For Clinical Research and Clinical Trial Data Management

the protocol centric information system

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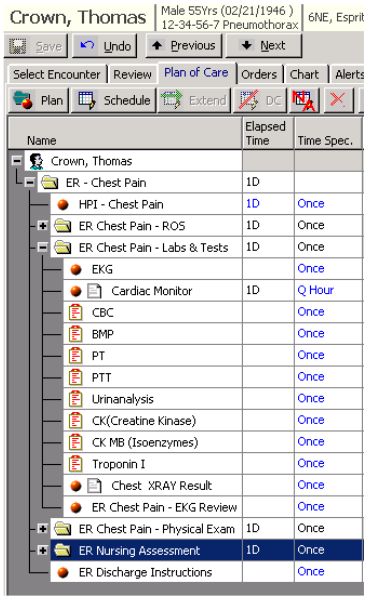
Overview

eSphere is a new paradigm for healthcare information systems – a single integrated system designed to create models that describe processes, from the simplest process to the most complex research algorithm. These models become the basis for data collection, monitoring, and analyses of the processes, forecasting resource utilization and determining costs.

Esprit's unique Care Module™ methodology provides the capability to model processes into hierarchical groupings enabling the ability to create complex and sophisticated structures. The system design incorporates a branching decision tree algorithm with dependencies and conditional decision points that can trigger other processes. With the sequence and timing of all events defined, the system creates a "schedule" for all activities.

The result is a model that is used to collect all data eliminating errors of omission and accounting for unexpected processes. Simply, ***eSphere*** "knows" what needs to be done, by whom, where, how, when and why.

eSphere is a new paradigm – one system that can be used to meet all of the needs of physicians and clinicians for patient care, principal investigators for clinical protocol research, as well as for safety, regulatory, and administrative needs.



Hierarchical Display of Process

Modeling Processes

- Describes the entire process, decision tree branches and paths, the sequence and timing of events (i.e. workflow), and the relationships between data elements
- A central repository of clinical elements that are used and re-used in the creation of all of the processes and maintains version control

Data Collection

- Errors of omission are eliminated from the data collection process because eSphere "knows" what should be collected and when
- Incorporates instructions, reminders and warnings into the data entry screens improving patient safety
- Workflow driven data collection improves timeliness and accuracy of care
- Charting by exception capability streamlines charting process while increasing comprehensiveness and quality of patient's health record

Monitoring

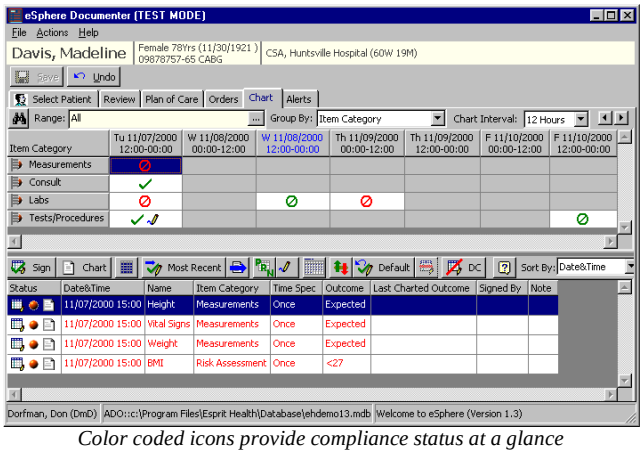
- Provides tools for real-time monitoring of the data collection process and of the documentation of patient care.
- Facilitates quality management checks from remote locations
- Chart status (e.g. Not documented, incomplete) communicated at a glance using color and symbols (circles, check mark, etc).

Data Analysis

- Standard and customized reports draw from patient demographic data, event/encounter data, and clinical data
- Transform data into information with powerful, easy to use wizards for ad-hoc queries, data extraction and export (e.g. XML, Excel, etc)

Information Management

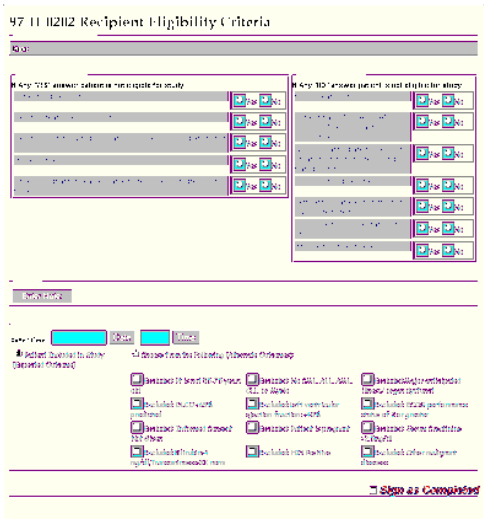
- Powerful web based "personal portals" enables clinicians to view the data they want, where and when it is needed.
  - ✓ *Comprehensive*. Relevant areas of the patient's clinical data presented in the format best suited to each practitioner
  - ✓ *Customizable*. From content to "look and feel" everything can be designed (and easily updated) to reflect needs.
  - ✓ *Web enabled*. Web pages generated using Esprit's unique technology for rendering database driven HTML.



Color coded icons provide compliance status at a glance

Research

eSphere is a complete clinical trial and data management system serving the needs of physician investigators, monitors, clinician caregivers, safety and regulatory monitors, data and project managers. It is designed and built with protocols at its core rapidly accelerating the clinical research process. ***eSphere*** assures the security and integrity of the research data while providing the researcher with real time access on demand.



Web based forms collect and verify data

Protocol Authoring, Tracking and Monitoring

- Assures that requirements for proper preparation of the clinical research protocol are met
- Follows process for protocol submission and IRB approval process
- Library of standard forms can be easily adapted, reused and shared across multiple protocols
- Maintains version control of the protocol and all amendments and automatically tracks history of all changes

Accelerated Research Study Design

- Simple drag and drop environment allows you to define database, metadata criteria, design form and test in real time.
- Ability to model complex patient and data flow processes, matching the actual protocol precisely.
- Incorporate instructions, reminders, and warnings into data entry screens.

Real Time Data Capture and Quality Data

- On-line patient registration and assignment to protocol facilitates easy identification of cohorts and eligibility determination.
- Coordinated collection of data assured elimination of wrong forms, errors of omission and prevalence of N/A's.
- Same patient, same encounter coordination increases patient safety
- Interfaces acquire data from other clinical databases eliminating redundant data entry errors.

Centralized Data Repository

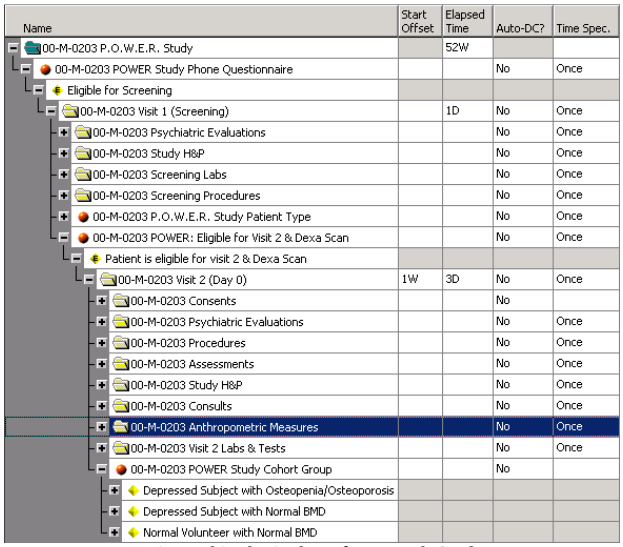
- Data Dictionary built upon unique, highly flexible data structure or "model" that enables users to exchange, compare, query and report on data from one protocol, across protocols, even from data originating in independent systems.
- Enables a single longitudinal patient record to integrate *all* data across current and prior studies
- Coordinated central knowledgebase of protocols
- Allows researcher's to access data and export to specialized database – with 100% protection of their ownership of data
- Capability to manipulate and analyze data via without impacting the original source

Effective Trial Control and Monitoring

- On-line forms enable instant source document verification
- Compliance with protocol flow and timing of events assured.
- Ability to conduct independent data quality checks from remote locations
- Automated triggers improve response to unplanned and adverse events

Analyses and Reporting

- Powerful, easy to use wizards provide tools for ad-hoc queries and analyses
- Data can be easily extracted and exported to Excel, SPSS, or SAS or other tools for sophisticated statistical analysis
- Web based portals are user defined, protocol specific, or defined by clinician location
- Standard reports are grouped into research reports and analyses, regulatory reports, clinical reports and administrative counts



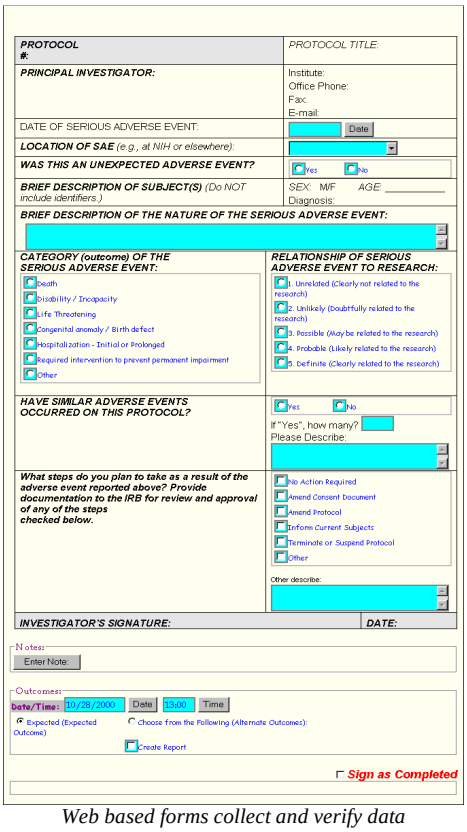
Name	Start Offset	Elapsed Time	Auto-DC?	Time Spec.
00-M-0203 P.O.W.E.R. Study		52W		
00-M-0203 POWER Study Phone Questionnaire			No	Once
Eligible for Screening				
00-M-0203 Visit 1 (Screening)		1D	No	Once
00-M-0203 Psychiatric Evaluations			No	Once
00-M-0203 Study H&P			No	Once
00-M-0203 Screening Labs			No	Once
00-M-0203 Screening Procedures			No	Once
00-M-0203 P.O.W.E.R. Study Patient Type			No	Once
00-M-0203 POWER: Eligible for Visit 2 & Dexa Scan			No	Once
Patient is eligible for visit 2 & Dexa Scan				
00-M-0203 Visit 2 (Day 0)	1W	3D	No	Once
00-M-0203 Consents			No	
00-M-0203 Psychiatric Evaluations			No	Once
00-M-0203 Procedures			No	Once
00-M-0203 Assessments			No	Once
00-M-0203 Study H&P			No	Once
00-M-0203 Consults			No	Once
00-M-0203 Anthropometric Measures			No	Once
00-M-0203 Visit 2 Labs & Tests			No	Once
00-M-0203 POWER Study Cohort Group			No	
Depressed Subject with Osteopenia/Osteoporosis				
Depressed Subject with Normal BMD				
Normal Volunteer with Normal BMD				

Hierarchical Display of Research Study

Regulatory

Federal regulations require continuing review of the research protocol, at intervals (at least annually) appropriate to the degree of risk. ***eSphere*** provides the tools to effectively monitor the collection of consent and assent documents, and assure that the collection of the research data is in compliance with the protocol. Alerts inform the Principal Investigator if the status of patients on the protocol changes due to complications, unplanned events, comorbid conditions, and adverse events.

As amendments to the protocol are stipulated from the ongoing review process, the system enables and tracks all changes maintaining a complete history of all changes. All reports and required written communications flow from the system. ***eSphere*** assures the security and integrity of the research data while providing the researcher with real time access on demand.



Web based forms collect and verify data

Compliance Monitoring

- Compliance with protocol flow and timing of events assured.
- Web-enabled ability to access data to conduct independent compliance checks from remote locations.
- Produce real-time Consent Forms (e.g. Consent/Assent) on demand.
- Errors of omission are eliminated from the data collection process because eSphere "knows" what should be collected and when.

Alerts and Triggers

- Automated triggers improve response to unplanned protocol events.
- Complete and appropriate documentation of unplanned events including: Description of Problem, Grading, Plan and Resolution.
- Adverse and Serious Adverse Event reporting is always assured because the system initiates the approved process.
- Can be used to send messages and emails.
- Rules can be defined which link data values (e.g. Toxicity levels) to conclusions and trigger actions.

Protocol Management Database

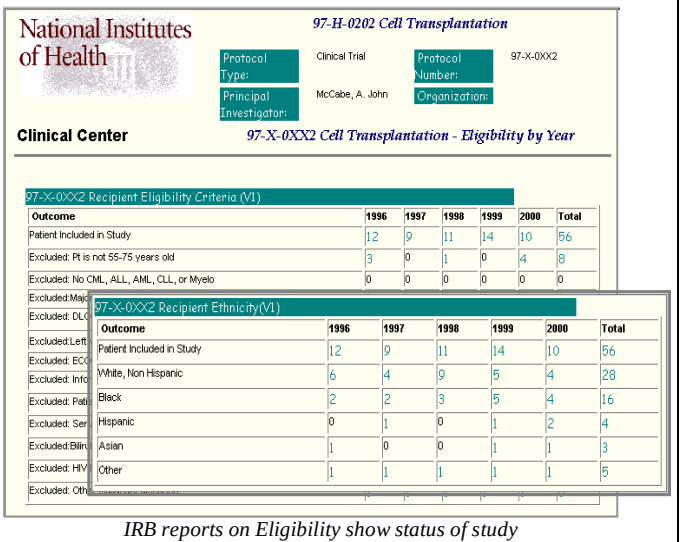
- Maintains historical database of approved protocols including goal, title, description and links to authoritative resources (e.g. clinical references).
- Tracks full amendment history (date and version control number) and Author and Contributors, audit trail and description of changes are included.
- The full study team and all participants are defined in the protocol ensuring privacy of patient data and protecting the researchers' ownership of the data.

Monitoring Study Progress

- Investigator determined protocol milestone can be setup and tracked real-time
- Real time "To Do" lists, automatically triggered reminders, and patient calendars insure protocol compliance
- Web-enabled ability to access data to conduct independent data quality checks from remote locations

Analyses and Reporting

- Regulatory reporting needs including AE/SAE reports met
- Standard and customized reports (e.g. Eligibility and administrative counts) satisfy IRB reporting requirements
- Powerful, easy to use wizards provide tools for ad-hoc queries analysis, data extraction and export
- Web based portals are user defined, protocol specific, or defined by clinician location



IRB reports on Eligibility show status of study

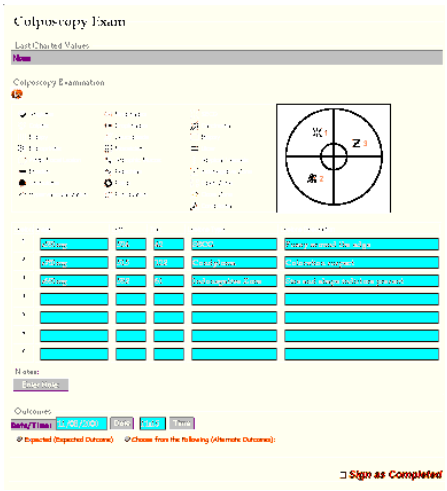
Clinical research trials that involve inpatient stays or ambulatory clinic visits create the need for clinical processes to take place as part of or as a byproduct of the research data collection process. These clinical processes may not be the focus of the research objectives but they are critical to the quality and safety of patient care.

Patients on a protocol require care for all of their current health problems, the protocol treatment itself, and the result (or side effects) of the interaction between the patient and the protocol. Clinical processes supported by ***eSphere*** include but are not limited to: assessments, observations, Notes, flow sheets, vital signs, specimen collection, patient education, procedures, tests, nursing care, discharge process, and follow-up calls.

System Wide Approach to Patient Safety

eSphere provides a system-wide approach to facilitate dramatic improvements to patient safety:

- **Authoring**: Clearly definition and agreement on processes eliminates duplicate orders
- **Order Entry**: Orders are patient and problem specific. Orders flow from the patient's integrated plan of care and are automatically displayed in the appropriate place and for the appropriate clinicians
- **Delivery of Care**: Charting by Exception approach, automatic calculations and conversions enable accurate charting
- **Monitoring:** Synchronous rules enable continuous monitoring of changes in patient condition



Example of Clinical Data Entry Form

Enhanced Patient Safety

- Clinical decision support capability provides automatic alerts to reduce adverse drug events. Alerts physicians and pharmacists on entry of order when an interaction or other medication related problem might arise.
- Protects patients from medication allergies.
- Clinically relevant information presented at order-entry time provides a complete picture of the patient's health status
- Automated charting improves the accuracy of documentation and makes more data accessible for medical decision-making.

Improved Patient Care

- Documentation is charted once, and the relevant information is automatically displayed in all of the right places
- Medication Administration Record always has up to the minute, real-time data.
- Clinicians gain accurate information at any point in the process, from current orders to assessment and examination data to the latest results and can produce task lists to manage individual activities and care plans on demand.
- Coordinated collection of data assured elimination of wrong forms, errors of omission, redundant data entry and prevalence of N/A's.

Coordination of Care

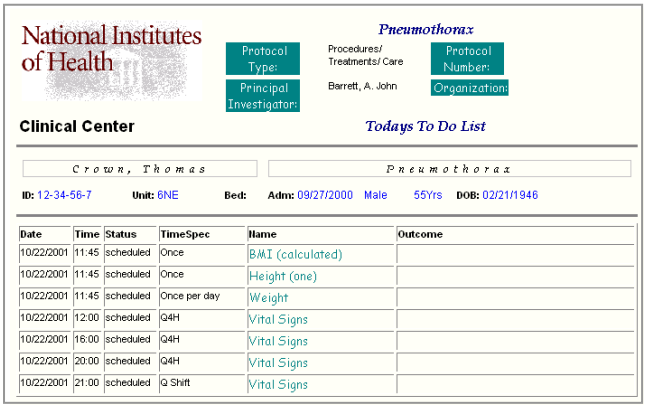
- Use of protocols enables coordination of care across the continuum – from the physician's office through the diagnostic phase, problem identification, treatment, and convalescence.
- Improved communication and increased efficiency result from multidisciplinary ability to access and use the integrated plan of care
- Every activity flows out of the plan of care and related protocols, so the timing and scheduling of events is assured.
- Care activities and related charting status can be monitored at-a-glance to quickly identify patient needs

Quality assurance and Outcomes Measurement

- Patient problems are related to specific goals and to the action plan designed to achieve the desired outcome

On-line Statistics and Reports

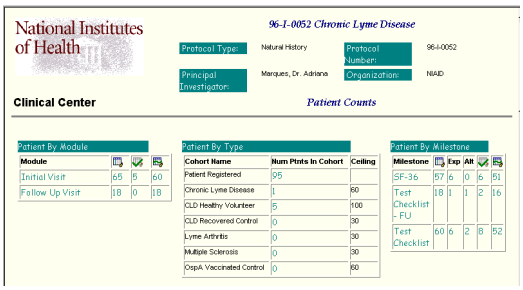
- Incidents (e.g. Medication Error) are tracked by time of day and by caregiver.
- Queries, analysis and reporting are available at all times



Example of To Do List

Administrative

Each clinical protocol can have a major impact on the resources and services provided by the organization that are needed to support the research study. ***eSphere*** provides the Principal Investigator and Administrators with the ability to understand and forecast the volumes of tests, procedures and activities that are required and help determine the number of subjects to study (i.e. sample size) needed for conclusions and findings to be meaningful.



Accrual Report – Cohort against Ceiling

To Do List and Checklists are easily produced

Resource Volume Forecasting

- Esprit approach for protocol driven resource planning and budgeting is focused on accurate projections of volumes.
- Protocols are used as the basis to relate clinical research programs with patient volumes and projected demand for resources and services.
- Forecast of resource consumption is calculated for an individual protocol and for all patients forecasted to be on the protocol.
- Prediction of patient enrollment requires the tools to predict the number of candidates and then the number of eligible patients in each cohort.
- Capability to change (re-forecast) patient projections at any time

Resource Utilization Monitoring

- Analyzes the variance between the actual resource consumption of patients in each cohort with the cohort "path".
- Enables the grouping or "roll-up" of detailed clinical and research data for ABC analyses (i.e. activity based costing).

Patient Eligibility and Forms

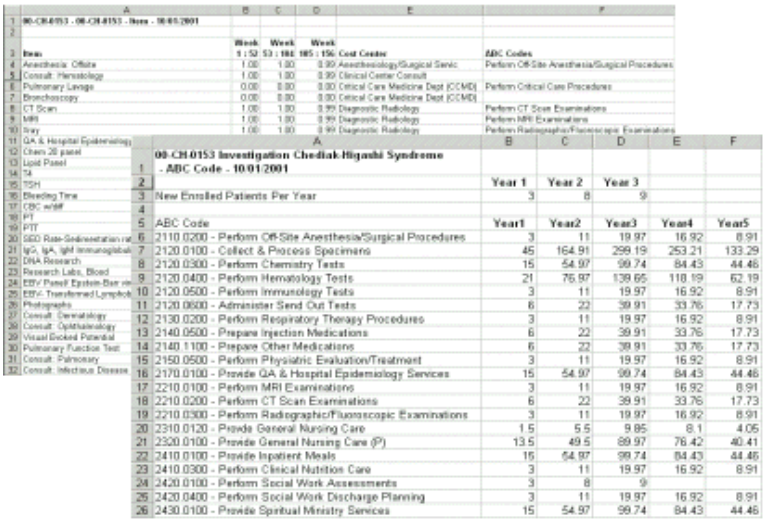
- All patient forms including Consent Forms (e.g. Consent/Assent) are retained in the centralized Data Dictionary ensuring that the current, approved form is always used.
- All forms are printed from within the system real-time, as needed.
- On-line patient registration and assignment to protocol facilitates easy eligibility screening and determination and identification of cohorts.
- Coordinated collection of data assures elimination of errors caused by using the wrong forms, errors of omission and prevalence of N/A's.

Patient Accruals

- Ability to designate patients as members of cohorts and enter IRB ceilings by cohort for each protocol.
- Enables the collection and tracking of candidates (both included and excluded from the study) and accrual rates against IRB ceilings.
- Standard reports can be generated on counts and statistics on recruitment, enrollments & accruals.
- Protocol amendments, changes in accrual rates, and dropout rates

Patient Lists and Reports

- Easy access to data coupled with standard reports and ad-hoc query capability provides the ability to generate a wide range of lists and reports
- Ability to define process and collect data to produce:
  - ✓ Letters to referring physicians
  - ✓ Patient Calendars
  - ✓ To Do lists and Follow-up Reminders



Example of ABC Report & Multi year Patient Forecast

Benefits

eSphere is more than a database, it is a well-thought out system that maps the protocol exactly as researchers think and work. The combination of the eSphere software and the Esprit Health data management services program enables researchers to:

- Focus on analyzing data by eliminating errors because data is entered correctly at the point of collection (with rules, range checking, automated calculations, etc)
- Publish results sooner by eliminating additional time spent merging, correcting and cleansing databases
- Assure complete security, integrity, accuracy and ownership of your research data

What Esprit Health can do for the Clinical Researcher

The start-up of every clinical research trial/project typically begins with the need for staff (full time, part time or both) and software tools to accomplish project goals. As a result, hiring costs, technology costs (computer/software) and the time and cost associated with acquiring knowledge (orientation, training, statistical software, data, etc) are incurred.

Esprit Health reduces start-up time and costs by providing all of the services and activities required to support your research.

The value of eSphere

- Manage and control the clinical trial with increased awareness of subject status, progress of data entry efforts and better coordination of the clinical efforts of all study team participants.
- Accelerate data entry.
- Reduce costs by eliminating transcription of data, paper forms and verification processes. Eliminate most paper forms, paper work and paper storage.
- Single database eliminates multiplicity of individual, standalone databases for each study/protocol.
- Flexible design enables use by one investigator or by an entire Institute – yet each individual has access to and maintains their own protocol with 100% protection of data ownership.
- Coordinated central library of protocols, forms, and dictionaries (Medications, Lab tests, etc) can be easily adapted, re-used and shared across multiple protocols.
- Shared interfaces provide ability to import data collected in other systems
- Can export data to specialized systems (e.g. SPSS, SAS) allows for experimental analyses without impacting source data.
- Easily convert paper based source data or standalone databases into researchable data that can be queried and analyzed.
- Patient demographic data is retained permanently in eSphere and does not need to be re-entered, even if the patient is later enrolled in additional studies. (But, it can be updated at any time.)
- Data can be collected on a PC and with Citrix on a MAC or on the Internet.
- Data entry forms do calculations (e.g. BMI, BSA), conversions (e.g. Weight) and complex scoring (e.g. SF-36).
- System can compute deltas from last visit to current visit (e.g. BMD, Osteporosis BMD)
- Every intervention in the protocol (planned and unplanned) is defined and scheduled so that errors of omission as well as errors due to the use of wrong forms are eliminated.
- Simple, yet powerful rules engine and outcome dependencies provide decision support on the basis of clinical data as well as physician directed decisions. For example, the system can automatically generate Adverse Event alerts and "trigger" the entire AE documentation process.
- Web based access enhances ability to monitor and review data remotely for quality control and compliance.

Esprit Health's Implementation and Consulting services focus on decreasing study start-up time and streamlining data collection and data management processes. The outcome of these efforts is the rapid creation of a central, secure database that enables immediate access to ALL research data for reporting and analyses.

Esprit provides a project manager and a cross-functional clinical and technical team that works to integrate the *eSphere* system with the current processes to maximize benefits from the very start. This approach requires no infrastructure investments and depending on the services chosen, can replace the need for:

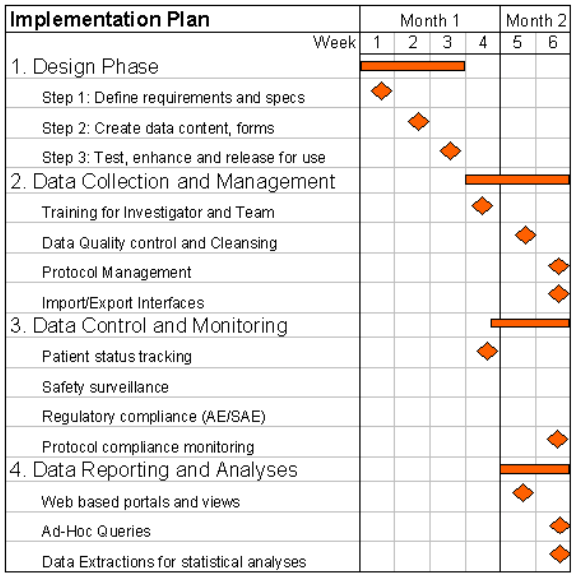
- Protocol manager
- Clinical Monitor
- Safety Monitor
- Statistician
- Database Administrator
- Data / Interface Analyst

From Design to Integrated Research Database

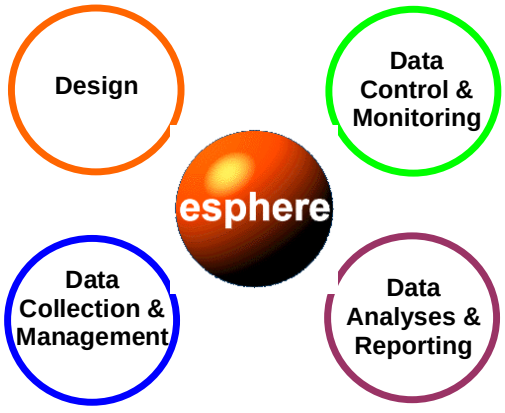
- Easy setup allows you to quickly define database, metadata criteria, design HTML forms and test.
- Generates protocol manual and related documents (Protocol description, data collection forms, and related procedures)
- Protects ownership of data yet facilitates sharing and re-use of common data dictionaries, standard forms and interfaces across multiple protocols.
- Maintain protocols, track amendments and disseminate changes

Data Collection and Data Management

- Esprit conducts training for ALL users: Investigator, Research Nurses, Clinical/Safety Monitors, and data entry.
- Convert paper files into researchable database
- Manage patient demographics, eligibility determination and cohorts.
- Coordinated collection of data assures elimination of wrong forms, errors of omission and prevalence of N/A's.
- Performs interactive, real time cleaning of data
- Import data from other clinical databases eliminating redundant data entry errors.



Implementation plan is customized to every protocol



Four Phased Approach

Data Control and Data Monitoring

- Patient/encounter coordination increases patient safety.
- Monitor patient status for unplanned and adverse events.
- Assure compliance with protocol flow and timing of events
- Conduct data quality and regulatory compliance audits
- Monitor protocol candidate eligibility and enrollment statistics (i.e. Accruals vs. Ceilings)

Data Analyses and Reporting

- Easy to use ad-hoc query tool and filter, sort and group by demographic, encounter and protocol data/.
- Prepare data extractions for export to Excel, SPSS, or SAS or other tools for sophisticated statistical analysis
- Develop Web based portals for the review and display of patient and cross protocol data

A New Paradigm

eSphere's new paradigm for healthcare information systems is built on the following core principles and concepts

Protocol Centric Design

- Creates a seamless infrastructure that gives researchers, clinicians and management timely data to successfully complete scientific investigations, empower decision-making and forecast personnel, material and capital needs.

Longitudinal Patient Record

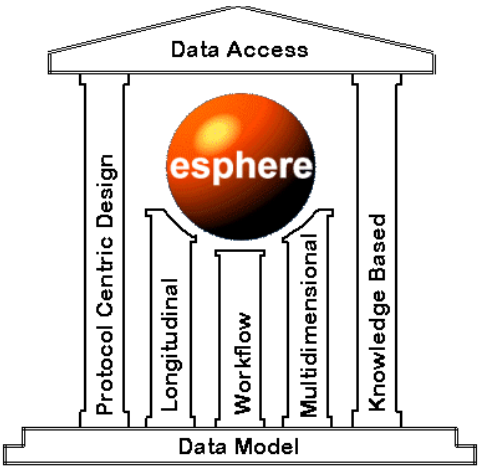
- Enables a single longitudinal patient record, encompassed by the research protocol, which integrates *all* data across current and prior encounters.

Seamless Workflow

- Integrates processes across clinical, nonclinical and departmental boundaries for efficient research and care.

Multidimensional

- Emulates the multidimensional and multidisciplinary nature of the healthcare process.
- Researchers, caregivers and administrators require the capability to shape and view a patient's health information as needed.



Knowledge Based Decision Support

- Provides access to clinical references and resources
- Incorporates a simple yet powerful If / Then rules engine and outcome dependencies to provide real time decision support on the basis of both clinical data and physician directed decisions.

Data Model

- A comprehensive set of linked data dictionaries and metadata that provides a common language for improved communication among all participants in the research and care process.

Access to Data

- Enable real time access to ALL data and export to specialized databases, while ensuring researcher's ownership of data.

Services

Implementation

- *eSphere* installation and configuration
- Protocol modeling and design workshops
- Training for Investigator/Study team and End users

Consulting Services

Esprit focuses on decreasing study start-up time, streamlining clinical and research processes, maximizing return on investment and improving the efficiency of data management.

- Design and creation of the protocol(s) in *eSphere* – from the metadata to data validation criteria
- Development of customized data collection tools using HTML and Javascript programming
- Design of Web portals and related views and reports for the protocol
- Monitor data collection process for compliance, data quality and timeliness
- Real-time, interactive data cleansing
- Develop customized Reports (e.g. Eligibility Counts, Outcomes Analysis)
- Prepare data extractions for statistical analyses

Technology

System Platforms

- Scalable SQL Database: Oracle
- Server: Unix, Windows NT, Citrix
- Client: Windows 98, 2000, NT, XP, MAC
- LAN: TCP/IP
- Web enabled

Architecture

- Object Oriented technology
- Three tier design
- Data Warehouse

HIPAA Privacy & Confidentiality

- User authentication, automatic logoff
- Role & context security access
- Audit trail

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