Enterprise SAE Requirements and Gap Analysis Report

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1 Overview

1.1 Purpose

SemanticBits has been tasked with performing a thorough review and analysis of NCI's needs with respect to the proposed Enterprise Data Management AE Reporting System (EDMAERS). The end result of this effort is this document, a detailed gap analysis between NCI's requirements and the current version of caAERS. It also includes a review of the administrative, analytical, reporting, and workflow related features and functionality of the AdEERS system and other supporting applications.

1.2 Background

The analysis efforts for this document were conducted in close concert with NCI-designated SMEs to understand the requirements and the current environment. Ann Setser, Nurse Consultant at NCICBIIT, shared here expertise on CTEP's requirements, the AdEERS system, current expedited reporting workflow, and NCI's requirements for expedited reporting. She helped determine the content to be provided in this document. Anne Thompkins from DCP, was a primary source of knowledge concerning DCP's expedited reporting requirements and workflows. She was a primary resource in performing a detailed review of the AdEERS system to understand the current system.

1.3 Requirements

NCI has performed a thorough requirements analysis for the EDMAERS. They have identified requirements in several different categories, including:

- Business
- Technical
- User
- Security
- Functional
- Ergonomic (or User Interface)
- Data
- Performance Quality
- Reporting
- Interface

This document will address each of these areas, identifying if caAERS meets the requirement, if it's fully or partially met, or if development still needs to occur before caAERS meets the requirement. In some areas, AdEERS and supporting tools/systems will also be discussed in relation to the requirements.

1.4 Current Adverse Event Tools

Groups across NCI currently use different tools and follow different workflows. No standard toolset is being used and paper-based workflows are still common.

1.4.1 Adverse event capture system

1.4.1.1 AdEERS

AdEERS (Adverse Event Expedited Reporting System) is NCI's web-based system for submitting expedited reports for serious and/or unexpected events. Reports entered into AdEERS are forwarded to designated recipients and the NCI for all trials using an NCI-sponsored investigation agent.

AdEERS is primarily used to capture and submit expected reports. It is used by CTEP, CIP, and DCP. It also has a powerful reporting system on the backend, allowing users to analyze different aspects of the information users enter in to AdEERS.

Communication occurs between other NCI tools and AdEERS. For example, protocol information collected in PATS (Protocol Authorization and Tracking System) and DESK (DCP's Enterprise System Knowledgebase) are accessed by AdEERS, allowing users to see the Treatment Assignment Codes (TAC), disease information, etc for the study when entering a report. This communication reduces manual work and data entry errors.

1.4.1.2 caAERS

caAERS (Cancer Adverse Event Reporting System) is an application that's used to collect, process, and report adverse events that occur during clinical trials. It supports the collection of 'routine' adverse events and the reporting of serious/unexpected adverse events.

As part of the Cancer Clinical Trial Suite (CCTS), caAERS integrates with a number of other tools to provide a full spectrum environment. caAERS can accept data from C3PR (Cancer Central Clinical Participant Registry), which collects protocol information; PSC (Patient Study Calendar), which collects information on a participant's status on a study (what cycle/course the person is on, appointments scheduled, etc); and LabViewer, which collects information on labs the participant has had run.

caAERS can be installed locally or centrally and supports importing data as well as real-time data transfer. When installed locally it can integrate with an organization's existing systems. This allows the organization to continue using their existing systems to capture information on participants, studies, and personnel, and use caAERS to record the AE data, since the real-time data transfer and import functions allow the systems to stay in-sync.

The built-in rules engine supports both regulatory reporting and local reporting needs. caAERS can be set up to automatically determine which reports are required, or a user can manually select the reports.

1.4.1.3 CDS and CDUS (https://cabig.nci.nih.gov/tools/CDS)

CDS (Clinical Data System), which replaced CDUS (Clinical Data Update System) in 2006, is the primary resource of clinical trial data for NCI Division of Cancer Treatment and Diagnosis (DCTD) and DCP. It is a web-based application, supported only on Internet Explorer, and is used to collect information on the protocols, participants, and adverse events that are experienced.

1.4.1.4 C^3D (https://cabig.nci.nih.gov/tools/c3d)

C^3D, Cancer Central Clinical Database, is a clinical trials data management system that collects clinical trial data using standard case report forms (CRFs) based on common data elements (CDEs).

C^3D has three web-based components, one for protocol building, one for data entry and management, and one for real-time access to clinical data. Users can use this tool to electronically submit clinical trials data to CDS and to the Clinical Trials Monitoring Service (CTMS/Theradex).

Adopters are able to use either a hosted version of C^3D, or they can install it locally.

1.4.1.5 Remote Data Capture (RDC) tools

NCI supports a centralized remote data capture (RDC) tool that can be used by internal groups (CTEP, DCP, CIP) or by organizations participating in clinical trials. The current

RDC tool is Oracle Clinical, although a new contract is in the process, and pending further appeals, will be awarded to Medidata. The RDC is used to collect all AE data, including routine, solicited, and serious AEs.

DCP currently uses the RDC for consortia trials, while older trials are reported via ITPR, an electronic spreadsheet. Data entered using these two tools is then transferred into DESK. All AE information collected has to be reconciled manually with what's entered in the RDC.

Many organizations that participate and run trials also use either an RDC or a local electronic data capture (EDC) tool. These might be off-the-shelf applications or custom built. Organizations often use these tools for both data capture and for in-depth analysis, since they provide both capabilities.

1.4.2 Adverse event data analysis

1.4.2.1 CDS and CDUS (https://cabig.nci.nih.gov/tools/CDS)

CDS also provides a mechanism for data access by stakeholders including cancer centers, cooperative groups, and single institutions via a data analysis interface. This interface enables users to view and generate reports about various aspects of the clinical trial process.

Each quarter, a cumulative report is compiled and submitted to CTEP for analysis and further evaluation.

1.4.2.2 C^3D (https://cabig.nci.nih.gov/tools/c3d)

J-review is a web-based tool associated with C^3D. It's used for ad-hoc querying, reporting, and analysis of clinical data.

1.4.2.3 CRIX (http://crix.nci.nih.gov/)

CRIX, the Clinical Research Information Exchange, is collaborative project between the government, academia, and bio-pharmaceutical industry to implement electronic infrastructure to support the sharing of clinical research data. As of September 2008, there are two modules in development, FIREBIRD and JANUS. FIREBIRD, the Federal Investigator Registry of Biomedical Information Research Data, automates the submission of FDA Form 1572. JANUS is a clinical data repository that provides a data collection and analysis warehouse for both clinical trial data submitted for protocols as well as clinical outcomes data.

1.4.2.4 caAERS

caAERS, as described in section 1.4.1.2 above, is an application that is used to collect, process, and report adverse events.

caAERS allows the collection of all Adverse Events, including solicited, 'routine', and 'serious'. AEs are grouped together based on user-defined timeframes, supporting the expedited reporting requirements, and the data reporting requirements.

APIs are currently being developed to support clinicians' reporting and analysis needs. APIs are also being developed to support the exportation of AE data in to other systems, such as an organization's local CTMS.

1.4.2.5 Remote data capture tools

As discussed in section 1.4.1.3 above, various remote data capture tools are used. In addition, many of these tools support analyzing the data after it's collected. All AE data must be reported on quarterly basis.

1.4.3 Supporting systems and elements

There are multiple systems that provide information necessary for AE collection and analysis. These systems can communicate with, be integrated with, or be part of the adverse event capture and analysis tools.

1.4.3.1 CTEP ESYS

CTEP ESYS, the CTEP Enterprise System is the primary data collection mechanism for NCI's large, complex extramural clinical trials program. CTEP-ESYS collects safety and clinical results data on 1,500 ongoing clinical trials that monitor more than 300,000 participants per year in more than 17 disease areas.

The CTEP-ESYS is composed of multiple integrated modules to support internal and external CTEP business operations. A module to support each Branch/office in CTEP has been developed, is in development or is scheduled for development. Additionally, several external modules for data collection, information distribution, correspondence and training have been developed or are scheduled for development. The following applications and services are all considered part of the CTEP ESYS:

- Protocol Authorization and Tracking System (PATS)
- Clinical Data Update System (CDUS)
- Drug Authorization, Review and Tracking System (DARTS)
- Clinical Trials Monitoring Branch- Audit Information Systems (AIS)
- Adverse Event Expedited Reporting System (AdEERS)
- Investigator Registration (Inv Reg)
- Dose Regimen (Dose Reg)
- Enterprise Query Wizard (EQW), Enterprise Information System (EIS)
- Enterprise Core Module (ECM)
- Clinical Investigations Branch Information System and Clinical IT (CIBISCIT)
- Regulatory Affairs Branch Information Tracking System (RABITS)
- Document Management, Assembly, Review and Tracking System (Docu-Mart)

1.4.3.2 DESK

DESK, DCP Enterprise System Knowledgebase, is a web-based custom Oracle database composed of multiple applications. DCP uses it to track information about protocols, organization, and people, including contact information, type of organization, investigator status, and organizational quality control status.

DESK is used daily to manage clinical trials. Information maintained in DESK is used by AdEERS and would need to be used by any additional tools to prevent duplication of work.

1.4.3.3 PATS

PATS, the Protocol Authorization and Tracking System, is used by CTEP to abstract key protocol data elements. This information is then made available to AdEERS to help AdEERS present information during the reporting of AEs.

1.4.3.4 caAERS – solicited AEs

caAERS allows solicited AEs to be associated directly to any study in caAERS, whether the study information is maintained in caAERS directly, or updated via an API. The study module allows authorized users to associated AEs to the study, based on a list of AEs provided by the investigator. This list of AEs will be presented to the user during the documentation of AEs.

1.4.3.5 C3PR

C3PR, the Cancer Central Clinical Participant Registry, is a web-based application for managing clinical trial data across multiple cancer clinical trials. It provides an efficient web-based clinical trials information management system available for use by multiple cancer research centers, and can support large-scale, geographically dispersed studies. C3PR provides current enrollment statistics and a repository for participant information across studies, sites, systems, and organizations.

C3PR is part of the CCTS suite and can be installed locally or used centrally. Information collected in C3PR can be used by other CCTS suite applications, either through direct communication or by exporting the data.

1.4.4 Other tools

1.4.4.1 Clinical Trials Database (CTDB)

The Clinical Trials Database is a proposed comprehensive, community accessible database that will contain complete, up-to-date information (including status, protocol, accrual, adverse events, etc) on all NCI-supported clinical trials. It is a CTWG Informatics Initiative, meant to centralize the work done in PATS, CTMS, CDUS, AdEERS, Summary 3/4 Reports, and PDQ (Physician Data Query). It is meant to be a centralized database that will reduce redundant data entry and reporting and provide authorized users with access to data and reporting.

1.4.4.2 Clinical Trials Monitoring Service (CTMS) / Theradex

CTMS/Theradex is used to collect participant level data for CTEP Phase I & II trials and is reported every 2 weeks. Theradex submits CDUS data to CTEP monthly.

1.4.4.3 Patient reported outcomes

This is a tool that is planned for development.

1.5 Current Workflows

Each NCI Organization has a set of procedures they follow when reporting SAEs.

1.5.1 CTEP

CTEP has specific workflows for determining if reporting is required, handling the creation and submission of expedited reports, and processing the reports after they've been submitted. The majority of the workflows for determining expedited reporting requirements and submitting the expedited reports are built in to the AdEERs. On the other hand, very little of the workflow surrounding processing the reports is built in to AdEERS, with most of it being paper-based.

1.5.1.1 24-hour notifications

If an AE requires a 24-hour notification, the users completes the 24-hour notification using AdEERS. The notification requires the user to enter a specific set of information (a subset of the information required for a 5-day and 10-day report). When the notification is submitted, AdEERS automatically sends it to the appropriate parties. While a 24-hour notification can be amended, it is not something that occurs frequently.

Once submitted, the 24-hour notification entry in AdEERS becomes a 5-day expedited report, requiring the user to enter additional information before the report can be submitted.

1.5.1.2 Expedited reporting (AdEERS/ABS/manual)

CTEP has a very in-depth workflow for handling expedited reporting of AEs. Entry of AEs and expedited report is done electronically through AdEERS. When a report is submitted through AdEERS, some reviewing may occur electronically. For example, if central processing is in place, the lead organization would review the report in AdEERS, send it back to the submitter for clarification, or send it on for processing.

In addition to data entry and reviewing, AdEERS also handles some decision making. For single-agent protocols, AdEERS has the ASAEL (Agent Specific Adverse Event List) programmed in to determine expectedness, which is one of the criteria for determining if an expedited report is required. It also allows you to enter some basic information about an AE to determine what, if any, expedited reporting is required (5-day versus 10-day for example).

Once the report is submitted in AdEERS and any central processing has been completed, some processing steps occur before the majority of the reports are turned over to their contractor, TRI. TRI processes the report, including submitting them to FDA where necessary. The majority of the steps are manual, including adding printed forms to color-code folders and multiple interoffice or courier deliveries. There are some electronically driven steps, including an exchange of email, information entered into ABS (AdEERS Backend System), and entering information into a database only used by TRI. When an expedited report has been completely processed, it will include additional forms and supporting document. The report plus this supporting information will be referred to as an expedited report package.

1.5.1.3 Do not process (DNP) workflow

After Expedited Reports are submitted, the AdEERS backend system (ABS) evaluates the report to determine what handling is required. If an Expedited report falls in to any category where detailed analysis is not required, it is marked as DNP. This means TRI will not activate the paper-based process of routing and reviewing. Instead, e-mail is sent to the site saying there's no further action required, and the report is added to the DNP list.

In the ABS, the IDB can run the IDB DNP report around a few parameters. The results of the search will show the AdEERS ticket number, the protocol number, agent name, AE information (category, AE, and grade), participant ID, date submitted, and location. This allows the IDB to quickly run through the expedited reports and mark them as reviewed, open them to view the entire report to determine if they want further information, or activate them to start TRI's processing workflow. If the IDB chooses to open an expedited report to get more details, it will automatically be marked as reviewed.

1.5.2 DCP

DCP currently supports two types of studies: CCOPs and Chemoprevention. Each has a specific workflow regarding reporting of SAEs.

1.5.2.1 CCOPs

CCOPs trials follow FDA regulations for reporting, using the CDUS-abbreviated reporting, or "AdEERS pathway" for actual reporting. This means an AdEERS 10-day report is used to report all SAEs, and does not include verbatim reporting. In general, the commercial pathway is followed for reporting, although some studies or groups may have additional limitations.

When an SAE occurs, it is (generally) reported using AdEERS. After it's been entered, the report will go to the research base, the AdEERS coordinator, the DCP Office, and the program director. DCP will review and store the report, but does nothing else with it. The program director may bring up reports with the group, such as when a trend is occurring, but it's up to the research base to process and manages the reports.

1.5.2.2 Chemoprevention program studies

There is one rule for all SAE reporting requirements: if an adverse event occurs that meets one of six "serious" indicators, an expedited report is required. When this happens, the NCI Medical Monitor (MM) and/or DCP Contractor must receive notification of the event within 24 hours of learning of it. The complete SAE form must be received by the MM and/or the DCP Contractor within 48 hours.

During processing, the expedite report becomes known as a case file, since additional information on top of the report is required. The contractor enters the information into a database and a tracking database. If they need clarification, they'll start a query spreadsheet and send it to the site for clarification. Then they send the report and a triage form (printed from tracking database) to the MM.

Medical Monitors review the SAE form and determine if the adverse event was unexpected. If they need additional information, they'll either contact the site directly or add their comments to the query spreadsheet.

When the MM has all the required information, they will then complete the write-up and triage form (and query spreadsheet if there are questions), and send it to the contractor. If the MM wants more info, the contractor sends the case file and any queries to the site. As the contractor receive responses, the information is added to the databases and sent to the MM.

Once the contractor has all the information concerning the AE, the contractor completes additional steps, as described below. These steps generally revolve around the expectedness and relatedness of the AE to the study.

- Expected or not related: submits to FDA as part of annual IND report
- Unexpected and related: submits IND Safety report to FDA within 15 days of initial report via written report
- Unexpected, related, and is fatal or life-threatening: submits IND Safety report to FDA within 7 days of initial report via telephone or fax
- Unexpected and related: notify participating investigators and update the IND

Note: There are some differences in the process based on the study and MM. Some MM prefer to receive the information before it goes to the contractor. Somme MM want to receive the information at the same time as the contractor, and some MM prefer the information goes to the contractor first before it's sent to them.

1.5.3 CIP

The Cancer Imaging Program (CIP) creates expedited adverse event reports using AdEERS or paper-based AdEERS reports. When 24-hour notification is required, notification is given by phone to both the contractor handling the expedited AE collection process, and the institution's SAE notification line. The completed expedited report is then due within 10 working days of first knowledge of the event.

As of mid-August 2008, CIP implemented a new process. The specific steps that are completed by the contractor after they receive the completed report are unknown.

If an AE does not required expedited reporting, it will be reported using the case report form (CRF). CIP also uses the abbreviated CDUS report system for their Phase 2 and Phase 3 studies. These reports are submitted quarterly to CTEP.

1.5.4 Cooperative Groups

Cooperative groups, such as North Central Cancer Treatment Group (NCCTG) and Cancer and Leukemia Group B (CALGB), consist of networks of cancer specialists at community clinics, hospitals, and medical centers. They support several types of trials, with various reporting requirements and methods. Some trials may be CTEP sponsored, some DCP sponsored, some sponsored by other groups. When this is the case, the sponsor's standard reporting method may be used, although deadlines for reporting could be different.

Cooperative groups have additional workfolk required, regardless of who sponsors the study. Since the studies could have participants at any of the group's locations, all documentation must be reviewed centrally before being forward to the sponsor. This includes standard CT Case Report Forms (CRF), entries into a remote data entry system, and expedited reports, both paper-based and electronic.

2 Requirements for AE Reporting

2.1 Overview

As cancer research has progressed and more trials are being run, NCI has evaluated their processes and has worked to improve the tools they provide to support cancer research. In 2006 they completed a thorough analysis of their adverse event reporting systems. This analysis led to the development of a detailed requirement document for an enterprise data management adverse event reporting system (EDMAERS). The authors grouped the requirements into several major categories, including:

- Business
- Technical
- User
- Security
- Functional
- Ergonomic (or User Interface)
- Data
- Performance Quality
- Reporting
- Interface

These categories serve to organize the needs of the various organizations involved, and identify all requirements that fall within the scope of that category. Several of the categories contain subcategories to further organize the requirements.

Since each category is all-inclusive, several requirements are documented in multiple categories. Where possible, cross references have been given to show the duplication.

This section of the document will provide an overview of each category, discussing the requirements in general. Sections 3-14 will discuss the detailed requirements for category and subsection, discussing how the requirements are currently met or how they will be met.

2.2 Organizations Involved

Various organizations sponsor clinical trials and use NCI's tools. Each group follows their own workflows and processes, but many pieces overlap. The challenge is to develop tools that are based on a shared set of requirements while still meeting each organization's individual needs.

The following organizations were considered as we analyzed the requirements for the EDMAERS and performed our gap analysis:

- CTEP
- DCP
- CIP
- FDA
- PhRMA (Pharmaceutical Research and Manufacturers of America)
- EORTC (European Organization for Research and Treatment of Cancer)
- ICH (International Conference on Harmonisation)
- General (Other Cancer Research Institutions)

Overall, the requirements are not separated by organization. If a requirement is organization-specific, we discuss possible alternatives and ways the requirement may affect other organizations.

2.3 Requirements Matrix

In 2006, CBIIT completed documenting the known requirements for the EDMAERS. These requirements, available in NCI_EDMAEReportingSystem.pdf (https://cabig.nci.nih.gov/workspaces/CTMS/Documents/CTMS_Documents/NCI_EDMAEReportingSystem.pdf), are the basis for this document. Requirements that were identified after the completion of that document have also been taken in to consideration.

Requirements may be duplicated in multiple categories, since the authors of the requirements document tried to ensure each category was all-inclusive, thus not requiring the reader to jump to different sections to understand the full requirements. In addition, since two years have passed since the requirements document was completed, some of the requirements may be obsolete or may have changed due to technological advancements or changes in directions at NCI.

2.4 Business Requirements

The business category discusses the business problems that need to be solved. There are two general categories here, contractual needs and overall needs to support the needs of the users of the system. Since the contractual needs aren't as pertinent to this document, they will only be discussed briefly.

The developer of the EDMAERS must have a history in the field. They should be familiar with development methodologies and requirements of caBIG and be able to develop an interoperable application, including customizing it as needed. They should also be known by organizations in the field who can recommend their services and expertise. Finally, they must be familiar with, and able to meet, all federal regulations.

Overall, the EDMAERS must meet, and really surpass, the capabilities of existing applications, specifically AdEERS. It must be able to:

- Support the printing of any AE report, old or new (versioning)
- Provide complete data management, including auditing, traceability, legacy migration, and archiving
- Be able to maintain the manual process workflows (where necessary)
- Generate an exhaustive list of reports (including ad-hoc reports) in both html and PDF format
- Support various vocabularies and workflows required by different groups
- Support the addition of attachments to expedited reports and provide automatic notifications used by various groups
- Come with complete documentation, including technical and end-user guides, online and in-line help, and a training cbt that includes the ability to track completion of training

2.5 Technical Requirements

The technology and technical infrastructure requirements that must be satisfied by the proposed solution are addressed in the technical category. In general, these relate to development practices that ensure a quality application that integrates smoothly into the existing technology suite while meeting required standards. Some of the basic requirements the developers of EDMAERS need to meet are:

- Provide a secure API interface to support messaging/communication with caDSR (Cancer Data Standards Repository), EVS, and CDEs
- Use a J2EE architecture, based on (and fully compliant with) the caBIG security model
- Be a web deployed, bilateral communication supporting system with SSO and an XML generator module for queries and retrieval of information; the preference is for the application to work in a Solaris or Linux environment, written with CORBA object model compliance
- Follow FDA and NCI standards (specifically called out were silver-level caBig compatible, ISO 11179, and E2B ICH standards)
- Include track-able and secure user access
- Have built-in change control and configuration management
- Work with a redundant server configuration, for backup, restoration, and disaster recovery

In addition, the application must be:

- Able to run as a hosted or stand-alone application, compliant with NCI architectural requirements and federal regulations
- Highly configurable and well documented, supporting multiple workflows, pathways, etc while allowing configurations to be easily modified without programming
- Capable of centralized and decentralized processing and approval (routing and reviewing)
- Able to import and export data in multiple formats
- Provide automated email and notifications of SAE and expedited reports for both various steps of the sponsors' different workflows, as well as routing and reviewing

2.6 User – AE Workflow Requirements

Requirements identified in the user category are generally found in use cases and process workflows. However, the initial identification of these is provided in list format. These requirements document the actions users must be able to perform to satisfy the business objectives. Some of the overarching user requirements include:

- When an AE is submitted, or a query is performed, users must be able to provide additional information via system updates or attachments, with automated notification to appropriate users built into the system based on process steps and/or record status
- Allow and support both the pre-review of an AE report before submission to RN for review, and the full AE workflow report intake process
- Support a complete IDB assessment, including requests for additional info, notifications, completion of assessment, and various IDB assigned statuses
- Support various workflows for different statuses and different workflows
- Provide full AE report lifecycles, including receipt of report, additions to the report, review and finalization of AE reports, and information distribution and archival

2.7 Security Requirements

Security of participant information is a high priority, so the system must prevent unauthorized access to the system and data. Considerations include authentication of users, restriction of data based on requirements for performing their work assignments, and auditing of access and data. Some of the high-level requirements documented in the security category are:

- Must support full auditing, role-based authorization and authentication, a diverse security module, and protection from viruses
- Must be able to pull identification info from the data for compliance with privacy laws, as well as meet other regulatory compliance issues
- Must be FISMA and NIST compliant, with an auto log-off feature
- Must have a login module that allows users to log in with a username and password, controlled by functionality
- Must support both local and remote access, with authentication and authorization built in

2.8 Functional Requirements

The authors of the requirement document thoroughly analyzed and documented the functionality requirements for the new EDMAERS. The requirement list is extensive and is based on business and user requirements. Some of the high-level requirements included in the functional category include:

- There must be an admin module that
  - Allows customization of screens and fields by a non-technical person
  - Supports configuring rules
  - Allows the changing of labels and/or pick lists
  - Verifies the user has adequate browser requirements
  - Is robust enough that few coding changes are required to support new workflows
- Must provide built-in, customizable reports and the ability to create ad-hoc reports; there needs to be a built-in screening/review process prior to submission of reports to NCI, and the ability to view and follow up on said reports
- Provide ability to create, search for, submit, copy, amend, and withdraw reports, with limitations built in on all functions based on user roles and statuses of the reports
- Have the ability to import various data items (AEs, reports, data for reports), and the ability to export the same items to multiple formats
- Provide a configurable review module for CTEP IDBs, DCP, CIP INDs, and CIP IDEs
- Provide built-in help for supporting all functional requirements
- Ability to provide different workflows for different types of protocols, agents, and devices
- Handle the current DNP module completely

- Provide a unique, 7-digit ticket number for all reports, with additional numbers for amendments
- Provide built-in error checking to validate data as entered
- Provide a built-in review system consisting of multiple levels and notifications, with the reviewer able to change the status of the reports at any point
- Support 24-hr notifications and creation of AEs and SAEs and expedited reports, with support for API integration into other systems to transfer the information
- Provide a method to include information for all sections of an expedited report

2.9 Ergonomic (or User Interface) Requirements

The look and feel of the application is important for adoption of the EDMAERS. The Ergonomic category discusses the requirements that must be met to ensure ease of use and accessibility by meeting 508 compliance and providing standardization of screen aesthetics, content layout, and navigation. High-level requirements include:

- Comply with NCI User Interface (UI) guidelines (http://www.usability.gov/pdfs/guidelines.html) and cancer.gov's page design standards (http://webresources.cancer.gov/), which requires including the cancer.gov mini banner on all pages
- Have complete 508 compliance (visually impaired users, color blind, etc), supporting full screen reader and keyboard-only mechanisms
- Should work in NCI's list of supported browsers (IE 5.0, Mozilla 1.0)
- Should conduct field-level validation through server side objects on each page, and avoid the use of frames
- Don't use JavaScript in place of business validation – ensure data integrity and validity
- Optimize screens for 1024x768, supporting 800x600 and up
- Support other languages in the future (no current requirement), and be NLM (National Library of Medicine) and NSL (National Science Library) enabled

2.10 Data Requirements

The data category discusses the high-level data requirements of the system. Specifically, it describes what data must be read, modified, stored, and produced within the system. The high level requirements include:

- Must provide complete data security
- Have the ability to maintain all data elements currently captured by AdEERS
- Provide complete data auditing; this includes but is not limited to
  - who changed what when
  - complete traceability
  - storing, tracking, and maintaining the workflow status automatically

- Ability to import and store legacy data, including user roles, AE info, and reports/histories
- Maintain a status and process history for all AEs entered, storing info in electronic format, with a 50-year data repository

2.11 Performance Quality Requirements

For the EDMAERS to be accepted by users, it will have to meet specific performance requirements, as documented in the performance quality category. These requirements include:

- An uptime of 95%, 7 days per week
- Easy to maintain and support
- Response time of less than 5 seconds per page, supporting 400 concurrent users
- User-friendly, supporting a variety of workflows
- Certified by a third party who's performed quality assurance and testing

2.12 Reporting Requirements

The DEMAERS is a data collection and reporting tool, so it must have high quality reporting built in. The high-level reporting requirements are documented in the reporting category, and include:

- Must be able to produce all existing AdEERS reports and include a report/query wizard for end-users to generate ad-hoc reports
- Reports need to be exportable to Excel, Access, CSV, or SAS, be viewable online, printable (all or certain pages), and savable locally as html or PDF
- Must be able to electronically submit reports to FDA and approvers

While these requirements may seem minimal, the reporting that is currently in place via AdEERS is extensive, and will be broken down further in section 12 below.

2.13 Interface Requirements

Interface requirements revolve around the need to integrate, communicate, or interact with hardware systems, procedures, or other software systems. These requirements are documented in the interface category and include:

- Ability to import/export data from existing AE collection/reporting tools
- Ability to communicate with the AdEERS system (until it is replace)
- Ability to electronically submit to FDA, either via email or by integrating with their electronic submission tools

Some additional requirements, based on interoperability factors, may also exist, even though they weren't documented. Interoperability requirements relate to the ability of diverse systems to work together without additional work by the customer. For the new tool to provide the maximum benefit, we believe the new tools needs to be able to work with lab data collection tools, protocol abstraction tools, and the centralized AE repository.

3 Requirements Gap Analysis Overview

The primary purpose of this section is to provide an introduction to the analysis sections of this document, where the authors discuss the extent to which the current version of caAERS (version 1.5) fulfills the requirements for the EDMAERS. The secondary purpose is to document how well the requirements are met by tools currently in use, such as AdEERS.

While Requirements for AE Reporting discussed the requirements at a high-level, Chapters 4 – 13 scrutinizes the requirements, decomposed them into sub-requirements to better describe the gaps.

Each chapter will include the following information:

- What the specific requirements are
- How caAERS meets the requirement and matches the functionality
- What gaps have been identified

In addition, the chapter may include information on:

- How the requirement is met by NCI's current toolset
- How caAERS is addressing the gap (if development is already planned for example)
- If a requirement requires more research to understand it
- If a requirement is obsolete and why

For ease of reference, the gaps will also be summarized in Appendix B - below.

4 Analysis of Business Requirements

4.1 AE Generation

The EDMAERS has to support the addition of new information and attachments to the expedited reports, with the ability to recall and print all versions of the reports.

4.1.1 How the requirement is currently met

AdEERS has the ability to print any report in the system. As reports are amended, they are given new AdEERS numbers, making the different versions easy to identify and print. There is a section that identifies any attachments that will be sent that should be included with the report.

caAERS collects and stores all changes made to a report, and provides the ability to print reports. Reports can be printed in multiple formats, and exported to XML. caAERS also has the ability to identify attachments that go with a specific report.

4.1.2 Identification of gaps and potential gaps

AdEERS and other existing systems completely meet the report printing capabilities. These systems are set up to easily identify the various versions of a report, enabling it to be viewed, updated, and printed. They do not allow the attachment of other information to the reports however.

caAERS supports the printing of reports, but additional development needs to occur to support identifying and printing various versions of the report. Information needed to support this capability is captured in the database, the development team just need to add access to it. This requirement is also discussed in sections 4.3 and 10.2 below.

Development also must occur to support adding attachments directly to an expedited report. This requirement is also discussed in sections 4.11, 5.3, 5.5, and 8.2.1 below. Adding this capability may also require additional development to the systems that would be receiving the expedited reports. For example, if caAERS attached files to an expedited report and sent it to AdEERS, AdEERS would not be able to handle the attachments, and may not even accept the report. If the reports are just being sent via email, there wouldn't be a problem.

4.2 Business

The EDMAERS must be caBIG silver-level compliant, with the application's development team providing any necessary customization without going through a third party. If the application that is being suggested to become the new EDMAERS is currently being used, the development team should have recommendations and references from the organizations currently using the application.

4.2.1 How the requirement is currently met

Modifications to AdEERS and other NCI tools are completed by the owner/developer of the tool. Most of these tools are not caBIG silver-level compliant, but they do have an extensive user base.

The caAERS development team provides all development to the caAERS application. They also provide assistance to modify an organization's existing tools so the tools can better integrate with caAERS. Each development cycle it recertifies as caBIG silver-level compliant.

caAERS is actively being tested by many organizations, both as a standalone application and part of the CCTS. As of September 2008, both Mayo Clinic and Wake Forest are completing pilot programs for tracking AEs and creating and submitting expedited reports.

4.2.2 Identification of gaps and potential gaps

Neither AdEERS nor other existing NCI tools completely meet the business requirements. While the development teams for all the tools perform customization and additional development, they have not made most of the tools caBIG silver-level compliant. In most cases, extensive development would need to occur to achieve the required compliancy.

4.3 Data Management

Complete data management must be supported. The following requirements address what aspects of data management must be supported:

- Full audit trail for entries into the database and all changes made to data
- Complete traceability of any document or analytical results submitted to regulatory agencies, with the data being stored, locked, and audited after submission
- Migration of legacy data from various sponsors and organizations, while still supporting interfaces into CTEP ESYS and other systems to reduce the impact of the repository change on other components
- Store, track, and maintain workflow status during updates to the system and/or to the expedited report package
- Have a 50-year repository for storing retired data
- Maintaining electronic versions of all AE reports, including status and processing history for reports that were imported in the system, and allowing access to said reports by authorized users
- Provide the ability to delete database items in two methods – soft(logical) and hard (permanent)

4.3.1 How the requirement is currently met

ABS (AdEERS backend) and the supporting database have full auditing and traceability. When reports are submitted to regulatory agencies, the data included in those reports can be easily identified and pulled up again. Since all changes are tracked individually, the changes are, in essence, being locked. The only way to remove or modify the data would be to go directly into the database and modify the individual record, something that wouldn't be easily achieved, and that few people have rights to do.

Since the workflow status is a separate field within the database, updates to the system and expedited report package do not affect this. Also, since each amendment is treated as a separate record, and all amendments are tied to the initial record, the status can be maintained across versions.

AdEERS backend provides access to all previous versions of the reports. If you have the ticket number, protocol number, and participant id, you can also access the report through the AdEERS front end.

caAERS supports the viewing of the current version of expedited reports. All changes are tracked and maintained in the database, so there is a history of older versions of the expedited report, it just isn't easily accessible. Given direct access to the database, a

complete history of a report and fields within the report can be gathered. Also, with the right access, records can be 'deleted'. However, few users have that level of access for the centrally maintained version of caAERS, and the access can be controlled at local institutions.

caAERS provides a method that allows organizations to import legacy data. The caAERS development team developed a schema to describe the formatting required to support importing the data.

4.3.2 Identification of gaps and potential gaps

caAERS needs some additional work in this area to fully meet the requirements. Specifically,

- Providing a 50-year data repository has to be examined. As discussed in section 5.8 below, the caAERS development team would only be required to provide this for the centrally installed version of caAERS. They would also need to ensure the data is maintained in a format that allows an organization to easily create this repository if they choose to install caAERS locally. Some of the questions the caAERS development team needs to answer include
  - What would be the format of the repository (backup server, backup tapes, duplicate repository of the current repository, etc)?
  - How many AE records and expedited reports would it need to hold?
- Allow access to, and printing off, all version of an expedited reports – caAERS only provides viewing and printing access of the current version of the expedited report. A method to review older versions of the report would have to be implemented. This requirement is also discussed in sections 4.1 above and 10.2 below.
- An interface with all of CTEP ESYS does not exist. Messaging and APIs support integration with AdEERS, but AdEERS is only one of many tools that make up CTEP ESYS. Additional research needs to occur to determine if the APIs and messaging the caAERS team has developed to support integration with other tools will be sufficient, or if more development needs to occur.
- The caAERS development team has started researching the best methods to provide auditing support for both AEs and expedited reports. Auditing has always been a consideration, so the database is already set up to support the required auditing. However, there's currently no easy way to provide the details necessary for an audit report. This requirement is also discussed in sections 4.6, 7.1, 8.3.4, and 10.2 below.
- Currently data isn't locked; only the primary keys are locked with all other fields able to be modified. More research needs to go in to the regulatory agencies traceability/data requirements to determine what additional development needs to occur to meet this requirement.

4.4 Documentation

The EDMAERS must be well documented to assist with the adoption and usage of it. Specific documents to be developed include:

- Standard operating procedures
- Detailed administrative manuals
- Documented procedures and standards

- End-user documentation
- Detailed design and technical spec document

4.4.1 How the requirement is currently met

AdEERS has built-in help to assist with actually using the system. There is also computer-based training to assist in learning how to use the AdEERS front-end.

caAERS is well documented. There is a very detailed design and technical spec document, with schemas provided for all modules. There are manuals for administrators to use with installing caAERS, setting it up, and maintaining it. There is a detailed user guide, and inline help to assist the users with understanding the requirements for specific fields. There's also a new online-help system that details the use of caAERS.

4.4.2 Identification of gaps and potential gaps

The front-end of AdEERs has help, but there doesn't seem to be any specific manuals for running through it. There are frequent training sessions and a test site to use to learn the system. The AdEERS backend (ABS) does not contain built-in help.

The authors of this report were unable to locate any documentation to support using the ABS or any of the other NCI tools. The same goes for technical documentation, such as the design and technical spec documentation, an administrative manual, and standard operating procedures. This is not to say that the documentation doesn't exist, access to it may be restricted, but if these documents exist, they aren't easily accessible.

The caAERS development team does a good job of providing technical and user-focused documentation. Documentation is updated as new development occurs and as adopters ask for clarification or assistance in performing tasks. Additional work will be done to provide a richer procedures and standards documentation.

4.5 General

For the EDMAERS to meet business needs, it must provide all the functionality currently available. This includes:

- Supporting printing and transmission of AE and expedite reports via FAX or courier
- Matching the functionality of AdEERS
- Allowing collaboration between diverse groups, based on authorization levels
- Providing a user friendly interface for infrequent users

4.5.1 How the requirement is currently met

caAERS has an interface that is basic and straight forward, allowing all levels of users to use it to enter AEs and create and submit reports.

caAERS allows users to enter AE information and then determine what reports are required. Users can complete the report in caAERS and send it electronically (through AdEERS for CTEP studies, or via email for other studies). caAERS submits expedited reports electronically through AdEERS, which requires it to use the same CDEs (if caAERS didn't map to AdEERS, reports couldn't be submitted).

caAERS can also be configured for various workflows, including CTEP, DCP, and CIP specific workflows, to help determine if an expedited report is required, and if it is, to create the specific report.

Users can print all reports in XML and PDF format, which can then be faxed or sent via courier to the appropriate parties. This means reports can be processed via both electronic and paper-based workflows.

4.5.2 Identification of gaps and potential gaps

caAERS still needs some work to meet the functionality of AdEERS. For submitting expedited reports, it still needs integration with ASAEL, or at the very least, provide a way to handle expected AEs. The ASAEL is important because it provides information on if an AE is expected, which in turn is used to help determine if an expedited report is required. Expectedness in addition to grade and hospitalization, determines if expedited reporting is required, and if it is, which specific report is required. The ASAEL is only valid for single modality protocols. For multi-modality protocols, AdEERS can not automatically determine expectedness of an AE. The information has to be located in the protocol and other supporting documents. The caAERS development team has a plan for handling expected AEs for single- and multi-modality protocols. This functionality will be available in caAERS version 2.0. This functionality is also discussed in sections 5.5, 8.3.2, and 10.1 below.

The big gap in functionality is caAERS lack of reporting and processing features that are included in ABS. These requirements are also discussed in sections 4.7, 6.2, 8.2.8, and 8.3.3 below. The ABS includes about a dozen modules to assist with analysis and reporting. The caAERS development team has started work on a reporting API, but functionality is limited and the interface is completely code based. caAERS also does not include any of the processing functionality that's built into ABS, such as marking expedited reports as DNP.

Some specific reports and processes that need to be added include:

- (IDB) DNP – Identifies which reports do not need to be fully reviewed, marks them as DNP, and provides a reports of the expedited reports for the IDB to go through
- Query New AE – check status, DNP status, general information
- Processing Data – shows phase information for the processing of an AE
- Assessments – shows the different assessments that have been made by various users
- ARA – allows users to create and print an ARA Summary (report)
- Additional info – way to track requests for additional information (and the responses)
- Various Statistical reports
  - Ticket Summary
  - Process Stage summary
  - AE comparison
  - DNP Summary
  - Attribution Summary
- Various General Reports
  - Print expedited report & blank evaluation forms
  - Handled expedited reports per x timeframe
  - AEs requiring expedited reports per x timeframe

- Expedited reports started but never completed
- Duplicate report check
- Pending reports
- Process completion report
- General AE report – used prior to audit

4.6 Regulatory Compliance

The new system must meet all applicable federal regulations. These requirements are also discussed in sections 4.3 above and 5.2.1.2, 7.1, 7.2, 8.1, 8.3.4, and 10.2 below. Specific regulations and requirements include:

- 21 CFR Part 11 (http://www.21cfrpart11.com/)
  - Electronic signatures (part of CFR part 11) using DHHS or SAFE credentials
  - Software validations
- HIPAA (http://www.hhs.gov/ocr/hipaa/) (also discussed in sections 5.2, 7.2, and 8.2.1 below)
- Federal Privacy regulations
- Federal information security requirements (FISMA) (also discussed in 5.2 and 7.3 below)
- Complete Auditing (this requirement is also discussed in sections 4.3 above, 7.1, 8.3.4, and 10.2 below)
- FDA 21 CFR 312 SAE (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312) ?
- Complete documentation of the application, from inception to release

4.6.1 How the requirement is currently met

As of September 2008, the authors of this document believe AdEERS is inline with most of the federal regulations. It provides full auditing on all data entered, has the ability to remove participant identification from the reports, and has multiple levels of data security. Further research needs to occur to determine the status of other NCI sponsored tools.

caAERS meets several federal regulations. It uses a public key infrastructure (PKI), which meets market and regulatory requirements for securing electronic information. Changes to information are tracked, and access to the data is limited by roles and responsibilities.

caAERS is based on the caBIG security model, which facilitate the achievement of requirements that are defined by regulations such as the FDA's 21 CFR Part 11, HIPAA, and FISMA. Further details on this can be found in section 5.2.1.2 below. caAERS provides functionality needed to support operating procedures that comply with many of these regulations.

The caAERS development team provides full access to all software documentation and all documentation used to develop and test caAERS.

4.6.2 Identification of gaps and potential gaps

At this time, none of the tools used for clinical trial management and support contain support for electronic signatures.

While caAERS provides functionality needed to support operating procedures that comply with many of these regulations, a complete analysis of how this support addresses the specific requirements of each regulation has not been completed. Such an analysis would also require a detailed description of the organizations in which caAERS will be used. However, a few areas the development team has identified as needing work include:

- Implement electronic signatures, one of two parts of 21 CFR Part 11
- Increase auditing features – basic auditing has been tested, but not fully integrated either in the front- or back- end of caAERS (this requirement is also discussed in sections 4.3 above, 7.1, 8.3.4, and 10.2 below)
- Provide the ability to strip participant identification from expedited reports, which would allow more investigators to use the information while maintaining participant privacy

4.7 Reporting and Analysis

Reporting and analysis are high priorities in cancer research. The EDMAERS must be able to provide a full suite of reports and support analysis of the AE data. Some of the key features that must be provided include:

- Ability to access key information from summary screens at multiple levels (case, report, study, etc)
- Provide a suite of built-in reports as well as the ability to create ad-hoc reports on the fly with no programming (some of the required reports are listed in section 4.5 above)
- Full query support, from field- to system-level querying, with users able to export and save the queries and results
- Ability to create reports in html and pdf, export to Excel, and print a full expedited report package (expedited report, supporting docs, attachments, IDB docs, etc) at any point through the workflow

4.7.1 How the requirement is currently met

As discussed in section 4.5 above, the ABS provides a full reporting and analysis suite. Reports created in AdEERS can be saved as PDFs or XML. There are many summary-level reports provided, which can then be drilled down into to get more specific information.

caAERS provides an API for searching the AE data. It comes with some preconfigured queries for the end-user, and will provide the ability to create their own queries.

The caAERS front-end provides some search capabilities as well, allowing the user to search for expedited reports or AEs, participants, studies, and personnel, with the results of the queries exportable to a .txt file. Expedited reports can be exported to PDF or XML, and electronically submitted to other systems via email or AdEERS.

All caAERS' modules include a summary screen of the data, allowing the users to quickly review the information before saving or editing it. The summary screen is available for studies, participants, research staff, and expedited reports.

4.7.2 Identification of gaps and potential gaps

The CTEP contractor handles most of the processing of expedited reports manually. They maintain a separate database with information about the processing of a report, with some, but not all, that information later being included in to AdEERS. Accessing the full AE package is possible, but not in an electronic manner. It doesn't appear AdEERS has the the ability to export reports or queries to HTML or Excel.

caAERS is in line with some of AdEERS deficiencies, although many of them will be addressed in future development. The key gaps are:

- caAERS does not provide a full suite of reports or a way to query data based on fields, studies, etc. The provided API needs to be expanded to include more of these features.
- caAERS does not export data to csv or html, allow adding this ability shouldn't be difficult since caAERS has the ability to export data to various other formats
- Summary screens will need to be built in for all reports and or queries

Some of these requirements revolve around the processing of submitted expedited reports, which is discussed in detail in sections 4.11 and 6 below. caAERS currently doesn't support the processing of expedited reports, but when the development team starts to implement it, they will address the following two requirements:

- Be able to provide information on the status of the expedited report package
- Be able to print and send electronically full expedited reporting packages

4.7.3 Obsolete and unclear requirements

With the changes in technology, it's our belief that exporting to HTML is now obsolete, having been replaced by being able to export to XML.

4.8 System Processing

To enter AEs and expedited reports, the system has to be able to handle and support the following:

- Medical term encoding
- Multiple coding dictionaries
- Imports of expedited reports
- Automatic notification to various personnel based on the status of reports

Entering AEs and expedited reports is only one part of the process. The EDMAERS also needs to be able to handle the workflow required after the report is submitted. This workflow is discussed in detail in sections 4.11 and 6 below. Some of the specific requirements documented as system processing requirements include:

- Workflow with or without centralized processing and approval (discussed in sections 4.11, 5.3, and 8.3.3 below)
- Handle adverse events and product complaints

- Support the addition of comments, corrections, supporting info, docs, query details, etc to an expedited report package (all supporting documentation for an expedited report)
- Automatic notifications to pre-determined users at various steps of the workflow (sections 5.6 and 8.2.6 below focuses on notifications, and sections 4.11, 6 , 8.2.8, and 8.3.3 below include similar requirements)

4.8.1 How the requirement is currently met

AdEERS has the ability to handle the various versions of CTCAE, which is mapped to MedDRA when there isn't a specific enough term available to describe the event. It's also configured to send out notifications based on when the expedited report is due.

There's a full workflow after an expedited report is submit which AdEERS also partially supports. It evaluates the report to determine if centralized processing is required and then goes through the proper workflow.

caAERS has the ability to use both CTCAE and MedDRA when documenting AEs and expedited reports. It also integrates CTEP's disease codes, pre-existing codes, agent codes, therapy codes, group codes, and country codes to support the reporting of AEs.

Once the expedited report has been created, caAERS is set up to send out notifications concerning the report and the status of the report. Notifications can be setup to go to a role-based recipient, or to a specific email address. caAERS currently submits expedited reports for CTEP-sponsored trials through AdEERS, which has centralized and decentralized processing and approval in place. In this sense, caAERS meets this requirement indirectly.

4.8.2 Identification of gaps and potential gaps

AdEERS does not support product complaints or attaching additional documents to a report after it has been submitted. Association to any additional documents is a paper-based process handled by CTEP's contractor when they process the submitted report.

caAERS currently only has the ability to import AEs that do not require expedited reporting (full import requirements are discussed in sections 5.5 and 8.2.5 below). The groundwork has been laid to support importing expedited reports, but it still needs to be developed.

Development needs to occur for caAERS to be able to handle the workflow associated with processing a report once it's been submitted. It currently does not support:

- Handling central processing, although it is an issue that is being addressed as caAERS works to integrate routing and reviewing into the system.
- Submissions of queries from the report processors to the site for more information
- Storage of, and association with, scanned documents and additional information gathered while the report is being processed
- Notifications to various parties based on the step the processing of the report is on

4.8.3 Obsolete requirements and requirements that need clarification

More research needs to occur to determine what is involved in handling product complaints before it can be integrated in to caAERS. It may simply require the creation of a report definition and its associated rules, which caAERS currently supports.

4.9 Training

Training is a big part of any application. Without training, it is harder for users to adopt a new tool. The training that should be available with the new system is:

- A computer-based training (CBT) module
- Training manuals
- Training activities

4.9.1 How the requirement is currently met

AdEERS has a CBT available on the web, http://ctep.cancer.gov/reporting/AdEERS_CBT_v3/welcome.html. Ann Setser has also created multiple PowerPoint training sessions which she delivers at various conferences and has made available on the internet.

The caAERS development team created training information, available at http://gforge.nci.nih.gov/docman/index.php?group_id=249&selected_doc_group_id=3113&language_id=1 (http://tinyurl.com/5vz4xk).

4.9.2 Identification of gaps and potential gaps

While the caAERS training information is a video available on the internet, it isn't a full blown CBT. The caAERS development team has plans to update the training information, including creating step-by-step videos, developing training guides, and putting together one or more CBTs.

4.10 User Access

Access to the system must be limited to only authorized users. Different levels of access should be allowed and configurable.

4.10.1 How the requirement is currently met

AdEERS requires a user name and password to access the backend system, which includes access to all the AE data.

caAERS provides various user roles to restrict access to different areas of the application. Only users with the right access to can add adverse events, view study and participant information, or make changes in the administration module. For future versions of caAERS, the development team is looking into expanding the roles and the changing the management of the roles to include more configurability. In addition, caAERS provides an authentication/authorization system that allows organizations to configure caAERS to use the organization's existing user names, passwords, and access.

4.10.2 Identification of gaps and potential gaps

There is no restriction on who can create an expedited report in AdEERS. Any user can access the system and submit a report.

4.11 Workflow

After an expedited report is created and submitted, there is an entire workflow for processing it. The workflow is different for each sponsor, so the new system must be able to support the following:

- Configuration of various workflows to support the different divisions of NCI
- Submission of electronic queries to the organizations/sites that submit electronic reports
- Determine if central processing is required and route accordingly (discussed in sections 4.8 above and 5.3 and 8.3.3 below)
- Support complex logic for routing expedited reports (multi modality including agents and imaging for example would need to go to CTEP and CIP)
- Support storage of scanned documents tied to the adverse event/expedited report (also reported in sections 4.1 above and 5.3 and 8.2.1 below)
- Configurable notifications based on regulatory deadlines (sections 5.6 and 8.2.6 below focuses on notifications, and sections 4.8 above and 6 , 8.2.8, and 8.3.3 below include similar requirements)

Many of these requirements actually overlap with section 4.8 above.

4.11.1 How the requirement is currently met

AdEERS currently supports CTEP and some CIP workflows. It can determine if central processing is required and route the information accordingly. Notifications are sent out based on submission deadlines and preconfigured recipients. It supports electronic queries of the data, and is able to handle multi-modality studies.

caAERS can be configured to handle CTEP, CIP, and DCP reporting requirements. Once a report is initiated, it will send out automated notifications to preconfigured recipients concerning the expedited report. Notifications will be delivered, as setup in the report definition, until a report is submitted. Once the report is submitted, any upcoming notifications are cancelled.

caAERS has the ability to submits expedited reports for CTEP-sponsored trials through AdEERS, which has centralized and decentralized processing and approval in place. In this sense, caAERS meets the requirement for central processing indirectly.

4.11.2 Identification of gaps and potential gaps

While AdEERS supports complex logic for routing AE reports, not all scenarios are taken into account. It also does not have the ability to store scanned documents to associate them with an expedited report. This is handled outside the application through a contractor-supported database.

As discussed throughout this document, and specifically documented in section 6 below, caAERS does not currently support processing a submitted expedited report, so the various workflows associated to processing a report still have to be developed. Specific requirements called out in this section that will be addressed when the development occurs include:

- Handling submissions of queries from the report processors to the site for more information
- Handling central processing (this will be addressed as the caAERS development team implements routing and reviewing, which could occur as early as caAERS 2.0)
- Storage association of scanned documents and additional information gathered while the report is being processed to an expedited report

5 Analysis of Technical Requirements

5.1 API

The EDMAERS must provide extensive API support. This includes:

- Automatic messaging APIs based on triggers
- Links to logon/security vendors or to an open source solution such as NCI CBIIT's Common Security Module
- All SAE data must be available to be pulled into custom apps and/or CTEP and DCP support systems (PATS, ESYS, Dose Regimen, DESK, and RDC)
- Maintain most current caDSR version for caBIG interoperability (also discussed in section 5.2 below)
- Connection to NCI CBIIT's EVS and dictionaries (also discussed in section 5.2 below)
- Connection to external applications, metadata, and vocabularies
- Integration with Oracle Clinical 4.5 and new RDC

5.1.1 How the requirement is currently met

caAERS provides a rich set of secure APIs that can be used to manage and query studies, participants, investigators and research staff. It also has APIs to query adverse events. A set of web and grid services are available that can be used to facilitate caAERS integration with external systems such as the RDC.

caAERS uses NCI CBIIT components where possible. For both authentication and authorization, the caAERS development team used Spring Security (formerly called Acegi) and NCI CBIIT's Common Security Module. caBIG standard CDEs have also been leveraged in caAERS. caAERS supports CTCAE (versions 2 and 3) and MedDRA versions (9, 10, and 11) for AE coding purposes. caAERS 1.0 data elements have been loaded to caDSR via the UML domain model loader, maintaining interoperability.

5.1.2 Identification of gaps and potential gaps

To fully meet the listed requirements, the caAERS development team needs to provide more integration. Specifically, the following features are missing:

- An API to manage adverse events and expedited reports
- Direct integration with EVS and additional dictionaries (this is partially met since the CDEs in caAERS are annotated with semantic concepts that belong to NCI Thesaurus)
- Integration with Oracle Clinical, RDC, and the new CDMS (which is slated to be Medidata pending the completion of protests).
  - The integration capabilities will be implemented using APIs provided by caAERS. Based on the integration use cases, additional APIs may need to be developed.

5.2 Architectural Constraints

There are specific architectural requirements the new application must meet to ensure caBIG interoperability and application stability. These include:

- Based on J2EE architecture and the current caBIG security model
- Ability to work as a central and stand-alone application

- Compliant with CFR Part 11, E2B, E2B(M) (http://www.fda.gov/CbER/gdlns/iche2bmqa.htm), HIPAA, and NCI technical requirements (A-130 http://www.whitehouse.gov/omb/circulars/a130/a130trans4.html, FISMA, and the overall C&A process); these requirements are also discussed in sections 4.3, 4.6, and and 5.2 above and 7.1, 7.2, and 7.3 below
- Compliant with GUI guidelines and Section 508 (http://www.section508.gov/) (also discussed in sections 5.3 and 9.2 below)
- Compliant with caBIG architecture and integrated with caDSR for CDE compliance (also discussed in section 5.1 above)
- Integration with EVS for terminologies and vocabularies (also discussed in section 5.1 above)

5.2.1 How the requirement is currently met

5.2.1.1 J2EE based

J2EE is the old name for what is now referred to as the Java Platform, Enterprise Edition (Java EE). From the Sun website:

> *Java Platform, Enterprise Edition (Java EE) is a set of coordinated technologies that significantly reduces the cost and complexity of developing, deploying, and managing multitier, server-centric applications. Building on the Java Platform, Standard Edition (Java SE), Java EE adds the capabilities that provide a complete, stable, secure, and fast Java platform for the enterprise.*

Essentially, Java EE consists of a standard specification (and set of related specifications) that is developed through the Java Community Process and reference implementations of the standard (and related standards). The Java EE specification defines the architectural elements of the platform. An application that is based on Java EE uses one or more of these elements. The platform elements include containers, components, standard services and APIs to services. Containers provide services to components through standard APIs.

caAERS is a Java EE based application. It is deployed as a servlet-based component in a Java EE web container. caAERS uses the standards services through the standard APIs such as JDBC, JMS, JNDI, JAAS, JPA, and many more. Additionally, caAERS uses the Spring Application Framework to facilitate use of Java EE technologies.

5.2.1.2 Compliance with various security-related regulations

The following regulations all define security-related requirements:

- HIPAA, Title II: Administrative Simplification
- Title 21, CFR Part 11
- The OMB's Circular No. A-130
- FISMA

Evaluating compliance with these regulations involves not just an evaluation of caAERS, but also the environment in which it is used. caAERS provides functionality needed to support operating procedures that comply with many of these regulations.

In addition, caAERS is based on the caBIG security model in that it uses Common Security Module (CSM) components to express and enforce authorization policy, and it supports the use of both CSM and GAARDS to manage identity (i.e. support

authentication). caBIG does not prescribe a common security model per se, but some of its components, including CSM and GAARDS, facilitate achieving the requirements that are defined by regulations such as the FDA's 21 CFR Part 11, HIPAA, and FISMA. CSM provides a very abstract model for expressing authorization policy, user provisioning tools, components for integrating with identity providers (through JAAS), and components for integrating authorization policy enforcement into caBIG applications. GAARDS provides components and services to support a PKI-based authentication and trust system, identity federation, and virtual organizations. CSM is most appropriate for managing identity and authorization policy within an organization. GAARDS is most appropriate for managing those issues across organizations.

5.2.1.3 Compliance with caBIG Architecture

caAERS is compliant with caBIG in the following ways:

- the caAERS domain model has been harmonized with BRIDG, semantically annotated with concepts from NCIt, and registered to the caDSR.
- The XML schemas that define all caAERS interchange formats have been registered to the Global Model Exchange.
- caAERS provides grid service APIs (both data and analytical) to expose caAERS data and functionality.
- caAERS uses caBIG security infrastructure (CSM and GAARDS).

In addition, caAERS is integrated with caDSR in that the caAERS domain model uses CDEs that are registered to the caDSR. The application does not dynamically interact with caDSR because no use cases have been identified that would require such interaction.

5.2.1.4 Integration with EVS

caAERS is integrated with EVS in that the caAERS domain model has been annotated with concepts from the NCIt and it uses one of the terminologies that NCIt serves (MedDRA).

5.2.2 Identification of gaps and potential gaps

5.2.2.1 Compliance with Various Security-Related Regulations

While caAERS provides functionality needed to support operating procedures that comply with many of these regulations, a complete analysis of how this support addresses the specific requirements of each regulation has not been completed. Such an analysis would also require a detailed description of the organizations in which caAERS will be used.

5.2.2.2 Compliance with E2B(M)

E2B(M), which subsumes E2B, defines rules for submitting individual case safety reports to the FDA. These rules have not yet been examined.

5.2.2.3 Section 508 Compliance

Effort has been made to adhere to the requirements defined in paragraph 1194.22 Web-based intranet and internet applications. However, a complete analysis has not been completed. As discussed in sections 5.3 and 9.2 below, the following 508 issues have been identified:

- Improve the tabbing and keyboard navigation. While tabbing is set up, it does not work consistently in either IE or Firefox
- There currently isn't a way setup that allows readers to skip lines or navigation. It has been recognized as a gap and should be an easy fix to implement
- Additional testing and research needs to be done concerning flickering of the application at the frequency specs

5.2.3 Obsolete requirements and requirements that need clarification

While caAERS partially meets 508 compliance, it's unclear the specifications for meeting the GUI guidelines. A reference to the list of GUI guidelines needs to be provided before the caAERS development team can determine what, if any development needs to occur.

5.3 Design

When designing the EDMAERS, the developers need to keep in mind some standard design principles:

- Make it highly configurable (individual fields, screens, pathways, workflows, etc) without requiring programming (also discussed in sections 8.1, 8.3.1, and 11.2 below)
- provide business rules based on unique characteristics (sponsor, agent, device, protocol, participant, etc)
- Have an extensible and flexible metadata model, which can provide for incorporation of CDEs
- Support multi-schemas that can be physically separated
- Support both centralized and decentralized processing and approval (discussed in sections 4.8 and 4.11 above and 8.3.3 below)
- Support electronic attachments to expedited report packages (also discussed in sections 4.1 and 4.11 above and 8.2.1 below)
- Comply with 508 and NCI UI guidelines (http://hcibib.org/hci-sites/GUIDELINES.html, http://www.usability.gov/pdfs/guidelines.html, and http://webresources.cancer.gov/index.html) (also discussed in sections 5.2 above and 9.2 below)
- Document the information and object models

5.3.1 How the requirement is currently met

caAERS is a highly usable application. As discussed in 5.2 above and 9.2 below, caAERS currently meets most 508 requirements. It also follows the general best-practices in web application design, including, but not limited to:

- Use of dark text on high-contrast backgrounds
- Ensure visual consistency
- Avoid horizontal scrolling
- Use of descriptive headings
- Differentiate and group navigational elements

caAERS currently submits expedited reports for CTEP-sponsored trials through AdEERS, which has centralized and decentralized processing and approval in place. In this sense, caAERS meets this requirement indirectly.

The caAERS team believes in documenting their application to increase the ease of additional development. They have fully documented the information and objects models. This information can be accessed through the caBIG gForge site, https://gforge.nci.nih.gov/plugins/scmsvn/viewcvs.php/docs/?root=caaersappdev. The team also believe in using existing functionality where possible, so has incorporated CDEs into caAERS, extending it where needed.

caAERs has many configurable features. The rules module can be setup to define when expedited reporting is required, and is done in a very easy to follow manner, with if-then statements. Different rules sets can be setup to address broader requirements, such as sponsors and organizations rules, and to address finer-grain requirements, such as an organization's specific rules for a single study. Using report definition files, users can define what fields are required for expedited reports. Currently, caAERS is setup to only display certain fields in the expedited flow based on the type of study (DCP-only fields for example).

The caAERS development team also implemented configurable screens in the expedited report flow for version 1.5. This is done during the setup of a report definition, and allows users to determine which fields show up on an ad-hoc basis: users can mark a field as mandatory, optional, or not applicable. If they mark it as not applicable, it will not appear on the screen

5.3.2 Identification of gaps and potential gaps

caAERS needs to warn users about timeouts to increase the appeal of the design. Users do not appreciate being signed out without notice. Best design practices all suggest having the main navigational items on the left. The caAERS development team is considering having a left-hand navigation, but it would be third level, not the main navigation.

caAERS does not at this time support the electronic attachments. Additional work needs to be completed before caAERS can support this.

As discussed in sections 5.2 above and 9.2 below, caAERS has a little additional work needed to fully comply with 508. This includes:

- Improve the tabbing and keyboard navigation. While tabbing is set up, it does not work consistently in either IE or Firefox
- There currently isn't a way setup to allow readers to skip lines or navigation. It has been recognized as a gap and should be an easy fix to implement
- Additional testing and research needs to be done concerning flickering of the application at the frequency specs

To fully meet the requirement for centralized and decentralized processing, caAERS needs do be modified. If caAERS is going to be a stand-alone reporting tool, this functionality needs to be built in. This is tricky, since it'll have to support it internally, but not duplicate the process as the report is being submitted through AdEERS.

While caAERS has more configurability than AdEERS, additional work needs to be done to fully meet this requirement. For example, caAERS needs to provide the following configuration methods:

- Allow/block modification of data by controlling the read/write features of different fields
- Determine what screens and information on screens appear based on protocol information
- Provide the ability to determine what fields/screens are available based on roles
- Provide rules that are based on other features besides sponsor, organization, or study (agent, device, participant, etc)

5.3.3 Obsolete requirements and requirements that need clarification

caAERS development is based on schemas. However, additional research needs to occur to understand the need behind multi-schema development that can be separated and to determine the importance of the requirement. This may be an obsolete requirement.

5.4 Documentation

The technical side of the EDMAERS also needs to be well documented, as also discussed in section 4.4 above. This includes documenting the API and providing all standard SDLC technical documents (schemas, requirements, designs, etc). The source code must be kept in the caBIG CVS repository, storing the different versions of the application.

5.4.1 How the requirement is currently met

caAERS is well documented. The standard SDLC documents are available, including a very detailed design and technical spec document, with schemas provided for all modules. All code is kept in the CVS repository, allowing for rollbacks, branching, and multiple versions. As of September 2008, caAERS has three main versions: version 1.0, the version being used, version 1.3.1, the CTMS version with Labviewer support, and version 1.5, the latest version.

Since the APIs have to be accessible by organizations who want to use them, they are well documented. There are wiki pages describing the APIs and messaging services.

5.4.2 Identification of gaps and potential gaps

Additional work needs to be done to the documents describing the APIs and messaging. These are important aspects of caAERS, and can be highly technical, so the documentation needs to be very thorough.

5.5 Import & Export Capability

It's important that data can be imported into and exported from the EDMAERS (also discussed in sections 8.2.4 and 8.2.5 below). Some of the applications it must be able to export to include: Excel, SAS, RDC, ESYS, DESK, Oracle clinical (and the new RDC), E2B Applications, CTSU, and Documentum/core dossier. The EDMAERS must be able to import data from custom applications in non-E2B format (SAE applications and systems such as DESK, ESYS, and ASAEL) and from lab and hospital systems. It would also be beneficial if it supports importing images, PDFs, and other documents to support AE data collection and the expedited report package (as discussed in sections 4.1, 4.11, and 5.3 above, and 8.2.1 below).

The system must be able to send and receive data via XML to support integration with other databases and systems.

Ideally, the HL7 Adapter will be used to perform export functionality.

5.5.1 How the requirement is currently met

caAERS has expanded import and export capabilities. Data associated with studies, participants, adverse events, expedited reports, investigators, and research staff can be exported to CSV and XML formats. These entities, except SAE reports, can also be imported into caAERS in XML format. The caAERS development team's most recent import addition is the ability to import CTEP studies captured in the CSV format. This addition significantly alleviates the burden of manually entering CTEP studies into caAERS, and eliminates the errors that are typically associated with manual entry of data.

caAERS specializes in sending and receiving data in XML. The integration with AdEERS to electronically submit expedited reports is in the form of XML documents and messages. In addition, a set of web services was developed that can be used to implement real-time integration of study, participant, adverse event, research staff, and investigator data with other systems. These services also use a combination of messages and XML documents.

5.5.2 Identification of gaps and potential gaps

caAERS does not include functionality to export directly to SAS, CTEP-ESYS, DESK, E2B Applications, CTSU, or Documentum/core dossier. The caAERS team needs to review the formats supported by the above-mentioned systems and devise an approach to convert the output from caAERS to those formats.

The caAERS team believes import functionality requirements are met, based on the development and publishing of a well defined set of XML schemas. As long as the input complies with the schema, caAERS can process it. Research has to be done to learn more about the data in various NCI applications, such as the ASAEL, to determine if additional development has to occur before caAERS can consume the data sent from the applications. The ASAEL is also discussed in sections 4.5 above and 8.3.2 and 10.1 below.

caAERS does not currently have a way to upload images and other documents (such as pathology reports, x-rays, or death certificates) into the system. To meet the requirements, the development team needs to implement a method for these uploads and the association of this type of material to an AE, SAE, expedited report, and expedited report package.

5.5.3 Obsolete requirements and requirements that need clarification

While the HL7 Adapter is not currently used, the export functionality seems to be adequate. Additional research needs to occur to determine if export methodologies need to be switched.

5.6 Notification Triggers

Notifications are an important part of the expedited AE reporting process and workflow, so supporting various types of notifications must be included in the EDMAERS. Section 8.2.6 below focuses on notifications, and sections 4.8 and 4.11 above and 6 , 8.2.8, and 8.3.3 below also include notification requirements. Specifically, the new reporting system must support:

- Automated configurable email and/or pager alerts and notifications
- Auto-notification based on preset methods (AE severity, frequency, source, etc)
- Notification to sponsor, cooperative group, consortia, FDA of SAE event, with notification times being configurable to include within 24-hours, immediately, and intervals

5.6.1 How the requirement is currently met

AdEERS has the ability to send out notifications when expedited reports are being created and when they're being processed. Reports can be sent automatically upon creation of an expedited report, and at specific intervals if the expedited has yet to be submitted. During the processing, notifications are also automatically sent based on the status and phase of processing, or can be manually triggered.

caAERS has a module that allows the user to set up notifications based on the report type. These notifications can be setup to send to specific addresses (email, web server, pager) or to a general role. For example, a report definition can include instructions to send notifications to the role research staff. When the notification is sent it will be sent to all individuals associated to that study who have the role of research staff.

Notifications in caAERS can be setup for specific timeframes based on the time a report is created. The notification timeline will be followed until the expedited report is submitted.

5.6.2 Identification of gaps and potential gaps

AdEERS does not have the ability to configure when notifications are sent – the notifications are built into the system. This also means notifications can't be sent at a user specified time. It also doesn't have built-in notifications based on AE details.

caAERS also does not fully meet these requirements. Since caAERS does not have processing built in, it does not have notifications that occur after an expedited report is submitted; the final notification is that the expedited report has been submitted.

caAERS also does not support notifications based on AE details. The caAERS development team needs to understand when this type of notification is needed and who the audience would be for it. Once they understand this, they will be able to start the development required to implement these additional notifications.

While caAERS provides a configurable notification system, based on the specific report being completed, additional development may be necessary to support sending notifications ad-hoc.

5.7 Quality

During the development of the EDMAERS, certain quality metrics must be met. There must be change control and configuration management, and the application must be certified (with quality assurance and testing) by a third party. Third party certification is also discussed in section 11.6 below.

5.7.1 How the requirement is currently met

caAERS has been following quality management practices since the very first phase of the project. For configuration management, the caAERS development team uses Subversion as a source control mechanism. For automatic build purposes, a continuous integration (CI) server called Hudson is used. As a part of the build process, all the unit tests are run and any failures are reported immediately to all the developers. This

insures any defective code is immediately identified and the developers can address the errors instead of propagating faulty code. In addition to the automatic build and unit tests, the caAERS development team performs various types of testing of caAERS.

The development team works closely with adopters and stakeholders and has a process in place for change control. Any changes, including new feature requests, go through the change control process.

The caAERS development team is using a defect management tool called JIRA to report and track any suspected and confirmed bugs. The reported bugs are further classified depending upon the module and functionality. JIRA has very good reporting capabilities, which helps management get a quick overview of the bugs in caAERS at any given time.

5.7.2 Identification of gaps and potential gaps

caAERS has very good quality management practices in place but is not formally certified for its quality by a thorough third party analysis. The testing that is done outside of the development team is completed by a group of adopters. That testing is limited to testing the functionality and user acceptance testing. Full third-party testing still needs to be scheduled.

5.8 Recovery Management

The data stored in the EDMAERS will be very important. As such, there must be a disaster recovery plan that includes a full backup and restoration of data. The EMAERS must be able to work in a redundant server configuration to protect the system from going down due to a server outage. These requirements are also discussed in section 4.3 above.

5.8.1 How the requirement is currently met

The caAERS development team does not have a version of caAERS that contains real data, which would require recovery management. When caAERS is installed locally, recovery management is handled by the organization that's using it.

5.8.2 Identification of gaps and potential gaps

At this time, the caAERS development team does not have a disaster recovery plan or method in mind for the centralized caAERS instance. The development of this plan could be assisted by working with the AdEERS team to go over existing disaster recovery plans. Once the team had a firm grasp on what needs to be done to the caAERS database to support disaster recovery, the could institute the changes, create the supporting documents, and put the plan in place.

Typically a backup server will be configured to take daily backups of the data and the software on physical tapes. These tapes will then be transported to a different facility at a regular interval.

The caAERS development team is looking into supporting running in redundant server configuration mode, where at least two more servers can be used for redundancy. This will only address the issue of the availability of the application if any one server goes down. If something goes wrong as a result of the disaster at the server facility, there will be latency in bringing up the application from the backed up physical tapes.

5.9 Standards

The new reporting system must be compliant with E2B ICH Standards (http://www.fda.gov/CbER/gdlns/iche2bmga.htm) for sending an SAE to FDA as well as ISO 11179 (http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=35347, which basically says it uses CDEs as a static download to the metadata layer of the application). It also must be caBIG silver-level compliant, which is also mentioned in section 4.2 above.

5.9.1 How the requirement is currently met

caAERS is certified silver-level compliant, and is reassessed and reconfirmed compliant after every development cycle. The caAERS development team loaded the domain model into CSR, which then converted the elements into CDEs. In addition, they made a point to use caBIG CDEs wherever possible.

At this time, it is believed that caAERS meets both E2B ICH Standards and ISO 11179. caAERS uses CDEs and is able to fill out the MedWatch forms to be submitted to the FDA for reporting serious expedited reports.

5.9.2 Identification of gaps and potential gaps

While the caAERS development team believes both E2B ICH Standards and ISO 11179 are met, there are multiple layers to these standards. Additional research needs to be complete during all phases of development to ensure these standards are met and supported.

5.10 Technology

The EDMAERS must meet the technological requirements that were defined in the requirement documents. The EDMAERS must:

- Have the ability to facilitate bilateral communication with local CTMS
- Be a web-deployed, thin-client
- Be developed for Solaris or Linux
- Be written with CORBA Object Model compliance (nice to have)
- Support single sign-on using active directory, LDAP, or similar technology
- Have a portal environment to surface key information

5.10.1 How the requirement is currently met

caAERS is a web application that supports a thin client (i.e. web browser) interface. It's completely Java based, so is compatible with Solaris and all major Linux distributions (since Java runtime environments are freely available and are usually installed by default).

caAERS supports single-on by using the WebSSO components of the caBIG GAARDS infrastructure. GAARDS provides another component that enables integration with Active Directory and LDAP technologies, using CSM. This component can be easily hooked in, but is not currently being used.

5.10.2 Identification of gaps and potential gaps

The caAERS user interface has been designed to present the right information to the user, when it is needed. However, some of the clinical workflows that have been identified in the CCTS project may be facilitated by having a customizable interface that allows the user to pull in pieces of functionality/data from each of the CCTS applications. To support this type of portal environment, the caAERS development team would need to evaluate the best way to expose this. Some options include creating portlets (based on the Java JSR 168 or 286 standards) or creating finer-grained web services.

caAERS provides APIs to consume protocol, person, and organization information from a local CTMS, but it does not export that information. There is no transactional communication with any CTMS. A good time to start this bilateral communication would be when the new NCI-sponsored clinical data management system becomes available.

5.10.3 Obsolete requirements and requirements that need clarification

The purpose of CORBA is to define a mechanism for achieving programming language and location independence. Since the caBIG program has chosen to use various web service standards to achieve these goals, CORBA no longer seems to be a valid requirement.

5.11 User Access

The user access technical requirements overlap with requirements mentioned in sections 4.10 above, and 7.1 and 7.4 below. The EDMAERS should store roles and user ids in the application database in a secure manner, and it should have the ability to create a unique identifier for each user.

5.11.1 How the requirement is currently met

caAERS has a module that controls access rights to the system. Each user can be assigned multiple roles to provide access to the various modules in the system. The authorization policy is stored in the caAERS database according to the CSM authorization model.

5.11.2 Identification of gaps and potential gaps

While caAERS meets or exceeds these requirements, the development team needs to enhance the user provisioning interface to enable expression of finer-grained policies, for example, to enable a field-level policy. This in turn means the team needs to enhance the policy enforcement points within the application code to enforce this finer-grained policy.

6 Analysis of User – AE Workflow Requirements

This section identifies various requirements for handling the workflow(s) necessary for processing an expedited report once it's been submitted. In general, caAERS does not meet any of these requirements at this time since the focus of caAERS development has been on entering and managing AEs and expedited reports. As this process is solidified, more focus will move to what happens after an expedited report is completed and is ready for processing.

The initial requirement document only covered CTEP's workflow and consisted of 39 requirements. It's important to understand the workflows that CIP and DCP use, so those are outlined here as well.

A detailed analysis on how NCI's existing systems and caAERS do or don't meet these requirements is not included in this section of the document. The authors of this gap analysis document recognize that caAERS does not have the processing workflow built in, and that existing systems only partially support the processing workflow since many of the steps are performed manually.

Instead, the processing workflows are completely outlined to illustrate the complexity of the workflows that the EDMAERS will need to address and support. A firm understanding of these process workflows will also assist the developers in providing the necessary support in the application.

6.1 All AE Processing Workflows

Regardless of which division's processing workflow, the EDMAERS must be able to support querying for information and responding to queries. This requirement is also discussed in sections 4.8 and 4.11 above. The main steps of this process include:

- A user receives a notification (via email, phone call, page, etc) that there's a query
- The user logs into the system to view the query about the AE
- The user provides the requested information either by entering it directly into the system or by uploading attachments
- The user indicates a response has been provided and saves any changes
- Notification is sent to the requestor that there's a response available.
- Requester logs into the system and reviews the response
- Requester approves the response or requests more information
- Requester makes any necessary changes or updates and saves
- Requester promotes the record to the next step in the processing workflow.

6.2 CTEP's AE Processing Workflow

The following steps are part of CTEP's AE Processing workflow and must be supported in the new system. These requirements are also discussed in sections 4.5 above, and 8.2.8 and 8.3.3 below.

6.2.1 Report intake

The first part of the EDMAERS is entering AEs and expedited reports. After an expedited report has been completed by sites and contributors and submitted for processing, the EDMAERS must begin the processing workflow. This includes:

- Storing the report with a unique ID
- Tracking receipt in the audit trail (this requirement is also discussed in sections 4.3 above, 7.1, 8.3.4, and 10.2 below)
- Sending out notifications to responsible parties (sections 5.6 above and 8.2.6 below focuses on notifications, and sections 4.8 and 4.11 above and 8.2.8 and 8.3.3 below also include notification requirements.)
- Support both centralized and decentralized processing (discussed in sections 4.8, 4.11, and 5.3 above and 8.3.3 below), including the ability to:
  - List a single report or a list of reports that need to be reviewed, are ready for review, or need to be promoted
  - query the original sender for additional information and receive notification when responses come in
  - Make changes and additions to the report and save all changes
  - Promote the report to the next step, which may or may not including assigning it directly to another user
- After the initial review, the system must support a more in-depth review of the reports by designated personnel, who would need to have the same access rights as the initial reviewers

It would be ideal if the EDMAERS could handle reports submitted via various methods in different formats, including submitting directly into the system, receiving a paper-based report, reports entered into existing systems and sent electronically to EDMAERS, and entered in the new CRIX Data Collection system and send electronically.

6.2.2 IDB assessment

After the initial and in-depth reviews by designated personnel, there is an IDB Assessment. IDB Monitor receive notifications when reports are ready for review, and once they've reviewed the reports, they have the ability to make changes, store the information, and change the status of the report (current statuses are File, Pending, and Hold) for further processing. The IDB Monitor performs a thorough review of the report and supporting information, decides if the information needs to go to the FDA immediately or be held for the annual report (thus the statuses), and promotes the report to the next step of the process.

AE Coordinators receive notification when the IDB has completed their assessment and takes appropriate action based on the status of the report. As long as the status of a report is "Pending", the report will cycle from the reviewer, to the IDB, to the AE coordinator. It will only move forward if the report is set to File or Hold.

6.2.3 Hold assessment decision

If personnel decide a report should be held, the EDMAERS must be able to handle the following steps:

- Notify the sites and designated personnel of the final status
- Print the final version of the expedited report package
- Provide verification of the assessment and mark it as complete

- Allow for a final QC of the data in the report and the assessment by qualified personnel
- Support both manual and electronic archiving, which would include notifying the AE status specialist for final archiving of the report package

6.2.4 File assessment decision

If personnel decide a report should be filed, the system must be able to handle the following steps:

- Creating a memo and filling out form 1571 for transmission to Regulatory Affairs Branch (RAB) (after completing and transmission of the Initial Safety Communication (ISC))
- Notifying designated personnel for a final review, with the reviewer having the full capabilities of any of the initial reviewers
- Creating an electronic version of the ISC (which can be printed if necessary), automatically sending it to the FDA and designated personnel, and tracking if the communication succeeds
- Allow the RAB to open the system, view the AE report, signoff on the 1571, assign a document number to the IND on the form, and approve the form
- Once the form has been signed and approved, store the information and transmit 1571 to the FDA and/or the Pharmaceutical company
- Change the status of the AE so it moves to the next step of the workflow

6.2.5 Review and finalization

After a report has been set up to move to the review stage, various personnel are involved in reviewing and finalizing the report.

- RN drafts an AEA Summary, which the system is capable of creating automatically when the status is set to review. When it's created, the QC person is automatically notified
- The person who is responsible for QCing the report reviews the AEA Summary, enters data for the 1571 and ISR or Action Letter, and approves moving the AE to the next step of the process
- IDB reviews the AE report, and receives notification that the report is ready for final signoff after the final QC. Once it's ready for final sign off, he/she provides final approval and changes the status to HOLD (if it wasn't already) and provides any final comments
- RAB is notified that a signature is required and signs into the system to provide the signature

The system must be able to handle all notification steps, store all transitions and interactions with the various personnel, and maintain a relationship between all supporting material and the AE/expedited report.

6.2.6 Distribute and archive

After the IDB has approved the AE/report, the RN performs one final QC on all entries and signs off on the report. Once it receives final signoff, the system automatically notifies all sites, organizations, and personnel involved in the processing workflow that the report and supporting material are available. In addition to the notification, the EDMAERS creates an archival copy of the report and supporting information, and sends it to the FDA, Pharmaceutical company, and sites, as long as they accept electronic versions.

6.3 DCP's AE Processing Workflows

DCP currently supports two types of studies, CCOPS and prevention studies. Expedited reports for these types of studies are handled with different workflows.

6.3.1 Processing CCOPS study AEs and expedited reports

CCOPs studies follow FDA regulations for reporting, using the CDUS-abbreviated reporting, or "AdEERS pathway" for actual reporting. This means an AdEERS 10-day report is used to report all SAEs, and does not include verbatim reporting. In general, the commercial pathway is followed for reporting, although some studies or groups may have additional limitations.

When an SAE occurs, it is reported using AdEERS. After it's been entered, the report will go to the research base, the AdEERS coordinator, the DCP office, and the program director. DCP will review and store the report, but does nothing else with it. The program director may bring up reports with the group, such as when a trend is occurring, but it's the research base that manages the reports and any processing required after they're submitted.

6.3.2 Processing chemoprevention program study AEs and expedited reports

There is one rule for all SAE reporting requirements: if an adverse event occurs that meets one of six serious indicators, an expedited report is required. Upon learning of a serious adverse event, an individual has 24 hours to send an initial notification and 48 hours to complete the full SAE form. The NCI Medical Monitor (MM) and/or DCP Contractor receive both the initial notification that an event has occurred and the completed SAE form.

When contractors receive a completed SAE form, they enter the information into a database and a tracking database. If they need clarification, they'll start a query spreadsheet and send it to the site for clarification. Then they send the report and a triage form (printed from the tracking database) to the MM.

Medical Monitors review the SAE form and determine if the adverse event was unexpected. If they need additional information, they'll either contact the site directly or add their comments to a query spreadsheet.

When the MM has all the required information, they will then complete the write-up and triage form (and query spreadsheet if there are questions), and send it to the contractor. If the MM wants more info, the contractor sends the case file and any queries to the site. As they receive responses, the information is added to the databases and sent to the MM.

Once the MM is satisfied with the case file and the contractor has all the information concerning the AE, the contractor completes additional steps, as described below. These steps generally revolve around the expectedness and relatedness of the AE to the study.

- Expected or not related: submits to FDA as part of the annual IND report
- Unexpected and related: submits IND Safety report via written report to the FDA within 15 days of initial report
- Unexpected, related, and is fatal or life-threatening: submits IND Safety report via telephone or fax to the FDA, within 7 days of initial report
- Unexpected and related: notify participating investigators and update the IND

Note: There are some differences in the process based on the study and MM. Some MMs prefer to receive the information before it goes to the contractor. Some MMs want to receive the information at the same time as the contractor, and some MMs prefer the information goes to the contractor first before it's sent to them.

6.4 CIP's AE Processing Workflow

The Cancer Imaging Program (CIP) creates expedited adverse event reports using AdEERS or paper-based AdEERS reports. When 24-hour notification is required, it is done by phone to both the contractor handling the expedited AE collection process, and the institution SAE notification line. The expedited report is then due within 10 working days of first knowledge of the event.

This is a new process released mid-August, so the specific steps that are completed by the contractor after they receive the completed report are unknown.

If an AE does not required expedited reporting, it will be reported using the case report form (CRF). CIP also uses the abbreviated CDUS report system for their Phase 2 and Phase 3 studies. These reports are submitted quarterly to CTEP.

7 Analysis of Security Requirements

7.1 Audit and Security

Requirements for this section overlap with requirements listed in sections 4.3 above and 4.6 above, and 8.3.4 and 10.2 below.

To meet one of the requirements of CFR part 11 compliance, EDMAERS must have full audit trails and audit reports. There must also be role-based authorization and authentication, with a security module that's robust enough to support multiple sponsors. The security must also be enough that it ensures that no viruses can get through. Finally, it must follow "Good Development Practices", a CDA created document.

7.1.1 How the requirement is currently met

The ABS and database have full auditing and traceability. When reports are submitted to regulatory agencies, the data that was included in that report can be easily identified and pulled up again. Since all changes are tracked individually, the changes are, in essence, being locked. The only way to remove or modify the data would be to go directly into the database and modify the individual record, something that would be difficult to achieve, and that few people have rights to do.

Since the workflow status is a separate field within the database, updates to the database and an expedited report package do not affect this. Also, since each amendment is treated as a separate record, and all amendments are tied to the initial record, the status can be maintained across versions.

Users do not require user names to submit expedited reports in AdEERS. However, to access the ABS, there is full user login/passwords implemented.

caAERS supports the viewing of the current version of expedited reports. All changes are tracked and maintained in the database, so there is a history of older versions of the report. However, this information isn't easily accessible. Given direct access to the database, a complete history of an expedited report and all fields within the report can be gathered.

Users are assigned roles when accounts are created in caAERS. To access various parts of the system and the data contained within, the user has to have the right permissions. caAERS has also developed a significant authorization and authentication system, which will allow users to integrate access control in to their existing systems.

It's the belief of the caAERS development team that caAERS does not have any vulnerabilities that can be exploited that will allow the application and data to be compromised. Completed virus protection is the responsibility of the organization that deploys caAERS.

7.1.2 Identification of gaps and potential gaps

caAERS needs additional development to support the required auditing functionality. Being able to audit the changes made to an AE and expedited report has been started, but is only at a basic level at this time.

The existing roles within caAERS may not be adequate for all users. As additional organizations adopt it, these roles are being evaluated to determine if additional development needs to occur.

7.1.3 Obsolete and unclear requirements

The caAERS development team needs clarification on what is meant by the CDA document, “Good development practices”. Good Development Practice regulations (GMPs) have been located, referring to FDA’s promulgated regulations. If this is what’s being referenced, the GMPs will be reviewed and caAERS evaluated to ensure the regulations are met.

7.2 Regulatory Compliance

The new reporting system must meet all regulatory requirements. Specific requirements include:

- De-identification of participant data to comply with HIPAA and other privacy laws (also discussed in sections 4.6 and 5.2 above and 8.2.1 below)
- Software validation, verified by the FDA audit team and/or NCI-ISSO, to comply with CFR Part 11

7.2.1 How the requirement is currently met

caAERS has validation in place. However, it still needs to be verified.

7.2.2 Identification of gaps and potential gaps

caAERS stores all data elements separately, so adverse event information can be separated from participant identifiers. However, this can only be done by a DBA directly accessing the database. Additional development must occur to support the exporting and querying information that shows all information except specific participant details.

While caAERS has software validation in place, the caAERS development team needs to have it verified by the FDA audit team and/or NCI-ISSO. The team also needs to examine the validation requirements of 21 CFR Part 11 to ensure full compliance is met.

7.3 Security

All NCI supported application must be considered secure. For this to happen, they must be FISMA (http://csrc.nist.gov/groups/SMA/fisma/index.html and http://iase.disa.mil/fisma/index.html) and NIST (http://www.nist.gov/) compliant, and should have completed a certification and authorization assessment form for NCI ISSO to review. The FISMA requirements are also discussed in sections 4.6 and 5.2 above.

7.3.1 How the requirement is currently met

As discussed in 5.2.1.2 above, evaluating compliance with these regulations involves not just an evaluation of the information system itself (caAERS), but also the environment in which it is used. caAERS provides functionality needed to support operating procedures that comply with many of these regulations.

7.3.2 Identification of gaps and potential gaps

While caAERS provides security functionality, a complete analysis of how the implemented security measures addresses the specific requirements of each regulation has not been completed. Such an analysis would also require a detailed description of the organizations in which caAERS will be used. The full analysis would require the caAERS development team to examine at least one deployment that should be FISMA compliant, and one deployment that should be NIST compliant.

7.3.3 Obsolete and unclear requirements

The caAERS development team is not familiar with the certification and authorization assessment form that needs to be reviewed by NCI ISSO, and whether this is still a standard process. Additional research needs to go into this requirement.

7.4 System Access

The EDMAERS must provide various levels of access. Access should be provided via a logon and password, with a built-in time-out mechanism. It must control access to the different modules and information based on role, group, and id. There should be a way for the users to remote login to the system, with full authentication and authorization in place. Users should be able to get a username and password easily when they access the system for the first time.

7.4.1 How the requirement is currently met

As discussed in various sections, caAERS requires a username and password to enter the application. There is full authorization and authentication, with the ability for organizations to integrate their existing authorization and/or authentication systems. This allows users to have one set of credentials across systems instead of having to maintain a separate username/password for caAERS. Rules are in place that prevent users from accessing data that is outside their scope. When users are idle for 30 minutes, they are automatically disconnected from the application and must log back in to access any data.

7.4.2 Identification of gaps and potential gaps

As previously discussed, additional work on the roles may be necessary to ensure the needs of all sponsors and organizations are met.

7.4.3 Obsolete and unclear requirements

The caAERS development team need more information concerning the ability to get a username and password instantaneously, as discussed in requirement SEC13. Currently, users do not have the ability to create an account in caAERS on-the-fly. An administrator must create the account and provide appropriate rights before a user can access the system. Once the requirement's meaning is clarified, how well caAERS meets it can be established.

Additional clarification is also necessary to determine what is meant by remote login capabilities. Since caAERS is a web-based system, users would have the ability to access it as long as they have access to the internet. When caAERS is installed locally by an organization, the limitation would be handled by the organization's IT group. For example, if a user was outside the network, the user would have to use whatever method was in place to access the network before being able to access caAERS.

8 Analysis of Functional Requirements

8.1 Admin Module

The EDMAERS must allow an administrator to make changes without having a programming background. Some of the changes and setup the system must support without coding changes include:

- Customize any or all screens and fields (also discussed in sections 5.3 above and 8.3.1 and 11.2 below)
- Dynamically setup business rules (AE reporting thresholds, CTC version, non-reportable AEs)
- Dynamically setup pathways, screens, and data fields
- Change labels or pick lists
- Verify and store users' systems information to ensure they meet browser/security requirements
- Allow GUI tools to have a signed relationship for end user screen changes
- View tracking

8.1.1 How the requirement is currently met

Admins have the ability to quickly and easily setup reporting rules based on sponsor, institution, and study. These rules drive reporting requirements, determining which reports are required when certain criteria is met, and what information must be included before a report can be submitted. When adding studies to caAERS, they can easily select the vocabulary used in that study, and therefore in reporting adverse events for that study. New versions of MedDRA can be easily imported into caAERS as they are released.

For September 2008, the caAERS development team introduced customizing the pages for the expedited reporting module. All fields for the pages are listed and the admin can mark the field as mandatory, optional, or not applicable. When the field is marked as not applicable, it will not appear on the screen when users go through the expedited reporting flow.

8.1.2 Identification of gaps and potential gaps

caAERS currently doesn't validate an end-user's system information. This has caused some frustration since users can access caAERS using unsupported browsers, which often leads to functionality issues. The caAERS development team needs to implement a way to check an end-user's system to ensure they meet requirements before allowing the user to access the tool. Since browser technology is constantly changing, this would require continual development, based on NCI's list of supported browsers and systems.

To meet the requirements documented for EDMAERS, caAERS needs to increase the custom configuration capabilities. At this time, most changes require programmatic changes. For example, as of September 2008, caAERS doesn't support:

- Customizing fields, including the labels and picklists (beneficial when new items are added or modified at a sponsor or national level)
- Dynamically adding CTC vocabularies (these are built into caAERS, so the addition of a new version, such as CTCAE v 4.0, would require a point release)
- Customizing screens (only supported within the expedited report module, and limited to adding/removing fields that are already built into the system)

8.1.2.1 Obsolete/Unclear requirements

The caAERS development teams needs clarification on the following requirements before it can be determined the status of the requirement:

- Allow GUI tools to have a signed relationship for end user screen changes
- View tracking

If the development team is understanding this requirement correctly, "GUI tools should have a signed relationship for end user screen changes," caAERS does not meet this requirement since electronic signatures are not currently supported. However, further clarification will be beneficial. To meet this requirement, the caAERS development team needs to implement support of signatures, and then require a signature when the user modifies anything that an end user would see (once that functionality had been introduced).

8.2 Analysis & Review

The following sections describe the analysis and review requirements that must be met. Many of these requirements overlap with requirements discussed throughout this document, covering reporting, user, data, and interface requirements. Since these requirements are so detailed, this area is broken into several sub-sections. This allows similar requirements to be grouped together and discussed in more detail, and allows readers to locate information of interest easier.

8.2.1 General requirements

There were several general analysis and review requirements for the EDMAERS. These include:

- Have a built-in online help module
- Track additional info from sites and sponsors (also discussed in sections 4.1, 4.11, and 5.3 above)
- Have built-in initial screening and review prior to submission to the NCI Access
- All sponsors to download protocol-specific data into the application
- Have a de-identifier module for compliance with HIPAA and other privacy laws (also discussed in sections 4.6, 5.2, and 7.2 above)
- Be able to include the complete workflow semantics in the database schema
- Have active workflow versioning
- Provide the ability for conditional path selection at event time
- Identify finite state machine based workflow modeling
- Ability to have single ownership assignment model

- Include security module for multiple sponsors
- Maintain current compliance standards and provide point releases to support updated standards

8.2.1.1 How the requirement is currently met

caAERS has an easy to use interface with built-in online and inline help. Users can get help on specific fields without leaving the page, or get more in-depth help by opening the online help.

For security, caAERS used a combination spring security and NCI CBIIT's Common Security Module. As such, it should support the various sponsors' security needs. caAERS also stores each data item in its own database field, which allows the separation of adverse event data from participant identification information, as required by HIPAA.

caAERS has a study/protocol module which allows users to add study specific information directly into caAERS. For example, users can add solicited AEs to the study, and have them appear in the adverse event module for data collection. Users can also define evaluation periods for a study. In future releases, users may be able to have different rules fire and actions occur based on the evaluation period.

The caAERS development team is continually increasing functionality, and addressing other bugs and compliance standards. The caAERS development team regularly releases new versions of caAERS, and provides patches in between regular releases to address critical bugs.

When looking at the database schema, developers will have the ability to see the complete workflow semantics.

8.2.1.2 Identification of gaps and potential gaps

caAERS does not currently have the ability to electronically add and associate attachments to an expedited report. This is functionality that needs to be built in.

caAERS submits completed reports for CTEP-sponsored studies electronic through the AdEERS system. In this way, there's a screening and review point before full NCI and FDA submission. Without using AdEERS, reports can only be submitted electronically via email, so there is no electronic review point before submission to the NCI and FDA. The caAERS development team will start addressing routing and reviewing with the release of caAERS version 2.0.

As discussed in sections 7.2 above, caAERS stores all data elements separately. However, there is no module that allows a user to separate the adverse event data from the participant data – only a DBA directly accessing the database can do this. Additional development must occur to support the exportation of, and querying of information that shows all information except specific participant details. caAERS also has no way to import expedited reports or serious adverse events at this time.

As discussed in several sections within this document, caAERS is not set up to handle the processing of completed expedited reports. Until it does so, it does not meet the following requirements:

- Be able to include the complete workflow semantics in the database schema
  Note: wherever necessary, such as in expedited reports, caAERS uses a status attribute to track the workflow status
- Active workflow versioning
- Provide the ability for conditional path selection at event time

- Identify finite state machine based workflow modeling
- Ability to have a single ownership assignment model

8.2.2 XML support

Specific requirements addressing XML support include:

- Generator module to allow query and retrieval of info from the system
- Workflow reconfiguration without recompiling
- Accept and transmit XML data to and from local databases

8.2.2.1 How the requirement is currently met

caAERS specializes in sending and receiving data in XML. As discussed in sections 5.1 and 5.5 above, caAERS provided XML schemas for importing and exporting the following elements: investigators, research staff, participants, studies. In addition, caAERS allows users to import routine AE information (AEs that didn't require expedited reporting).

The integration with AdEERS to electronically submit expedited reports is in the form of XML documents and messages. In addition, a set of web services were developed which can be used to implement real-time integration of study, participant, adverse event, research staff, and investigator data with other systems. These services also use a combination of messages and XML documents.

The caAERS development team has also provided an API for querying AE data. The results of the queries are delivered in XML format. All APIs the caAERS team have developed have both web and grid service interfaces, where the data transport format is XML.

8.2.2.2 Identification of gaps and potential gaps

While there is an API for querying AE data, additional work needs to be done on the API. The querying capabilities are limited, and there is no front-end for the query tool.

caAERS hasn't implemented the processing of submitted expedited reports. As such, there are no workflows available to reconfigure without recompiling data. However, the caAERS team will use this requirement to drive the implementation

8.2.3 Search capabilities

Users of EDMAERS will want the ability to search for information various ways. Some of the specific search methods and constraints that must be included in the EDMAERS front-end include:

- Ability to search for protocol, agent, and device
- Search results should only display studies that have not closed
- Ability to search for new AEs and new expedited reports

8.2.3.1 How the requirement is currently met

Within the caAERS front-end, there are multiple search modules. Users can search for participants, studies, research staff, investigators, and studies. There's also an advanced search module that allows the user to search across studies to locate expedited reports and routine AEs.

8.2.3.2 Identification of gaps and potential gaps

While caAERS includes integrated search capabilities that is accessible to users via the front-end, there is additional development that needs to occur to fully support the requirements.

- Currently, the search results can be saved, but only as a .txt file. For the results to be useable outside of caAERS, the results need to be savable in more formats
- There isn't a way to exclude closed studies. When you search for a study, you can filter based on the status of the study, but you can't eliminate just one status
- There isn't a way to search for an agent or a device. Additional protocol criteria needs to be included as searchable fields

8.2.4 Export capabilities

These requirements overlap with requirements discussed in section 5.5 above. The new reporting tool must be able to export data. It should be ablep to export SAE info into various applications, and should include an HL7 Adapter. Some of the applications and formats it needs to export to include:

- E2B applications
- CDUS (clinical data update system)
- DESK
- ESYS
- EXCEL
- ORACLE CLINICAL (C3D, CTSU, DCP OC)
- SAS
- Oracle Clinical Remote Data Capture (RDC)
- XML

8.2.4.1 How the requirement is currently met

caAERS has expanded export capabilities. Data associated with studies, participants, adverse events, SAE reports, investigators, and research staff can be exported to CSV and XML formats.

As illustrated by caAERS integration with AdEERS, caAERS is able to export data for use in other systems. XML documents and messages (web services) allow caAERS to export data to various applications.

8.2.4.2 Identification of gaps and potential gaps

caAERS currently does not include functionality to export directly to most of the listed applications. Additional research needs to occur to determine if export methodologies need to be modified to support providing data to these applications. The caAERS team needs to review the formats supported by the above-mentioned systems and devise an approach to convert the output from caAERS to those formats.

caAERS does not currently include an HL7 adapter for use when exporting data. If current export capabilities are found inadequate, or if it's mandatory that an HL7 adapter be included, additional research will need to occur to determine specific changes required to include and use this adapter.

8.2.5 Import capabilities

The EDMAERS must have specific import capabilities (also discussed in section 5.5 above). The import capabilities that must be supported include:

- Migrate legacy data into the EDMAERS from existing systems (AdEERS, local CTMS)
- Import images, PDFs, etc and associate them with expedited reports
- Import from
  - CTS (clinical trials system)
  - Custom applications
  - Hospital systems (HL7 or LIMS)
  - Lab systems

8.2.5.1 How the requirement is currently met

As more users adopt caAERS, more data will need to be imported into caAERS. caAERS provides an XML-based import method to import legacy routine AEs and various data elements required to support the collection of AEs.

In general, caAERS has well-developed import capabilities. Data associated with studies, participants, adverse events, investigators, and research staff can be imported into caAERS in XML formats. In September 2008, the caAERS development team added the ability to import CTEP studies captured in the CSV format. This addition will significantly alleviate the burden of manually entering CTEP studies into caAERS. It will also eliminate the errors that are typically associated with manual entry of data.

8.2.5.2 Identification of gaps and potential gaps

The caAERS team believes import functionality requirements are mostly met, although some additional research needs to occur concerning importing from hospital systems. However, as long as the input complies with the schema, caAERS can process it.

The caAERS development team also needs to provide a method for importing expedited reports, and, once impletement, a way to import processing information for those expedited reports.

caAERS does not currently have a way to upload images and other documents (such as pathology reports, x-rays, or death certificates) into the system. To meet the requirements, the development team needs to implement a method for these uploads and the association of this type of material to an AE, SAE, expedited report, and expedited report package.

8.2.6 Notifications

The EDMAERS must be able to meet various notification requirements. These requirements overlap with requirements discussed in section 5.6 above, and are also mentioned in sections 4.8 and 4.11, and 6 above, and 8.2.8 and 8.3.3 below. The following notification requirements were specifically called out as functional requirements:

- Generate automatic notifications of AEs based on preset thresholds (frequency, severity, source, etc), with preconfigured people to notify and the ability to add people ad-hoc
- Allow asynchronous event processing
- Notify sites and investigators when submissions are made to the FDA
- Support the 24-hour notification process for both CTEP and DCP (discussed in section 8.3.2 below)

- Push reports and workflow to appropriate parties via email or pager
- Send notification to the reporter when the report is created, copied, or amended

8.2.6.1 How the requirement is currently met

AdEERS has the ability to send out notifications when expedited reports are being created and when they're being processed. Notifications can be sent automatically upon creation of an expedited report, and at specific intervals if the expedited has yet to be submitted. During the processing, notifications are also automatically sent based on the status and phase of processing, or can be manually triggered.

caAERS has a module that allows the user to set up notifications based on the report type. These notifications can be setup to send to specific addresses (email, web server, pager) or to a general role. For example, a report can be set to go to the primary investigator. Then, when a report is submitted concerning an AE on a specific study, the person or people assigned the primary investigator role in caAERS for that study will be notified.

caAERS uses asynchronous event processing to a limited extent to implement caAERS to AdEERS communication. Expedited reports are submitted to AdEERS asynchronously and caAERS also process the results from AdEERS asynchronously.

Notifications in caAERS can be setup for specific timeframes based on the time a report is created. The notification timeline will be followed until the expedited report is submitted.

caAERS partially supports the 24-hour notification process for both CTEP and DCP. 24-hour notification reports have been created and can be used to document the required information. DCP can receive these via email, or print them to send via fax.

8.2.6.2 Identification of gaps and potential gaps

Additional notification development needs to occur for caAERS to fully meet these requirements. Since caAERS does not have processing built in, it does not have notifications that occur after an expedited report is submitted; the final notification is that the expedited report has been submitted.

caAERS also does not support notifications based on AE details. Additional research and development must be completed to fully understand the audience for these notifications and at what various points in the AE collection and expedite report creation modules this functionally needs to be added. The caAERS development team can see multiple points where this would be beneficial while processing a submitted expedited report.

The caAERS development team needs to complete more work to fully support the 24-hour notification process for AdEERS, and to support amending reports that are sent via AdEERS. This development involves collaboration with the AdEERS development team, since these need to be process by AdEERS. Development is slated to be completed in version 2.0, but the date can't be completely controlled since the AdEERS development team's schedule also has to be considered. The same can be said about amending reports and sending notifications concerning the status of the amendment.

While caAERS provides a configurable notification system, based on the specific report being completed, additional development may be necessary to support sending notifications ad-hoc.

While caAERS supports asynchronous workflow when sending expedited reports to AdEERS, additional work needs to occur before caAERS supports it in general.

8.2.7 AE report creation

The requirement document called out many specific requirements the EDMAER must meet concering creating adverse event reports. These include:

- Select sections appropriate for the AE report
- Complete expedited reports in multiple settings
- Able to be edited, reassessed, withdrawn (if not submitted), and have information added to the expedited report
- Require the protocol number and participant ID to create a report
- Require the protocol number, ticket number, and participant ID to withdraw a report
- Require the protocol number, ticket number, participant ID, agent information, primary investigator inforamtion, and author details to amend a report
- Only submitted reports can be amended and copied
- When amending a report, be able to copy all the information from the previous version and make changes where necessary
- Support different workflows simultaneously, displaying specific message and fields depending on the type of study; study types that must be supported include:
  - Commercial agent only
  - Non-NIH/NCI investigational only
  - Multi-sponsor
  - Surgery only
  - Radiation only
  - Device only
  - Prevention
  - CTEP IND
  - Multi-modality
  - Imaging
- Always capture reporter info before AE report is created or copied
- Generate a random 7+ digit ticket number for each report generated, and maintain the ticket number, adding a unique amendment number for each amendment
- Support edit checks to validate the data in real-time
- Accommodate reporting of any AE, even if it doesn't fulfill expedited reporting requirements
- Describe AE using protocol-defined vocabulary method (term for MedDRA, category, term, and other for CTC), grade, comments, verbatim description, and reporter
- Ability to attribute the AE to causal factors with standard indicators
- Support protocol-specific exceptions to expedited report requirements
- Provide a way to view toxicities, by toxicity and grade
- Mechanism to select the classification level (classification of reaction) from available classification, which contain standard grade levels; this must be mandatory

8.2.7.1 How the requirement is currently met

caAERS supports the creation of expedited reports. Expedited reports can be created, submitted, amended, and withdrawn. Each expedited report contains necessary information, determined by the sponsor of the study, and study based rules. All reports require the documentation of the reporter and are assigned a 5-digit ticket number.

Any AE can be submitted as an expedited report, even if the rules say a report is not required. Users can select the grade of the AE, attribution to the study, and hospitalization to help identify the AE before determining if expedited reporting is required. The vocabulary used to describe the AE is based on the study, and caAERS supports multiple versions of CTC and MedDRA. Users are also able to record comments and verbatim descriptions about the AE.

Based on the rules and report definition setup, caAERS denotes which fields, sections, and screens are required before the expedited report can be submitted. As the user moves through the pages of the expedited report, caAERS validates the data entered to ensure the data matches the database requirements.

caAERS supports multiple workflows for creating expedited reports. Currently it fully supports the following types of studies:

- Commercial agent only
- Non-NIH/NCI investigational only
- Prevention
- CTEP IND
- Multi-modality

8.2.7.2 Identification of gaps and potential gaps

caAERS has the capability to create expedited reports. However, to fully meet the requirements outlined for the EDMAERS, it needs to add the following functionality:

- Allow users to select sections of the report (although the way caAERS will be streamlined in version 2.0, this may not be necessary)
- Support the assessment and addition of information to the report after the report has been submitted and is in processing
- Fully support the amending of a report
- Fully support the withdrawal of a report
- Support the copying of a report
- Change their ticket numbering schema from 5-digits to 7-digits
- Support the following workflows, including adding specific messages and fields:
  - Multi-sponsor
  - Surgery only
  - Radiation only
  - Device only
  - Imaging

- Increase functionality associated with the following workflows (adding specific messages and fields based on the type of study)
  - Commercial agent only
  - Non-NIH/NCI investigational only
  - Prevention
  - CTEP IND
  - Multi-modality

caAERS only allows users to search for AEs by first identifying a participant-study combination. To meet the requirements, the caAERS developers need to extend this functionality to allow users to locate expedited reports by searches that include ticket number.

8.2.8 Processing expedited reports

After an expedited report is submitted, it needs to be processed to validate the information, be reviewed, and then be submitted or stored. Some of the functionality requirements for the EDMAERS address this processing workflow, and are listed below. In addition, these requirements are discussed in sections 4.5 and 6.2 above, and 8.3.3 below.

- Assessments
  - Users can conduct assessment/reassessment of Section Head Review, and copy assessment
  - Investigator and NCI comparison assessment
  - Provide a way to indicate if assessment is complete
  - Provide a way to view details of assessment (date, assessed by name)
  - Provision of a reassessment and workflow module for review and/or approval of AE reports by sponsors
  - Customizable assessment logic by sponsor/pathway/protocol
  - AEs can be added if assessment is not complete or has been changed (amended) but not saved
  - During assessment, sponsor must be able to delete, change, or add an AE, conmed, or other cause
- Back-end (analysis) report creation
  - Build custom reports in standard format and as a saved canned report
  - Generate, schedule, and save batch report jobs
  - Include canned (20+) and custom reports (which can be saved for future use)
  - Have statistical and analytical reports
  - Produce existing AdEERS reports
  - Support extensive reporting and querying capabilities
  - Ability to do milestones tracking

  - Ability to view AE processing stages for a particular ticket
    - Allow automatically selecting ticket number
    - Show only tickets submitted to NIH/NCI
    - Display by ticket number ascending, status descending, and amendment number descending
- Report reviewing
  - View AE reports
  - Ability to review protocol info:
    - NIH/NCI Protocol number
    - Vocabulary version
    - Local Protocol number
    - Are investigational agents present?
    - Are investigational devices present?
  - Ability to view andenter comments
  - Ability to view agent/drug by NSC, name, or IND#
- Report Processing
  - Able to prepare the submission packet sent to the FDA (ARA summary, section head review, actions recommended, etc)
  - Ability to further process all new/amended AE reports submitted to NIH/NCI
  - Produce and print FDA (and others as described in section 12 below) reports
  - Add and display ARA Summary text
  - Ability to print expedited reports that have completed processing
  - Ability to track and record all communication that takes place concerning an expedited report
  - Provide a way to view and enter actions recommended and associated comments
  - Provide a way to view abd enter protocol violation details and the nature of those violations
  - Provide a way to display the lead organization's protocol aliases and participating organizations' aliases for displaying the local document number
- Report Routing
  - Identify user-specified target recipients of AE reports
  - Acknowledgement of receipt of AE reports
  - Flag AEs that meet defined criteria as DNP, based on AE, expectedness, IND agent, grade, attribution, and hospitalization

- DNP Module
  - Configurable electronic review for CTEP Investigational Drug Branch (IDB) physician drug monitors that includes functionality of AdEERS DNP Module with similar modules for DCP, CIP INDs, and CIP IDEs
  - Process
    - Receive notifications
    - Review reports online through the application
    - Mark as reviewed, enter comment and mark as review, or mark as activate to start full processing
  - Ability to produce summary report
  - CTEP's process is only valid for protocols under a NCI IND
  - Must include indication that IND agent was administered

8.2.8.1 Identification of gaps and potential gaps

These requirements all focus on the processing of submitted expedited reports. As discussed previously in this document (specifically in section 6 above), caAERS does not support the processing of expedited reports. Additional development needs to occur for these requirements to be met.

8.3 Data Capture and Reporting

The requirements here cover general data capture needs, initial data collection, submitting the data, and analyzing/reporting on the data. Since these requirements fall into four general categories, the requirements will be discussed in several sub-sections. This allows a more detailed discussion and allows readers to quickly locating specific requirements.

8.3.1 General Data capture and reporting requirements

Concerning data and reporting, in general, the EDMAERS must:

- Include an integrated comprehensive online help module
- Support all LOVs (list of values) required by NCI, and the real-time updates of the LOVs on a local system
- Provide user name/password for authentication and multiple levels of authorization for multiple rule-based tracks, including:
  - NIH/NCI-IND
  - Non NIH/NCI-IND
  - Commercial (MedWatch)
  - Radiation
  - Surgery
  - Device
  - Prevention (DCP)
  - Imaging trials
  - Image guided intervention trials
  - CIP INDs
  - CIP IDE
- Provide access to participants who don't have usernames, allowing them to submit AEs they experience

- Have different interfaces for DCP, CTEP, and CIP, customized to meet business processes (also discussed in sections 5.3 and 8.1 above and 11.2 below)
- Include secure workload tracking and SAE query wizards for all sponsors and their designated trail sites; sponsors and sites include:
  - NIH
  - NCI
  - CTEP
  - CIP
  - NCI CBIIT
  - CCR
  - Cooperative groups
  - Cancer centers
  - Consortia
  - Other cancer organizations
- Have hot key functionality to allow users to get through the application quicker after they become familiar with it
- Provide the ability to print expedited reports
- Provision an XML generator function that's based on a meta-model approach
- Have search functionality
- Be semantically and syntactically interoperable with the silver-level compliant SAE system
- Include various modules and screens, including a summary screen, transmit screen, and participant screen
- Support workflow modifications based on sponsor and consortia needs
- Be able to abstract the protocol PI from CDUS and institutions from the protocols

8.3.1.1 How the requirement is currently met

To access caAERS, users must log in with a user name and password combination. Once in the application, users will be able to access a full online help system, including inline help to provide information about various fields. The system is easy to use and has been programmed to show only fields specific to the sponsor, in the case of CTEP and DCP. For September 2008, the caAERS development team introduced customizing the pages for the expedited reporting module. When setting up a report definition, all fields for the pages are listed and the admin can mark the field as mandatory, optional, or not applicable. When the field is marked as not applicable, it will not appear on the screen when users go through the expedited reporting flow.

As part of the CCTS, it is silver-level certified, supporting CDEs and standard LOVs. There's also a robust search engine available that summarizes the search results. In addition, each module includes a summary page that details the information contained in the element the user is accessing. This summary page is the first thing the user sees when editing information, and the last thing the user sees when initially creating something.

Users have the ability to print an expedited report at any stage of the report (incomplete, ready for submission, submitted, amended, withdrawn, etc). Users can also save reports as PDF or XML files.

In preparation for creating expedited reports, users have the ability to import an excel spreadsheet containing a list of protocols. If an investigator isn't in caAERS but is included on the spreadsheet, the investigator will be created within caAERS. caAERS

uses CTEP's list of organizations to populate the organizations within caAERS. caAERS also supports importing other data elements, such as investigators, research staff, studies, and participants.

8.3.1.2 Identification of gaps and potential gaps

caAERS does not support an anonymous login, which would allow a participant to log in to the system and enter an AE they're experiencing. This has been discussed as a possible addition for a release in the near future. caAERS also does not have differences in their login methods based on the tracks. Conversations would need to occur to understand the full requirements here. If it's a matter of access, this could be controlled by the existing roles. If it's a matter of sponsors and single-sign-on capability, caAERS has built that capability in.

While caAERS does support NCI's LOVs and vocabularies, it does not support real-time updates. Updates would require a point release. caAERS has run into issues with this already, related to organizations, so is looking at modifying the system to support either imports of the information, real-time updates (which would require development by caAERS and NCI), or a combination of the two.

caAERS supports some general customization based on study and sponsor, such as customizing the fields that appear on the expedited report pages. However, these customizations are limited to adding and removing fields that are already built into the system. To fully meet the requirements, additional development needs to occur, extending the existing functionality to include changing field labels, adding items to lists, adding fields to pages.

This work could also be a step toward allowing full workload tracking and SAE query wizards for sponsors and trial sites. caAERS does provide some query functionality, but it needs to be further developed to fully meet the requirements.

While the UI is very user friendly, it is the same for all levels of users. Additional work can be done to make it even easier for experienced users to use, such as shortcut keys to open searches, go to specific modules, copy items for reuse, etc.

8.3.2 Initial data collection

The initial data collection requirements for the EDMAERS are listed here and in section 8.2.7 above. Specific ones list here include:

- Support the 24-hr notification process for both CTEP and DCP (discussed in section 8.2.6 above)
- Be able to create AEs, SAEs, and expedited reports
- Be able to save interim and incomplete version of expedited reports, and support AE versioning
- Be able to withdraw expedited reports
- Connect via API to custom dictionaries (CTCAE 2.0, CTC 3.0, MedDRA 9, MedDRA 10, etc)
- Include a drug/agent screen
- Be integrated with (via API) the ASAEL (for determining expectedness of an adverse event on a CTEP IND trial) and other predictive apps to help determine processing (this is also discussed in sections 4.5 above and 5.5 above and 10.1 below)
- Be able to report deaths unrelated to adverse events

- Be able to capture AE data related to multi-IND and multi-sponsor studies

8.3.2.1 How the requirement is currently met

caAERS is a tool that has the ability to capture any type of AE and to create reports for the AEs it captures. It is developed to support the various types of studies for CTEP and DCP. To support this ability, it comes pre-loaded with CTCAE 2.0 and CTC 3.0, and has the ability to import MedDRA 9, 10, and 11. As new versions of CTC and MedDRA are released, they will also be supported.

Users have the ability to save draft versions of AE collections, where attribution is not fully provided, and incomplete versions of reports, where reports aren't completed in one setting.

8.3.2.2 Identification of gaps and potential gaps

caAERS supports the 24-hour notification process required for both CTEP- and DCP-sponsored studies, with built-in reports, which can be sent via email to the recipients. However, additional development is on-going to enhance the support, providing direct notification through AdEERS for CTEP, and investigating a different method of supporting the requirement that doesn't require a separate 'report' in caAERS.

caAERS tracks all changes made within the system. However, the developers need to implement a way for users to be able to view this information. So, if an attribute of an AE changes, or a report is modified in any way, a user would be able to view what changed and when it was changed.

Similarly, caAERS provides the ability to withdraw an expedited report. However, it only marks it as withdrawn; it does not modify the version sent to AdEERS or notify AdEERS that it has been withdrawn.

caAERS uses custom dictionaries to support documenting AEs and creating expedited reports. However, they are either programmed in, or have to be imported. Supporting a connection to these dictionaries via API needs to be researched further. The APIs for CTC could always be available, but limits would need to be placed on the ones supporting MedDRA since it is a proprietary vocabulary.

CTEP's ASAEL is currently not integrated into caAERS, but is slated for development for caAERS 2.0. Support will be in phases, first allowing users to directly associate 'expected' AEs to a study. Then the team will look into connecting to the ASAEL via API.

caAERS is setup to associate a study to one sponsor. Studies can be assigned multiple identifiers, thus providing a method to document more than one sponsor. However, additional development needs to occur to directly support the association of a study to multiple sponsors.

8.3.2.3 Obsolete requirements and requirements that need clarification

At this time it's unclear what the authors of the requirement document meant by "be able to report deaths unrelated to adverse events". caAERS has the ability to capture "Death" as an AE, since Death is included as a term within the CTC vocabularies. If this is what the authors meant when they made this a requirement, caAERS does meet the requirement. However, the caAERS team wants to get some clarification on the requirement to ensure it is met.

In addition, the caAERS team needs a clearer understanding of what is meant by "include Drug/Agent screen". caAERS allows the user to enter information about all agents used during the period of time being reported on, including study agents and concomitant drugs. However, it's not clear if this is what is meant by the requirement.

8.3.3 Submitting the data

Once data is collected, the EDMAERS must support submitting it to various parties. This involves:

- Providing an API to allow integration and cross verification with other systems:
  - ESYS
  - ESYS components (PATS, Dose Regimen, etc)
  - DESK
  - Local patient data systems
    - Oracle Clinical for Cancer Trials Support Unit (CTSU)
    - Remote Data Capture (RDC)
    - C3D
    - DCP Oracle Clinical
- Include an autocoder in the expedited report package, and links via API to COTS autocoders, with the ability to track which have a signed relationship
- Supporting email alerts and notifications (sections 5.6 and 8.2.6 above focuses on notifications, and sections 4.8, 4.11, 6 , and 8.2.8 above include similar requirements)
- Communicate to spell checkers via API
- Be able to copy and amend adverse event reports
- Support both a centralized and decentralized processing and approval (discussed in sections 4.8, 4.11, and 5.3 above)
- Receive automated, electronic submissions of expedited reports from cancer centers' clinical trials systems (both legacy and the caBIG SAE solution)
- Provide a field to capture the verbatim toxicity terms
- Capture system changes (comments, notes logs)
- Allow web-based reporting of AEs, to be submitted through the new system

8.3.3.1 How the requirement is currently met

caAERS is a web-based application that supports the submission of expedited reports and allows the reports to be amended as necessary. It has built-in email alerts and notifications, and supports CTEP's current centralized and decentralized processing and approval via its connection with AdEERS. It recognizes who sponsors the study and processes the reports accordingly. As long as a user has a user name and password with access to reporting, the report can be accessed directly and modified.

When reporting AEs, a verbatim field is included to allow the users to record the AE as described by the participant.

8.3.3.2 Identification of gaps and potential gaps

The caAERS development team is working on an API that allows the integration of AE data and expedited reports with other systems. Under the current development plan, the API should be available for beta use in March of 2009. In addition, caAERS has an API for importing historic AE information, but not historical expedited reports. The

development team will be investigating extending this API to support importing current AE and expedited data. This API is necessary to receive information from various CTMS.

While caAERS does allow a report to be amended, it is not integrated with AdEERS to support the submission of that amended report for CTEP studies. There's also no way to identify the report as amended. As of September 2008, this functionality is currently being worked on by both the AdEERS and caAERS teams. caAERS also doesn't support copying an expedited report or AE. This requirement was reviewed for caAERS 1.5, but has been moved to a later development period.

While caAERS currently supports centralized and decentralized processing and approval of expedited reports, this functionality will be enhanced in the future to support non-CTEP studies. A method that doesn't involve AdEERS is also being investigated.

The caAERS development team needs to look into supporting the following functions in caAERS:

- Spell checking within caAERS
- caAERS also doesn't support copying an expedited report or AE. This requirement was reviewed for caAERS 1.5, but has been moved to a later development period.
- It also needs to provide a way for users to annotate an expedited report, so they can provide comments and ask questions without directly modifying the report. This features is being looked into as the caAERS team addresses routing and reviewing requirements.

8.3.3.3 Obsolete requirements and requirements that need clarification

The specific needs of the various users for AE case follow-up needs to be broken down into more detailed requirements to determine if additional development is required to fully meet the requirement.

To fully determine what level caAERS meets or doesn't meet the autocoder requirement, the caAERS team needs further clarification. However, it can be noted that caAERS does not have a way to recognized signed relationships.

The current reporting tool is web-based, so there were questions concerning the requirement that the new tool allows web-based reporting of AEs. Does this mean a separate website that would communicate to the new system, or is it just reiterating that the tool needs to be web-based? If it's the former, the development of the API should support submissions made via a website. If it's the latter, caAERS fully meets the requirement.

8.3.4 Reporting on/analyzing the data

When reporting/analyzing the data collected, the EDMAERS must:

- Supporting AE case follow-up for site personnel, regulatory NCI vendors, NCI personnel, etc
- Include distribution logic determining the sponsor of the study (CTEP, CIP, or DCP), and if CTEP, if it goes to TRI, Do not assess, or IDB DNP for batch processing (also discussed in sections 4.5, 6.2, and 8.2.8 above)
- Support customizable assessment logic by sponsor, pathway, protocol, or a combination of all three
- Have the ability to report the number of local system failures to capture NCI's required data (Reconciliation of record by field data)

- Have an event screen
- Provide full audit trail and audit reports, including reports that compare versions of reports to account for differences

8.3.4.1 How the requirement is currently met

caAERS supports very basic auditing of the data collected. Most of this requires a DBA to access the database directly for the information.

8.3.4.2 Identification of gaps and potential gaps

The majority of these requirements involve processing submitted reports, functionality that does not currently exist within caAERS. Some specific items that need to be addressed in relation to this, and give the appropriate priority include:

- The various distribution requirements for CTEP – Go to contractor, Do not assess, and Do not Process; these are important for managing the workload associated with processing expedited reports for CTEP-sponsored studies, so will have high priority.
- Comments or note logs, to capture comments concerning the processing of an expedited report package

While basic auditing is in place, the caAERS development team is starting to explore the expansion of auditing all data collected. The auditing requirement is also discussed in sections 4.3 above, 4.6, and 7.1 above, and 10.2 below.

8.3.4.3 Obsolete requirements and requirements that need clarification

What is meant by “Event screen”, requirement FN151, needs to be clarified before it can be determined if the requirement is met or not.

9 Analysis of Ergonomic (or User Interface) Requirements

9.1 General

Some of the general user interface requirements for the EDMAERS were discussed in sections 5.3 above and 11.5 below. Specific items that need to be addressed include:

- The application must follow NCI UI guidelines and run in the supported browsers (IE 5.0, Mozilla 1.0)
- The home page must include a disclaimer addressing privacy and retention of information collected
- The JavaScript must behave the same in IE, Netscape, and Mozilla
- No browser modification should be required to display the application in its optimal presentation (1024x768 pixel resolution), and no horizontal scrolling should be required
- At a minimum, each screen should be conducting field-level validation through a server side object, to ensure that data integrity and validity is not compromised before it's added to the database
- When working with graphics, set the graphics' dimensions in the graphics' HTML tags and avoid using pixilated, improperly compressed or scaled graphics
- Style sheets should be used to help create a consistent look and feel, and should influence the presentation of documents without sacrificing device-independence or adding new HTML tags
- When data is placed side-by-side, rows and columns must be aligned and where possible, the input controls should be of an identical length
- Frames should be avoided unless justified by specific user needs

9.1.1 How the requirement is currently met

caAERS is a very user friendly application, with an intuitive interface, inline and online help, and an easy to follow workflow. It is 508 compliant, as further discussed in 9.2 below. Cascading style sheets (css) are used to help present a consistent look and feel across the application. These style sheets also allows the caAERS development team to quickly make updates to the look and feel, with minimum coding required.

Layout is optimized for 1024x768, with almost no use of frames. This supports both 508 needs and the general equipment setups of most sponsors and organizations. Columns are used to reduce vertical scrolling, but not to the point that the page requires horizontal scrolling. Where columns are used, fields line up vertically for a clean look and feel.

Javascript is used, and works the same regardless of the supported browser in use. Field-level validation is used to ensure data validity and integrity, so the database does not become corrupted.

caAERS fully supports field-level validation through server side objects. A significant number of server side validations are implemented using the business rules engine (Drools). caAERS has also provided client side validation wherever necessary, leveraging the Prototype Javascript library to complete the implementation.

9.1.2 Identification of gaps and potential gaps

caAERS currently does not have any disclaimers about the information added and stored in the system. This is something that needs to be added to meet requirements.

9.1.3 Obsolete requirements and requirements that need clarification

The requirement documented in the requirement document stated NCI's supported browsers were IE 5.0 and Mozilla 5.0. Since technology has improved, the authors of this document believe NCI's supported browsers have changed.

caAERS runs in IE 7.0 and Firefox 2.0 and up. However, it is not guaranteed to work in IE 6.0. Pending the clarification of NCI's supported browsers, additional development may be required, based on the planned timeline for the EDMAERS.

9.2 508 Compliance

As a government application, the EDMAERS must be 508 compliant. These requirements are also discussed in sections 5.2 and 5.3 above. Some specific items that must be addressed include:

- Information cannot be conveyed solely through color – if color indicators are used, there must be statements that provide the information without it being reliant on color
- Links must make sense on their own – they can't rely on the context of the text surrounding them
- There must be a skip navigation link feature allowing screen reader users to move directly to the content of the new page
- All images must have alt descriptions, and complex images must be made accessible by the use of longdesc tag or "d" links
- Forms must be accessible (labels, text description, tabbing order, etc) so they can completed with the use of a screen reader and keyboard-only mechanisms
- Tables should be used only minimally, relying on text tags primarily
- Application should be designed so it doesn't flicker with a frequency greater than 2 Hz and lower than 55 Hz
- All navigational images must have clear Alt Tags
- If checkboxes are required to support the selection of an individual row, the checkbox should appear as the left-most column

9.2.1 How the requirement is currently met

caAERS meets most 508 compliance regulations. It was designed to ensure maximum usability for those who use alternate methods to access the web.

- Where color is used, explanations are provided.
- When images are used (both for illustration and navigation), ALT tags are used to explain the purpose of the image.
- Tables and frames are used minimally, with the layout controlled by style sheets and text tags.

9.2.2 Identification of gaps and potential gaps

To further improve 508 compliance, caAERS needs to make the following adjustments:

- Improve the tabbing and keyboard navigation. While tabbing is set up, it does not work consistently in either IE or Firefox
- There currently isn't a way setup that allows readers to skip lines or navigation. It has been recognized as a gap and should be an easy fix to implement

9.2.3 Obsolete requirements and requirements that need clarification

Additional testing and research needs to be done concerning flickering of the application at the frequency specifications documented in the requirement. With the improved technology, it is unclear if this is even a valid requirement.

9.3 Language Support

At this time, the EDMAERS is only required to support English. However, it's possible that additional languages will need to be supported in the future, specifically for entering AEs and expedited reports. The EDMAERS must be NLM (National Library of Medicine) and NSL (National Science Library) enabled.

9.3.1 How the requirement is currently met

caAERS is being developed to support multiple languages. Error messages, inline help, instructions, and labels are all being kept in separate property files. Handling the information this way allows for easy translation in the future.

9.3.2 Identification of gaps and potential gaps

caAERS is not currently NLM or NSL enabled. Additional development needs to occur for the application to support using these two libraries.

9.4 Navigation

The navigation elements in the system must be very clear. The image used to access help must be the right-most item of the page. There should be a menu area, which separates the header from the page content area. The menu area should be composed of navigation elements that take the user directly to another base screen, application, document, or website. The navigation buttons must be distinctive and clearly identified, with the text centered within the button.

9.4.1 How the requirement is currently met

AdEERS navigation is straight-forward. There is no menu area, no header information. To access reports, you click buttons in the middle of the screen. Once in the report, high-level navigation is controlled by a menu on the left-hand side of the screen. Help is always accessed from the upper right-hand corner of the page, and the buttons to control the actions done on the page are centered at the bottom of the page.

caAERS navigation is also very straightforward. It has a high-level navigation menu at the top of the screen, with sub-level navigation areas beneath it that change based on which high-level element is selected. Visual cues in the navigation elements allow the user to know where they are in the application quickly. Logging out of the application and accessing help is done consistently from the top right-hand corner of the screen. In addition, each page has help in the top corner of the page area, and inline help exists next to many fields. Buttons that control the action of the pages themselves are

consistently found at the bottom of the page, in both the left- and right-hand corners. If a field has a button associated to it, the button is always found to the right of the field.

One nice element of caAERS navigation is the site map, which is available when you click on the logo in the upper left-hand corner. The site map organizes the different modules of caAERS, showing the users only the elements they have access to.

9.4.2 Identification of gaps and potential gaps

Navigation may need to change to meet the requirements, since using the main navigation doesn't take a user to separate pages. Instead, the user has to access second-level navigation before the main page changes. Before the caAERS development team changes the navigation to meet the requirement, extensive usability testing would need to be completed.

9.5 Page Layout

The EDMAERS must have certain layout features to meet requirements. These requirements are:

- The general layout must include a window title (application name & NCI, plus any additional identifying info about the screen) with six areas: header, sub-navigation, main navigation, page content area, action area, and footer
- All pages should have the same basic underlying structure
- The layout of the application must include main navigation, provide application specific controls, and have intuitive navigation that requires minimal training
- There should be a way to add default information that can be displayed as a reminder to the user
- The cancer.gov mini banner must be included on every page, and the overall layout (footer, header) should be consistent with cancer.gov design standards
- The content area should be customized on each screen, with the layout being constrained only by the style sheet
- Ordering of fields and flow should be familiar to users and support comfortable navigation

9.5.1 How the requirement is currently met

AdEERS is a very consistent application, which users find easy to use. Before users can access the application, they must go through multiple pages, one of which includes most of the required standard elements.

The pages in the AdEERS application are very similar to each other, with a consistent look and feel. The types of fields used and the layout are both consistent from page to page. Users find the flow intuitive, and are able to navigate through the sections confidently after a little training.

caAERS is a fairly intuitive application. The layout is clean and the consistent from page to page and module to module. While each page's content is different, the look and feel doesn't deviate from the styles setup in the CSS. Navigation elements are consistent throughout the application, and the title bar provides the application name as well as information on what screen is being accessed.

Entering an expedited report was setup in caAERS to match the functionality and feel of AdEERS, so is familiar and easy to navigate through. Each iteration release of caAERS

brings new changes, which makes creating the report more clean, more simple, and more intuitive, while requiring less time.

As of September 2008, the caAERS development team added the ability to enter information to be displayed when entering AEs. This information is tied to the study and the evaluation period, so is fairly customizable.

9.5.2 Identification of gaps and potential gaps

AdEERS was developed as a stand-alone application and does not include many of the page layout elements necessary to meet the requirements for the new application. There is only one level of navigation, it doesn't have the header or the footer, and there's no mention of the cancer.gov mini banner. The layout is also controlled by frames, with no style sheets associated to the application. While there is a window title, it doesn't change from page to page, and only includes the name of the application. However, it is still straightforward and easy to use.

caAERS is missing a few elements required to meet the page layout requirements. The following changes need to occur to caAERS to meet the requirements:

- Add the standard header and footer navigation elements
- Include the cancer.gov mini banner
- Add NCI to the window title

While caAERS does support adding information to display during the AE flow, additional investigation needs to occur to determine the full requirement. The development team is also looking in to adding alerts, which may not be limited to a study-level addition, it may be per patient.

10 Analysis of Data Requirements

10.1 Elements

The EDMAERS must be able to capture and maintain the data elements currently captured by the AdEERS application.

10.1.1 How the requirement is currently met

caAERS was built around the AdEERS system, so captures the same data elements for AE collection and expedited reporting as AdEERS.

10.1.2 Identification of gaps and potential gaps

While caAERS captures the elements used for creating an expedited report, it is missing some elements captured by AdEERS. For example, it does not have the ASAEL integrated into it, as discussed in sections 4.5 above and 5.5, 8.3.2 above. caAERS also does not capture any of the AE and report processing elements, since that functionality hasn't been added to caAERS yet.

10.2 Auditing

To satisfy federal regulations, it's important that full auditing is in place in the EDMAERS. All changes must be captured, and all updates made to an expedited report once it has been submitted must be automatically stored, tracked, and maintained. Anything submitted to the FDA or any regulatory agency must be traceable, so the source data and creation method can be determined, down to field-level changes.

These requirements are also discussed in sections 4.3 above, 4.6, 7.1 above, and 8.3.4 above.

10.2.1 How the requirement is currently met

The ABS and database have full auditing and traceability. When reports are submitted to regulatory agencies, the data that was included in that report can be easily identified and pulled up again. Since all changes are tracked individually, the changes are, in essence, being locked. The only way to remove or modify the data would be to go directly into the database and modify the individual record.

Workflow status is maintained separately within the database, so updates to the expedited report and expedited report package do not affect this. Also, since each amendment is treated as a separate record, and all amendments are tied to the initial record, the status can be maintained across versions.

AdEERS provides access to all previous versions of the reports. If you have the ticket number, protocol number, and patient id, you can also access the report through the AdEERS front end.

caAERS supports the viewing of the current version of expedited reports. All changes are tracked and maintained in the database, providing a history of the report. However, accessing this information requires having direct access to the database.

10.2.2 Identification of gaps and potential gaps

caAERS needs some additional work in this area to fully meet the requirements. Specifically:

- Electronic versions of all AE reports – caAERS only provides viewing/printing access of the current AE report. A method to review older versions of the report would have to be implemented. This requirement is also discussed in sections 4.1 and 4.3 above.
- Being able to audit the changes made to an AE and expedited report has been started. While all the information lives in the database, there isn't an easy way to access it.
- Currently data isn't locked; only the primary keys are locked with all other fields able to be modified. More research needs to go in to the regulatory agencies traceability/data requirements to determine what additional development needs to occur
- caAERS doesn't trace where the data comes from. So, if something is imported from an XML file, or added via API and messaging, it won't be marked any different than if it's entered manually. This will need to be built to support FDA's requirements

10.3 Access

All information stored in the new reporting tool, including supporting documents, must be retrievable and analyzable.

10.3.1 How the requirement is currently met

All data in the caAERS database can be retrieved. All changes are tracked, and all information is available for analysis by a DBA. End-users can easily bring up and view all adverse events associated to a patient-study combination.

10.3.2 Identification of gaps and potential gaps

At this time, additional information can't be associated electronically to an expedited report. When the caAERS development team implements this feature, they will insure the information will be retrievable and analyzable.

While data can be retrieved, there isn't a user-friendly way for a user to retrieve it or analyze it. Methods have to be developed to:

- Allow a user to retrieving all versions of all elements stored in the database, for example, be able to compare two versions of the same report, or changes to the medical history associated to a participant-study combination
- Provide a method to analyze the data that is retrieved

10.4 Migration

There must be a way to import legacy data into the EDMAERS, so interfaces with existing tools are minimally impacted. This needs to occur for CTEP, DCP, and CIP. This requirement overlaps with a requirement in section 4.3 above.

10.4.1 How the requirement is currently met

caAERS also has the ability to import legacy AE information, as well as information on studies, participants, investigators, and research staff. The information just needs to be properly formatted so it can be imported into caAERS.

10.4.2 Identification of gaps and potential gaps

An interface between caAERS and CTEP-ESYS and DCP-ESYS do not exist. APIs and messaging have been developed to support integration with other tools, but these have not been applied to either CTEP's or DCP's existing components. The caAERS team is not familiar with the systems used by CIP, so more research needs to go into understanding integration needs.

The caAERS development team also needs to develop methods for importing legacy expedited reports. When the processing of expedited reports is built in, migration will be considered.

10.5 Maintenance

This requirement overlaps with a requirement in section 4.3 above. The new system must be able to retire data to a data storage system for 50 years. It must store and managed AE reports in electronic format while maintaining all versions of the expedited reports along with the status and process history for reports entered directly or imported in to the system.

10.5.1 How the requirement is currently met

caAERS supports the viewing of the current version of expedited reports. All changes are tracked and maintained in the database, so there is a history of older versions of the report. Given direct access to the database, a complete history of an AE report and fields within the AE report can be gathered. Also, with the right access, records can be 'deleted', but few users have that access for the centralized caAERS, and the access can be controlled at local institutions.

10.5.2 Identification of gaps and potential gaps

A 50-year data repository has to be examined. If installed locally, the specific methods on how this would be done would be determined by the adopter. The caAERS development team needs to develop a method that enables the data to be exported in a format that is easily persisted, or just enable the persisting of the database files since any SQL programmer could work with the data even if caAERS is no longer deployed. If caAERS is set up centrally, the methodology would be determined by NCI in correlation with the caAERS development team.

caAERS only provides viewing/printing access of the current AE report. A method to review older versions of the report would have to be implemented.

11 Analysis of Performance Quality Requirements

11.1 Availability

NCI's applications must have a high availability. Cancer treatment occurs 24x7x365, so adverse events could be entered at any time of the day. That's why the applications must be available 7 days a week, 95% of the time. The only time the applications should go down is for scheduled maintenance. This ensures 24-hour notification is always available, reports can always be accessed for updates or review, and users are informed about the status of their patients.

11.1.1 How the requirement is currently met

Current applications meet the availability requirements. caAERS has also been developed to meet the availability requirements. The centralized instance of caAERS version 1.1.3 is only brought down to push updates and enhancements to it. Future versions of caAERs will continue to maintain availability requirements, and will strive to exceed 95% uptime.

Proper configuration of caAERS is required to ensure 24-hour notification availability, since all notification and reports for CTEP-sponsored studies are being routed through AdEERS. The configuration process is being modified and well documented to increase the ease of setup, ensuring availability is at the level it needs to be.

11.1.2 Identification of gaps and potential gaps

caAERS appears to be at the same level of availability as existing systems. However, since it is a new application, additional testing needs to continue to verify future versions of caAERS continue to meet availability needs.

11.2 Maintainability

For applications to continue to be useful, they must be easy to modify and configure. This includes:

- Providing configurable workflows (also discussed in sections 5.3, 8.1, 8.3.1 above)
- Having a module for maintaining reference tables
- Having a module for user access management
- Providing online support for dynamic setup of business rules and workflow configuration

11.2.1 How the requirement is currently met

The caAERS development kept maintainability in the forefront when developing caAERS. Users' roles and access is maintained directly in caAERS, with authentication and authorization APIs developed to allow integration with individual organization's existing systems. Report definitions and requirements can be imported into caAERS or documented and implemented using the Rules module. While some rules were hard-coded in version 1.1.3, development is occurring in future versions to bring everything into the rules module. This moves the control to the users' hands.

Since caAERS can be installed locally at an organization or be used in a hosted environment, it is highly configurable. Organizations can quickly configure it to use their e-mail services, and add only the investigators, studies, and end users they need to support the trials they're involved in. Most information can be imported, although there is a manual entry option as well.

11.2.2 Identification of gaps and potential gaps

As common knowledge in software development, if a system is not easy to maintain, additional development becomes increasingly difficult. Modifying AdEERS to support CIP's reporting needs and processing workflow took months of development time. Even changing an option in a dropdown can be problematic. These changes can also affect integration with other systems. For example, a recent change to an ethnicity value in AdEERS prevent caAERS from submitting expedited reports through AdEERS.

As caAERS is being developed, the developers are constantly considering maintainability. To this end, much of the configuration can be done within the interface of the application. Most configurations are now available via the interface, but additional coding needs to occur to complete the process.

caAERS has been designed in light of the lessons learned from the AdEERS system. In particular, special emphasis has been placed on enabling a high degree of configurability in order to avoid some of the maintenance issues that plague AdEERS. While caAERS is currently very flexible, more work in this area should be done to support alternative workflows.

11.2.3 Obsolete requirements and requirements that need clarification

Part of this requirement identifies reference tables. The authors of this gap analysis were not able to determine what was meant by reference tables. When clarification is received, the caAERS development team can determine if it's met.

11.3 Performance

Since a large number of organizations are involved in cancer research, applications must be able to handle at least 400 concurrent users while maintaining a response time of less than 5 seconds per page.

11.3.1 How the requirement is currently met

caAERS is being developed to meet the performance requirements.

11.3.2 Identification of gaps and potential gaps

The response time within AdEERS is not always below 5 seconds when being used. Specifically, when a search field is being brought up, or when a page is being saved, the response time often exceeds 5 seconds.

caAERS does not have the current user base to verify it meets the performance requirements. It has been developed with performance in mind, so should meet/exceed the performance of existing tools. However, load testing has not been completed on caAERS, so it is uncertain how many users can be logged in at once while maintaining page refresh time requirements.

11.4 Quality

Any tool being used for cancer research should be reliable and produce the same results time and time again. This doesn't mean all workflows perform the same, just that if the same data is entered multiple times, the same results should be achieved.

11.4.1 How the requirement is currently met

AdEERS is a very stable, quality driven application. It has been in use for many years, giving the developers plenty of time to work out any bugs that may have been in place.

The same can be said about most other tools currently in use at NCI – in general, the tools have been in place for multiple years, so the bugs have been worked out. This allows for consistent performance by new and experienced users.

caAERS is in its second year of development. The various workflows work fairly consistently, although there are some occasional glitches. However, users generally know what to expect and see what they expect as they enter adverse events and expedited reports. New development will continually improve the quality of the application, and increased usage will identify any remaining bugs, allowing the developers to resolve them.

11.4.2 Identification of gaps and potential gaps

Currently, existing systems are more stable and have a higher quality than caAERS. As caAERS development continues and usage increases, the quality will continue to improve, bring caAERS up to the standards of current systems. This is simply the standard growing pains felt when new applications are developed and user requirements are identified and/or modified.

11.5 Usability

If an application is not easy to use, it will take longer for users to adopt it. The EDMAERS must support multiple groups and various workflows, while still remaining easy to use.

11.5.1 How the requirement is currently met

AdEERS and other NCI tools are fairly user friendly. Many groups have their own support systems, but all use AdEERS (to some extent) for expedite reporting. Supporting systems weren't developed separately due to usability issues, so each of the systems could be considered easy to use (just not as easy to maintain).

AdEERS has been considered a fairly straight-forward, easy to use system. The front-end UI is intuitive, with help built in. The search functionality is not always clear, but is workable. AdEERS supports workflows for various organizations and types of trials, with the pages being reused ~95% of the time across workflows. Entering the information for the various workflows seems to require extensive code changes, so in that point, the usability is not has high as it could be.

The ABS is also fairly straight-forward to use, with controlled access. Although the module is easy to use, there are not instructions provided for most of the reports. In addition, consortia and co-ops have a separate backend reporting tool which allows them to handle their central processing requirements as well as view expedited reports across organizations.

caAERS is in the process of combining two modules into one, centralizing the initial collection of all AEs. The first version of caAERS separated routine AE collection and

expedited reporting into separate modules, which introduced some usability and reporting issues. Making the initial collection point centralized addresses these concerns and reduces duplicate entry requirements. This allows users to enter AEs only once while still having the ability to associate them to other AEs in an evaluation period and include them in expedited reports.

caAERS also supports the various workflows of the different organizations. The flow remains the same, with different fields showing up and different rules firing to support the user as he/she goes down the different path. The various workflows are mainly configured when setting up caAERS the first time, by entering different report definitions and rules. When the user adds a study to the system, it provides more information on the steps required for the workflow.

On the technical side, caAERS has import functionality. This may be considered difficult for the lay person, since the files to be imported must be in a specific format. However, technical users should find the import functionality fairly intuitive and easy to use, with the files easy to generate. This includes both the messaging and in-system importing. Reporting, on the other hand, is not as user friendly. There have been APIs set up to assist with reporting, but there is no GUI to go with it to assist users to perform their queries.

11.5.2 Identification of gaps and potential gaps

AdEERS and other NCI tools have their strengths and weaknesses. Overall, these tools are found to be user friendly. However, some of the backend tools that AdEERS provides, and the various search methods, can be seen as needing some work.

As for caAERS, usability continues to improve as new versions are released. The development team needs to improve the usability of querying and reporting on data collected. In addition, users have expressed some frustration with the import functionality and integration caAERS with their existing tools.

11.6 Validation

It's important that any tool that's adopted by NCI has been tested and validated by an outside third party. This allows for an unbiased evaluation of the system.

11.6.1 How the requirement is currently met

The AdEERS development team has adopters test the application before release.

Various cancer organizations are part of the caAERS team as potential adopters of the system. Not only do they provide functionality expert, they also provide QA/usability information. This includes testing caAERS centrally as well as installing it locally and testing that part of the process. Test cases and User Acceptance Testing material are provided to the adopters to support their evaluation.

11.6.2 Identification of gaps and potential gaps

caAERS has third-party testing for usability and compliance in the form of potential adopters of the system. This should meet the requirements. However, as discussed in section 5.7 above, full third-party testing still needs to be scheduled.

12 Analysis of Reporting Requirements

The reporting requirements here overlap with requirements posted in section 4.7 above.

12.1 Generation

The new system must be able to produce all existing AdEERS reports, including specific layout and output formats, as well as ad-hoc reports. There should be a user-friendly report wizard to assist users in building and accessing their reports. The user must also be able to specify the criteria for the report, and be able to sort by the various fields.

12.1.1 How the requirement is currently met

caAERS currently has an API with several reports pre-configured.

12.1.2 Identification of gaps and potential gaps

Additional development and research needs to go into a reporting module in caAERS. While there is a reporting API, it does not have a user friendly interface and requires technical knowledge to use. The reports provided by the API are also limited. Additional development needs to occur to provide all current AdEERS reports and ad hoc reporting.

12.2 Output

Being able to create reports is only part of the picture. Users also need to be able to use the information. To support this, the new tool needs to be able to:

- Export query results in various formats, including excel, access, cvs, and SAS, as well as copy reports into various word processing tools
- View reports online, as well as print one or more pages of the report
- Save and store electronic copies of the reports locally, in pdf and html format
- Electronically submit reports to FDA and approvers

12.2.1 How the requirement is currently met

caAERS has mechanisms to support saving expedited reports as PDF and XML. If users make slight configuration changes, they'd be able to modify the data in word processing tool. Without configuration, they'd still be able to view the data in word processing tools.

Users can also view the expedited reports and choose to print pages from the report, as well as send the report to the FDA and approvers via e-mail.

12.2.2 Identification of gaps and potential gaps

While caAERS support the standard expedited report, it does not support the backend reports that AdEERS has. More development needs to occur to provide these reports, as well as provide the mechanism to export the data for analysis.

To support the submission of reports to the FDA and other approvers using their online submission tools, discussions need to be held with the individual groups to determine what integration needs to occur. caAERS has messaging capability, and currently submits expedited reports directly to AdEERS, so these modifications may be easy to make.

13 Analysis of Interface Requirements

At the time of the initial writing of the requirements for the EDMAERS, there were no specific requirements for the interface. However, since this section of requirements addresses the need to integrate, communicate, and interact with hardware systems, procedures, and other software systems, it's believe that some specific requirements can be inferred.

13.1 Communication with CCTS

A new suite of tools is being developed to assist with cancer research, the CCTS (Cancer Clinical Trial Suite). This suite supports the management of study participant information through the clinical trial lifecycle and helps connect software tools to existing data management systems and the caBIG infrastructure. The EDMAERS should be able to integrate/communicate with the tools of this suite.

13.1.1 How the requirement is currently met

Most of the existing tools, including AdEERS, DESK, and PATS, are not part of the suite, nor can they communicate with the tools of the suite. Additional development would need to occur before this would be possible.

caAERS is one of the tools of the suite. As such, it's been built to communicate and integrate with all tools of the suite, as well as other tools that are part of the caBIG infrastructure.

13.1.2 Identification of gaps and potential gaps

AdEERS and other supporting systems would need additional development to be able to communicate with the CCTS.

13.2 Communication with Existing AE Repositories

Many organizations have organization-based and maintained clinical trial and AE repositories. It would be ideal if communication could be established between the EDMAERS and these organization-based systems.

NCI also supports a centralized data collection and management repository. Tools should be able to communicate with this repository, where all AE information will be stored.

13.2.1 How the requirement is currently met

AdEERS does not currently integrate with any organization-based repositories. However, it does have some integration with NCI's centralized repository.

The caAERS development team, has developed APIs that allow communication between caAERS and other systems. For communication to occur, some development is required by the organization. There is also development occurring that will allow other systems to receive all AE data that is entered in caAERS.

13.2.2 Identification of gaps and potential gaps

At this time, both existing systems and caAERS partially meet the requirements. Depending on the viewpoint, AdEERS meets the requirement better since it can currently communicate with NCI's centralized repository. However, with minimal additional development, caAERS should also be able to communicate with NCI's centralized repository.

13.3 Electronic Submission of Various Reports

CTEP, CIP, DCP (for CCOPs trials), and the FDA currently support electronic submission of expedited reports. All organizations want electronic submission of expedited reports to be the primary method they receive reports.

13.3.1 How the requirement is currently met

AdEERS currently sends a copy of all submitted reports to the reporter, the physician, the lead investigator, and any other pre-determined parties, including the FDA. It can not handle all workflows though, such of DCP's non-CCOPs trials and some of CIP's trials.

caAERS has the ability to email the various reports to the different organizations. The reports have to first be set up within caAERS, which the main CTEP, DCP, and FDA forms are. caAERS also has the ability to send reports to other systems electronically through web services, such as sending reports to AdEERS. Sending the reports to other systems just requires extra configuration by the other system to receive the information.

13.3.2 Identification of gaps and potential gaps

AdEERS was initially developed to just handle CTEP sponsored trials, so it does not support the electronic submission of expedited reports for all organizations. At this time, none of NCI's tools can support all organizations' needs.

caAERS has been developed to support electronic submission to various organizations. However, at this time, only CTEP reports are being submitted electronically, and these are going to the AdEERS system, and will continue to be routed through AdEERS until such a time as AdEERS is replaced. DCP and FDA reports can be sent via e-mail, and integration with their systems is feasible, with a little development/setup by both the caAERS team and the organizations' tools teams.

13.4 Additional Possible Required Interfaces

13.4.1 Protocol abstraction

Information found in protocols is used when documenting AEs and SAEs, and when creating expedited reports. Elements from the protocol, such as TACs and TADs, are used during the submission of expedited reports through AdEERS.

Currently, protocols are stored electronically in numerous places, with no standards. In the past, this has caused problems, with information stored in a local CTMS being different than information stored by CTEP.

It's possible that the EDMAERS may also need to act as a centralized place for protocol information. This way, no mater where it the protocol is developed, systems will have a central location to gather the information from, thus maintaining format and details.

caAERS has the ability to centralize the electronic storage of protocol information. It has the ability to receive protocols from C3PR and local CTMSes, and allows users to manually enter the protocol into caAERS. There's also a method to import the protocol as provided by CTEP via excel spreadsheet. With a little work, caAERS could also have a method to export protocol information to other systems.

13.4.2 Lab data collection

Lab values can be the basis of AEs, or be supporting material for an AE to allow the investigator to get the full picture. The EDMAERS should be able to integrate with any tools that collect lab information. It would not be a good tool for all lab data collection, but the information should be available.

The collection of lab data for cancer research is not standardized. Currently AdEERS only supports a limited LOV, while others tools have open collection. PSC, for example, has a different LOV. It may be best if the EDMAERS supports multiple LOVs for labs.

caAERS still operates under the AdEERS LOV for labs. However, it has integrated with PSC to accept alerts that labs are available for a participant-study combination. In the future, caAERS developers want to provide a way to automatically create adverse events based on lab values, and automatically import lab values into expedited reports and/or as attachments to AEs, SAEs, and expedited reports.

14 Planned Enhancements

14.1 AdEERS enhancements

AdEERS will officially be releasing an updated version in September 2008. This release includes the following additions, changes, and enhancements:

- Accommodate and support submission of expedited reports for CIP/ACRIN trials to NCI for processing, where ACRIN is a participating or lead organization
- Support of a device-only pathway
- Modification of screens, reports, help text, and message to include NCI's generic information rather than information for a specific program
- Course information screen is now mandatory, although fields will be mandatory based on the type of study
- Changes to how medical devices are handled, including allowing multiple devices to be added, stating how the device is being used, dropdowns based on the protocol abstraction instead of text fields, and additional required fields
- Modifications to the expedited report and MedWatch report to show multiple devices

14.2 caAERS version 2.0 enhancements

caAERS is in constant development. The enhancements that are being considered for version 2.0, which will be released March 2009, include:

- Incorporate changes made to AdEERS, released in September 2008
- Complete support of CIP/ACRIN reporting
- Increased integration points with other CCTS applications
- Further streamlined/simplified expedited reporting
- Continued improvements to UI and usability
- Internal (institutional) Routing and Review
  - Support review and approval workflows for AE
  - Central Processing
- External Agency Reporting
  - Support amending a previously submitted AdEERS report
  - Support 24-hr notification through AdEERS
  - Providing identification of the source of the expedited report (submitted via caAERS through AdEERS for example)
- Automated Decision Support for Expectedness of AEs
  - Support protocol based configuration of expectedness
  - Develop rule sets to automatically determine expectedness
- Improvements to ensure easy and lo- cost install and configuration

- Ensure compliance is being met
  - 21 CFR Part 11
  - HIPAA
  - Section 508
- Interface between caAERS and local CTMS
  - Further simplified services to integrate data
  - Support import of organization and ID
  - caAERS-to-local CTMS integration of AE data

14.3 caAERS future enhancements

After caAERS version 2.0 is released, there is still additional work to be done. Areas that are being considered for development include:

- Refactoring to support use of COPPA services
- Increased integration points with other CCTS applications
- Adverse Event Data Capture
  - Ability to upload photos and documents and attach to reports and as part of submission
  - Enhanced usability of AE capture flow
- Vocabulary Mapping Service
  - Support update of organization IDs with CTEP identifier
  - Obtain Study Agents (CTEP List of Agents and EVS)
  - Obtain TAC info from CTEP
  - Support FDA Drug List
  - Support WHO Drug List
  - Update CTEP Investigator Lists
- Interface Between caAERS and Local CTMS
  - Further simplified services to integrate data
  - Support import of organization and ID
  - caAERS-to-local CTMS integration of AE data
  - Disable UI for entry of certain data
- External Agency Reporting
  - Improved report generation tool for custom report generation
  - ICH Reporting Support
  - Pharmaceutical Reporting Support

- Internal (institutional) Routing and Review
  - Support definition of new institutional roles (i.e. IRB, Safety Review Board, etc)
  - Support ad-hoc notification of AE to specific roles
  - Support rule-based notification of AEs to specific roles
  - Support review and approval workflows for AE
  - Central Processing
- Automated Decision Support for Expectedness of AEs
  - Implement ASAEL for automating determination of expectedness
  - Develop rule sets to automatically determine expectedness
- Data Sharing
  - Support for multi-site access and/or hosted caAERS instance
  - Support for caAERS-to-caAERS integration
- Support for analysis of AE data
  - Improved reporting API
  - UI development for back-end reporting API
  - Addition of back-end reports specific for analysis
- Refactoring and improvements to security to simplify local system integration
- Continued improvements to UI and usability
- Improvements to ensure easy and low cost install and configuration
- Compliance
  - 21 CFR Part 11
  - HIPAA
  - Section 508
- Auditing reports and support

15 Conclusions

15.1 Overview

This gap analysis document provides a detailed examination of the requirements gathered for NCI's proposed Enterprise Data Management AE Reporting System (EDMAERS) in relation to the current version of caAERS. A thorough review of the requirements was performed and then compared to the current version of caAERS. Several sections also include information on the functionality of AdEERS and other NCI tools.

This analysis work would not have been possible without the assistance of Ann Setser, who shared her expertise on CTEP's workflow and requirements, and Anne Tompkins, who shared her expertise concerning DCP's requirements.

15.2 Summary of Findings

Analysis was performed around the 10 categories of requirements defined in the EDMAERS requirement document. These categories are:

- Business
- Technical
- User – AE Workflow
- Security
- Functional
- Ergonomic (or User Interface)
- Data
- Performance Quality
- Reporting
- Interface

The document contained 478 requirements. However, this does not mean there are 478 unique requirements, because several of them are listed in multiple sections. In addition, many requirements were a compilation of multiple requirements. In addition, some requirements were unclear, or were obsolete due to a change in direction or improvement of technology. Some new requirements were also identified in the process of creating this gap analysis document. A total count of unique requirements could not be established due to these factors.

The analysis of caAERS against the EDMAERS requirements resulted in the identification of 171 gaps (or possible gaps). These gaps do not map 1-to-1 to the documented requirements, as illustrated by looking at the Interface category. The requirement document did not have any requirements listed for the Interface category, but 2 gaps were identified. The gaps identified were also not unique. For example, the requirementn for centralized processing was mentioned in several categories, so the gap was also identified in several categories.

The following table summarizes the requirements documented in the EDMAERS requirement document and the gaps identified during analysis. This is just an overview to provide some reference. The two numbers should not be compared directly since they do not map 1-to-1.

Requirement Section	Number of Requirements documented	Number of Gaps or Potential Gaps Identified (not mapped 1-to-1)
Business	78	30
Technical	66	28
User – AE Workflow	39	4
Security	17	9
Functional	186	64
Ergonomic	59	12
Data	12	12
Performance Quality	9	8
Reporting	12	4
Interface	0	2
Total Requirements:	**478**	**171**

Summary of EDMAERS requirements gaps identified (not for direct comparison)

15.3 Major Gaps

The analysis performed identified several major gaps between caAERS and the requirements for the proposed EDMAERS. While caAERS partially met most requirements, extensive work needs to be done in the following areas:

- Processing expedited reports
- Analyzing collected data on AEs
- Integration with existing NCI tools

These areas are discussed in detail below.

15.3.1 Processing workflows

The EDMAERS needs to support both the collection of AEs and expedited reports and the processing of submitted expedited reports. There is a history of tying this functionality together, since the processing of expedited reports is supported by AdEERS.

Several sections of the requirement document included requirements revolving around the processing of expedited reports; User – AE Workflow exclusively discussed the requirements. Of the 39 requirements documented in that section alone, caAERS met none of them. If you look at the gaps identified for that section, it is clear caAERS doesn't support the functionality because the gaps state:

- Does not handle queries to the submitter and notification back to the requestor
- Does not have workflow for processing completed expedited reports for CTEP
- Does not have workflow for processing completed expedited reports for DCP
- Does not have workflow for processing completed expedited reports for CIP

As discussed in sections 1.5 and 6 above, each sponsor has a different workflow for processing submitted reports. Several of the steps are currently paper-based. Extensive analysis work will be required to discover the best way to support the various workflows electronically before it can be added to caAERS.

15.3.2 Analysis of data

The focus of the caAERS development through September 2008 has been to support the collection of adverse event data and the generation of expedited reports. caAERS is now able to capture extensive adverse event data, but has limited ways to provide the data for analysis. Few reports exist in caAERS, and the reporting API is in its earliest stages, usable only by people with a technical background.

Now that caAERS readily captures AEs and expedited reports, more works needs to go into making the data readily accessible for analytical purposes. Priority needs to be determined for the various analysis requirements, so progress can be made in this area. The resulting development must be accessible by all level of users, both technical and non-technical, which means a reporting interface must be built to support any methods developed.

15.3.3 Integration with existing NCI systems

The EDMAERS must integrate with existing systems; it will not contain all functionality required to support all users. While it may eventually replace some systems, it will happen in a phased approach, so it must be able to integrate with those systems. There should only be one “source of truth” for each data type, so EDMAERS must be able to connect to the various applications that are sources of truth for any elements it uses.

caAERS is part of the CCTS, and it is caBIG silver-level certified, but the only existing tool used by NCI that it integrates with outside of the CCTS is AdEERS. It does have messaging and APIs available, but they have not been tested against other systems in use.

15.4 Next Steps

There are several steps that must be taken as NCI moves forward with creating the EDMAERS, including, but not limited to the following:

1. Revisit and redraft the requirement document
2. Prioritization of requirements
3. Expedited report processing analysis - job shadowing
4. Integration analysis – conversations with existing tools teams
5. Security review – environmental considerations
6. CCTS considerations

Steps 1 and 2 can be completed before the EDMAERS development team is chosen, although it is better to involve the development team in the requirement gathering so they can gain a better understanding of the complexities of the requirements. Additional information is listed below concerning the necessity of the steps.

15.4.1 Revisit and redraft the requirement document

The requirement document, as-is, would be difficult to develop from for multiple reasons:

- Requirements are duplicated across multiple categories

- Requirements are not always concise and clear
- Some requirements are obsolete
- Some requirements actually document several requirements
- 99% of the requirements are listed as High-priority and mandatory

As an initial pass at identifying requirements across the groups, it has served its purpose. The initial categorization and duplication also is understandable, since it allows readers to identify all the requirements for a category without jumping around in the document.

Several things need to occur to develop a requirement document developers could work from:

- Identify the development area or functionality being supported, and use that as the category
- Clearly identifying functional and non-functional requirements
- Remove duplicate requirements, maintaining a matrix to identify any requirements that fall into several categories
- Create clear, concise requirements, with each requirement identifying a single concept
- Remove obsolete requirements
- When referring to existing documents or resources, provide links to the material
- Identify any requirements that were not captured in the initial drafting of the requirement document

15.4.2 Prioritization of requirements

Once the requirement document has been reworked, the priority items and preferred workflows need to be identified. Questions should be asked, such as:

- Is it more important to be able to analyze collected data, or process submitted reports?
- Which group is having the most problems so their requirements need to be addressed first?

This type of information allows the development team to identify which items to address first, what prerequisites exist, and what factors need to be considered before developing an item a certain way. It also allows them to develop iteratively, adding functionality every release.

15.4.3 Expedited report processing analysis - job shadowing

To fully understand the requirements for processing expedited reports, the development team will need to work with the sponsors and the contractors that manage the processing workflows. There will be overlap across the various sponsors, and there will be individual considerations. The best way to identify the overlaps and the individual needs is to go through the process multiple times, following several expedited reports through the entire process.

This type of analysis will require extensive cooperation and coordination, as sensitive data will be involved. Time will need to be factored in to gain the necessary approval.

This type of analysis may be beneficial in others areas as well, such as using analytical tools, submitting expedited reports, entering AE data. Shadowing personnel as they do their jobs will always allow the development team to better support the user's needs.

15.4.4 Integration analysis – conversations and coordination with existing tools teams

Integration can not occur without knowledge of the tool trying to be integrated with. Even with the knowledge, integration is difficult without access to the tool's code. This means it's important to work with the various tools teams to support the integration.

A complete list of tools that the EDMAERS will need to integrate with needs to be created, listing the team that supports it and a main contact. This will allow the EDMAERS development team identify the various groups involved and start communicating with them to learn about the tools, any existing support available for integration, and any work going on that may affect being able to integrate with a tool.

Meetings can be coordinated with various parties to discuss the integration requirements, and potentially reduce the work if the groups can make use of their respective development efforts.

Integration timelines will be a production of both the EDMAERS development team and the tools' support teams, since both parties will have to invest time into the project.

15.4.5 Security review – environmental considerations

Once an environment is decided on for the EDMAERS, a full security review needs to take place. Without being in the final environment, only an initial security review can take place.

Appropriate time and funding must be allocated for this to take place.

15.4.6 CCTS considerations

The caBIG Clinical Trial Suite (CCTS) should be taken into account when considering the EDMAERS. Several questions come to mind when considering the CCTS:

- If the EDMAERS is part of the suite, what additional requirements are there?
- If it is not part of the suite, what integration points should exist?
- What integration points will be available between a locally installed version of the application, and the version of the application that is the EDMAERS?

Appendix A - Glossary

Term / Abbreviation	Description
ABS	AdEERS Backend system
AdEERS	Adverse Event Expedited Reporting System; The adverse event reporting system developed by the NCI for expedited reporting of SAEs on CTEP sponsored trials.
AE	Adverse Event
AIS	Clinical Trials Monitoring Branch- Audit Information Systems
ARA	Adverse Reaction Assessment
ASAEL	Agent Specific Adverse Event List
caBIG	Cancer Biomedical Informatics Grid. The acronym given to the project sponsored by the NCI and managed by Booz Allen Hamilton to develop a set of tools for use by the cancer community.
C3D	Cancer Central Clinical Database
C3PR	Cancer Central Clinical Participant Registry
caAERS	Cancer Adverse Event Reporting System. The subject of this document; a system being developed by the SemanticBits for NCI/caBIG to capture and report Adverse Events for the cancer clinical trials community
caDSR	Cancer Data Standards Repository
CALGB	Cancer and Leukemia Group B
CBIIT	Center for Biomedical Informatics and Information Technology
CCOPS	Community Clinical Oncology Program
CCR	Center for Cancer Research
CCTS	caBIG Clinical Trial Suite
CDEs	Common data Elements
CDISC	Clinical Data Interchange Standards Consortium
CDMS	Clinical Data Management System
CDS	Clinical Data System
CDUS	Clinical Data Update System
CI	Continuous integration
CIBISCIT	Clinical Investigations Branch Information System and Clinical IT
CIP	Cancer Imaging Program
COH	City of Hope National Medical Center; developer of first release of caAERS
CRFs	Case Report Forms
CSM	Common Security Module
CSS	Cascading Style Sheets
CSV	Comma-separated values
CT	Clinical Trials
CTC	Common Toxicity Criteria

Term / Abbreviation	Description
CTCAE	Common Terminology Criteria for Adverse Events (replaced "CTC" with the 3rd version of this system)
CTDB	Clinical Trials Database
CTEP	Cancer Therapy Evaluation Program---a program within the Division of Cancer Treatment and Diagnosis within the NCI.
CTEP ESYS	CTEP Enterprise System
CTMS	Clinical Trials Management System. Often used to refer to a computer application developed by a cancer center or other entity to record clinical trials data. Also refers to the caBIG workspace by the same name that is working to develop a comprehensive system for the cancer CT community.
CTMS/Theradex	Clinical Trials Monitoring Service
CTS	Clinical Trials System
CTSU	Cancer Trials Support Unit
CVS Repository	Version control system
DARTS	Drug Authorization, Review and Tracking System
DCP	Division of Cancer Prevention.
DCTD	Division of Cancer Treatment and Diagnosis
DESK	DCP's Enterprise System Knowledgebase
Docu-Mart	Document Management, Assembly, Review and Tracking System
DNP	Do not Process
Dose Reg	Dose Regimen
E2B	Standard that discuses Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports
ECM	Enterprise Core Module
EDC	Electronic Data Capture
EDMAERS	Enterprise Data Management AE Reporting System – new system to be developed, focus of this gap analysis
EIS	Enterprise Information System
EORTC	European Organization for Research and Treatment of Cancer
EQW	Enterprise Query Wizard
EVS	Enterprise Vocabulary Services
FDA	Food and Drug Administration
FISMA	Federal Information Security Management Act
GAARDS	Grid Authentication and Authorization with Reliably Distributed Services
GMPs	Good Development Practice regulations, FDA regulations
HIPAA	Health Insurance Portability and Accountability Act
HL7	Health Level 7
ICH	International Conference on Harmonisation
IDB	Investigational Drug Branch
Inv Reg	Investigator Registration

Term / Abbreviation	Description
ISC	Initial Safety Communication
ISSO	Information Systems Security Officer
LOV	List of Values
MM	Medical Monitor
NCI	National Cancer Institute
NCCTG	North Central Cancer Treatment Group
NLM	National Library of Medicine
NSC	The unique identifier of an agent; numerical identifier
NSL	National Science Library
Participant	Used throughout the document to represent participants, patients, and subjects that are participating in studies/protocols
PATS	Protocol Authorization and Tracking System
PDQ	Physician Data Query
PhRMA	Pharmaceutical Research and Manufacturers of America
PI	Principal Investigator
PKI	Public Key infrastructure
PSC	Patient Study Calendar
QC	Quality Control
RAB	Regulatory Affairs Branch
RABITS	Regulatory Affairs Branch Information Tracking System
RDC	Remote Data capture
SA	Systems Analyst. A specially trained group of individuals who are responsible for obtaining user requirements and documenting these for the purpose of developing a 'blue print' for software development.
SAE	Serious Adverse Event. An Adverse Event that requires expedited reporting to the Study Chair, Sponsor and/or other entities.
SIG	Special Interest Group. A group within the caBIG community focused on a special application or area of interest.
SSO	Single Sign On
TAC	Treatment Assignment Code
UML	Unified Modeling Language
UPMC	University of Pittsburgh Medical Center
XML	Extensible Markup Language

Appendix B - Gap Matrix

All gaps identified in this document have been compiled into an easy to read spreadsheet format. This format allows the person reading this report to easily identify:

- Gaps identified and organized by section of this gap analysis
- Where the gaps are duplicated, since the same requirement may have been in multiple sections

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
4	**Business**			
4.1	**AE Generation**	Need to be able to attach information to reports. Problems with this would be if the system receiving the report could handle attachments	y	4.1, 4.11, 5.3, 5.5, 8.2.1
		Need to easily view all versions of a report (initial version, amendment 1, amendment 2, etc)	y	4.1, 4.3, 10.2
4.3	**Data management**	A 50 year data repository has to be examined. Would this be a backup server, backup tapes, duplicate repository of the current repository. How many AE records would it need to hold?	y	4.3, 5.8
		Electronic versions of all AE reports – caAERS only provides viewing/printing access of the current AE report. A method to review older versions of the report would have to be implemented	y	4.1, 4.3, 10.2
		An interface with all of CTEP ESYS does not exist. Messaging and APIs support integration with AdEERS, but AdEERS is only one of many tools that make up CTEP ESYS. Additional research needs to occur to determine if the APIs and messaging the caAERS team has developed to support integration with other tools will be sufficient, or if more development needs to occur		
		Being able to audit the changes made to an AE and expedited report has been started. While all the information lives in the database, there isn't an easy way to access it.	y	4.3, 4.6, 7.1, 8.3.4, 10.2

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		Currently data isn't locked; only the primary keys are locked with all other fields able to be modified. More research needs to go in to the regulatory agencies traceability/data requirements to determine what additional development needs to occur		
4.5	**General**	caAERS doesn't have 'expectedness' built in (ASAEL, etc)	y	4.5, 5.5, 8.3.2, 10.1
		caAERS doesn't have the backend reporting that is in AdEERS	y	4.5, 4.7
		caAERS doesn't have the DNP built in	y	4.5, 6.2, 8.2.8, 8.3.3
4.6	**Regulatory Compliance**	caAERS doesn't support electronic signatures	y	4.6, 8.1
		caAERS needs increased auditing capabilities	y	4.3, 4.6, 7.1, 8.3.4, 10.2
		caAERS doesn't have a way to provide a version of reports without patient identity markers	y	4.6, 5.2, 7.2, 8.2.1
		a complete analysis of how caAERS addresses the specific requirements of each regulation has not been completed. Such an analysis would also require a detailed description of the organizations in which caAERS will be used.	y	4.6, 5.2, 7.3
4.7	**Reporting & Analysis**	caAERS does not provide a full suite of reports or a way to query data based on fields, studies, etc. The provided API needs to be expanded to include more of these features.	y	4.5, 4.7, 8.2.2
		caAERS does not export data to csv or html, allow adding this ability shouldn't be difficult since caAERS has the ability to export data to various other formats		
		Summary screens will need to be built in for all reports and or queries		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		Some of these requirements revolve around the processing of submitted expedited reports, which is discussed in detail in sections 4.11 and 6 below. caAERS currently doesn't support the processing of expedited reports, but when the development team starts to implement it, they will address the following two requirements: • Be able to provide information on the status of the expedited report package • Be able to print and send electronically full expedited reporting packages	y	4.7, 4.11, 6
4.8	**System Processing**	caAERS currently only has the ability to import AEs that do not require expedited reporting (full import requirements are discussed in sections 5.5 and 8.2.5 below). The groundwork has been laid to support importing expedited reports, but it still needs to be developed.	y	4.8, 5.5, 8.2.1, 8.2.5
		caAERS needs to support notifications based on the step of the workflow for processing an expedited report	y	4.8, 4.11, 5.6, 6, 8.2.6, 8.2.8, 8.3.3
		Handling central processing, although it is an issue that is being addressed as caAERS works to integrate routing and reviewing into the system.	y	4.8, 4.11, 5.3, 8.3.3
		Submissions of queries from the report processors to the site for more information	y	4.8, 4.11, 6
		Storage of, and association with, scanned documents and additional information gathered while the report is being processed	y	4.1, 4.11, 5.3, 5.5, 8.2.1
		More research needs to occur to determine what is involved in handling product complaints before it can be integrated in to caAERS. It may simply required the creation of a report definition and its associated rules, which caAERS currently supports.		
4.9	**Training**	caAERS needs to provide more thorough training material, including a (or multiple) CBT modules		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
4.11	**Workflow**	As discussed throughout this document, and specifically documented in section 6 below, caAERS does not currently support processing a submitted expedited report, so the various workflows associated to processing a report still have to be developed.	y	6
		Handling submissions of queries from the report processors to the site for more information	y	4.8, 4.11, 6
		Handling central processing	y	4.8, 4.11, 5.3, 8.3.3
		Storage association of scanned documents and additional information gathered while the report is being processed to an expedited repor	y	4.1, 4.11, 5.3, 5.5, 8.2.1
5	**Technical**			
5.1	**API**	caAERS does not have APIs to manage adverse events and expedited reports		
		caAERS is not directly integrated with EVS (CDEs are annotated with semantic concepts that belong to NCI theasurus)	y	5.1, 5.2
		caAERS is not directly integrated with Oracle Clinical or Medidata CDMS (requires APIs, and may require new APIs to be developed)		
		Need to create a disaster recovery plan and implement it. Should work with NCI/AdEERS team to see if the existing plan can be used		
		caAERS and redundant server configuration?		
5.2	**Architectural Constraints**	*While caAERS provides functionality needed to support operating procedures that comply with many of these security regulations, a complete analysis of how this support addresses the specific requirements of each regulation has not been completed. Such an analysis would also require a detailed description of the organizations in which caAERS will be used.*	y	4.6, 5.2, 7.2, 7.3

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		E2B(M), which subsumes E2B, defines rules for submitting individual case safety reports to the FDA. These rules have not yet been examined.		
		caAERS has a little additional work needed to fully comply with 508 compliancy. This includes: • Improve the tabbing and keyboard navigation. While tabbing is set up, it does not work consistently in either IE or Firefox • There currently isn't a way setup that allows readers to skip lines or navigation. It has been recognized as a gap and should be an easy fix to implement • Additional testing and research needs to be done concerning flickering of the application at the frequency specs	y	5.2, 5.3, 9.2
5.3	**Design**	To fully meet the requirement for centralized and decentralized processing, caAERS needs do be modified. If caAERS is going to be a stand-alone reporting tool, this functionality needs to be built in. This is tricky, since it'll have to support it internally, but not duplicate the process as the report is being submitted through AdEERS.	y	4.8, 4.11, 5.3, 8.3.3
		While caAERS does have more configurability than AdEERS, additional work needs to be done to fully meet this requirement. For example, caAERS needs to provide the following configuration methods: • Allow/block modification of data by controlling the read/write features of different fields • Determine what screens/information on screens appear based on protocol information • Provide the ability to determine what fields/screens are available based on roles • Provide rules that are based on other features besides sponsor, organization, or study (agent, device, participant, etc)		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		While the caAERS team believes both E2B ICH Standards and ISO 11179 are met, there are multiple layers to these standards. Additional research needs to be complete during all phases of development to ensure these standards are met and supported.		
		caAERS has a little additional work needed to fully comply with 508 compliancy. This includes: • Improve the tabbing and keyboard navigation. While tabbing is set up, it does not work consistently in either IE or Firefox • There currently isn't a way setup that allows readers to skip lines or navigation. It has been recognized as a gap and should be an easy fix to implement • Additional testing and research needs to be done concerning flickering of the application at the frequency specs	y	5.2, 5.3, 9.2
		Best design practices all suggest having the main navigational items on the left. The caAERS development team is considering having a left-hand navigation, but it would be third level, not the main navigation.		
		caAERS does not at this time support the electronic attachments. Additional work needs to be completed before caAERS can support this.	y	4.1, 4.11, 5.3, 5.5, 8.2.1
		caAERS needs to warn users about timeouts to increase the appeal of the design. Users do not appreciate being signed out without notice.		
5.4	**Documentation**	Additional work needs to be done to the documents describing the APIs and messaging. These are important aspects of caAERS, and can be highly technical, so the documentation needs to be very thorough.		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
5.5	Import & Export Capabilities	caAERS does not include functionality to export directly to SAS, CTEP-ESYS, DESK, E2B Applications, CTSU, or Documentum/core dossier. The caAERS team needs to review the formats supported by the above-mentioned systems and devise an approach to convert the output from caAERS to those formats		
		While the HL7 Adapter is not currently used, the export functionality seems to be adequate. Additional research needs to occur to determine if export methodologies need to be switched.	y	5.5, 8.2.4
		caAERS does not currently have a way to upload images and other documents (such as pathology reports, x-rays, or death certificates) into the system.	y	4.1, 4.11, 5.3, 5.5, 8.2.1
5.6	Notification Triggers	Since caAERS does not have processing a submitted expedited report built in, it does not have notifications that occur after an expedited report is submitted; the final notification is that the expedited report has been submitted.	y	4.8, 4.11, 5.6, 6, 8.2.6, 8.2.8, 8.3.3
		caAERS also does not support notifications based on AE details. Additional research and development must be completed to fully understand the audience for these notifications and the point(s) in the process this belongs to.	y	4.8, 4.11, 5.6, 6, 8.2.6, 8.2.8, 8.3.3
		While caAERS does provide a configurable notification system, based on the specific report being completed, additional development may be necessary to support sending notifications ad-hoc.	y	4.8, 4.11, 5.6, 6, 8.2.6, 8.2.8, 8.3.3
5.7	Quality	caAERS has very good quality management practices in place but is not formally certified for its quality by a thorough third party analysis. The testing that is done outside of the development team is completed by a group of adopters. That testing is limited to testing the functionality and user acceptance testing. Full third-party testing still needs to be scheduled.	y	5.7, 11.6

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
5.8	Recovery Management	At this time, the caAERS development team does not have a disaster recovery plan or method in mind for the centralized caAERS instance. The development of this plan could be assisted by working with the AdEERS team to go over existing disaster recovery plans. Once the team had a firm grasp on what needs to be done to the caAERS database to support disaster recovery, the could institute the changes, create the supporting documents, and put the plan in place.	y	4.3, 5.8
5.9	Standards	The caAERS development team is looking into supporting running in redundant server configuration mode, where at least two more servers can be used for redundancy. This will only address the issue of the availability of the application if any one server goes down. If something goes wrong as a result of the disaster at the server facility, there will be latency in bringing up the application from the backed up physical tapes. *While the caAERS development team believes both E2B ICH Standards and ISO 11179 are met, there are multiple layers to these standards. Additional research needs to be complete during all phases of development to ensure these standards are met and supported.*		
5.10	Technology	The caAERS user interface has been designed to present the right information to the user, when it is needed. However, some of the clinical workflows that have been identified in the CCTS project may be facilitated by having a customizable interface that allows the user to pull in pieces of functionality/data from each of the CCTS applications. To support this type of portal environment, the caAERS development team would need to evaluate the best way to expose this. Some options include creating portlets (based on the Java JSR 168 or 286 standards) or creating finer-grained web services.		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		provides APIs to consume protocol, person, and organization information from a local CTMS, but it does not export that information. There is no transactional communication with any CTMS. A good time to start this bilateral communication would be when the new NCI-sponsored clinical data management system becomes available.		
6	**User - AE workflow**			
		does not handle queries to the submitter and notification back to the requestor	y	4.8, 4.11, 5.6, 6, 8.28, 8.3.3
		Does not have workflow for processing completed expedited reports for CTEP		
		Does not have workflow for processing completed expedited reports for DCP		
		Does not have workflow for processing completed expedited reports for CIP		
7	**Security**			
7.1	**audit and security**	caAERS needs additional development to support the required auditing functionality. Being able to audit the changes made to an AE and expedited report has been started, but is only at a basic level at this time.	yes	4.3, 4.6, 7.1, 8.3.4, 10.2
		The existing roles within caAERS may not be adequate for all users. As additional organizations adopt it, these roles are being evaluated to determine if additional development needs to occur.		
		The caAERS development team needs clarification on what is meant by the CDA document, "Good development practices". Good Development Practice regulations (GMPs) have been located, referring to FDA's promulgated regulations. If this is what's being referenced, the GMPs will be reviewed and caAERS evaluated to ensure the regulations are met.		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
7.2	regulatory complaince	caAERS stores all data elements separately, so adverse event information can be separated from patient identifiers. However, this can only be done by a DBA directly accessing the database. Additional development must occur to support the exportation of, and querying of information that shows all information except specific patient details. While caAERS does have software validation in place, the caAERS development team needs to have it verified by the FDA audit team and/or NCI-ISSO. The team also needs to examine the validation requirements of 21 CFR Part 11 to ensure full compliance is met.	yes	4.6, 5.2, 7.2, 8.2.1
7.3	Security	*While caAERS provides security functionality, a complete analysis of how the implemented security measures addresses the specific requirements of each regulation has not been completed. Such an analysis would also require a detailed description of the organizations in which caAERS will be used. The full analysis would require the caAERS development team to examine at least one deployment that should be FISMA compliant, and one deployment that should be NIST compliant.* *The caAERS development team still needs to complete the certification and authorization assessment form for NCI ISSO to review. The development team will contact the NCI ISSO to receive the form.*	y	4.6, 5.2, 7.3
7.4	System Access	*Users do not have the ability to create an account in caAERS on-the-fly. An administrator must create the account and provide appropriate rights before a user can access the system.* *As previously discussed, additional work on the roles may be necessary to ensure the needs of all sponsors and organizations are met.*		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
8	**Functional**			
8.1	**Admin Module**	caAERS only provides limited capabilities when it comes to customizing screens caAERS currently doesn't support customizing fields, including changing the labels and picklists (beneficial when new items are added/modified at a sponsor/national level) caAERS currently doesn't support dynamically adding CTC vocabularies (these are built into caAERS, so the addition of a new version, such as CTCAE v 4.0, would require a point release) caAERS currently doesn't validate an end-user's system information. This has caused some frustration since users can access caAERS using unsupported browsers, which often leads to functionality issues. The caAERS development team needs to implement a way to check an end-user's system to ensure they meet requirements before allowing the user to access the tool. Since browser technology is constantly changing, this would require continual development, based on NCI's list of supported browsers and systems. *Requirements also state that GUI tools should have a signed relationship for end user screen changes. If this is understood correctly, caAERS does not meet this requirement since electronic signatures are not currently supported. So, to meet this requirement, the caAERS development team needs to implement support of signatures, and then require a signature when the user modifies anything on a screen/page an end user would see.* *Doesn't support view tracking*		
8.2	**Analysis and review**			
8.2.1	**General Requirements**	caAERS does not currently have the ability to add attachments to provide additional information for an expedited report. This is functionality that needs to be built in.	y	4.1, 4.11, 5.3, 8.2.1

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		caAERS electronic submission goes to the AdEERS system. In this way, there's a screening/reviewing point before full NCI/FDA submission. Without AdEERS, this is no direct submission to the NCI/FDA and no review point before submission. Routing and reviewing is being added starting with caAERS version 2.0.		
		As discussed in sections 7.2 above, caAERS stores all data elements separately. However, there is no module that allows a user to separate the adverse event data from the patient data – only a DBA directly accessing the database can do this. Additional development must occur to support the exportation of, and querying of information that shows all information except specific patient details.	y	4.6, 5.2, 7.2
		caAERS also has no way to import expedited reports/serious adverse events at this time.	y	4.8, 5.5, 8.2.1, 8.2.5
		As discussed in several sections within this document, caAERS is not set up to handle the processing of completed expedited reports. Until it does so, it does not meet the following requirements: • Be able to include the complete workflow semantics in the database schema Note: wherever necessary, such as in expedited reports, caAERS uses a status attribute to track the workflow status • Active workflow versioning • Provide the ability for conditional path selection at event time • Identify finite state machine based workflow modeling • Ability to have single ownership assignment model	y	6
8.2.2	**XML Support**	caAERS hasn't implemented the processing of submitted expedited reports. As such, there are no workflows available to reconfigure without recompiling data. However, the caAERS team will use this requirement to drive the implementation	y	6

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		While there is an API for querying AE data, additional work needs to be done on the API. The querying capabilities are limited, and there is no front-end for the query tool.	y	4.5, 4.7, 8.2.2
8.2.3	**Search capabilities**	Currently, the search results can be saved, but only as a .txt file. For the results to be useable outside of caAERS, the results need to be savable in more formats		
		There isn't a way to exclude closed studies. When you search for a study, you can filter based on the status of the study, but you can't eliminate just one status		
		There isn't a way to search for an agent or a device. Additional protocol criteria needs to be included as searchable fields		
8.2.4	**Export Capabilities**	caAERS currently does not include functionality to export directly to most of the listed applications. Additional research needs to occur to determine if export methodologies need to be modified to support providing data to these applications. The caAERS team needs to review the formats supported by the above-mentioned systems and devise an approach to convert the output from caAERS to those formats.	y	5.5, 8.2.4
		caAERS does not currently include an HL7 adapter for use when exporting data. If current export capabilities are found inadequate, or if it's mandatory that an HL7 adapter be included, additional research will need to occur to determine specific changes required to include and use this adapter.	y	5.5, 8.2.4
8.2.5	**Import Capabilities**	*The caAERS team believes import functionality requirements are met, although some additional research needs to occur concerning importing from hospital systems. However, as long as the input complies with the schema, caAERS can process it.*		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		caAERS does not currently have a way to upload images and other documents (such as pathology reports, x-rays, or death certificates) into the system. To meet the requirements, the development team needs to implement a method for these uploads and the association of this type of material to an AE, SAE, expedited report, and expedited report package	y	4.1, 4.11, 5.3, 5.5, 8.2.1
		The caAERS development team also needs to provide a method for importing expedited reports, and, once impletement, a way to import processing information for those expedited reports.	y	4.8, 5.5, 8.2.1, 8.2.5
8.2.6	**Notifications**	Additional notification development needs to occur for caAERS to fully meet these requirements. Since caAERS does not have processing built in, it does not have notifications that occur after an expedited report is submitted; the final notification is that the expedited report has been submitted.	y	4.8, 4.11, 5.6, 6, 8.2.6, 8.2.8, 8.3.3
		caAERS also does not support notifications based on AE details. Additional research and development must be completed to fully understand the audience for these notifications and the point(s) in the process this belongs to.	y	4.8, 4.11, 5.6, 6, 8.2.6, 8.2.8, 8.3.3
		caAERS currently doesn't fully support 24-hour notification for CTEP-sponsored trials. Notifications are sent based on the status of the 24-hour 'report' status, but the notification itself can't be delivered via AdEERS. This is a feature the caAERS team is hoping to support in version 2.0, but implementation is dependent on the AdEERS team.	y	8.2.6, 8.3.2
		caAERS currently doesn't fully support amendments of reports. caAERs can start the amendment process, but it can not be process through AdEERS. This is a feature the caAERS team is hoping to support in version 2.0, but implementation is dependent on the AdEERS team	y	8.2.6, 8.2.7, 8.3.3

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		While caAERS provides a configurable notification system, based on the specific report being completed, additional development may be necessary to support sending notifications ad-hoc.	y	4.8, 4.11, 5.6, 6, 8.2.6, 8.2.8, 8.3.3
		While caAERS supports asynchronous workflow when sending expedited reports to AdEERS, additional work needs to occur before caAERS supports it in general.		
8.2.7	AE Report Creation	caAERS only allows users to search for AEs by first identifying a participant-study combination. To meet the requirements, the caAERS developers need to extend this functionality to allow users to locate expedited reports by searches that include ticket number.		
		Allow users to select sections of the report (although the way caAERS will be streamlined in version 2.0, this may not be necessary)		
		Support the assessment and addition of information to the report after the report has been submitted and is in processing		
		Fully support the amending of a report	y	8.2.6, 8.2.7, 8.3.3
		Fully support the withdrawal of a report	y	8.2.7, 8.3.2
		Support the copying of a report	y	8.2.7, 8.3.3
		Change their ticket numbering schema from 5-digits to 7-digits		
		Support the following workflows, including adding specific messages and fields: - Multi-sponsor - Surgery only - Radiation only - Device only - Imaging		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		Increase functionality associated with the following workflows (adding specific messages and fields based on the type of study) - Commercial agent only - Non-NIH/NCI investigational only - Prevention - CTEP IND - Multi-modality		
8.2.8	**Processing expedited reports**	caAERS doesn't support the processing of submitted expedited reports	y	4.5, 6, 8.2.8, 8.3.3
8.3	**Data Capture and Reporting**			
8.3.1	**General data capture and reporting requirements**	caAERS does not support an anonymous login, which would allow a patient/subject to log in to the system and enter an AE they're experiencing. This has been discussed as a possible addition for a release in the near future. *caAERS also does not have differences in their login methods based on the tracks. Conversations would need to occur to understand the full requirements here. If it's a matter of access, this could be controlled by the existing roles. If it's a matter of sponsors and single-sign-on capability, caAERS has built that capability in.* While caAERS does support NCI's LOVs and vocabularies, it does not support real-time updates. Updates would require a point release. caAERS has run into issues with this already, related to organizations, so is looking at modifying the system to support either imports of the information, real-time updates (which would require development by caAERS and NCI), or a combination of the two.		

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
8.3.2	Initial data collection	caAERS supports some general customization based on study and sponsor, such as customizing the fields that appear on the expedited report pages. However, these customizations are limited to adding and removing fields that are already built into the system. To fully meet the requirements, additional development needs to occur, extending the existing functionality to include changing field labels, adding items to lists, adding fields to pages.	y	5.3, 8.1, 8.3.2, 11.2
		Allow full workload tracking and SAE query wizards for sponsors and trial sites. caAERS does provide some query functionality, but it needs to be further developed to fully meet the requirements.		
		While the UI is very user friendly, it is the same for all levels of users. Additional work can be done to make it even easier for experienced users to use, such as shortcut keys to open searches, go to specific modules, copy items for reuse, etc.		
		caAERS supports the 24-hour notification process required for both CTEP- and DCP-sponsored studies, with built-in reports which can be sent via email to the recipients. However, additional development is on-going to enhance the support, providing direct notification through AdEERS for CTEP, and investigating a different method of supporting the requirement that doesn't require a separate 'report' in caAERS.	y	8.2.6, 8.3.2
		caAERS tracks all changes made within the system. However, the developers need to implement a way for users to be able to view this information. So, if an attribute of an AE changes, or a report is modified in any way, a user would be able to view what changed and when it was changed.	yes	8.3.2, 10.3
		Similarly, caAERS provides the ability to withdraw an expedited report. However, it only marks it as withdrawn, it does not modify the version sent to AdEERS or notify AdEERS that it has been withdrawn.	y	8.2.7, 8.3.2

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		caAERS uses the custom dictionaries. However, they are either programmed in, or have to be imported. Supporting a connection to these dictionaries via API needs to be researched further. The APIs for CTC could always be available, but limits would need to be placed on the ones supporting MedDRA since it is a proprietary vocabulary. CTEP's ASAEL is currently not integrated into caAERS, but is slated for development for caAERS 2.0. Support will be in phases, first allowing users to directly associate 'expected' AEs to a study. Then the team will look into connecting to the ASAEL via API. caAERS is setup to associate a study to one sponsor. Studies can be assigned multiple identifiers, thus providing a method to document more than one sponsor. However, additional development needs to occur to directly support the association of a study to multiple sponsors. *At this time it's unclear what the authors of the requirement document meant by "be able to report deaths unrelated to adverse events". caAERS does have the ability to capture "Death" as an AE, since Death is included as a term within the CTC vocabularies. If this is what the authors meant when they made this a requirement, caAERS does meet the requirement. However, the caAERS team wants to get some clarification on the requirement to ensure it is met.* *In addition, the caAERS team needs a clearer understanding of what is meant by "include Drug/Agent screen". caAERS allows the user to enter information about all agents used during the period of time being reported on, including study agents and concomitant drugs. However, it's not clear if this is what is meant by the requirement.* The caAERS development team is working on an API that allows the integration of AE data and expedited reports with other systems. Under the current development plan, the API should be available for beta use in March of 2009.	y	4.5, 5.5, 8.3.2, 10.1
8.3.3	**Submitting the data**			

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
		caAERS has an API for importing historic AE information. The development team will be investigating extending this API to support importing current AE and expedited data. This API is necessary to receive information from various CTMS.		
		The caAERS development team needs to look into supporting spell checking within caAERS.		
		While caAERS does allow a report to be amended, it is not integrated with AdEERS to support the submission of that amended report. As of September 2008, this functionality is currently being worked on by both the AdEERS and caAERS teams.	y	8.2.6, 8.2.7, 8.3.3
		caAERS also doesn't support copying an expedited report or AE. This requirement was reviewed for caAERS 1.5, but has been moved to a later development period.	y	8.2.7, 8.3.3
		While caAERS currently supports centralized and decentralized processing and approval of expedited reports, this functionality will be enhanced in the future to support non-CTEP studies. A method that doesn't involve AdEERS is also being investigated.	y	4.8, 4.11, 5.3, 8.3.3
		The specific needs of the various users for AE case follow-up needs to be broken down into more detailed requirements to determine if additional development is required to fully meet the requirement.		
		To fully determine what level caAERS meets or doesn't meet the autocoder requirement, the caAERS team needs further clarification. However, it can be noted that caAERS does not have a way to recognized signed relationships.		

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		The current reporting tool is web-based, so there were questions concerning the requirement that the new tool allows web-based reporting of AEs. Does this mean a separate website that would communicate to the new system, or is it just reiterating that the tool needs to be web-based? If it's the former, the development of the API should support submissions made via a website. If it's the latter, caAERS fully meets the requirement.		
8.3.4	**Reporting on/analyzing the data**	The various distribution requirements for CTEP – Go to contractor, Do not assess, and Do not Process; these are important for managing the workload associated with processing expedited reports for CTEP-sponsored studies, so will have high priority. (part of processing expedited reports)	y	6
		Comments or note logs, to capture comments concerning the processing of an expedited report package (part of processing expedited reports)	y	6
		Provide full audit trail and audit reports, including reports that compare versions of reports to account for differences	y	4.3, 4.6, 7.1, 8.3.4, 10.2
		What is meant by "Event screen", requirement FN151, needs to be clarified before it can be determined if the requirement is met or not.		
9	**Ergonomic/User Interface**			
9.1	**General**	caAERS needs to add information on the home page/when logging on about privacy and retention of info collected		
		The requirement documented in the requirement document stated NCI's supported browsers were IE 5.0 and Mozilla 5.0. Since technology has improved, the authors of this document believe NCI's supported browsers have changed. caAERS runs in IE 7.0 and Firefox 2.0 and up. However, it is not guaranteed to work in IE 6.0. Pending the clarification of NCI's supported browsers, additional development may be required, based on the planned timeline for the EDMAERS.		

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9.2	**508 Compliance**	Improve the tabbing and keyboard navigation. While tabbing is set up, it does not work consistently in either IE or Firefox	y	5.2, 5.3, 9.2
		There currently isn't a way setup that allows readers to skip lines or navigation. It has been recognized as a gap and should be an easy fix to implement	y	5.2, 5.3, 9.2
		Additional testing and research needs to be done concerning flickering of the application at the frequency specifications documented in the requirement. With the improved technology, it is unclear if this is even a valid requirement.	y	5.2, 5.3, 9.2
9.3	**Language Support**	caAERS needs to become NLM and NSL enabled		
9.4	**Navigation**	Navigation may need to change to meet the requirements, since the main navigation doesn't go to separate pages; you have to access second-level navigation before the main page changes.		
9.5	**Page Layout**	The standard header and footer navigation elements are also not included at this time.	maybe	
		Missing the standard header and footer navigation elements		
		missing the cancer.gov mini banner		
		doesn't include "NCI" in the window title		
		While caAERS does support adding information to display during the AE flow, additional investigation needs to occur to determine the full requirement. The team is also looking in to adding alerts, which may not be limited to a study-level addition, it may be per patient		
10	**Data**			
10.1	**Elements**	caAERS does not include the ASAEL	yes	4.5, 5.5, 10.1
		caAERS also does not capture any of the AE and report processing elements, since that functionality hasn't been added to caAERS yet.	yes	6, 10.1

Section #	Section or Sub-section Title	Identified Gap (possible gaps are in italics)	Duplicate?	Section(s) it is shared with
10.2	Auditing	Being able to audit the changes made to an AE and expedited report has been started. While all the information lives in the database, there isn't an easy way to access it.	yes	4.3, 4.6, 7.1, 8.3.4
		Electronic versions of all AE reports – caAERS only provides viewing/printing access of the current AE report. A method to review older versions of the report would have to be implemented	yes	4.1, 4.3, 10.2
		Currently data isn't locked; only the primary keys are locked with all other fields able to be modified. More research needs to go in to the regulatory agencies traceability/data requirements to determine what additional development needs to occur	yes	4.3, 4.6, 7.1, 8.3.4
		caAERS doesn't trace where the data comes from. So, if something is imported from an XML file, or added via API and messaging, it won't be marked any different than if it's entered manually. This will need to be built to support FDA's requirements		
10.3	Access	Allow a user to retrieving all versions of all elements stored in the database, for example, be able to compare two versions of the same report, or changes to the medical history associated to a participant-study combination	yes	8.3.2, 10.3
		Provide a method to analyze the data that is retrieved		
10.4	Migration	An interface between caAERS and CTEP-ESYS and DCP-ESYS do not exist. APIs and messaging have been developed to support integration with other tools, but these have not been applied to either CTEP's or DCP's existing components.	yes	4.3, 10.4
		The caAERS development team also needs to develop methods for importing legacy expedited reports.	yes	4.3, 10.4

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10.5	**Maintenance**	A 50-year data repository has to be examined. If installed locally, the specific methods on how this would be done would be determined by the adopter. The caAERS development team needs to develop a method that enables the data to be exported in a format that is easily persisted, or just enable the persisting of the database files since any SQL programmer could work with the data even if caAERS is no longer deployed. If caAERS is set up centrally, the methodology would be determined by NCI in correlation with the caAERS development team.	yes	4.3, 10.4
		caAERS only provides viewing/printing access of the current AE report. A method to review older versions of the report would have to be implemented.	yes	4.3, 10.4
11	**Performance Quality**			
11.2	**Maintainability**	As caAERS is being developed, the developers are constantly considering maintainability. To this end, much of the configuration can be done within the interface of the application. Most configurations are now available via the interface, but additional coding needs to occur to complete the process.		
		Part of this requirement identifies reference tables. The authors of this gap analysis were not able to determine what was meant by reference tables. When clarification is received, the caAERS development team can determine if it's met.		
		caAERS has been designed in light of the lessons learned from the AdEERS system. In particular, special emphasis has been placed on enabling a high degree of configurability in order to avoid some of the maintenance issues that plague AdEERS. While caAERS is currently very flexible, more work in this area should be done to support alternative workflows.		

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11.3	**Performance**	*Additional testing has to be done to determine if caAERS can support the load that's required while maintaining response times (400 user, 5 sec response time)*		
11.4	**Quality**	caAERS needs to be used by actual adopters more to increase the quality of the application. The more it's used, the more bugs will be found and addressed. Standard problem of new application		
11.5	**Usability**	Work needs to be done ti improve the usability of the limited reporting available in caAERS (API)		
		Setting up data for messaging and importing is still seen as highly technical and difficult.		
11.6	**Validation**	Full third-party testing still needs to be scheduled.	y	5.7, 11.6
12	**Reporting**			
12.1	**Generation (of Reports)**	While there is a reporting API, it does not have a user friendly interface and requires technical knowledge to use.	yes	4.7, 12.1
		The reports provided by the API are also limited. Additional development needs to occur to provide all current AdEERS reports and ad hoc reporting.	yes	4.7, 12.1
12.2	**Output**	caAERS does not support the backend reports that AdEERS has. More development needs to occur to provide these reports, as well as provide the mechanism to export the data for analysis.	yes	4.7, 12.2
		To support the submission of reports to the FDA and other approvers using their online submission tools, discussions need to be held with the individual groups to determine what integration needs to occur. caAERS does have messaging capability, and currently submits expedited reports directly to AdEERS, so these modifications may be easy to make.	yes	4.7, 12.2
13	**Interface**			
13.2	**communication with existing AE repositories**	caAERS needs additional development to be able to communicate with NCI's newly adopted centralized AE repository		

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13.3	**Electronic submission of various reports**	caAERS may need additional development to support electronic submission of expedited reports directly (not via email) to other organizations' systems		