SWIFT CTMS & PAYMENTS TRIGGERS FOR NEUROVASCULAR PRODUCT TESTING

A Dissertation

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*By*

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# DECLARATION

I hereby declare that the work being presented in the dissertation report entitled SWIFT CTMS & PAYMENTS TRIGGERS 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 Dr. Ashish Indani. 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: 29-06-2022 Aarushi Mehtani

# CERTIFICATE

This is to certify that the dissertation titled **"**SWIFT CTMS & PAYMENTS TRIGGES, by Aarushi Mehtani, in partial fulfilment for the award of the degree of Master of Technology in Biotechnology Engineering, is a record of candidate's own work carried out by her under the supervision of **Dr**. **Ashish Indani**, Sr. Manager Clinical Affairs, Stryker Neurovascular**.** The matter embodied in this dissertation has not been submitted for the award of any other degree or diploma to the best of my knowledge and belief.

Signature of Industrial mentor:

**Dr. Ashish Indani**

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Stryker Neurovascular

Gurugram

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Aarushi Mehtani

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# ABBREVIATIONS

| | |
|---|---|
| **ACA** | Affordable Care Act |
| **ADaM** | Analysis Data Model |
| **ADR** | Adverse Drug Reaction |
| **AE** | Adverse Event |
| **AMC** | Academic Medical Center |
| **ARO** | Academic Research Organization |
| **CCEA** | Complete, Consistent, Enduring, Available |
| **CDASH** | Clinical Data Acquisition Standards Harmonization |
| **CDISC** | The Clinical Data Interchange Standards Consortium |
| **CDS** | Clinical Data System |
| **CMO** | Contract Manufacturing Organization |
| **COA** | Clinical Outcome Assessments |
| **CRA** | Clinical Research Associate |
| **CRC** | Clinical Research Coordinator |
| **CRF** | Case Report Form (less frequently |
| **CRO** | Contract Research Organization |
| **CSDD** | Center for the Study of Drug Development |
| **CSO** | Contract Safety Organization |
| **CTMS** | Clinical Trial Management System |
| **CVM** | Center for Veterinary Medicine |
| **DDC** | Direct Data Capture |
| **DM** | Data Manager |
| **DSMB** | Data and Safety Monitoring Board |
| **eCOA** | Electronic Clinical Outcome Assessments |
| **eCRF** | Electronic Case Report Form |
| **ePRO** | Electronic Patient-Reported Outcome |
| **EDC** | Electronic Data Capture |
| **EHR** | Electronic Health Record |

| | |
|---|---|
| **eICD** | Electronic Consent Document |
| **EMR** | Electronic Medical Record |
| **eSource** | Electronic Source Data |
| **eTMF** | Electronic Trial Master File |
| **FDA** | Food and Drug Administration |
| **FIH** | First in Human |
| **FPI** | First Patient In |
| **GCP** | Good Clinical Practice |
| **GDP** | Good Documentation Practices |
| **GDPR** | General Data Protection Regulation |
| **HHS** | Department of Health and Human Services |
| **HIPAA** | The Health Insurance Portability and Accountability Act |
| **IC** | Informed Consent |
| **ICD** | Informed Consent Document |
| **ICF** | Informed Consent Form |
| **ICH** | International Council for Harmonization |
| **IEC** | Independent Ethics Committee |
| **IIT** | Investigator-Initiated Trial |
| **IND** | Investigational New Drug |
| **IRB** | Institutional Review Board |
| **MD** | Doctor of Medicine |
| **MDR** | Medical Devices Regulation (EMA) |
| **NBE** | New Biopharmaceutical Entity |
| **NCE** | New Chemical Entities |
| **NDA** | New Drug Application |
| **NIH** | National Institutes of Health |
| **OCT** | Office of Clinical Trials |
| **OHRP** | Office for Human Research Protections (Overseen by the Department of Health and Human Services) |
| **PCR** | Pending Changes Report |

| | |
|---|---|
| **PDUFA** | Prescription Drug User Fee Act |
| **PHI** | Protected Health Information |
| **PII** | Personally Identifiable Information |
| **Pl** | Principal Investigator |
| **PRO** | Patient-Reported Outcome |
| **RTSM** | Randomization and Trial Supply Management |
| **SAE** | Serious Adverse Event |
| **SDTM** | Study Data Tabulation Model |
| **SDV** | Source Document Verification |
| **SOP** | Standard Operating Procedure |
| **tSDV** | Targeted Source Document Verification |
| **TMF** | Trial Master File |
| General Software Terms | |
| **API** | Application Program Interface (also |
| **CSV** | Comma-Separated Values |
| **EDC** | Electronic Data Capture |
| **GUI** | Graphical User Interface |
| **IRT** | Interactive Response Technology |
| **IVR** | Interactive Voice Response |
| **ODM** | Operational Data Model |
| **SaaS** | Software as a Service |
| **SAS** | Statistical Analysis System |
| **SPSS** | Statistical Package for the Social Sciences |
| **TFS** | Team Foundation Server |
| **UAT** | User Acceptance Testing |

# TERMINOLOGY

This section gives a short overview of the nomenclature, actors, processes, events and documents involved with clinical trial management file.

1. **Clinical Trial Management System** (CTMS) is a software system used by biotechnology and pharmaceutical industries to manage clinical trials in clinical research.
2. eTMF an electronic master file or eTMF is a Trial Master File in electronic or digital format. It is a way of digitally capturing, managing, sharing and storing those essential documents and content from a clinical trial.
3. Payments: The date that the first person in Stryker becomes aware of an event.
4. Electronic Data Capture is just one of the steps in that process - creating protocols and case report forms, recording patient data, and sending it to where it belongs.
5. Trial registration and approval When initiating a clinical trial, multiple registrations and approvals are mandatory. A registration at an authority is usually bound to deadlines and yields some file number returned by the authority. A remarkable written permit is the ethics committee vote, which clarifies ethic concerns and commensurability and has a limited validity period. At the end of the trial, the sponsor has to provide a final study report to authorities. Trial registries such asclinicaltrials.gov allow searching for ongoing and closed trials.
6. Trial site The local organization or department, whose personnel effectively performs investigations with subjects will be denoted as trial site or center. A trial site can be a department of pharmaceutical company, clinic, medical school or an (interdisciplinary) CRO.
7. Trial protocol A trial protocol is a document provided by the sponsor, which defines the trial's procedures
8. The visit schedule defines the chronological sequence of investigation visits. Typically, detailed work instructions and a Case Report Form (CRF) are attached for each visit
9. Eligibility criteria Eligibility criteria comprises inclusion and exclusion criteria for participants of a concern trial, which are examined during the initial visit (screening visit).

"[Inclusion and exclusion Criteria] are based on such factors as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions."

10. Recruitment The recruitment is the systematic establishment of a candidate stock with a volume required for the trial. When registering a candidate, storing Personally Identifiable Information (PII) such as contact details will require a data privacy consent signed by the candidate. Recruitment can be started for a particular trial by means of dedicated contacting or public appeals, such as advertisement campaigns. Since sponsors may choose a contracting site according to the volume of their established registry of readily available candidates, the CRO's recruitment strategy may rely on a permanent recruitment process.
11. Candidate, Subject A candidate is a person interested in participating trials, who is registered during recruitment. If eligibility and regulatory criteria are met, the candidate is enrolled for a particular trial.
12. Informed Consent After education about the trial's process, details and risks and the proband's rights, a candidate approves his knowledge and agreement by signing the Informed Consent (IC). A signed IC is a precondition for participation, usually expressed as a particular inclusion criterion. The IC may also stipulate a financial compensation for participation and expenditures, if allowed by regional regulations.
13. SOP Standard Operating Procedures (SOPs) are written work orders for general tasks, device usage or established procedures at the trial site and represent an essential QM instrument. Specific SOPs may be created for a particular trial or even provided as part of the trial protocol.
14. Visits Trial site staff performs actual interventions and examinations during a sequence of investigation visits (e.g. screening visit, treatment or dosing visits), under surveillance of the investigator.
15. Source data, CRF Source data and completed CRFs represent the valuable outcome of investigations Source data like questionnaire answers, medical assessments or lab reports is collected according to visit SOPs. Finally, the source data is aggregated and entered into CRF documents, attached to the trial protocol. Coding is the task of assessing or normalizing data according to scores or schemes in the course of infilling CRFs. Both source data and CRFs are prepared for delivery when completed. In terms of a CDMS, the CRF data entry will be locked and exported at this point (database release). The sponsor receives data in

raw paper and/or electronic format for subsequent review at reading centers and analysis. The workflow for tracking caveats and inconsistencies of CRFs follows a structured resolution workflow, which is sometimes referred to as query management.

16. Audit Audits are performed by internal monitor personnel (internal audits) as well as external Clinical Research Associates (CRAs) (external audits) or commissioners (authoritative audits6). External and authoritative audits can be scheduled by a sponsor or regulator without announcement or on a regular basis. An audit should confirm the proper adherence to the trial protocol and regulations such as GCP.Violations identified during an authority's audit have to be reported (finding) and may inflict a penalty.

# ABSTRACT

The study is based on the clinical Function of the Stryker Neurovascular division.

Conducting a clinical trial can be tedious, CTMS helps us to conduct a clinical trial more efficiently and reduce the cost. CTMS can be used for all four phases of a clinical trial. Research sites, institutions, sponsors, and contract research organizations (CROs) use clinical trial management systems to ensure studies' success. Some of the many reasons a CTMS is important are that it saves time and reduces frustration over the course of a study by Providing ready access to an overview of the progress of a study with continuous and up-to-date reporting, Allowing study leaders to plan tasks and activities as well as assign responsibilities, and track and monitor activities, Organizing all of the study's relevant documents and information, Managing a range of different assets and associated clinical trials, Facilitating compliance with regulatory requirements. Configuration of different modules

As a part of implementation of CTMS, Stryker set up a Project SWIFT that was targeted to onboard various studies, their electronic data capture systems, electronic trial master file and invoicing and payments for the clinical sites using CTMS module. This project included configuration of the payments and invoicing module, assigned as an internship project and was the basis of this thesis.

# Contents

# 1 Introduction

## 1.1 Neurovascular diseases and their transcatheter treatment

In USA, Stroke is the fifth leading cause of death contributing to over 142,000 incidents and approximately 5% (1 in 19) death In Australia, 1.2 million (4.8%) population had Heart, stroke and vascular disease [1] of which, 141.4 persons per Million are stroke alone[1]. The Statistics also demonstrate (for Australia) that the incidence suddenly raises after 65 years of age Similar incidence can be observed in various European (1.12 /512 million incidence 9.53/512 Million prevalence) [2] and Asian countries [3]. Major concerns about stroke associate with its high mortality and post-survival morbidity Hence, it has taken an additional highlight in space of Medicine. Over last two hand half decades, stroke research has progressed in understanding stroke pathophysiology, multiple pathways causing stroke and its treatment, through animal experimental models, therapeutic drugs, clinical trials and post-stroke rehabilitation studies. However, the research is continuing to reach to mitigate gaps still existing in the knowledge about stroke especially towards inability to translate the outcomes of current research into clinical settings[2]. The hemorrhagic stroke which contributes to about 20% of the stroke incidence the world, is mainly caused by rupture of aneurysm in cerebral vasculature leading to intracranial hemorrhage and further a stroke. Ischemic stroke which precedes reduced blood supply to the brain due to thrombosis or stenosis of the arteries supplying brain, contributes to about 80-87% of the stroke incidence [3].

The treatment of stroke has off-late gained major leap pertaining to the changes produced by evidence-based therapy[3]. Along with various medicinal management options, the surgical and endovascular treatment options have significantly advanced. The advancement in endovascular therapy like Aspiration-retriever technique for stroke (ARTS), Distal aspiration with Catheters, Mechanical thrombectomy, and Recanalization are considered to have improved the treatment for stroke more efficient despite unclear patient reported outcomes[4]. Hence, several clinical bodies followed a systematic approach to formalize guidelines for stroke treatment. Among these guidelines, the major and well accepted are guidelines issued by American Heart association / American Stroke Association (AHA/ASA)[5], Royal College of Physicians UK (RCP), European

Stroke Organization (ESO), Indian Stroke Association (ISA), Australian Stroke Foundation (SF) and Australian Institute of health and welfare (AIHW). These guidelines are important artefacts not only in determining the clinical course of the treatment but also to understand the met and unmet needs in the therapy of stroke.

## 1.2 Stryker Corporate and Stryker Neurovascular

Stryker Corporation is a global medical technology firm with a mission focused on customers and the statement is “Together with our customers, we are driven to make healthcare better.” Stryker is head quartered in Kalamazoo, Michigan, USA and operates in numerous markets such as in North and South America, Europe, the middle East, Africa and Asia. Stryker has set up a generation improvement middle in India that typically cognizance on design, improvement and production help of Stryker merchandise for worldwide market. Stryker procedures are properly aligned to conventional of ISO 13485:2016 for medical gadgets and has additionally been constantly progressed thru auditing manner over more than one decade. Also, the procedures meet the necessities of 21CFR820 as consistent with U.S FDA and different regulatory our bodies of various international locations wherein Stryker conducts such commercial enterprise activities.

Stryker's global net sales grew to $17.1 billion U.S. dollars billion in 2021, the 42nd consecutive year of growth. Stryker employs approximately 40,000 people worldwide. Stryker sells its products in more than 100 countries and has 30 manufacturing and R & D bases worldwide. Stryker offers innovative products and services through the design and manufacture of a variety of orthopedic, medical, surgical, neurotechnology, and spinal devices that help improve patient and hospital outcomes. Neurotechnology is a business that falls into the cranial and neurovascular divisions.4

## 1.3 Medical devices

A medical device can be a machine, instrument, apparatus, or an article that is used to diagnose, monitor, and therapeutic purposes. A medical device plays an essential role, such as detection, measurement, restoration, and modification of the structure or a function of the body

due to health problems or chronic medical conditions. Stryker promotes minimally invasive treatment practices through innovative products and services for ischemic and hemorrhagic stroke. Stroke is a condition in which blood vessels that carry oxygen and nutrients to the brain are blocked or ruptured (or ruptured) by blood clots. When that happens, the brain and brain cells die because parts of the brain cannot get the blood (and oxygen) they need. [5] There are also two types of strokes: ischemic stroke and hemorrhagic stroke. In ischemic stroke, the blood supply to a part of the brain is reduced, causing dysfunction of brain tissue in that area. It is caused by thrombosis, embolism [6], systemic hypoperfusion [7], and cerebral venous sinus thrombosis. Hemorrhagic stroke is caused by bleeding in the brain and causes brain dysfunction [12]. There are also two types of hemorrhagic stroke [8] ie. Intracerebral hemorrhage (intracerebral hemorrhage) and subarachnoid hemorrhage (intracranial hemorrhage outside the brain tissue). According to WHO, 15 million people worldwide suffer from stroke each year. Of these, 5 million have died and another 5 million are permanently disabled. High blood pressure causes more than 12.7 million strokes worldwide. Stryker NV's product range includes a broad, balanced and successful product portfolio for HEM, AIS, ICAD treatment areas, and access products to reach affected sites. They are categorized as follows: Access: As the word means “A way to Approach” these products are used to approach the site. Because the insertion site for these intravascular procedures is the femoral artery, these access devices are required for the implant to reach the target site in the brain. It includes:

Catheters: These are catheters designed to help and assist the device in rapidly accessing the target site. There are AXS Catalyst 5, AXS Catalyst 6, AXS Catalyst 7, AXS Infinity LS, AXS Infinity plus, AXS Offset. There are several microcatheter designed to provide high performance and versatile performance. It also provides smooth tracking and stable delivery. There are Excelsior 1018, Excelsior SL-10, Excelsior XT-17, Excelsior XT-27

*Figure 1: Excelsior XT- 17*

*Figure 2: AXS Catalyst*

Guidewires: Synchro guidewires are designed to enhance torque transmission through its microfabricated outer structure while Transend offers control and responsiveness Those coatings facilitate advancement through the microcatheter. They serve as a guide for the catheter to reach the target site. The doctor follows these guide wires in the fluoroscopy and advances the catheter backwards. Once in place, the guidewire is pulled out of the lumen of the catheter.

Figure 3: Transend

*Figure 4: Synchro*

Balloon Catheters: These catheters are designed to Track high, protect well and designed for rapid access and reliable proximal flow control e.g., Flow gate 2. There is also have Merci balloon guiding catheter for protection and support.

*Figure 5: Flow Gate*

Angioplasty & Stenting: An endovascular procedure with minimal invasion to widen narrowed or occluded vessels, mainly used to treat arterial atherosclerosis is known as angioplasty. A deflated balloon catheter is passed over a guide-wire into the narrowed vessel and then inflated to a fixed size. This balloon helps in expansion of the blood vessel and the surrounding muscular wall which increases the blood flow. To ensure that the vessel remains open at the time of ballooning a stent is inserted and then the balloon is deflated and withdrawn. Angioplasty includes all manner of vascular interventions that are typically performed transcutaneous. This includes:

Stents: The stent system is designed to provide improved compatibility, stability, and ease of use. Flexible design with self-expanding Nitinol stent. The unique adaptive cell design provides the coil support and wall juxtaposition needed to perform safe and effective stent-assisted coil embolization. e.g., Neuroform Atlas and Neuroform EZ (pre-loaded on the delivery wire)

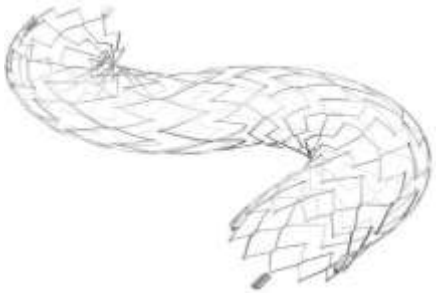

*Figure 7: Neuroform Atlas*

*Figure 6: Neuroform EZ*

Flow Diverters: A technology used to redirect blood flow to avoid rupture of an aneurysm in a blood vessel. They are designed to provide optimized flow diversion e.g. Surpass Streamline.

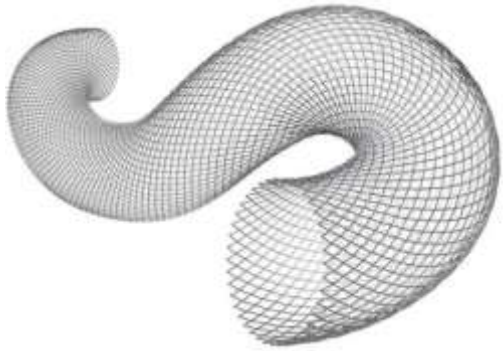

*Figure 8: Surpass Streamline*

ICAD Stent: Wingspan is designed for intracranial atherosclerotic disease. This stent system is with gateway PTA balloon catheter which facilitates access through challenging neurovascular anatomy.

*Figure 9: Wingspan Stent*

Embolization: This is a procedure that blocks blood vessels that cause tumors and abnormal growth. This procedure uses a coil and a balloon catheter to block blood flow. There are various coils for filling an aneurysm, depending on the size and structure required to fill the aneurysm. B. Target 360, Target 3D, Target Nano, Target XL, Target XXL. A balloon catheter, i.e., Transform, is also used in this procedure to block blood flow.

*Figure 11: Target 360*

*Figure 10: Transform*

Thrombectomy: An intervention procedure used when a blood clot or blood clot is blocking a blood vessel in the brain. The procedure is to surgically remove the blood clot from the blood vessels. Therefore, thrombectomy includes a retriever (Trevo XP) specifically designed to remove thrombi in patients with ischemic stroke. There are also suction systems; AXS Universal and AXS Vecta71. It provides more power for suction with next-generation vacuum technology to improve the aspiration of thrombus in the neurovascular system.

*Figure 12: Trevo XP*

*Figure 13: AXS Universal*

## 1.4 Clinical Research for Medical device

A medical device clinical study or study is defined as a systematic study of a subject performed to assess performance or safety. Clinical trials conducted on pharmaceuticals and medical devices are similar, but they are designed or conducted differently, and product regulatory assessments are different from pharmaceutical regulatory assessments. Less product research is required to demonstrate efficacy and safety than drug research. Clinical evidence shows the

consistency and accuracy of the level of effectiveness that meets the application requirements described on the device. The proposed trials of the new device will be subject to a review and notification process prior to initiating clinical trials to ensure the safety of enrolled subjects.

The clinical proof of proof-of-concept research in early product development is limited to pre-finished initial product designs for specific applications. Prototype devices go through a cycle of preclinical testing and redesign to create a sophisticated, tested design that is ready for manufacturing and human testing. Pilot clinical trials are preliminary studies of device design efficacy and safety to properly plan appropriate and important studies that help collect clear statistical evidence of device efficacy and safety. Commonly used to collect information. The number of participants is used. Post-marketing clinical trials are conducted after the product has been approved for sale by a regulatory agency. Medical devices based on surgical implants cannot be used on healthy subjects. Instrument testing is initiated by a small pilot study and then expanded to a larger population of relevant diseases.

To enable display and guarantee the desired functionality of the device, medical device research sponsors incorporate at least one diagnostic imaging technique. Manufacturers of in vitro and implanted diagnostic equipment ought to do safety studies on any potential negative impacts on a patient's health. The medical issues that research participants dealt with during their participation must also be reported, even though they have nothing to do with the technology. Depending on the device and study design, device research incorporates medical experts such as researchers, psychologists, physiotherapists, clinical trial coordinators, device engineers or programmers, medical imaging or pathology staff. is necessary. Investigators and field staff must receive practical training on the device and methodology in order to evaluate the device's effectiveness and safety.

## 1.5 Need for Standard systems to manage clinical research

The management of clinical trials must include safeguards for human subjects. Institutions and people engaged in clinical research involving human subjects must receive approval from regulatory organizations like the Food and Drug Administration (FDA) and from supervision organizations like regional Institutional Review Boards (IRB). To conduct research with human beings, researchers must also establish, document, and uphold the proper credentials, training,

and precautions. Regulatory documentation could be manually managed for a single clinical trial with a small number of participating clinical sites with the aid of a Microsoft Excel spreadsheet or relational database program like Microsoft Access.

However, a multicenter clinical trial or clinical trial network, where numerous clinical sites may carry out numerous studies concurrently, poses unique challenges for regulatory document management due to the volume of documents that must be gathered and maintained, the difficulty of managing several projects at once, the requirement for multiple owners to share document files, and the dynamic nature brought on by unavoidable changes in the study's design.

The system described below was created as a module of a comprehensive Clinical Trial Management System (CTMS) created for a clinical trial network supported by the National Institutes of Health (NIH). Utilizing a computerized RDM system is ultimately intended to facilitate project and data management tasks and to better control and monitor regulatory compliance. [15]

The FDA's Center for Devices and Radiological Health (CDRH) oversees the regulation of medical devices in the United States. The FDA/mandate CDRH's is to advance and safeguard public health by rapidly distributing safe and efficient medical devices. The risk connected to the equipment in question influences the requirement for proving safety and effectiveness. A three-tiered method is used to categories devices according to their assessed risk (class I, II, or III) [ ]

General controls, which are written requirements for labelling, manufacture, post-Market surveillance, and reporting, are applied to Class I devices (lowest risk). When there is a reasonable certainty that general controls alone are sufficient to ensure safety and efficacy, devices are classified as class I. The broad regulations that usually apply to class I devices include restrictions on adulteration and misbranding, specifications for creating registration and device listings, requirements for adverse event reporting, and best manufacturing practices. Additionally, FDA has access to remedies like seizure, injunction, criminal prosecution, civil penalties, and recall authority. Most class I devices don't need an official FDA review before going on the market. Devices classified as Class II are those with a higher risk for failure, for which general controls alone have been deemed to be insufficient to provide a fair level of assurance of their effectiveness and safety, but for which sufficient data is available to construct special controls. Performance benchmarks, design restrictions, and Post-Market observation programmers are examples of special controls. Additionally, before the device may be commercialized, the FDA must

approve a premarket notification application (PMA or 510[k]). The medical device producer must submit evidence in the 510(k) application that the new product is "substantially equivalent" to one that is lawfully marketed. About 10% of 510(k) submissions contain clinical data, even though considerable equivalence can typically be proven solely by bench and animal research.

The class III devices with the highest potential for risk are heart valves, pacemakers/implantable cardioverter-defibrillators, and coronary stents. These items either maintain or sustain life, play a significant role in protecting human health, or pose a significant risk of disease or injury. Therefore, relying just on general and specific controls to ensure safety and effectiveness does not suffice. Before they can be legally marketed, most class III devices need FDA approval of a PMA. Clinical data indicating a reasonable level of assurance that the device is safe and effective in the target population is often required for PMA approval.

# 2 Review of Literature

## 2.1 Current challenges in clinical trial management

Clinical trial management has been difficult for those working for pharmaceutical companies, contract research organizations, sites, and vendors over the past year. Clinical trial administrators are under pressure to create trials "that offer the proper answers, in the most straightforward and unobtrusive way for patients, that are acceptable to regulators and payers" as clinical trials have become more complex over the years. Many respondents feel confined by the intricacy of the regulations they follow, which is to be expected in an industry that is so extensively regulated. Additionally, the differences among various regulatory agencies and the difficulties they present are a recurring theme. Due to the seriousness of patient outcomes in the healthcare system, the healthcare sector is one that is closely watched. Clinical trial outcomes include medicines, vaccines, therapeutic procedures, and medical equipment, all of which are subject to stringent regulations. Although the existence and significance of the regulations are understandable, strictly adhering to them is a tremendous task. Even the smallest inaccuracy could jeopardize the case and result in millions of dollars in losses financially. Even with an endless number of imposed requirements, maintaining and assuring compliance remains a significant task. There is also a need to comprehend completely new sets of requirements as trials increasingly focus on rising markets in new nations. The cost of trials is at an all-time high as a direct result of the previous two problems. More emphasis is being put on the "demand for resources to implement and control every stage" due to growing complexity and short deadlines.

Another significant issue for those managing trials is the recruitment and retention of patients, with a high percentage failing to fulfil goals and drop-out rates rising. Finding and training the correct employees is becoming more difficult as trial complexity and change rates continue to rise.[10]

## 2.2 Landscape of current solutions

Clinical trial support software consists of RDBMS-based applications for process mapping and data management specific to the trial location (the "client"). Options might be viewed as related work in a broader sense when selecting to switch from spreadsheet- or paper-based workflows to a database system. CDMS The most crucial task of filling out CRFs via electronic data capture is supported by a clinical data management system (CDMS) (EDC). Site personnel (end users) are presented with input forms by an EDC software UI, allowing them to enter clinical data for each subject. There is no need for intermediary paper-based Source Data Forms because data is already available in electronic form (eCRF), which is appropriate for further processing (data analysis) (SDFs). Electronic Patient Reported Outcome (PRO) capabilities assist trial designs where participants must submit their own data, similar to eCRF. The term "CTMS" (Clinical Trial Management System) refers to database systems that cover processes involved in the organization and management of study and trial locations. When opposed to CDMSs, these processes often have a lower estimated risk. The greater range of supported processes results in a variety of possible CTMS solutions and the creation of custom software, in contrast to CDMSs that have a defined focus on EDC. A CTMS may integrate CDMS features or even interact with a different CDMS instance.

## 2.3 Requirements of CTMS in a medical device company

The crucial set of tools for efficiently planning, managing, and tracking your clinical research portfolio is the clinical trial management system. The study team uses this unique, all-inclusive project management tool from the beginning to the end of the study, including enrollment and monitoring.

Clinical trial sponsors can more effectively manage and maintain the planning, execution, and reporting of clinical trials with the help of CTMS. The CTMS is a centralized dynamic system that provides numerous uses for various participants in a clinical trial procedure. For instance, project managers can monitor and oversee the clinical trial's progress, enabling them to guarantee that investigations are carried out as planned. Authoring visit reports and submitting them for review and approval is a capability of Clinical Research Associates (CRA). Users of CTMS will

have easier access to operation statistics, milestones, and related information with increased organizational transparency.

### 2.3.1 Requirement of eTMF in medical device company.

A trial master file in electronic or digital format is known as a "electronic master file," or "eTMF." It is a method of gathering, managing, distributing, and keeping those crucial records and content from a clinical study digitally.

Every business engaging in a licensed clinical trial, often a pharmaceutical or biotech corporation, is required to abide by the regulations set forth by the government. Maintaining and storing specific crucial papers pertaining to that clinical trial is one of the fundamental requirements to satisfy regulatory compliance. A Study Master File is essentially a collection of critical records and information that demonstrates how a clinical trial was managed, carried out, and compliant with regulatory standards. These crucial records make it possible to assess the efficiency and caliber of the clinical experiment.

Using paper-based or network-based TMFs to capture and store clinical trial documentation can be time-consuming, challenging to manage, and may result in costly errors that jeopardize your clinical studies. Adopting an eTMF enables continuous document management and oversight in real-time, ensuring compliance and audit preparedness. The following are some of the main advantages:

- Manage, exchange, and approve clinical records via a web-based application at any time.
- From a web-based application, access, approve, share, and manage clinical documents whenever you want.
- Better TMF quality thanks to digital technologies' lower error rate compared to manual/paper processes
- Increased effectiveness while conducting a study

- Reduce regulatory risk: Documents and reports may be audit-ready much faster with digital systems than with paper ones.
- Less time is spent starting and ending trials.
- Quicker document retrieval and searching
- Cost savings through less paper and labor use and improved filing efficiency
- Regulatory agencies state that the following specifications must typically be met by systems and software used to hold electronic records, digital documents, and content: digital content archiving, security and access controls, change controls, audit trails, and system validation. The majority of eTMF solutions differ in how they go about digitizing and maintaining the TMF, but. the fundamental needs are nearly always there.

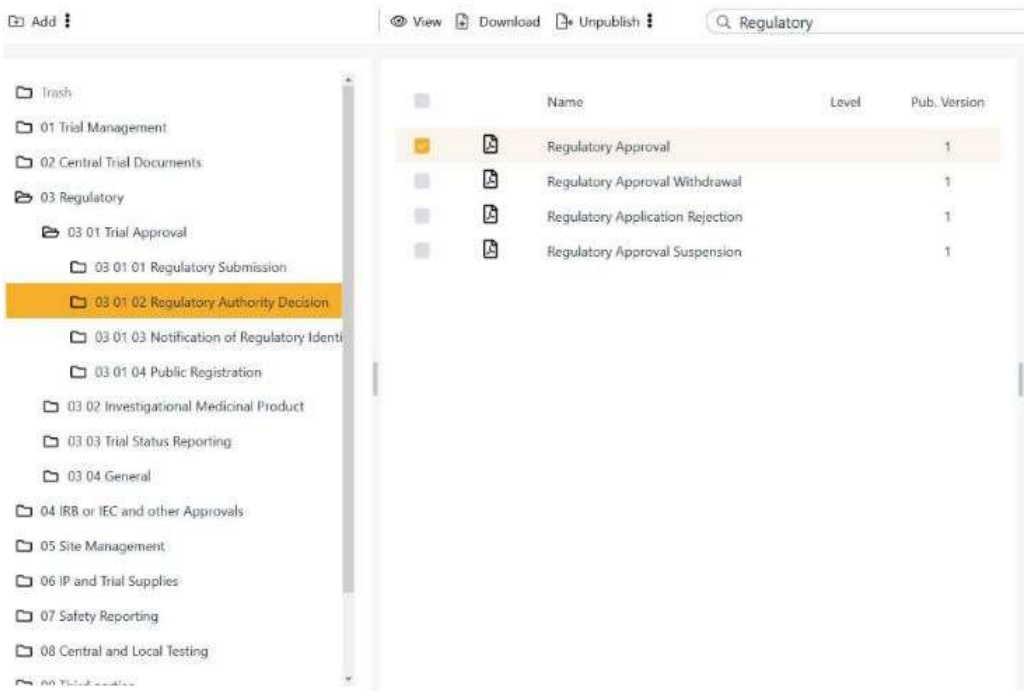


*Figure 14: CTMS Dashboard*

## 2.4 Structure of CTMS

The CTMS is a hierarchical structure of data modules where data can be entered and shared in a useful manner to make relevant data available throughout the system. This reduces redundancy by allowing common data to be associated with several components. Additionally, it automates and improves the efficiency of the data management process Six key parts make up the CTMS structure, and each one has features for entering, monitoring, and managing data. These parts work together to make it possible to enter information, manage it, and associate it across CTMS quickly, efficiently, and in an orderly fashion.

**An overview of each element and how they relate is given in the list below.**

Organization-Tracks and handles information about organizations. A sponsor site, hospital, lab, internal review board (IRB), and other entities are examples of organizations. A company usually has one or more physical locations as well as staff (workers) connected to it. Once an organization has been created, you can link it to one or more current addresses and pertinent contacts. The addresses and contacts that go along with them are tied to that organization. In this manner, the selected organization's linked addresses and contacts are displayed.

Addresses – controls and keeps track of physical addresses. An address can be linked to numerous contacts or organizations and only needs to be added once. For instance, an address may be connected to an already-existing Organization A and, if appropriate, may also be connected to an Organization B. An address can be used with numerous current contacts in the same way. It's crucial to realize that the organization name, not the actual address, appears when an address is linked to a contact or an organization.

Contacts- Organizes and tracks personnel data. Contacts are typically members of an organization's workforce, such as investigators, vendors, sponsors, and CRO staff. When contacts are created, the appropriate organization is assigned as their employer. Additionally, contacts may be individually linked to research and locations.

Study(ies) – Manages and tracks study data. A study is defined by its name, therapeutic research focus, sponsor, and other relevant details including study status and study locations. A study is connected to an existing company once it has been founded to serve as the study sponsor.

Additionally, pertinent study contacts, often those linked to the chosen organization, might be added (in other words, the study sponsor). Additional study data, including milestones and remarks, can be independently added.

Country(ies) – Keeps track of and organizes study-related country data. To keep track of recruitment efforts across all study countries, national planning enables site and subject enrollment numbers for each nation. Once a country is added, resources with roles at the country level are linked to it (such as, Lead CRA, Local Trial Manager, Country Manager). The addition of additional national data, such as national milestones, is optional.

Site(s) – keeps track of and organizes site data for every study nation. Each site has a distinct site number, information on the primary investigator, and other crucial details about the site visit (monitoring) process, like the visit schedule, visit reports, and subjects. The creation of a site makes it a dependent child-object of an already-existing study country. A single research country may contain multiple sites. A site is connected to an existing organization after it has been added, and this association is indicated by the site URL. The institution where subjects are housed is probably the one that was chosen as the site address. An existing organization contact can also be linked to the site contact in the same way.

Organizations, addresses, contacts, research, nations, and places have a straightforward relationship with one another. Organizations, contacts, and addresses can be linked to several

research, nations, and sites once they have been developed. Once a study is formed, one or more country sites may be added, and the relevant contacts and organizations may be linked to them.

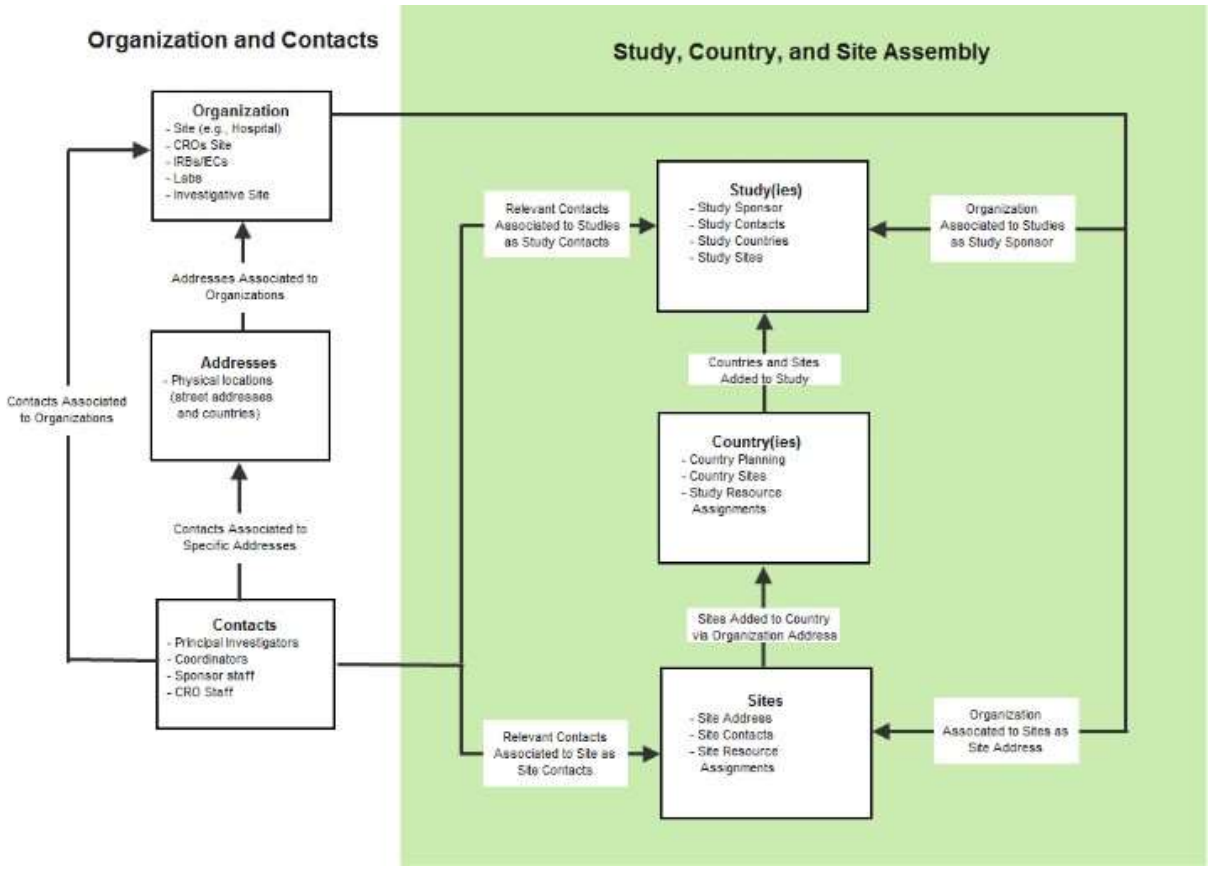


*Figure 15: CTMS workflow*

CTMS provide the following capabilities:

- Study Manager Homepage: Provides a single page for Study Managers to view key information, status, metrics, and data at the Study, Study Country, and Study Site levels.
- Study Management: Provides the ability to track and manage events, milestones, metrics, performance, and compliance across a study.

- Issue Management: Provides the ability to capture, track, and manage observations, risk mitigation actions, protocol deviations, and follow up items for a study.

- CRA Homepage: Provides a single page for CRAs to view key information, including status, enrollment metrics, deviations, and monitoring visits at the Study, Study Country, and Study Site levels.

- Site Monitoring: Provides the ability to manage all aspects of routine monitoring visits (Pre-Study Visit, Site Initiation Visit, Interim Monitoring Visits, and Close Out Visit), including confirmation and follow up letters, monitoring visit reports, and tracking of on-site monitoring activities.

- Study Communication: Provides the ability to manage study personnel and their contact information, and to track all communication regarding the study.

- CDMS & Clinical Operations Connection: Allows for the exchange of Studies, Study Countries, and Sites from Clinical Operations CTMS to CDMS EDC, and the exchange of Subjects, Subject Visits, Procedures, and Visit Definitions from EDC Vaults to CTMS.

- Subject Visits: Provides the ability for study managers to define visits for a Study, create and track visits and related source data verification (SDV) activities for a given Subject, and use this data in monitoring reports and other study management reports.

- Vault Payments: Provides the ability for study managers to manage payment requests, expenses, and budgets related to a trial.

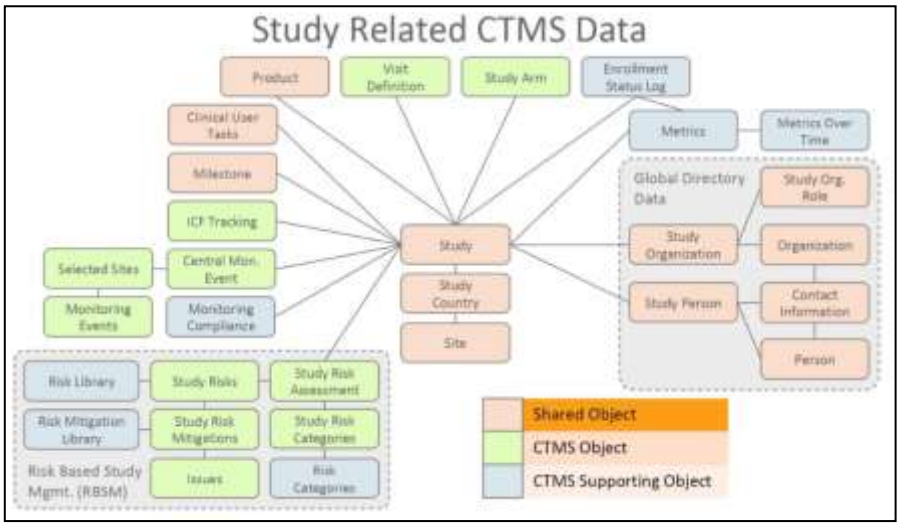


*Figure 16: Study related data*

## 2.5 Structure of Electronic trial management file.

A trial master file in electronic format is known as an eTMF. It is a collection of crucial trial-related papers that enables verification of the trial's conduct and the caliber of the data produced. The European Union (EU) mandates that a Trial Master File (TMF) be kept up-to-date throughout a trial. The Food and Drug Administration (FDA) of the United States mandates that clinical trials be carried out in accordance with the ICH GCP standards. It is anticipated that an eTMF containing those papers will be maintained for compliance reasons given that the ICH GCP stipulates necessary records for the conduct of a clinical trial.

The site and the sponsor should both prepare trial master files at the start of a study in accordance with the ICH GCP. Only once the monitor has examined and verified that all required documents are present and kept in the proper location is a trial's close-out possible. Additionally, during a trial, the regulatory authorities have the right to ask for an audit of any or all of the paperwork listed in the ICH GCP. This procedure is accelerated and made more effective by a well-managed eTMF.

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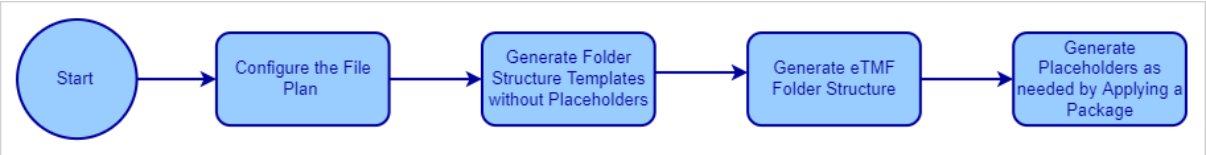


*Figure 17: eTMF Workflow*

## 2.6 Payments in clinical trials

One of the trickiest parts of managing a clinical trial is the investigator payment. Area of interest, trial length, clinical phase, and patient recruitment are important considerations by pharmaceutical and medical device companies for investigator payments. The investigators must get remuneration that are fair, reasonable, and commensurate to their fair market value.

Investigator salaries, overheads, and administrative costs are the three parts of an investigator grant. The cost of the entire trial is made up of these expenses, with the investigator remuneration component accounting for 40% to 50%. It covers salaries for researchers, doctors, and other workers.

Businesses like to compensate researchers on a milestone basis. Depending on the study type, the initial payment can often range from 40 to 50 percent of the overall award, with the remaining instalments contingent on enrolment or other milestones. (9)

These payments are made in accordance with the terms of the Clinical Trial Agreement for completed subject visits and subject activities (CTA).


*Figure 18: Payment workflow*

You can generate costs for the subject activities listed in the Clinical Trial Agreements (CTA) at the site level using Site Payments. Site Payments and MEDS are connected to produce costs from certain subject visits and activities.

A Payee is a person or business that needs to be charged for services rendered at the clinical trial location. The site payees are formed at the site-level on Cloud Administration and already exist there. CROs can operate and administer their research within a division of Platform thanks to cloud administration. The Client Division creates a Site Payee. Site payees can be utilized for many studies and study sites after being created on Cloud Administration.

Based on the criteria provided in the CTA, costs are created for the relevant actions. Autogenerated expenses are the costs that are generated. Additionally, for subject activities that are not covered by the CTA, you can set ad hoc subject expenses.

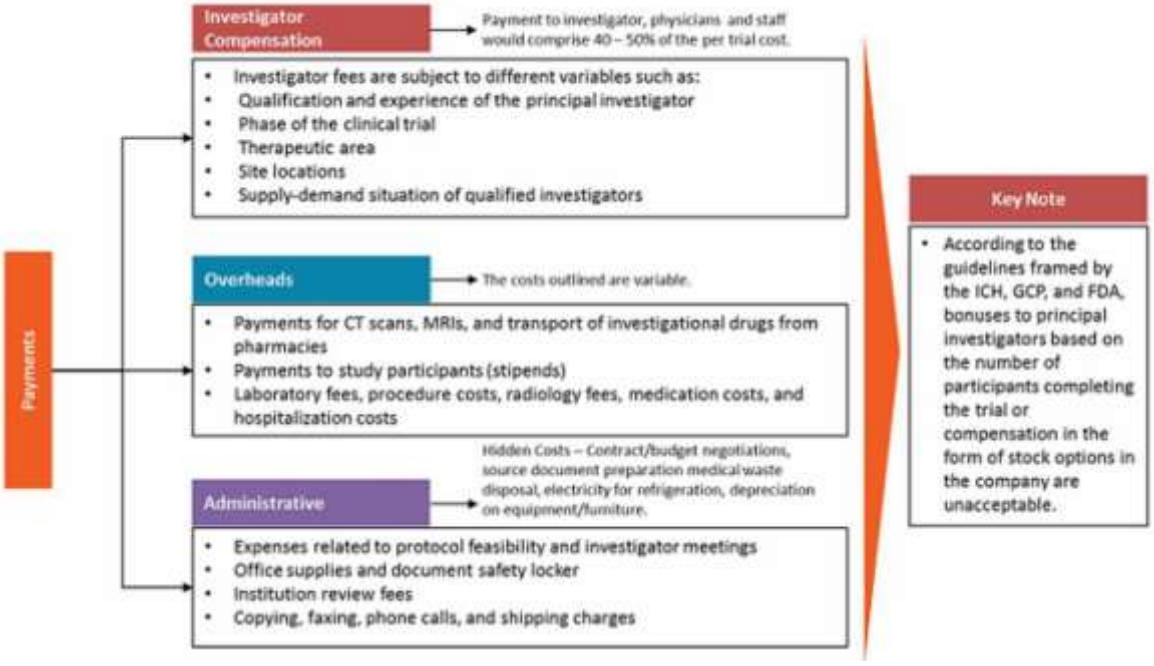


*Figure 19:Clinical Investigator Payment flowchart*

# 3 Materials and Methodology

## 3.1 Platform

Clinical trial management tasks have been eased thanks to CTMS. All organizational data, tracking data, and reports are now accessible from a single, reliable location. As a result, managing the survey requires less work, less time, and less money. In order to develop leaner organizations, pharmaceutical and biotechnology corporations typically minimize their employment needs. The solution supports timely reporting and data export if the CTMS is updated as the inquiry develops. Since the early 2000s, enhanced electronic system connections have reduced the amount of manual work needed to manage clinical studies. By reducing the number of individuals needed to enter data, CTMS also lowers the chance of human mistake.
Inconsistency across data sources was one of the key issues that existed prior to CTMS. Since the implementation of CTMS, this has either disappeared or been greatly diminished. The collection of all clinical trial data in a single location is significantly more convenient and reliable. This makes it possible for audits and inspections by health authorities to use trustworthy documentation and evidence of test monitoring and execution.

## 3.2 Spreadsheet

1. Trackers for clinical studies often used spreadsheets and worksheets. Use worksheets to enter, display, and change data quickly and easily. Although they are a useful tool, worksheets for clinical trial management soon become constrained as your team and research expand and your business strives to reduce risk through quality and compliance. Here are some benefits of using a CTMS rather using worksheets:

2. Collaboration with User Roles

The CTMS offers a safe space where team members can communicate in a managed setting where users can be limited to specific data views and/or studies.

3. Integrated, Consistent Data

The CTMS offers a data warehouse that can be utilized consistently both within and between studies, and across different data perspectives.

4. Secure and Reliable

The CTMS offers regulated user accounts to ensure that only authorized individuals can access data. The data is kept accessible when you need it thanks to redundancy, backups, and high availability cloud computing technology.

5. Compliant

The CTMS effortlessly implements controls for 21 CFR Part 11 compliance while your team is engaged in study management tasks. Audit trail, electronic signatures, data archiving, and user account controls are examples of controls.

## 3.3 User stories creation

A specific user goal can be effectively expressed through user stories. They are written in the form of a single sentence that describes the user, their objective, and their motivation.

To aid with the process, user stories are created. User stories are employed, and triggers are developed in accordance with the demand and the pre-defined necessity of clinical trials. Requirements and roles are pre-defined to provide an output.

*Table 1:User story for Payments Configuration*

| **As a** | **I want to** | **So that** | **My outcome parameter is** |
|---|---|---|---|
| Clinical Trial Associate / Business Analyst | Configure a study in the CTMS invoicing module | Information from EDC can be used for automation of Invoicing and payments for the study | Availability of study in the study with requisite documents in the system to add sites and users under it |

| | | | |
|---|---|---|---|
| Clinical Trial Associate / Business Analyst | Add study sites under the configured study | Invoicing as per the clinical trial agreement of the site can be configured | schedule of payments for addition of milestones and amount is available in the system |
| Clinical Trial Associate / Business Analyst | Ingest the clinical trial agreement | Payment schedule of the site as milestone and amount is configured for respective site | have complete payment schedule for each site by milestones and amounts |
| Clinical Trial Associate / Business Analyst | Link the field(s) in EDC with the invoicing process | The trigger for payment is automatic on completion of respective action | automated addition of pertaining to completion of milestone to the invoice |
| Clinical Trial Associate / Business Analyst | Populate the invoice template when invoice is due by time or threshold | A cumulative invoice of all payment units (milestone x number of subjects completing that milestone x amount as per agreement for the site at that milestone) is generated at the first pass of the information in the identified fields for | All milestones in a respective period populated as a row item for a given period |

| | | | |
|---|---|---|---|
| | | that milestone in the EDC | |
| Clinical Trial Associate / Business Analyst | Validate the populated data for each invoice report | The correct amount is triggered for payment as per the clinical trial agreement as per the payment SOP | Correct invoice generated |
| Clinical Trial Associate / Business Analyst | Configure user with their rights for invoicing system for each study site and overall study | The users can view, validate, approve and act as per their responsibility | Correctly set generation and approval of the final invoice |
| Clinical Trial Associate / Business Analyst | Configure the approval flow for the invoice | Responsible approvers can review and approve the invoice and payment | Configured user approval flow as per SOP |
| Clinical Research Associate | View and validate the invoice generated in the system against the clinical trial agreement | payments can be completed for the sites timely | Validated and approved invoice |
| Clinical Research Associate | Approve, call for modification or stopping the payment for a site | The invoicing process is error free | Invoice action completed as required |

*Table 2:SIPOC for payments*

| | Source | input | Process | outcome | Customer |
|---|---|---|---|---|---|
| Clinical Trial Associate / Business Analyst | Study Protocol and CRF | Preliminary study information EDC fields sites and users information | The data is manually added to the CTMS module or fetched from other modules of CTMS | Study available for addition of sites and users | System |
| Clinical Trial Associate / Business Analyst | Clinical Trial Agreement for each site Payments SOP tax regulation for country | Preliminary data of the site Payee bank and tax details EDC link of the site | Create a Site manually or import >> add the payee details >> add bank details >> add tax rules as per country's laws >> add notes >> create approval process flow | Site with primary payment information | System |
| Clinical Trial Associate / Business Analyst | Clinical Trial Agreement for each site Payments SOP | Preliminary data of the site Payee bank and tax details EDC link of the site | Identify payment milestone for the study>>create the milestone for invoicing>>identify the EDC field(s) which associate with the milestone>>add the edit check on EDC or BO4 report to trigger milestone completion alert>>use the alert for populating an event of payment >> add amount value for each | Structure for milestone x amount created | System |
| Clinical Trial Associate / Business Analyst | EDC field list | Milestones for payment in the study flow EDC link of the milestone completion Amount at completion | | | System |

| | | | | | |
|---|---|---|---|---|---|
| | | of milestone | completed event>>amount for each milestone as per sites CTA to be added | | |
| Clinical Trial Associate / Business Analyst | CRF / BO4 report | Signal for competition of field of interested | | All Milestones by CRF | System |
| Clinical Trial Associate / Business Analyst | System | System generated proforma invoice<br><br>BO4 report | Cross check information and identify differences if any | Validated invoice | System |

## 3.4 Test Plan

A test plan is a written document that outlines the goals, materials, and procedures for a particular test of a piece of software or hardware. Usually, the strategy includes a thorough understanding of the ultimate workflow. The following things were used to create a test plan:

- Examine the current workflows, processes, and data sources that are expected or documented.
- Speak with representatives from all functional areas, such as project management, finance, governing bodies, site management, and data management, to obtain information.
- Go over and show off the typical features of an electronic CTMS.
- "Gap Analysis" should be used to identify configuration needs for best practices.
- Create a budget for the CTMS's deployment and ongoing operations.

## 3.5 Study configuration requirements

Payment processing for clinical trials is covered by the study configuration in Site Payments, which includes:

- The establishment of event costs, triggers, and event payees,
- Cost approvals
- Invoices for non-US sites,
- Payment's approval, and
- Payments Distribution.
- Sites
- Clinical trial agreements

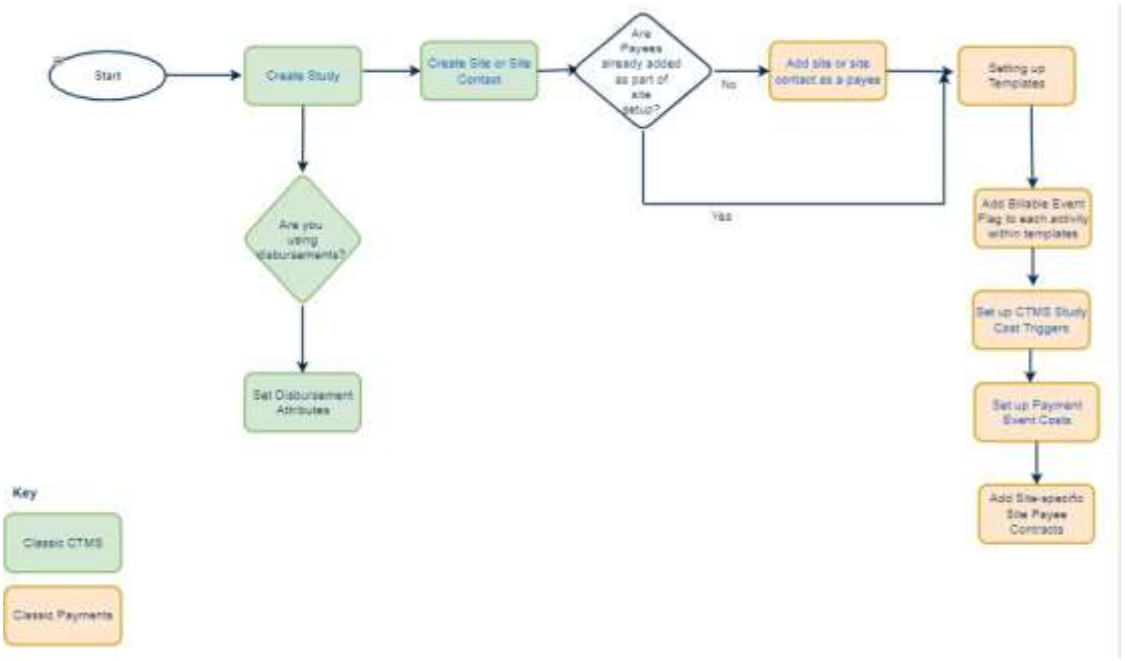


*Figure 20:Study Configuration flow chart*

## 3.6 Configuration process

Once the study configuration requirements are generated. Configuration is done to get into testing environment.

1. To Configure a study, we have to have access for the study, Environment and suitable roll to add the required field into the system.
2. Visit to CTMS app to get initiated with CTMS configuration
3. Reference documents must be available during the time of configuration
4. There should be CTA for each site.
5. Once all the requirements are checked. Add the milestones to get it configured
6. We can also collect the data from Cloud administration (if available)
7. All the sites are added and verified from the smart sheet.
8. Add all the payees
9. Adding costing triggers
10. Adding additional event cost
11. Configuration must be done for each site (Triggers can differ from site to site)
12. To generate triggers milestones must be identified in CRF and verified so that it should not generate query.
13. Detection of completion of Milestone.

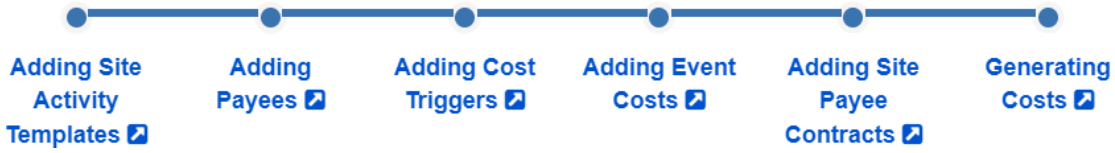


*Figure 21:Payment Generation workflow*

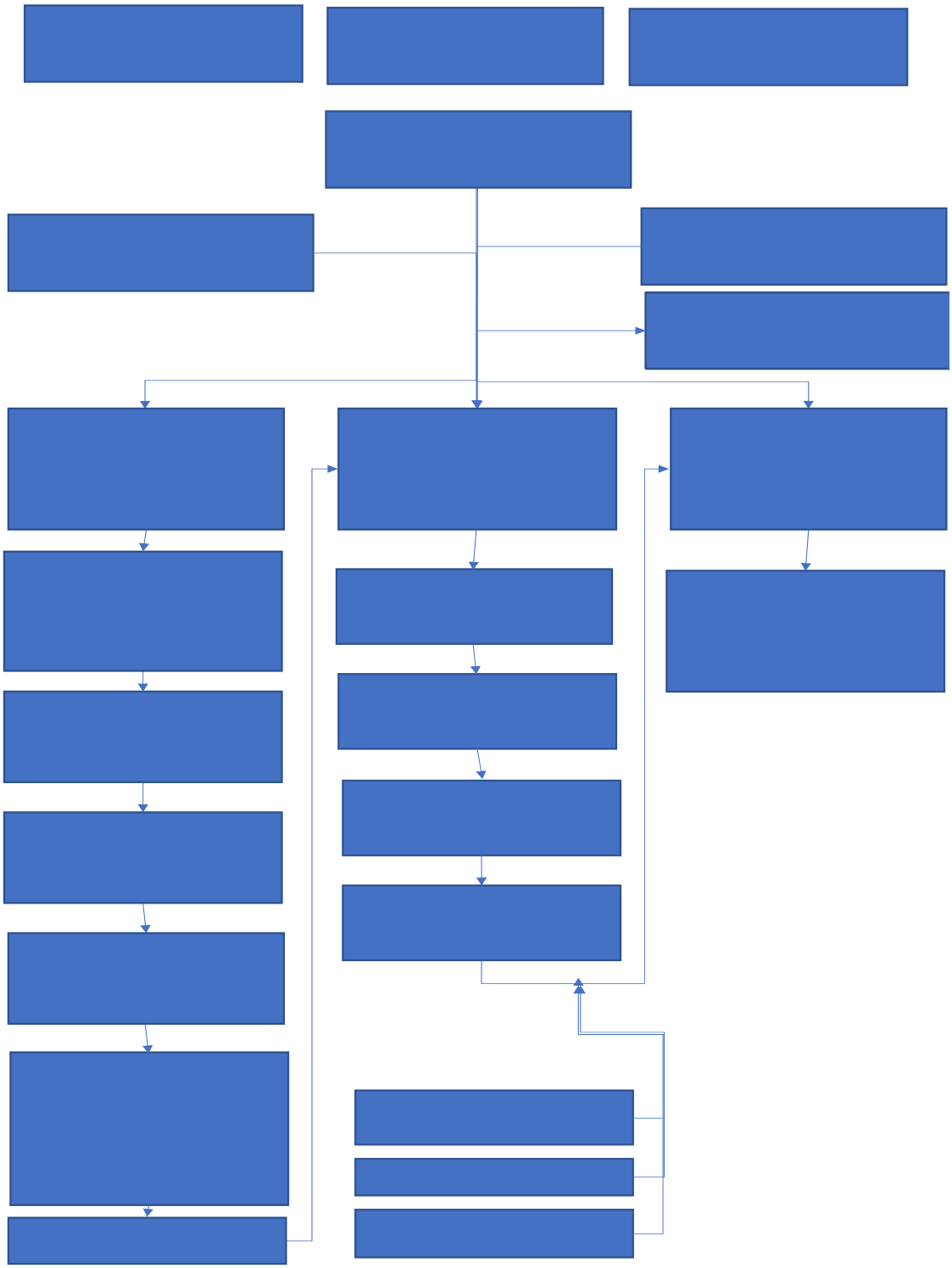

*Figure 22: Configuration workflow of payments*

## 3.7 Validation plan

Payment files must be legitimate and properly formatted before being submitted to payment systems and financial institutions for processing. If this isn't done, the payment process is hindered, which adds time and money to fix the problem.

The following choices are available for assigning validations:

- Setting up validations
- establishing user-defined checks
- Select a predefined library of validations

# 4 Results

The SWIFT-CTMS payments were developed in accordance with procedures that Stryker had repeatedly put through clinical trials over the course of many years. The introduction of a common baseline was added to data to assist users avoid errors and save time when they are expected to interact.

A number of objectives were created, met, and put into practice.

*Table 3: Results of Implementation of payments and invoicing module*

| Outcome | Status |
|---|---|
| Availability of study with requisite documents in the system to add sites and users under it | Achieved |
| Schedule of payments for addition of milestones and amount is available in the system | Achieved |
| Have complete payment schedule for each site by milestones and amounts | Achieved |
| Automated addition of pertaining to completion of milestone to the invoice | Achieved |
| All milestones in a respective period populated as a row item for a given period | Achieved |
| Correct invoice generated | Achieved |
| Correctly set generation and approval of the final invoice | Achieved |
| Configured user approval flow as per SOP | Achieved |

| | |
|---|---|
| Validated and approved invoice | Achieved |
| Invoice action completed as required | Achieved |

# 5 Discussions

## 5.1 Technologies

For a CRO, using these technologies can be extremely beneficial. Many times, professionals that are able to offer technology to support various stages of a clinical trial process are more suited to satisfy the needs of the entire research operations spectrum. Some of the most helpful technologies that can collaborate to speed up your study include business intelligence systems, electronic data collection, participation payments, regulatory management, and participant payments.

The operations and outcomes improve when technology like those stated above are integrated. It is possible to improve workflow efficiency, improve the quality of your data, and reduce any form of redundant data entry by using a CTMS to transfer data between systems. You must therefore search for system integrations as well. In reality, you should seek out manufacturers who offer integration not only among the products in their own line but also with the various enterprise systems you often use. By strengthening team interactions, billing and regulatory compliance, and patient safety, integrations like IRB, EMR, and financial software linkages can create new efficiencies inside the businesses.

## 5.2 Standard and Regulations

- A clinical trial management system aids firms in complying with legal obligations. The three most significant regulatory requirements for the CTMS and compliance are for:
- In the European Union and the European Economic Area, the General Data Protection Regulation (GDPR) enforces data protection and privacy laws.
- Good Clinical Practice (GCP) makes ensuring that the values of morality, professionalism, and patient safety are upheld. , ,
- The Health Insurance Portability and Accountability Act (HIPAA) outlines the conditions under which electronic protected health information (ePHI) may be disclosed and safeguards ePHI.

- The requirements under which electronic records and electronic signatures are regarded as trustworthy, dependable, and equivalent to paper records are defined in Title 21 of the Code of Federal Regulations (21 CFR Part 11).

## 5.3 Increasing Needs

- It is obvious that a clinical trial management system is essential for today's research. Not only does the CTMS manage data effectively; it also standardizes the entire process, aids in innovative healthcare solutions, and provides IT services for the healthcare industry. Using such a software system benefits everyone involved in the clinical trial because everything is interrelated.

- CTMS can lower the costs associated with managing clinical trials within particular units by facilitating an additional level of openness between the study and finance teams. The management process will become simpler and more precise as a result. The CTMS is used to provide the Principal Investigator (PI) with consistent and practical reports and financial data that is pertinent to the PI. Centralized systems can benefit the clinical trial by improving billing accuracy, accelerating invoicing, and reducing payment delay.

# 6 Conclusion

This thesis described the CTMS system, an electronic content management system. The user knowledge assessment results showed that a CTMS should be used to centrally manage everything required for general trial oversight. This uses fewer resources and makes life considerably simpler for trial teams and upper management. One of the main characteristics of CTMSs is reporting. A CTMS makes it easy to create reports, and reports may be easily altered. Adopting an eTMF makes it possible to handle documents continuously and monitor them in real-time, assuring compliance and audit readiness. With the aid of software, you can keep track of every single clinical trial expense and study budget, including payables for clinical sites, ad hoc costs, and vendor payments to CROs and IRBs. This gives you a detailed picture of the costs associated with clinical trials within your CTMS.

# Reference


1. National Health Survey: First Results, 2017–18 — Australia available from: 4364055001do003_20172018.xls (live.com)

2. Kuriakose, D., & Xiao, Z. (2020). Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. International journal of molecular sciences, 21(20), 7609. https://doi.org/10.3390/ijms21207609

3. Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJ, Demaerschalk BM, Khatri P, McMullan PW, Qureshi AI, Rosenfield K, et al.; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.**Stroke**. 2013; 44:870–947. doi10.1161/STR.0b013e318284056a

4. Venketasubramanian, N., Yoon, B. W., Pandian, J., & Navarro, J. C. (2017). Stroke Epidemiology in South, East, and South-East Asia: A Review. Journal of stroke, 19(3), 286–294. https://doi.org/10.5853/jos.2017.00234

5. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2009 Jan 27. 119(3):480-6.

6. Koton S, Schneider AL, Rosamond WD, et al. Stroke incidence and mortality trends in US communities, 1987 to 2011. JAMA. 2014;312(3):259-268. doi:10.1001/jama.2014.7692.

7. Introduction to Stroke (https://www.nhlbi.nih.gov/health-topics/stroke) retrieved on 12th January, 2020.

8. Kuriakose, D., & Xiao, Z. (2020). Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. International journal of molecular sciences, 21(20), 7609. https://doi.org/10.3390/ijms21207609

9. Ga, D., 2008. Fisher m, macleod m, Davis Sm. “Stroke. Lancet”, 371(9624), pp.1612-23.

10. Hatem A. Wafa, MPH, Charles D.A. Wolfe, MD, Eva Emmett, MPH, Gregory A. Roth, MD, Catherine O. Johnson, PhD, Yanzhong Wang, PhD, Burden of Stroke in Europe

11. Thirty-Year Projections of Incidence, Prevalence, Deaths, and Disability-Adjusted Life Years. StrokeVol. 51, No. 8Burden of Stroke in Europe https://doi.org/10.1161/STROKEAHA.120.029606Stroke. 2020;51:2418–2427

12. Mehta T, Male S, Quinn C, Kallmes DF, Siddiqui AH, Turk A, Grande AW, Tummala RP, Jagadeesan BD. Institutional and provider variations for mechanical thrombectomy in the treatment of acute ischemic stroke: a survey analysis. J Neurointerv Surg. 2019 Sep;11(9):884-890. doi: 10.1136/neurintsurg-2018-014614. Epub 2019 Feb 13. PMID: 30760625.

13. Shuaib, A. and Hachinski, V.C., 1991. "Mechanisms and management of stroke in the elderly" CMAJ: Canadian Medical Association Journal, 145(5), p.433

14. Stam, J., 2005. Thrombosis of the cerebral veins and sinuses. New England Journal of Medicine, 352(17), pp.1791-1798.

15. Clinical Investigator Payment Best Practices (clinicalleader.com)

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| W | URL: https://www.sofpromed.com/how-much-does-a-clinical-trial-cost<br>Fetched: 2021-11-09 00:04:48 | 2 |
| W | URL: https://www.simpletrials.com/what-is-a-ctms<br>Fetched: 2020-11-19 01:33:36 | 2 |
| W | URL: https://doi.org/10.3390/ijms21207609<br>Fetched: 2022-06-30 06:12:00 | 2 |
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