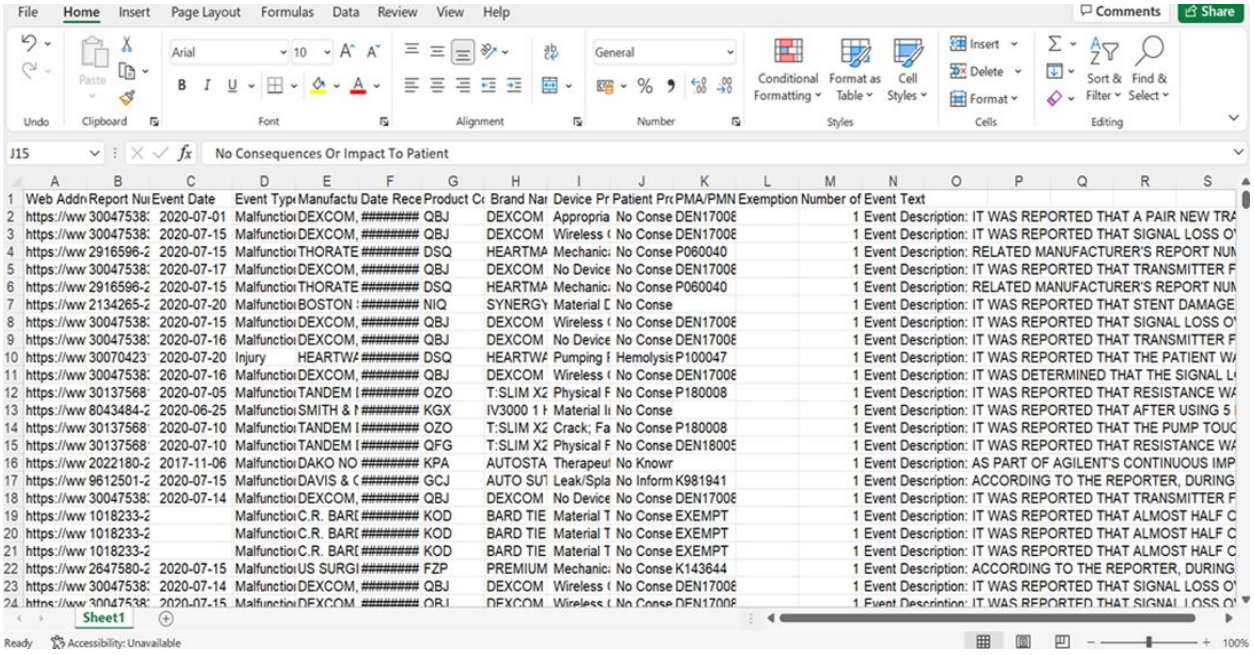


Figure 32: Showing the data exported into excel file

viii. After the data is retrieved in excel, the data is cleaning was done. The data was filtered based on the required.

3.2.1.3 TPLC:

Total Product Life Cycle database combines data from several databases to create an integrated record of medical device premarket and post market activity. It includes details such as the number of recalls, premarket submissions, adverse event information, and so on.

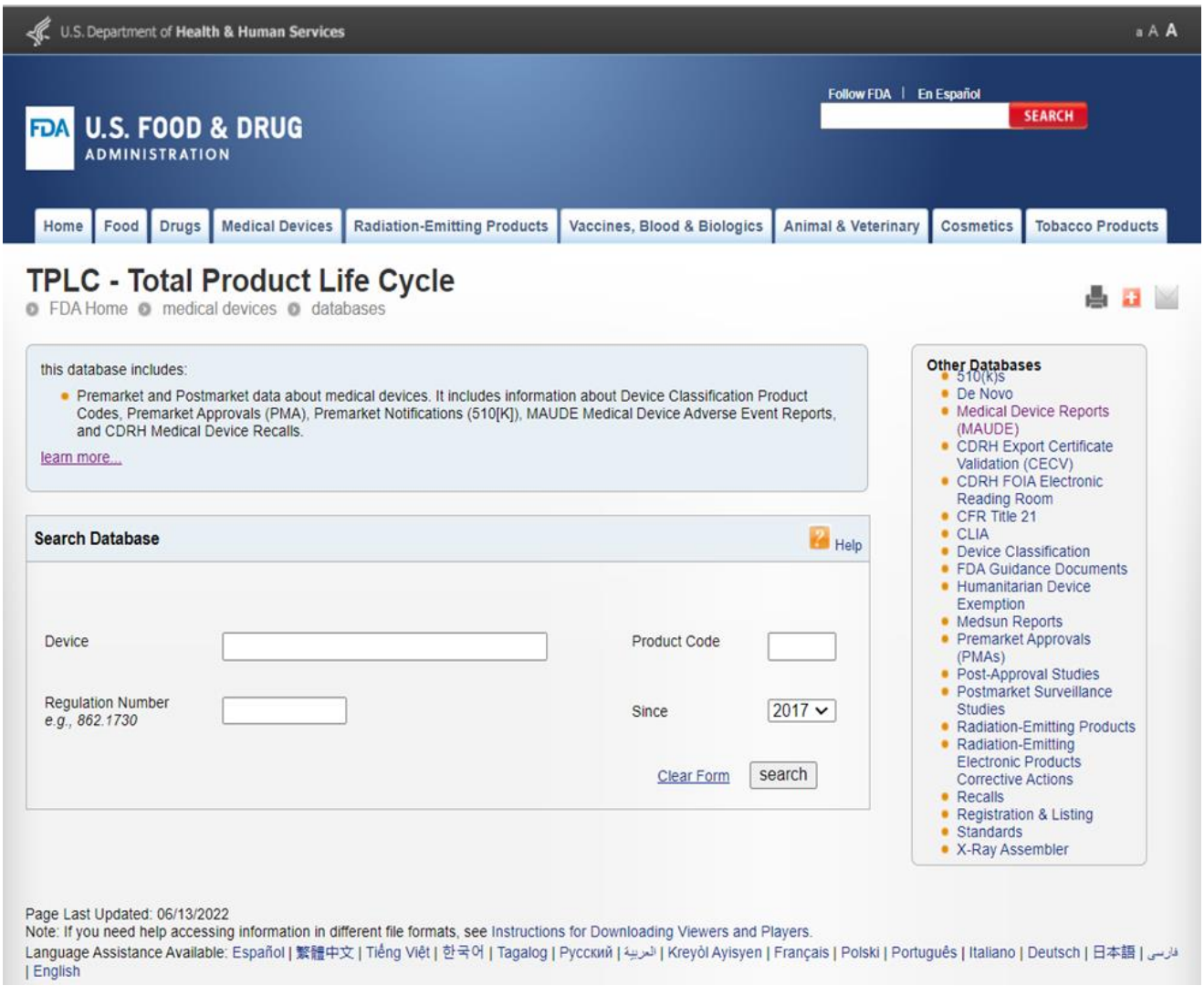


Figure 33: TPLC homepage

i. Data was also retrieved from TPLC data base.

ii. In the homepage of the TPLC database, the product code DQY was entered.

iii. The time frame was entered since 2016 as the per the requirement.

iv. Then enter search.

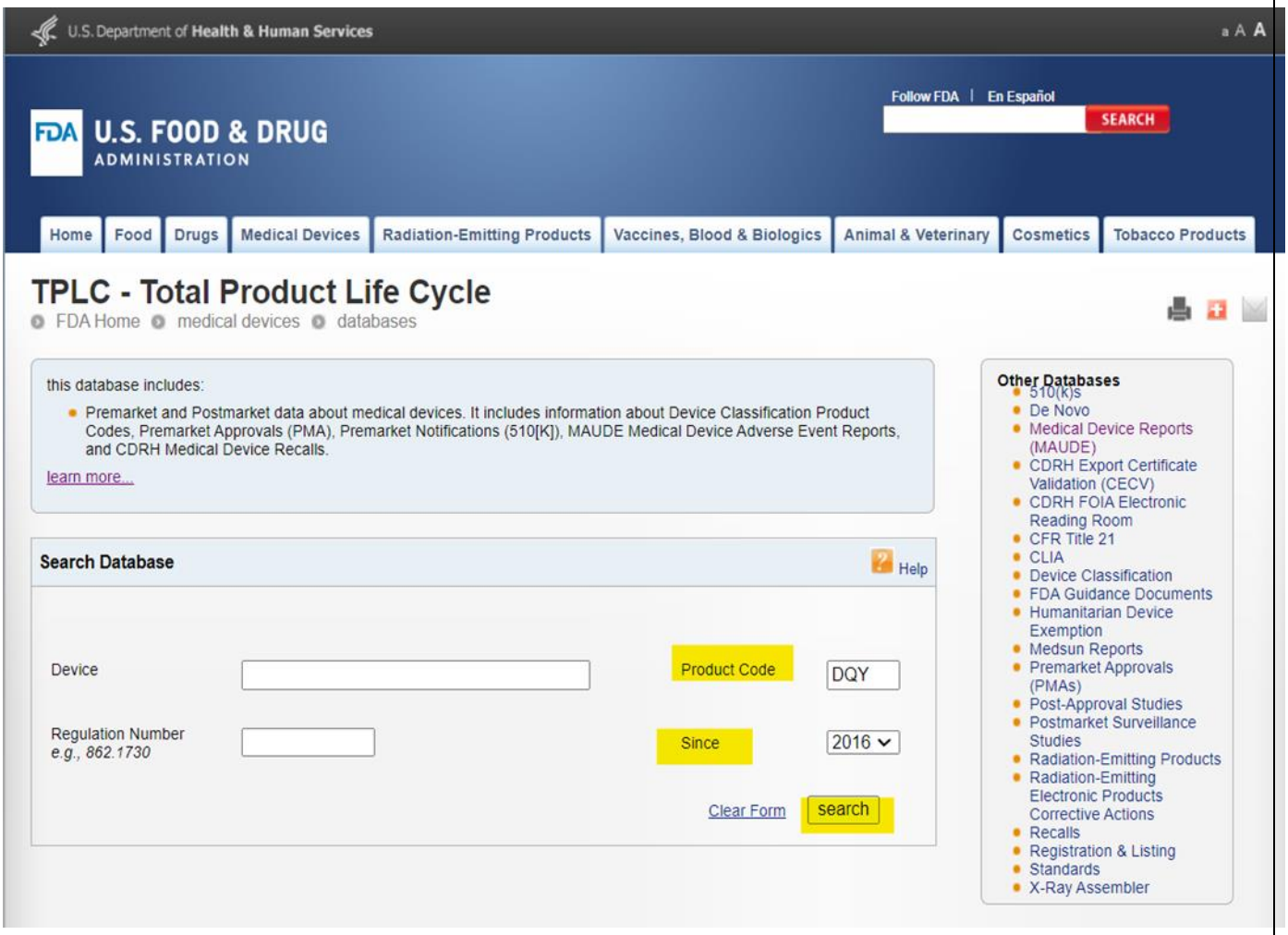


Figure 34: Showing search criteria for TPLC

v. When search is done, another tab opens in which click on the hyperlink of the device name.

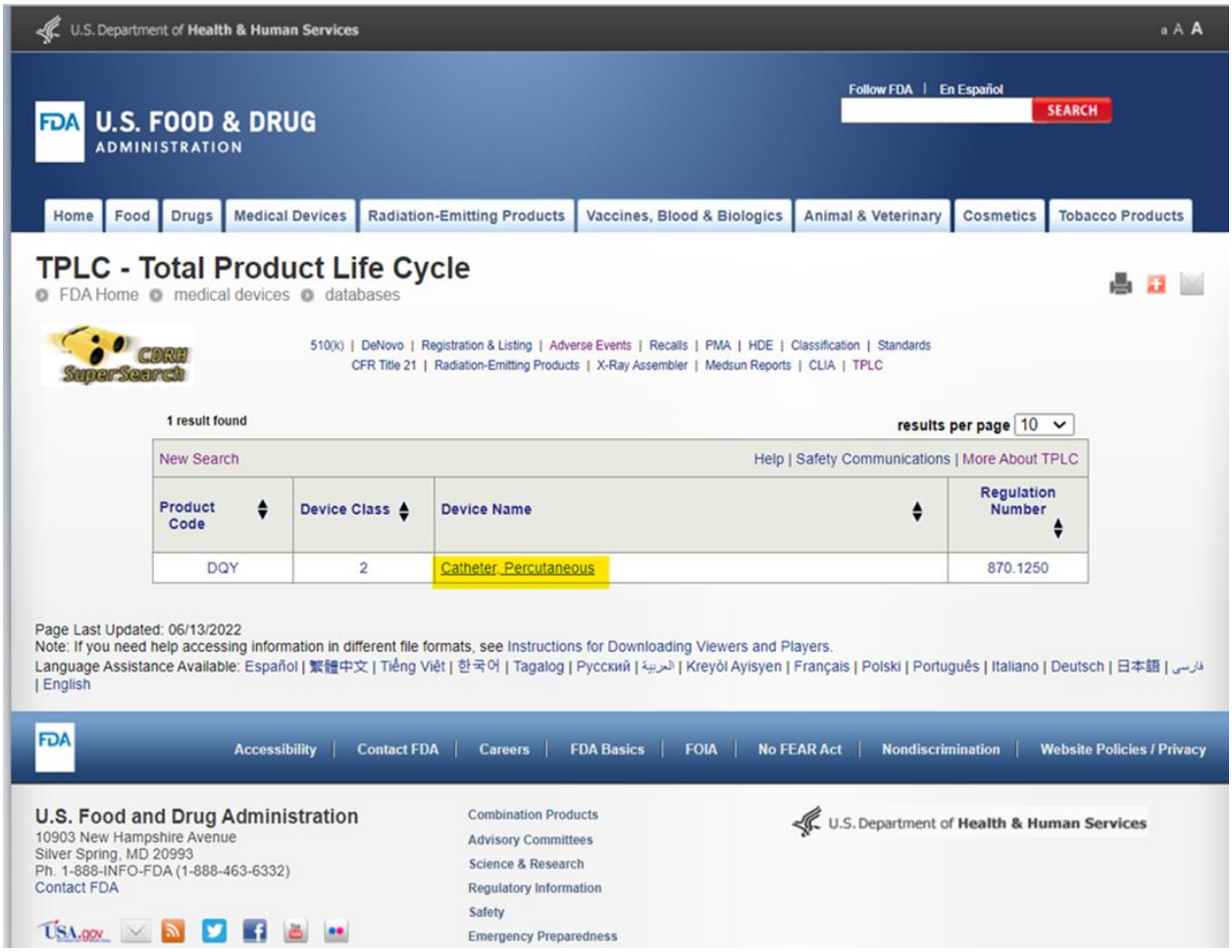
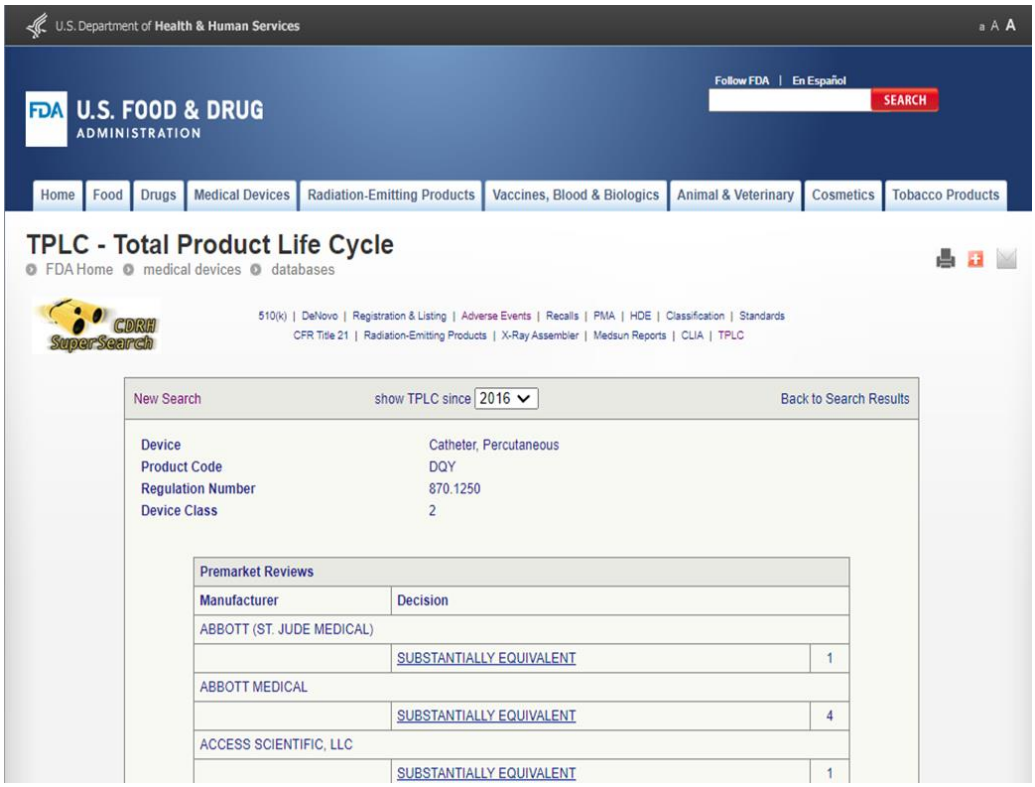


Figure 35: Showing the search result of TPLC

vi. Upon clicking on the hyperlink of device name another page opens up containing the information as per the search criteria.

vii. The whole data was retrieved into the excel sheet and then the data cleaning and sorting was done.



Device Problems	MDRs with this Device Problem	Events in those MDRs
Material Rupture	3465	3465
Adverse Event Without Identified Device or Use Problem	1865	1865
Break	1858	1858
Material Deformation	1392	1392
Detachment of Device or Device Component	1028	1028
Leak/Splash	825	825
Kinked	696	696
Physical Resistance/Sticking	681	681

Recalls			
Manufacturer		Recall Class	Date Posted
1	Abbott	II	Apr-07-2022
2	Arrow International Inc	II	Feb-14-2020
3	Arrow International Inc	II	Apr-10-2019
4	Arrow International Inc	II	Jan-11-2019
5	Arrow International Inc	II	Jun-29-2018
6	Arrow International Inc	II	May-30-2018

Patient Problems	MDRs with this Patient Problem	Events in those MDRs
No Consequences Or Impact To Patient	8196	8196
No Clinical Signs, Symptoms or Conditions	3225	3225
No Known Impact Or Consequence To Patient	2022	2022
No Patient Involvement	937	937
Vascular Dissection	420	420
Device Embedded In Tissue or Plaque	397	397

Figure 36: Showing search results of TPLC

3.3 Automated statistical tool for the estimation of product usage in the field:

This project was done to establish a statically sound tool for estimating the product usage, based on the available historical data (sales, complaints, change) that will eliminate the need for time consuming manual analyses. When a change has been made to product and the new and old version are in circulation in the market, and the data that come from market is in mixture of both old and new version of the product. So, it becomes very difficult and time consuming to assess the effectiveness and progress of the change made to the products. This automated tool will help in doing all the analyses within fraction of time. Following are the various steps that were followed:

- Data collection: First step was the collection of different data sets such as Sales data, Complaint's data, distribution data.
- After the data collection, data was compiled, sorted and filtered as per the requirement.
- Then the lead time of use (i.e., time from product manufacture to actual use) was calculated.
- Using the change data, the data was differentiated into different versions in order to see the trends and patterns of the past.
- Multiple Pivot charts were created in excel to visual the data better.
- Using the Minitab, data analysis was done.
- Multiple regression analysis was done in Minitab to get the prediction equation.

Chapter: 4 RESULTS & DISCUSSION

4.1 Effect of CMC – Complaint Submission

Month	Team Total	Submitted by Hinan	Contribution
January	449	40	9%
February	431	37	9%
March	722	66	9%
April	494	41	8%
May	585	60	10%

Table 12: Effect of Complaint submission by CMC coordinator

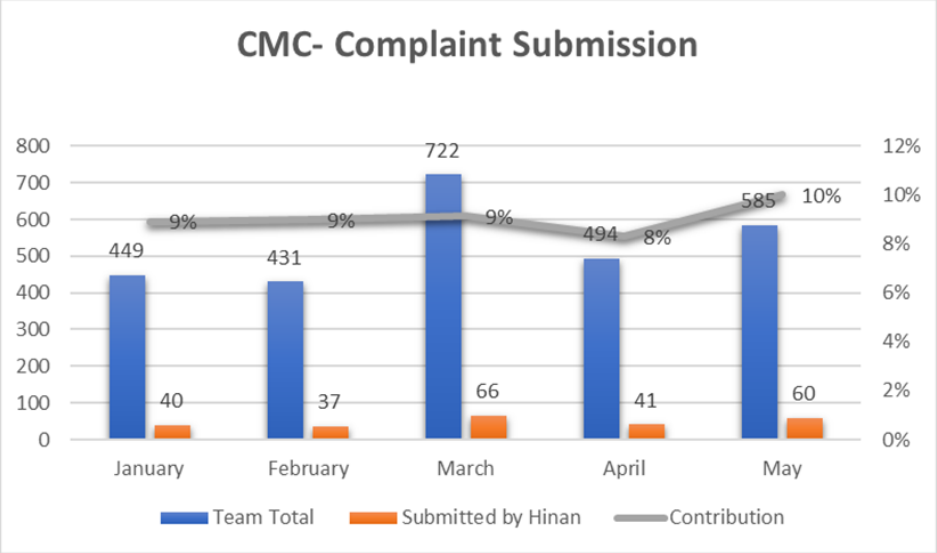


Figure 37: Effect of Complaint submission by CMC coordinator

Inference: The recorded data is for 5 months, the complaint handling team submitted 449 complaints total in the first month, of which I, as a CMC coordinator, submitted 40. My

contribution in this month was 9%. The complaint handling team submitted 431 complaints total in the second month, of which I, as a CMC coordinator, submitted 37. My contribution in this month was 9%. The complaint handling team submitted 722 complaints total in the third month, of which I, as a CMC coordinator, submitted 66. My contribution in this month was 9%.

the complaint handling team submitted 494 complaints total in the fourth month, of which I, as a CMC coordinator, submitted 41. My contribution in this month was 8%. The complaint handling team submitted 585 complaints total in the fifth month, of which I, as a CMC coordinator, submitted 60. My contribution in this month was 10%. As a result, the complaint submission was successfully done.

4.2 Effect of Complaint Closure

Month	Submitted by Hinan	Team Total	Contribution
January	0	498	0%
February	11	586	2%
March	44	625	7%
April	52	562	9%
May	52	625	8%

Table 13: Effect of Complaint Closure by CMC coordinator

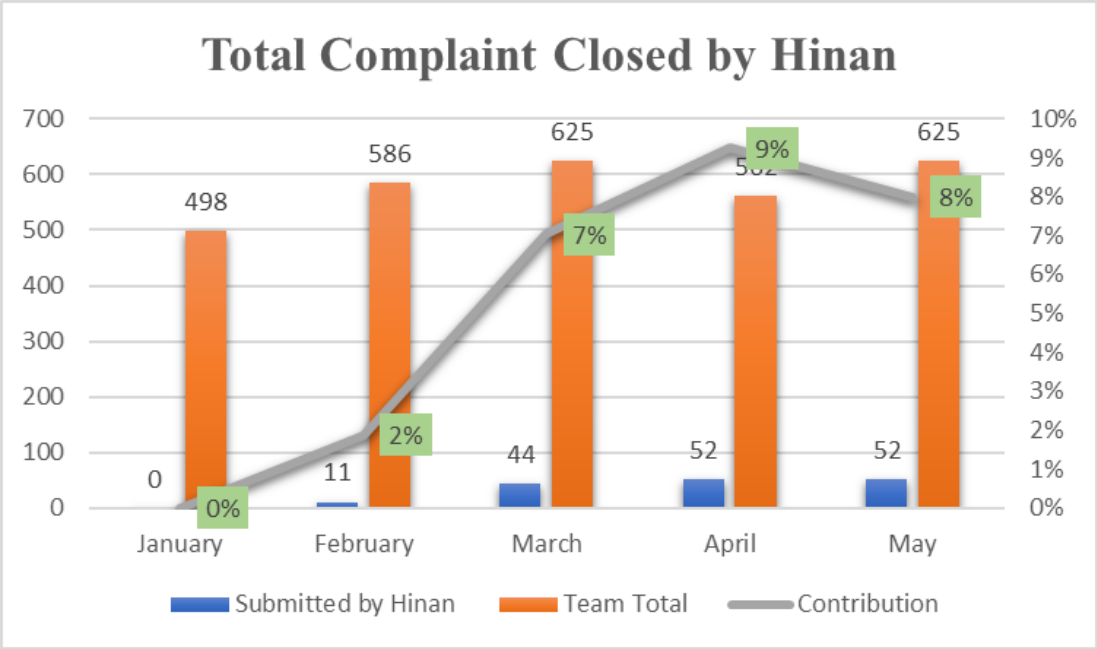


Figure 38: Effect of Complaint Closure

Inference: This data is recorded for 5 months, as the complaint requires at least 30 days for all the investigation to be done, so no complaint was closed in the first month. In second month, 11 complaints were closed by me. In third month, 44 complaints were closed by me. In fourth month, 52 complaints were closed by me. In fifth month, 52 complaints were closed by me. Therefore, in total I have closed 159 complaints in 5 months.

4.3 Effect of MDR submission

Month	Submitted by Hinan	Team Total	Contribution
April	1	76	1%
May	3	96	3%

Table 14: Effect of MDR by CMC coordinator

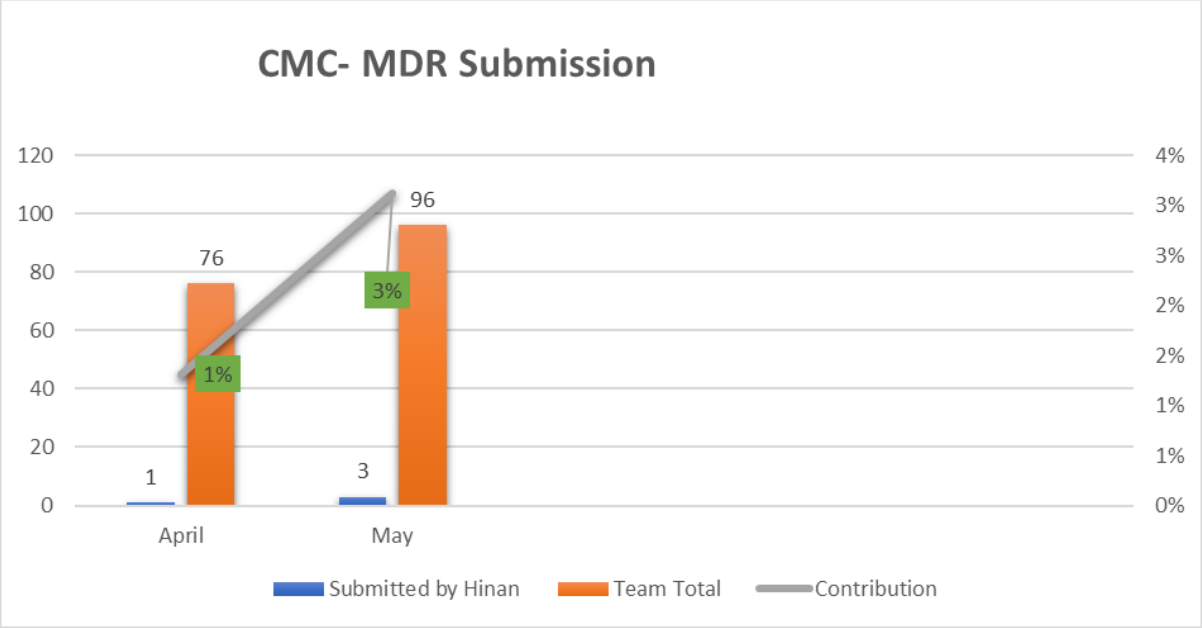


Figure 39: Effect of MDR Submission

Inference: This data is recorded for 2 months, the complaint handling team submitted 76 MDR total in the first month, of which I, as a CMC coordinator, submitted 1. My contribution in this month was 1%. The complaint handling team submitted 96 MDR total in the second month, of which I, as a CMC coordinator, submitted 3. My contribution in this month was 3%. Therefore, the MDR submission was successfully done.

4.4 Periodic Safety Update Report

Evaluation Period:- AUG 2016- JUL 2021

Incidents Summary (MAUDE)

Product Code	Product Type	Death	Injury	Malfunction	NA/ Other	Total
DQY	Guide Catheter	46	587	3880	2	4515
DQY	Intermediate Catheter	24	182	1212	0	1418
DQY	Balloon Guide Catheter (BGC)	52	539	3987	0	4578
DQY	Microcatheter	46	823	1899	0	2,768
Grand Total		**168**	**2,131**	**10,978**	**2**	**13,279**

Figure 40: Showing Incident summary from MAUDE of DQY

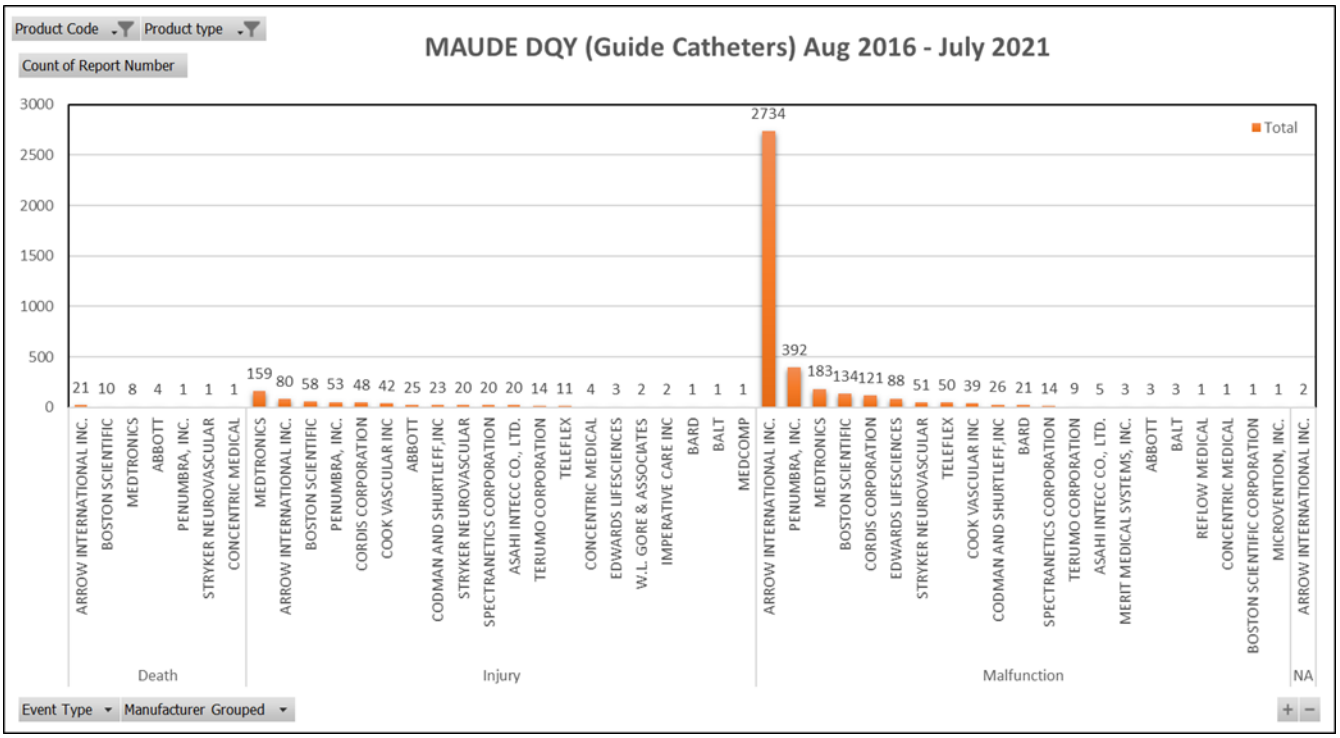


Figure 41: Showing MAUDE data for Guide catheters

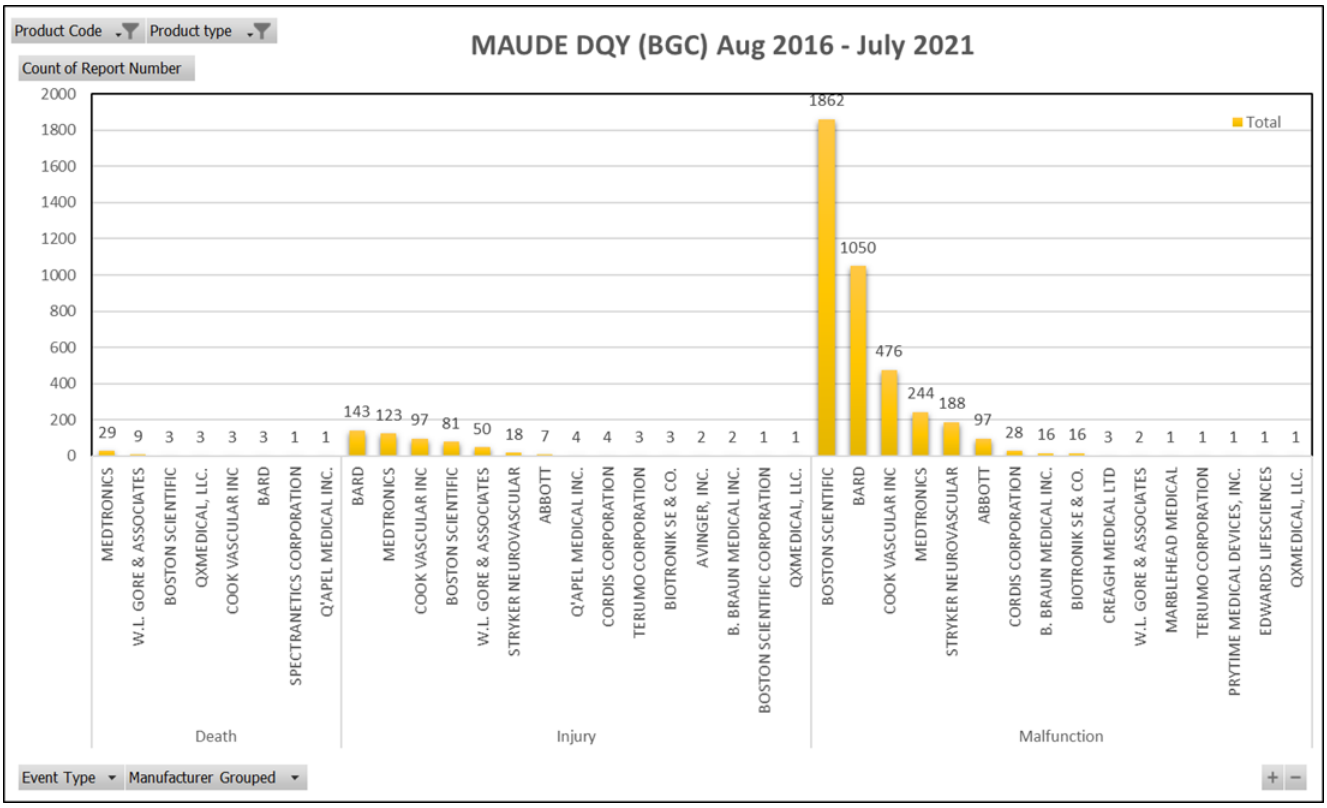


Figure 42: Showing MAUDE data for Balloon Guide catheters

1	**TPLC for DQY**			Data Retrieved on: 18-OCT-2021
2	**Device**	Catheter, Percutaneous		
3	**Regulation Description**	Percutaneous catheter		
4	**Product Code**	DQY		
5	**Regulation Number**	870.125		
6	**Device Class**	2		
7				
8		**Recalls**		
9	**Manufacturer**	**Recall Class**	**Date Posted**	
10	Arrow International Inc	II	Feb-14-2020	Arrow FlexTip Plus(R) Epidural Catheterization Kit, Arrow Pressure Injectable Two-Lumen PICC Kit 5, Arrow M
11	Arrow International Inc	II	Apr-10-2019	Arrow® Two-Lumen Central Venous Catheterization Set With Blue FlexTip® Catheter
12	Arrow International Inc	II	Jan-11-2019	Arrow CVC 2 Lumen, Pediatric Two-Lumen Central Venous Cauterization Set With Blue FlexTip Catheter, 4 Fr
13	Arrow International Inc	II	Jun-29-2018	Multi-Lumen Central Venous Catheterization Set With Blue FlexTip Catheter
14	Arrow International Inc	II	May-30-2018	Catheter Hemostasis Valve For Use With .038" (.096 Cm) Dia. And Smaller Guide Wires, Continuous Nerve Blc
15	Arrow International Inc	II	Apr-10-2018	MAC Two-Lumen Central Venous Access Kit, ARROWg+Ard Blue(R) MAC(TM) Two-Lumen Central Venous Acc
16	Arrow International Inc	II	Feb-20-2018	Pressure Injectable ARROWg+Ard Blue PLUS Multi Lumen Central Venous Catheterization Kit, Multi Lumen Ce
17	Arrow International Inc	II	Jun-12-2017	Arterial Catheterization Kit, Single-Lumen Central Venous Catheterization Kit With Blue FlexTip(R) Catheter,
18	Bard Peripheral Vascular Inc	II	Oct-08-2020	Bard Conquest PTA Balloon Dilation Catheter
47	**Device Problems**	**MDRs with this Device Problem**	**Events in those MDRs**	
48	Material Rupture	3049	3049	
49	Break	1726	1726	
50	Adverse Event Without Identified Device or Use Problem	1506	1506	
51	Material Deformation	1283	1283	
52	Detachment of Device or Device Component	909	909	
53	Leak/Splash	730	730	
54	Kinked	696	696	

Figure 43: Showing TPLC recall summary for DQY

Inference: The data for DQY was successfully retrieved from MAUDE and TPLC databases. Further, the data compilation was also done. Various Pivot table and charts were created to better analyses and comparison of how Stryker Neurovascular products are doing in the Market as compared to the competitor products. It was seen that incase of the guide catheters, for example the death cases for SNV were 1 as compared to the competitor Arrow international which has 21 death cases in. In case of serious injury SNV has 20 cases as compared to Medtronic which has 159 cases. In Malfunctions, SNV has 51 cases as compared to Arrow International which has 2734 cases.

Furthermore, for Balloon guide catheters, SNV 0 death cases as compared to Medtronic which has 29 death cases. In the case of serious injury, SNV has 18 as compared to Bard having 143 cases. Also, for the Malfunctions, SNV has 188 cases as compared to Boston Scientific having 1862.

Overall, it was concluded after the data analysis that the Stryker Neurovascular products are having less risk over benefits compared to the competitor devices.

4.5 Automated Statistical tool for product usage in the field

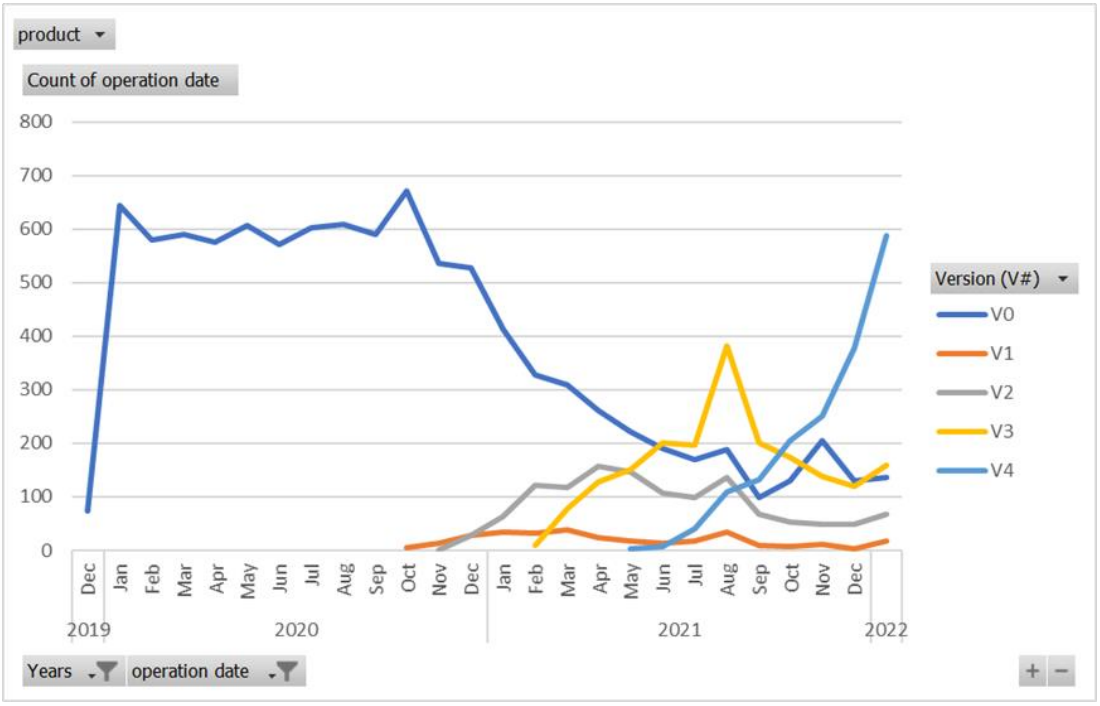


Figure 44: Showing the distribution of sales of different versions of same product across the timeline.

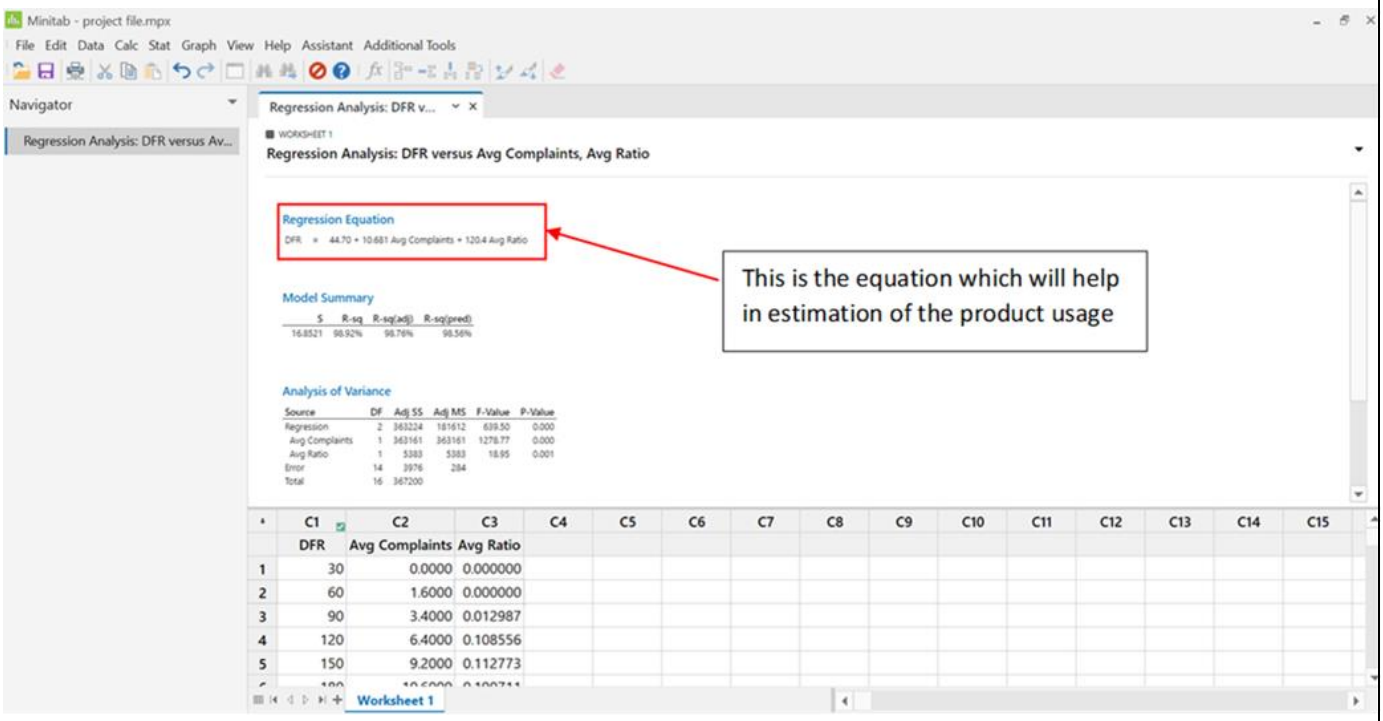


Figure 45: Showing the equation for the estimation of product usage.

Inference: The data analysis was done in Minitab and the equation was successfully obtained for the estimation of product usage. Furthermore, the automation of this tool will be done in the PowerBI. This is an ongoing project for automation which will be taken care by other team in division. Hence, the statistical method was successfully developed from our end.

CONCLUSION

Complaint handling is another crucial Quality Function that supports in identifying issues or risks related with Stryker Neurovascular products so that improvements can be made to the product and the best possible service can be provided to the customer. Every complaint about a Neurovascular product is taken into account, regardless of the causes, and is assessed, reviewed, and investigated according to processes, with corrective and preventative actions taken as needed. The organization investigates the complaints, which assists in the improvement and enhancement of the condition. The current project focuses on the Stryker Neurovascular' s complaint management.

- I have submitted total of 244 complaints in 5 months and my overall contribution is 9% in the team.
- I have closed _ PIs and 159 Complaints in 5 months.
- I have submitted total of 4 MDRs in 2 months and my overall contribution is 2% in the team.

A Periodic Safety Update Report is a report that summarizes essential actions and conclusions generated from medical device post-market surveillance data. Even if the product is no longer on the market, all associated preventative and corrective activities should be documented throughout its lifetime. For each device, manufacturers of class IIa, class IIb, and class III must prepare a periodic safety update report. Stryker Neurovascular also prepares PSUR for its products and the data retrieval is the first step in PSUR formation and is very important step. I have successfully retrieved data from various public databases (MAUDE, TPLC) for catheter file. After data retrieval, I have complied, sorted the data, and plotted various Pivot graphs for better visualization and analysis of data.

Statistical analysis is a type of data analysis that helps to derive usable conclusions from unstructured and raw data. Statistical analysis is the process of working with data to obtain valuable information from data. It is utilized by businesses and other organizations. So, this project focuses on creating such statistical tool for the estimation of future usage of product in the field which will help in reducing the ad hoc manual process which are very time consuming.

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Document Information

Analyzed document	Final Thesis Hinan (602004010) pdf (D141295466)
Submitted	2022-06-27 06:56:00
Submitted by	Sumanta Sarathi Sharma
Submitter email	ss.sharma@smvdu.ac.in
Similarity	13%
Analysis address	ss.sharma.smvdu@analysis.urkund.com

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28/06/2022