

IMPROVING AND ACCELERATING THE CLINICAL TRIAL PROCESS

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CTIS has provided informatics support since 1988 and has built powerful clinical trial and research management informatics applications that helps in improving and accelerating the clinical trial process. These CTIS solutions provide monitoring, management and day to day decision support to the the various stakeholders. While CTIS has provided informatics solution to its clients and its research community, Clinical development still is largely paper based (for example: Investigator registration, IRB reviews) or mixed electronic and paper based. Geographically dispersed stakeholders performing paper based processes delays the study. Redundant data entry and lack of data sharing also delays the clinical research and reduces efficiencies and data quality.

CASE STUDY: CANCER THERAPY EVALUATION PROGRAM – ENTERPRISE SYSTEM (CTEP-ESYS)

CTIS provides CTEP with mission support through 22 clinical trial and research management informatics applications, of varying age and technology. These applications share a common data warehousing solution that is certified secure, which stores information on over 700,000 patients, 15,000 investigators, 10,000 protocols, 8,000 sites, 3,000 drug agents, and 250 Investigational New Drugs (INDs).

To achieve a major reduction in the protocol authoring cycle time, CTIS has developed a powerful and flexible protocol authoring and management tool, the Document Management, Assembly, Review and Tracking System (Docu-MART). The goal of Docu-MART is to expedite rapid protocol development by effectively connecting all stakeholders involved in the process and eliminating paper based processes as well as streamlining protocol development processes. There are areas where paper based processes can further be eliminated and the processes can be integrated and streamlined to achieve further acceleration in the clinical trial process.

Data is stored in disparate, incompatible systems and formats, hence data exchange / communication among stakeholders and data reconciliation during trial conduct is virtually impossible. Lack of access to existing data such as prior protocols, single and multi-agent toxicity data, clinical outcome data, safety, efficacy are obstacles and causes delay in the trial progress. Optimum Quality suffers due to lack of real or near real time data not available to the sponsor and researchers. Highlighting of non-performing, problematic sites to facilitate decision making early is not available.

The functionality of CTEP-ESYS currently is of limited use to outside systems and their

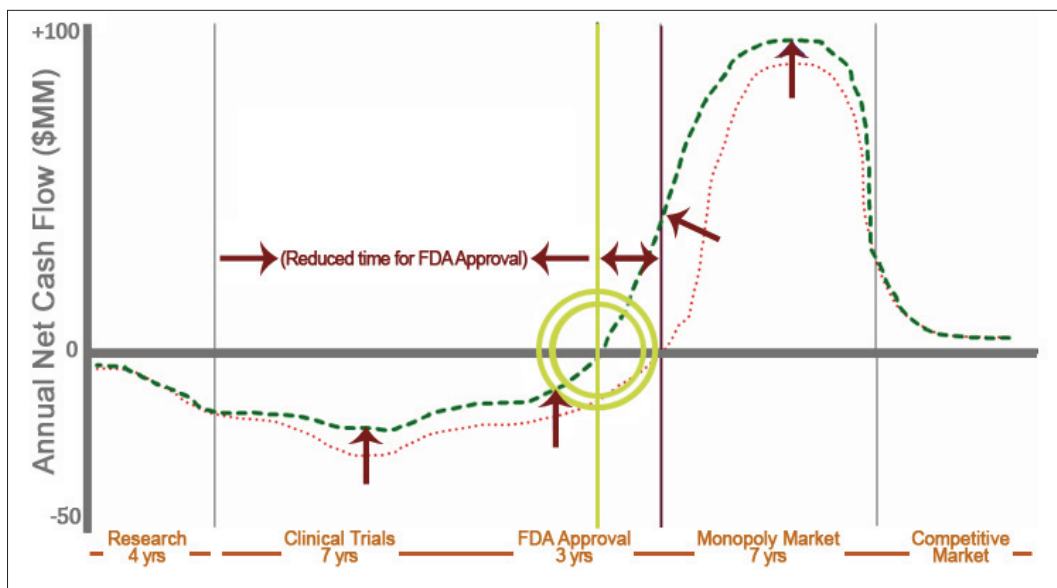
stakeholders. CTIS is interested in supporting CTEP with a standard, scalable, and robust architecture framework to encourage data sharing and interoperability beyond the current CTEP stakeholder community. This initiative will put CTEP in a unique position to have a broader vision and to do “more with less.” It will also assist the broader cancer community in its goals for better research, outcome management, and improvement through productivity improvements and efficiencies that provide even higher return.

The constraints above causes delays in the scientific review processes and data reporting, redundancy in the Institutional Review Board (IRB) processes, slow patient accrual, and suboptimal communication between sponsor (within divisions) and sites, thus causing the postponement of the clinical trial development milestones.

Understanding the challenges and the opportunities, CTIS is placed in a unique position to support CTEP-ESYS expand in functionality, integrate and harmonize with external systems, thus helping CTEP further achieve considerable improvements to causing the postponement of the clinical trial development milestones. CTIS recognizes that the targets for improvement listed below will further streamline studies and shorten timelines.

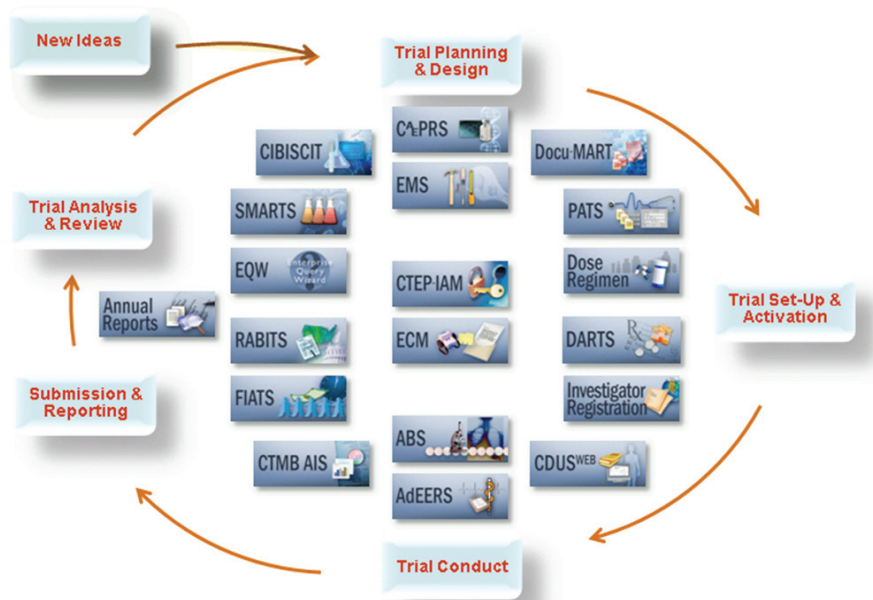
- Protocol Design and Study start up
- Patient and Investigator recruitment
- Clinical Trial Management
- Data Management, Analysis and sharing
- Drug Ordering and Inventory
- Regulatory submissions
- Integrated workflow and collaboration
- Real time metrics and site visibility

The figure below shows the improvement that can be achieved by implementing the target functions as discussed below.



Proper Clinical Informatics: Saves Costs & Increases Profits

The figure below represents the current landscape of the CTEP-ESYS applications supporting the clinical trials.



CLINICAL TRIAL LIFE-CYCLE AND CTEP-ESYS APPLICATIONS

Docu-MART is a system of software applications utilizing both desktop and web technologies to enhance the authoring, reviewing, and tracking of clinical trial protocol documents. The application is planned to assist in reducing the administrative burden of protocol development so that investigators can focus on scientific integrity. Docu-MART will help increase the efficiency of clinical trial document development and approval processes by leveraging the use of standard templates, standard document structure, auto content generation, online reviewing & approval, automated notifications, and tracking of the document through its lifecycle.

The Clinical Investigations Branch Information System and Clinical IT (CIBISCIT) is an Internet-based application used to assist the Clinical Investigations Branch (CIB) in the real time maintenance (i.e. data entry, storage, reporting, analysis, retrieval) of information related to diseases to be studied in Concepts and Phase III protocols.

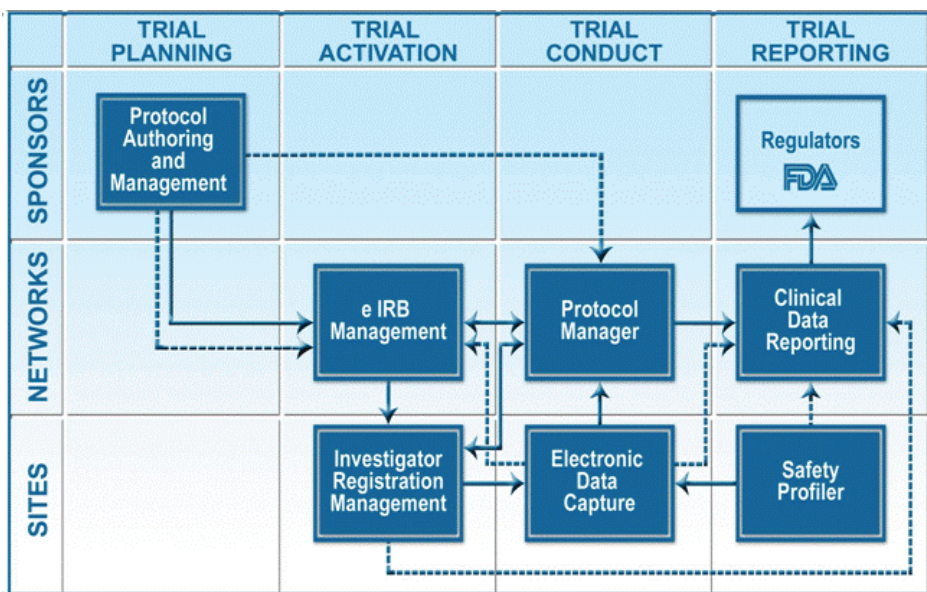
The Protocol Authorization and Tracking System (PATS) provides CTEP the ability to enter, modify, and retrieve data on letters of intent, concepts, protocols, revisions, and amendments received from physicians conducting clinical trials. PATS tracks these documents as they pass through protocol lifecycle from review and approval to activation and completion. Trial details are entered including information about physicians, sites, and investigational agents used on the protocol.

The CTEP Investigator Registration (CTEP-IR) system is a component of Drug Authorization and Review Tracking System (DARTS) and is used to electronically collect, store, and manage data about registered investigators who are eligible to receive National Cancer Institute (NCI) supplied investigational agents from the Pharmaceutical Management Branch (PMB) of CTEP.

The Clinical Trials Monitoring Branch Audit Information System (CTMB-AIS) is a web based system that facilitates oversight and compliance monitoring of Cooperative Groups and CCOP Research Bases with NCI’s monitoring guidelines. The CTMB-AIS enables audit scheduling and reporting in a standard format and provides ability to review and assess the audit reports. The system raises flags to alert CTEP of sites that are not complying with NCI guidelines and ensures that sites are regularly audited.

The Adverse Event Expedited Reporting System (AdEERS) is a web based system that facilitates timely reporting of Adverse Events (AEs) and increases the efficiency, completeness, and accuracy of safety monitoring and reporting to NCI/CTEP and the Food and Drug Administration (FDA). All NCI sponsored protocols are required to use AdEERS for reporting expedited AEs.

While maintaining the current operations, the CTEP-ESYS must undergo technology adaptation to resolve the outstanding issues. CTEP-ESYS should unify clinical data, mine it for specific indications and share this data effectively. To achieve this, a new technology platform that addresses data sharing, that builds on industry standards, reliable middleware, role based integrated workflow, end to end communications must emerge. The figure below depicts integration of applications across various stages of clinical trial life-cycle and collaboration across the various stakeholders.



The Standards-based (e.g., Medical Dictionary for Regulatory Activities (MedDRA), Systematized Nomenclature of Medicine(SNOMED), International Classification of Diseases (ICD), Health Level Seven (HL7), Clinical Data Interchange Standards Consortium (CDISC), Biomedical Research Integrated Domain Group (BRIDG), etc.) end-to-end solutions enable higher data integrity, allowing better trial data portability, better data readability, better data maintenance, lower maintenance costs, streamlined and simplified data collection processes, increased collaboration, improved data capture, reduced trial time, improved data storage and data management. The proposed architecture will support clinical data exchange standards, streamline the processes and will provide ability for easy integration.

Providing access to endpoints and statistics will help in the study definition and design phase. The study library would provide information about similar trials and background information that would provide a jump start to study definition and design. Providing a workflow based peer review and editing will present the opportunity to considerably reduce the time for protocol development. Integration with an electronic IRB system would expedite the ethical and safety review. Several improvements can be achieved in the trial activation phase by automating and streamlining the investigator registration process, by implementing a work flow based drug distribution and inventory system. Considerable savings in time can be achieved by integrating the clinical trial systems to the electronic data capture system and implementing a powerful collaboration process.

Another area of improvement would be to provide more effective Data Management, Analysis and Monitoring. This can be achieved by providing an executive dashboard to track progress by study, site, and group. It can also integrate with different site systems for faster data exchange, resolution, and data reconciliation, provide the sponsor of the trial with greater visibility and powerful data mining capabilities. Recent work by David Dilts, Ph.D. highlights the advantages of being more selective about what clinical research work to undertake. Dilts' work suggests that CTEP is now in a position to accomplish an even better job of determining what clinical trials to approve, activate, and execute to completion given the richly detailed data generated from the informatics system now facilitating program administration.

Finally, trial progress can also be achieved by integrating with Patient Registration systems such as Oncology Patient Enrollment Network (OPEN), Cancer Central Clinical Participant Registry (C3PR) and promote electronic flagging of eligible patients in Electronic Medical Record (EMR) systems, facilitate rapid patient eligibility determination, automated drug ordering for registered patients (integration with DARTS). The performance of a site can readily be accessed by making available the accrual rates on the trial dashboard.