

New dimensions in EDC/eClinical Systems

Enhanced Study Management Functions

#1 Document Management

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Since the first Babylonian recorded inventory on wet clay tablets in cuneiform text all those thousands of years ago, humans have gradually improved their data collection methods over the millennia - from clay to papyrus to vellum to paper, and now, at this juncture in history, as cleverly arranged electrons in a computer. What is common about all these technologies, including the computer enabled ones, is that a human agency is required to make the data useful. That's a fancy way of saying *someone* has to look at the data, think about it, and do something with it - otherwise it has no value.

Until very recently, what that meant was that each specific group of users would take the data and place it into their own system (electronic or paper process, but in this case, electronic) in order to help them organize the data, act upon it, and derive value. Thus, in the realm of clinical software systems to support clinical trials, EDC, CTMS, IVRS, CDMS, etc. are marketed and sold as different products to meet those needs.

Automated computer based systems enable the organization of large volumes of data, and assist in the quality execution of clinical trials. Computers are highly efficient at moving and organizing all those 1's and 0's with precision and speeds no human being can hope to match. So, we have different systems available to meet different needs, which represent a fairly linear, paper-based thought process. Data goes from one to the other to the other - but how does it get there and what if two or more groups require access for different needs at the same time? The CRAs need to collect data, and the Study Manager needs to manage studies operationally.

These two groups could have their needs met with the simple example of a pure EDC system and a CTMS. In the ordinary course of events, these are two separate software entities performing two different functions. In order for the data in one to be present in the other, one of two things must occur - either an interface is developed to allow data exchange, or the data is keyed in manually. Both of these have issues - in the first instance, such interfaces are often difficult to construct and burdensome to maintain, and in the second, whilst computers are highly precise, humans are generally not, so errors are introduced during the re-keying process. Both methods suffer from a lack of immediacy - they take time to perform, which in turn causes inefficiencies in the trial process.

As computer systems have evolved over the last decade or two, it has become increasingly obvious that the old linear methods of thinking no longer have to apply. Data can be used in many different ways, at the same time, and within the same system - this not only obviates the problems of interfaces and rekeying, but also tends to cost considerably less than two separate systems alone. Automated systems are including more and more features that leverage the many things in common that arise from using the same data, but for different purposes - all managing data relating to sets of patients, the clinical trial process, and events within or arising from the process. Thus, simple EDC begins to morph into an eClinical product in the breadth of its capabilities. It makes sense that this is happening, at least in some vendors, as Sponsors, shopping for efficiency, rightly expect more "bang for the buck" and greater efficiency.

An example of the expanding dimension of EDC automation into the eClinical realm is illustrated by a request from Steve Mayo, CEO of Emissary, a CRO in Austin, Texas [<http://www.emissary.com>]. Dr. Mayo wanted to extend the EDC data collection and management into managing the study's TMF (Trial Master File):

- "To reduce the burden on the study coordinators and to simplify our regulatory compliance efforts, we would greatly like to keep all the clinical data in this one EDC system, where my staff can then monitor and follow-up on missing data" to include notifications when items are due.

A few days later:

- "It's fantastic!!!! This is really good stuff!!! I think with a little testing and some training videos we can start using this right away!"

A characteristic of a modern system, designed without a fundamental linear paradigm, is that requests such as the above can be executed in a relatively short timeframe. What that means to the purchaser of such a system is that costs are generally a few single digit percentage points of a stand-alone system and they have access to something that is exactly how they wanted it - tailored solutions at a cheaper than off the rack price.

It's arguable then, that with appropriate Sponsor and provider vision of what can be achieved, even more exciting changes may be just around the corner, and at a price and a timeline to accommodate the needs of all parties. Prelude Dynamic's VISION (yes, called that for a reason) is coming to fruition on many different levels - in this paper, we will overview Document Management within a single "EDC" system.

Document Management Extension to Vision EDC system

- Study-level Trial and Project Team document forms (each of which can optionally be separated into different categories/binders)
- Project Manager Definition form for Site, Personnel, and Patient documents (with up to 3 defined dates or other fields for each document)
- Site, Personnel, and Patient document forms based on Definition above
- Site, Personnel, and Patient document listings at study level - summaries from the above forms but over all sites and patients
- Site, Personnel, and Patient summaries of documents submitted (checklist)
- Project Manager and Monitor roles can see all the pages, and can edit all except the patient source documents, but the permissions are easily changed.

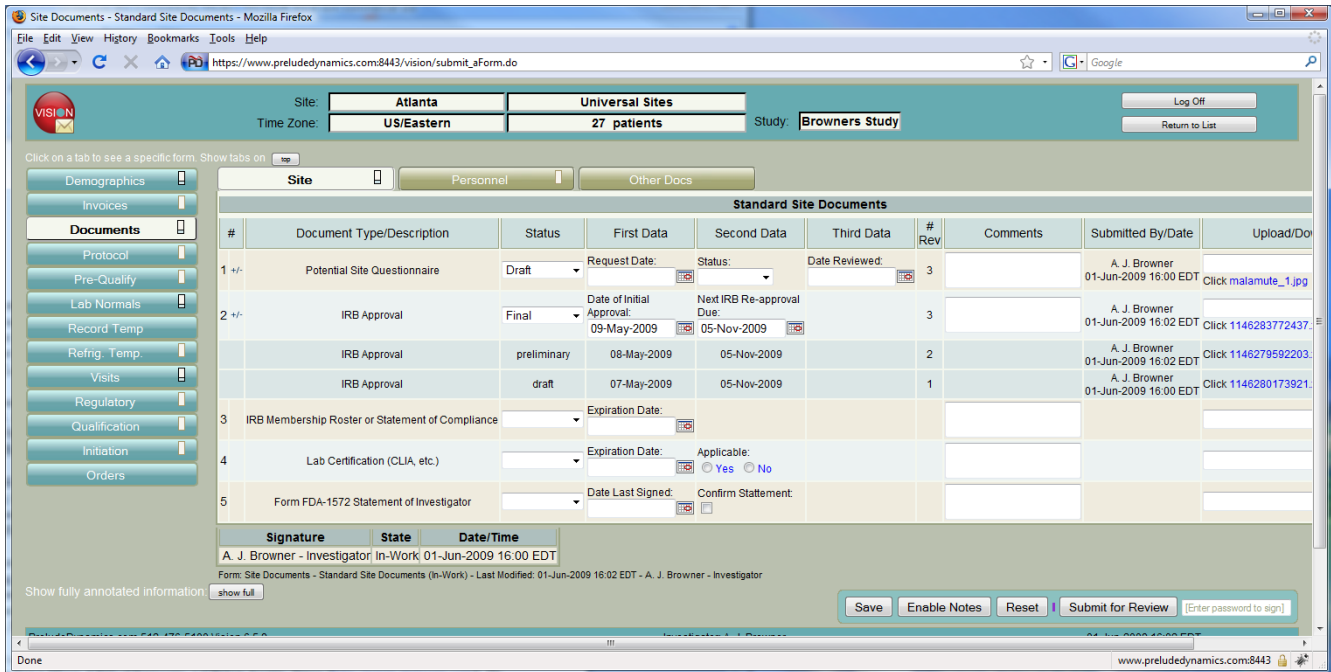
There are parts of the feature in the following locations:

1) **Patient Level (e.g., source documents)**. Select a patient and the "Source Docs" tab. Here, the Coordinator or Investigator can upload standard and ad-hoc documents for the patient. Click "Summaries" to view the document status of the patients, toggling "Condensed" and

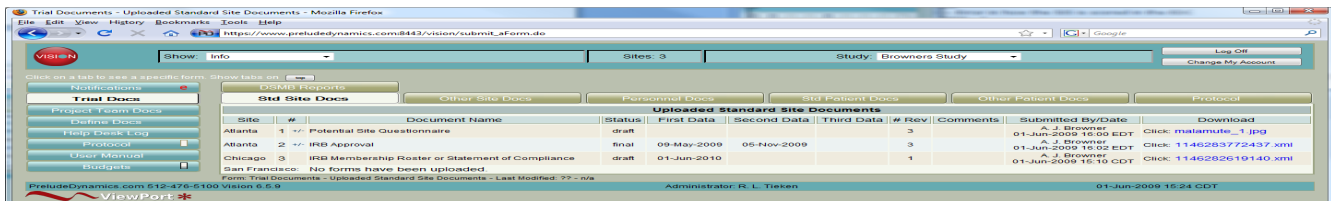


"Expanded" to see amplifying detail about the documents.

2) **Site Level (e.g., site initiation, IRB).** Select a site and the "Documents" tab. Here, you can upload standard site, personnel, and ad-hoc documents for the site and site personnel. Look at "Summaries" to view the document status of the sites, toggling "Condensed" and "Expanded".

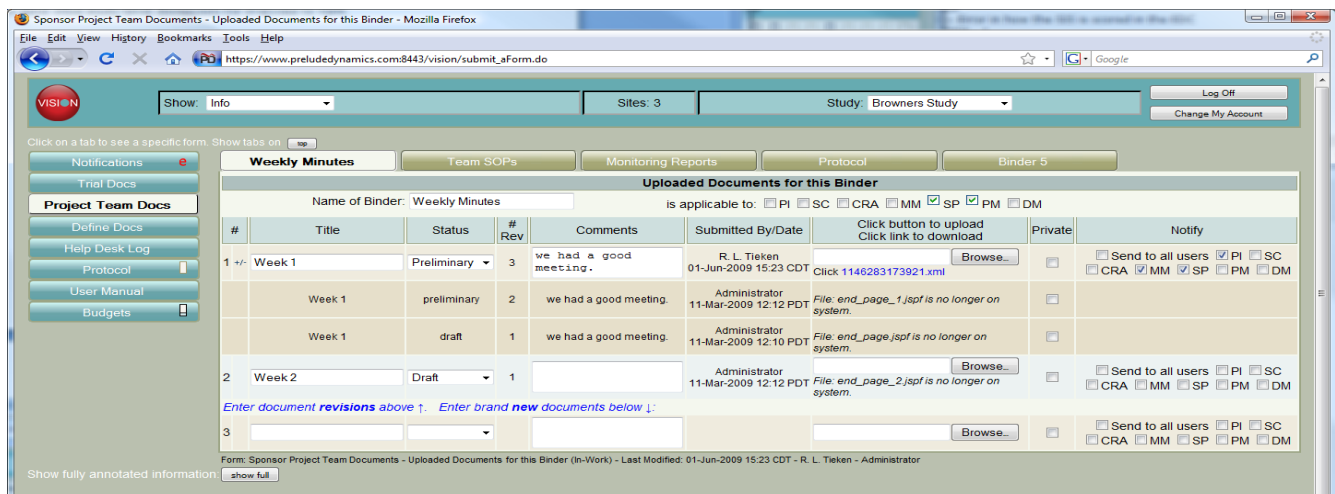


At the study level, the uploaded patient, site, and personnel documents can be viewed, along with study binders.



3) **Study Level (e.g., protocol).** The "Trial Docs," "Project Team Docs," and "Define Docs" are all the main study-level document tabs.

- "Define Docs" allows you to specify the site, personnel, and patient documents that are expected.
- "Project Team Docs" are only viewable by the Sponsor, Project Manager, Monitors, and Medical Monitors, and you can specify different Binders, which are groupings of documents.
- "Trial Docs" summarizes the site, personnel, and patient documents, and enables entry of other study-level documents for everyone to view.



All document upload pages have the following similar features and capabilities:

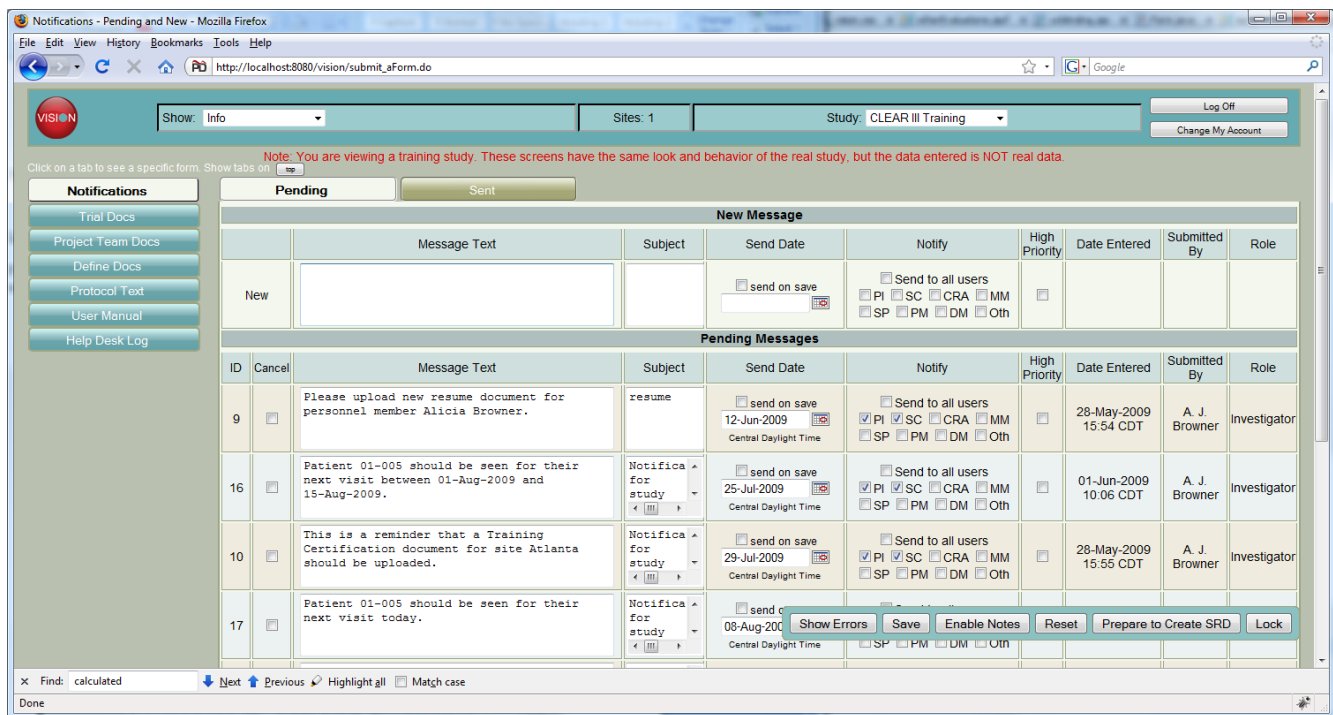
- Users may upload multiple versions of the same document, with Vision storing all versions and the meta-data associated with each. The display will show a list of current documents, and revisions are viewable (read-only) by clicking to "expand" in-line the view for that document. All revisions (versions) can be downloaded to view the document.
- The meta-data for each document/revision includes a title, type/category, status (e.g., draft, final), submitter (auto-populated), submitted date (auto-populated), comments, and the uploaded file.
- Each document/revision is limited by role as to which roles can see the reference; and sites as to which sites can see the reference.
- Each document type/category can be associated with user roles (investigator, monitor, etc) that are notified (email, and on-line list) when an upload of that type occurs. (For site and patient forms, this is defined by the Project Manager.)
- Each document can be marked "private" so only the user that uploads it can view it (until it is "published/public").
- When a document is uploaded, and is not private, and roles for that document are defined, those roles will receive a notification that the document has been uploaded
- Each revision (once not current) will have read-only meta-data and users may only download older versions, but may not replace or upload over older versions.

Furthermore, for study-level documents,

- The system supports multiple, user-named groupings/containers of documents (e.g., IRB documents, staff documents, etc.)

In addition:

For each document, notifications can be specified either as reminders to upload a standard document or as roles to notify when an upload event occurs.



Existing sites get a notification whenever the study form changes with new additions. When designated for a new site (e.g., status drop-down on demographics form is set to "Active" from "Planned"), users assigned to the site get a notification about the documents needed. (This needs to happen after users are assigned to the site!)

When a new site or new patient is added, Vision creates a "documents" page at the corresponding site/patient level. The entries on these match the individual items set by the Project Manager list in 1). Each document has a title and description from what the Project Manager entered in 1), along with the other standard document fields. From then on, uploads by the site staff trigger a notification back to the people listed by the Project Manager.

The study level has a summary form that lists all the site documents that have been uploaded and has a clickable "download" link. This summary will have sortable columns. Similarly, the study level has a summary for the patient documents. The summaries will display for a selected site or for all the sites and will also list the "other" from #5 below.

For each site and patient, independently, the user will be able to upload documents that aren't in one of the pre-defined Project Manager lists (similar to the standard documents except there are no labels set by the Project Manager). These will be "other" documents.

There is a site and a patient summary that itemizes by site/patient, the documents that have and have not been uploaded. There is a column to show the date and the number of days since the notification date so people will know what is expected, missing, and how "behind" they may be.

Site Document Status - Mozilla Firefox
 https://www.preludedynamics.com:8443/vision/process_list.do

VISION | Show: Sites | Sites: 3 | Study: Browners Study | Log Off | Return to List

Click on a tab to see a specific form. Show tabs on top | Viewing Summaries

Documents | Site | Personnel | Delegation

Enroll vs. Time | Total Enroll | Form Status | Queries | Visit Status

Site Document Status Condensed

To navigate to the list of documents for the site, click on a row.
 For document name and upload date, hover the cursor over the number or the icon.

Site	1	2	3	4	5
Atlanta	✓	✓	✗	✗	✗
Chicago	✗	✗	✓	✗	✗
San Francisco	✗	✗	✗	✗	✗

PreludeDynamics.com 512-476-5100 Vision 6.5.9 | Investigator: A. J. Browner | 01-Jun-2009 15:11 CDT

ViewPort*

Done | www.preludedynamics.com:8443

Site Document Status - Mozilla Firefox
 https://www.preludedynamics.com:8443/vision/summaryChoice.do

VISION | Show: Sites | Sites: 3 | Study: Browners Study | Log Off | Return to List

Click on a tab to see a specific form. Show tabs on top | Viewing Summaries

Documents | Site | Personnel | Delegation

Enroll vs. Time | Total Enroll | Form Status | Queries | Visit Status

Site Document Status Expanded

To navigate to the list of documents for the site, click on a row.

Site	Potential Site Questionnaire	IRB Approval	IRB Membership Roster or Statement of Compliance	Lab Certification (CLIA, etc.)	Form FDA-1572 Statement of Investigator
Atlanta	01-Jun-2009 16:00 EDT	01-Jun-2009 16:02 EDT			
Chicago			01-Jun-2009 15:10 CDT		
San Francisco					

PreludeDynamics.com 512-476-5100 Vision 6.5.9 | Investigator: A. J. Browner | 01-Jun-2009 15:12 CDT

ViewPort*

Done | www.preludedynamics.com:8443

CONCLUSION

The real "value" behind automation continues to evolve, and expand in dimension.

The definition of EDC is changing, or rather, EDC as a single entity is becoming extinct - quality systems are evolving into e-Clinical systems offering hitherto unaffordable speed and efficiency to Sponsors of all sizes and needs. From time savings to overhead burden, data visibility enabling early corrective action, to regulatory compliance, a modern eClinical solution encompasses proven abilities to achieve what just a few years ago none thought possible.

Next article: Automated Honoraria and Payment Calculations - based on Patient Visit milestones and Site Coordinator/Investigator completion.