Roadmap for study startup

Deploying Adobe technology to automate clinical study startup procedures

Section 1: Introduction and overview

1.1 Introduction

Effective management of the clinical trials process can significantly affect a company's bottom line.

According to a study by Cutting Edge Information, companies stand to lose between $600,000 and $8 million for each day that clinical trials delay a product's development and launch. Furthermore, only 6% of clinical trials are completed on time, and 72% of trials run more than one month behind schedule (Cutting Edge Information 2004). A key challenge is that the clinical trials process spans so many different parties, including study sponsors, contract research organizations (CROs), site management organizations (SMOs), patient recruiters, investigators, and patients.

By observing and working with customers across many industries over the last decade, Adobe has developed solid technologies that can help decrease cycle times and reduce errors by automating key manual tasks and processes.

If you currently have a process that's manual and heavily paper-based or one that involves a legacy IT infrastructure, the task of automating different steps in the clinical trials process may seem daunting. This roadmap focuses on one key area of the clinical trials process—study startup—and shows how Adobe technology can help you gain a significant competitive advantage in new product development.

The study startup phase, which includes investigator enrollment and submission of new investigator packages, is a time-consuming component of the clinical study process. The Signatures and Authentication for Everyone (SAFE) BioPharma Association recently identified Form 1572, used by clinical investigators participating in trials, as the single most redundant paper form received by the FDA. The newsletter goes on to state that between 220,000 and 240,000 1572 forms are received each year by the U.S. agency and that conversion from paper to an electronic form would save an average of $159 per form—or more than $38 million per year (Shields-Uehling 2006).

This roadmap identifies opportunities to develop pilot projects and implement larger strategies to streamline your company's study startup process while simultaneously delivering immediate ROI.

This roadmap is a guide for deploying Adobe technology to automate certain processes associated with the initiation of clinical studies. It is not a substitute for agency-issued regulations or guidances, nor is it a substitute for in-house SOPs that have been created in accordance with any government regulations or guidances. Rather, this roadmap is intended to be a supplement that provides step-by-step instructions for implementing Adobe technology to streamline certain procedures. Many factors outside the scope of this document must be considered to successfully complete the processes associated with the initiation of clinical studies. Please refer to the appropriate government and industry regulations and guidances concerning the conduct of clinical studies:

- *www.fda.gov/cder/index.html*
- *www.fda.gov/cber/index.html*
- *www.emea.eu.int*
- *www.safe-biopharma.org*
- *www.phrma.org/updated_principles_for_conduct_of_clinical_trials_and_ communication_of_clinical_trial_results*

This document explains how Adobe technology can help automate the well-defined, repetitive processes associated with getting a clinical trial up and running. It provides information concerning the technical implementation of Adobe technology as well as guidance for modifications to the overall processes.

1.2 Overview of the clinical study process

The Guidance for Industry—E6 Good Clinical Practice: Consolidated Guidance (referred to in this guide as the guidance) is an "international ethical and quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects." The full guidance can be found at *www.fda.gov/cder/guidance/959fnl.pdf*. The guidance was developed within the Expert Working Group (Efficacy) of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and has been subject to consultation by the regulatory parties, in accordance with the ICH process.

As detailed in the guidance, all clinical studies require the development and approval of a protocol, which is "a document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial," and usually includes the background and rationale for the trial. The protocol should describe the scientific basis for the study in a clear, detailed manner.

The protocol also details the requirements for identifying the appropriate Institutional Review Board/Independent Ethics Committee (IRB/IEC) and for identifying and enrolling investigators to assume responsibility for the proper conduct of the trial. Before initiating a trial, investigators are required to provide written approval from the IRB/IEC for the protocol, written informed consent, subject recruitment procedures, and any other written information to the subjects. Investigators are also required to provide the IRB/IEC with their current investigator's brochure.

1.3 Investigator responsibilities

The term investigator is defined on page 5 of the guidance as, "A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator."
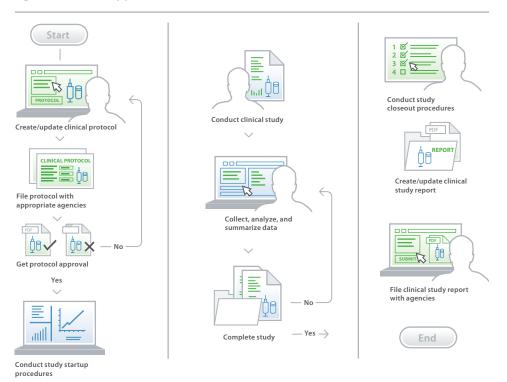
Investigator responsibilities include:

- Subject recruitment
- Medical care of subjects
- Collection of subjects' informed consent forms
- Communication with the IRB/IEC
- Protocol compliance
- Investigational products
- Randomization and blinding procedures
- Data reporting
- Safety reporting

1.4 Clinical trial timelines

Although the end-to-end timeline for clinical trials varies depending on the type of trial, the number of patients, and the length of the trial, the process steps required to initiate, conduct, and complete any clinical trial are consistent across all trials (see Figure 1). This roadmap focuses on the activities associated with conducting study startup procedures, with an emphasis on enrolling investigators, filing the IND amendments for new investigator packages, and performing duties surrounding drug accountability. Because these processes are repetitive and consistent across all clinical trials, once process efficiencies are implemented for these procedures, savings can be realized across all clinical trials, regardless of the project, type, or length of the trial.

Figure 1. Clinical study process overview

Section 2: Study startup procedures

Adobe technology helps automate study startup procedures (which are illustrated in Figure 2). These technologies are flexible; they can be implemented incrementally to achieve optimal process efficiency over time. This roadmap provides detailed descriptions to help you implement some or all of those technologies based on your desired level of automation.
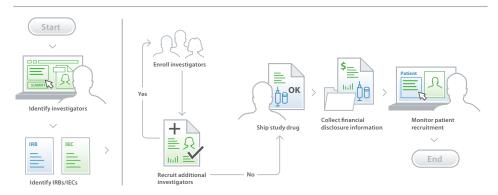
Details concerning the implementation of Adobe technology are provided in each step described in this guide. It is important to note that the only software required for investigators is the free Adobe® Reader® and an e-mail account to send and receive forms and documents.

Sponsors and CROs may need additional Adobe infrastructure components, including:

- **LiveCycle® PDF Generator ES**—Enables investigator packages to be assembled as Adobe PDF files for submission to the agency
- **LiveCycle Rights Management ES**—Enables document-level version and access control of Adobe PDF files and Microsoft Word and Excel documents, so confidential information is restricted to intended recipients
- **LiveCycle Reader Extensions ES**—Enables the use of the free Adobe Reader client
- **LiveCycle Process Management ES**—Enables the management of ad hoc processes with investigators
- **Adobe Acrobat® Professional**—Enables creation of PDF files as well as commenting and digital signatures
- **LiveCycle Digital Signatures ES**—Enables the validation of digital signatures
- **LiveCycle ES Connectors for ECM**—Enables seamless integration between LiveCycle ES solution components and your ECM system

For more information about Adobe LiveCycle ES solution components, visit *www.adobe.com/lifesciences/solutions/livecycle*. For details on Acrobat Professional, visit *www.adobe.com/acrobat*.
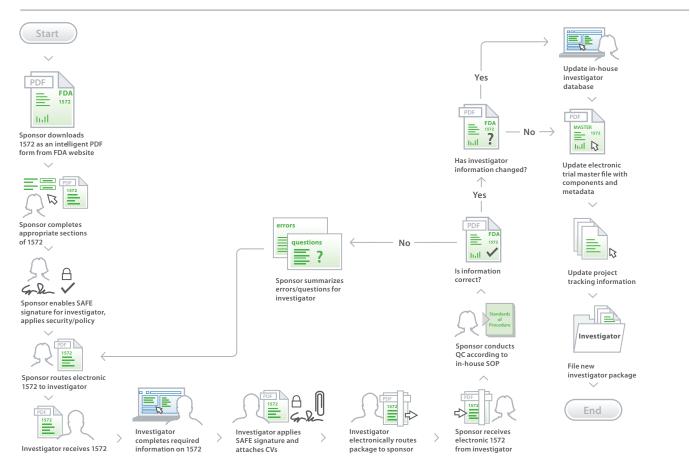
Figure 2. Study startup procedures

2.1 Identifying and enrolling investigators

The process of identifying and enrolling investigators is linear in nature and is consistent across all therapeutic areas. The process is well defined by the U.S. FDA and is repetitive, which allows efficiencies to be implemented across all therapeutic areas. Figure 3 shows an overview of the process.

Figure 3. Enrolling investigators

2.1.1 Identifying investigators

Investigators whose expertise qualifies them for the study are identified. Section 4, Page 13, of the guidance details investigator qualifications as follows:

> 4.1.1 The investigator(s) should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB/IEC, and/or the regulatory authority(ies).

> 4.1.2 The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information, and in other information sources provided by the sponsor.

Sources of information for identifying investigators include, but are not limited to:

- In-house investigator databases
- *www.clinicaltrialnetwork.com*
- CROs enlisted to assist in the conduct of the clinical trial

2.1.2 Enrolling investigators

Once the investigators are identified and the site initiation procedures have been completed, the procedures to enroll investigators for the purpose of conducting the trial are complete. For trials conducted under the regulations of the FDA (both CDER and CBER), the steps illustrated in Figure 3 must be followed. This section first examines each of these steps and then identifies how Adobe technology can help streamline the process.

1. The sponsor starts Form 1572, which is available on the FDA website at *www.fda.gov/opacom/ morechoices/fdaforms/default.html*. Form 1572 must be completed for each investigator to be enrolled. Certain fields can be prepopulated with data (such as fields 1–5, 7, and 8). The form can be sent electronically or printed and physically mailed to each investigator.

2. The investigators receive the form. Investigators who receive an electronic form can use Adobe Reader to complete it, print it, attach any required documentation such as CVs, sign it, and return it to the sponsor. Investigators who receive a paper form in the mail need to fill out the paper version, sign it, attach the CVs, and mail it back.

3. Once the sponsor receives the paper version, the individual responsible for the study does the following:

   • Reviews the new investigator package to ensure that the form has been completed correctly, the information is valid, and the appropriate supporting documents have been attached. If errors or questions are identified that require changes to the 1572, the sponsor must contact the investigator and often must route an updated form to the investigator for a new signature.

   • Verifies that any updated information (such as the investigator's address) is entered into the in-house database(s) used to create the 1572.

   • Retains a copy of the 1572 with attachments for the trial master file.

   • Retains investigator CVs for the trial master file and the product application to the FDA.

This roadmap identifies high ROI areas based on past customer implementations in the pharmaceutical industry and other industries. In addition, it provides options to automate the manual process described in the previous section to reduce the cycle times and cost for enrolling investigators in a clinical study. Similar problems and challenges have been addressed in other industries, such as financial services and telecommunications. Mobile phone applications and mortgage applications are two examples of processes that Adobe has helped streamline to provide significant ROI in terms of costs savings in paper and processing time. Many challenges at the core of these processes are also present in the study startup process.

Adobe technology offers several opportunities to dramatically streamline the investigator enrollment process, enabling you to reduce cycle time and resources required to complete investigator enrollment for clinical studies:

• **Information collection and tracking.** Each study may require many investigators to be recruited, and each investigator must complete a 1572. It is time-consuming and costly to prepare and route paper versions of the form. Once routed, the forms must be tracked to ensure that investigators return the forms in a timely manner. While e-mailing electronic forms to investigators is an improvement, utilizing fill-and-print forms still restricts optimal functionality.

• **Information management.** Whether e-mailing or mailing the form to the investigator, the sponsor must still process the paper version of the form and attachments when they are returned. If there are errors, the sponsor must work with the investigator to correct the information, which may include reprocessing the 1572. The returned information may also be compared with database information used to create the form. If the information has been modified, the sponsor must manually update any in-house databases used to create the 1572. Finally, sponsors must ensure that copies of the returned documents are placed in the appropriate repositories for maintaining the trial master file as well as ensuring the availability of investigator CVs for inclusion in a future application.

The investigator enrollment process, while well-defined and repetitive in nature, presents many challenges that can add considerable delays in getting a clinical trial started. The manual process could easily result in weeks of elapsed time for each 1572 form that you process. Multiplying the number of investigators recruited each year with the elapsed time spent by an organization for each investigator, results in a significant cost. These delays in completing the study startup phase can also lead to delays in submission, approval, and product launch—meaning potential lost revenues of millions of dollars. Additionally, allocating resources to the manual routing and tracking of the 1572 forms is costly in terms of both money and valuable resources that could be allocated to other more critical tasks.

Adobe technology can improve the investigator enrollment process. This roadmap describes the improvements in phases, which enable incremental implementation. As each phase is implemented, ROI increases exponentially.

2.1.2.1 Phase 1: Improving information collection

Phase 1 focuses on facilitating the three steps for enrolling investigators that are outlined in section 2.1.2. The current 1571 and 1572 PDF forms on the FDA website are locked by the FDA, so their functionality cannot be enhanced by adding functionality such as data saving, digital signatures, and dynamic barcodes. The versions of forms 1571 and 1572 supplied with this roadmap have been revised using Adobe LiveCycle Designer ES to add advanced PDF functionality. To use the 1572 provided with this roadmap:

1. Add an e-mail button on the 1572 with the e-mail address set to the individual in your organization that will receive the completed forms. Add additional data validation to the form with LiveCycle Designer ES to verify user input and completeness on the form, such as adherence to acceptable values for a particular field and completion of fields that are mandatory before a signature can be applied.

2. Enhance the form using Adobe LiveCycle Reader Extensions ES or Acrobat Professional (version 8 or later) to provide investigators with the following rights:

   - Attach documents (available only with LiveCycle Reader Extensions ES)
   - Update form fields
   - Apply an electronic signature

   Details on using Acrobat Reader-enablement and Adobe LiveCycle Reader Extensions ES can be found at *www.adobe.com/products/livecycle*.

3. E-mail the form to the investigator or make it available via a portal if a website portal has been set up for the clinical study.

Once the PDF form has been enhanced, the investigator can use the free Adobe Reader to fill out the form, sign it using a digital signature (such as SAFE), attach the appropriate supporting CVs, and send the form with attachments back to the sponsor. These simple steps eliminate the exchange of paper documents resulting in a reduction in cycle time, errors, and costs.

For more information about SAFE, visit *www.safe-biopharma.org or www.adobe.com/ lifesciences/safe.html*.

2.1.2.2 Phase 2: Enhancing information management

Phase 2 provides the capability to automatically manage the 1572s with attachments, as they are received from investigators. The steps in this phase are:

1. Complete the three steps from Phase 1 (see section 2.1.2.1).

2. Within your existing e-mail system, set up an e-mail address for LiveCycle Process Management ES to accept the completed forms.

3. Set up LiveCycle Process Management ES Server to route the attachment (new investigator package) to the appropriate individual to conduct a quality control inspection.

4. Configure LiveCycle Process Management ES to route the attachment to LiveCycle Forms ES Server on approval of QC inspection.

5. Set up LiveCycle Forms ES Server to accept tasks from LiveCycle Process Management ES and extract the data (as an XML data stream) from the 1572 form.

6. Configure LiveCycle Process Management ES to route the completed new investigator package as a PDF file for inclusion in the 1571 package.

2.1.2.3 Phase 3: Enhanced integration with existing ECM or project management software

Organizations that do not currently use a repository for managing forms can benefit from Adobe's process management suite, which includes LiveCycle Process Management ES and LiveCycle Content Services ES. This suite is a good starting point for electronically managing the status of the forms being sent out and returned across one or many clinical trials. LiveCycle ES can be configured for event notification and exception reporting and can provide a dashboard view of the status. Additionally, LiveCycle Content Services ES includes an enterprise content management repository and enables your team to rapidly implement end-to-end processes that heavily interact with content and automate the assembly and generation of PDF packages to share with regulators or process participants. For more information, visit *www.adobe.com/products/livecycle*.

For organizations that currently have a database for investigators, an electronic trial master file, and/or an electronic project tracking system, LiveCycle ES Connectors for ECM can be configured to integrate with any or all of these systems to automatically update the attributes, data, and components. Not only can the investigator automatically fill out and sign the form with the free Adobe Reader, but LiveCycle ES can automatically manage the new investigator packages being returned. You can configure LiveCycle Process Management ES to automatically:

- Update in-house investigator databases
- Route the appropriate documents to the trial master file—the workflow can be configured to update the trial master file with the attachments (such as CVs) and data from the new investigator package
- Update any in-house project tracking database

For specifications concerning these integrations, see *www.adobe.com/devnet/livecycle/workflow/articles/lc_workflow_qpac_overview.pdf*.
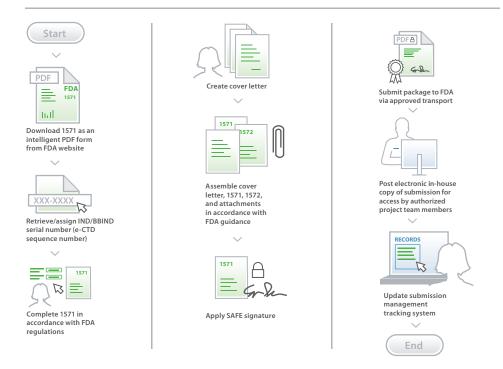
2.1.2.4 Other challenges

Adobe's digital signature technology and partnerships with key security vendors ensure that Adobe products support high-assurance and standards-based methods for applying digital signatures—including SAFE-compliant digital signatures. However, not all processes require or support digital signatures. In these situations, Adobe LiveCycle Forms ES can be used to place a 2D barcode on an Adobe PDF form during form design. These high-capacity barcodes capture data as information is entered into the Adobe form. When complete, the form can be printed, signed with a "wet" signature, and returned to the sponsor. When the paper form is received, the sponsor can scan the barcode and extract the information as an XML data stream for processing. For more details about Adobe LiveCycle Forms ES, visit *www.adobe.com/products/livecycle*.

Once the investigator package is complete, it can be filed with the Investigational New Drug (IND) application.

2.2 Filing new investigator submissions

The documentation supporting studies conducted under a U.S. IND application must be filed with the FDA in accordance with existing regulations. New investigator enrollments must be approved by the agency prior to the initiation of the study at the investigator's site. The following section details the process for filing the new investigator package with the FDA and describes how Adobe technology can automate the process steps. Figure 4 shows an overview of this process.

Figure 4. Filing a new investigator package

Start

Download 1571 as an intelligent PDF form from FDA website

Retrieve/assign IND/BBIND serial number (e-CTD sequence number)

Complete 1571 in accordance with FDA regulations

Create cover letter

Assemble cover letter, 1571, 1572, and attachments in accordance with FDA guidance

Apply SAFE signature

Submit package to FDA via approved transport

Post electronic in-house copy of submission for access by authorized project team members

Update submission management tracking system

End

2.2.1 Submitting and updating the IND application

Submitting and updating a paper-based IND application is labor intensive and error prone. An IND application consists of multiple submissions detailing the progress of the project. The FDA-defined hierarchy for describing the series of submissions across an IND application is detailed here:

- Initial IND application: ID assigned by agency plus initial sequence or serial number, such as IND 12345, Serial 0000

- First update: ID assigned by agency, plus sequence or serial number incremented by one, such as IND 12345, Serial 0001

- Second update: ID assigned by agency, plus sequence or serial number incremented by two, such as IND 12345, Serial 0002

The 1571 is required for submitting or updating an IND application. Multiple new investigator packages can be included with a single submission or update. The steps for submitting the IND application are:

1. The serial or sequence number is assigned to the submission.

2. All components (cover letter, if applicable, 1571, and 1572s with attachments) are assembled in accordance with existing agency regulations.

3. The form and package are signed and sent to the FDA.

4. The package, including all revisions and updates, is posted internally for in-house consumption.

Adobe technology can help streamline the assembly and submission of IND amendments and facilitate internal review, approval, and tracking of submissions across your organization. The next section shows how Adobe technology can optimize this process.

2.2.1.1 Assembling, posting, and tracking the IND package

The enhanced 1571, supplied with this roadmap, can be prepopulated with the correct project and sponsor information. The entire package can then be assembled in one of two ways:

- On the desktop with Adobe Acrobat

- On a server using LiveCycle Process Management ES and LiveCycle PDF Generator ES

For organizations that process a large number of new investigator packages, using a server is preferable. Because LiveCycle Process Management ES and PDF Generator ES are server-based applications, they can be integrated with other enterprise applications or automated processes to operate with little or no manual intervention.

Once the package is assembled, 1571 forms can be signed with a SAFE digital signature in Acrobat or Adobe Reader and submitted to the FDA via the e-submission gateway. The ability to submit the package electronically offers significant savings by eliminating many paper-based processes. In addition, the electronic package can then be posted to in-house repositories (as detailed later in this section).

In addition to automating the submission of the new investigator package to the FDA, Adobe technology can automate repetitive tasks such as posting the submission for in-house consumption and updating an in-house submission management tracking system.

Adobe LiveCycle Process Management ES can be integrated with in-house repositories posting submission updates and updating submission status to automatically update both the components and the associated metadata. In addition to automating the assembly and submission of IND amendments, Adobe LiveCycle ES can automatically manage and track submission components. You can configure LiveCycle Process Management ES to automatically:
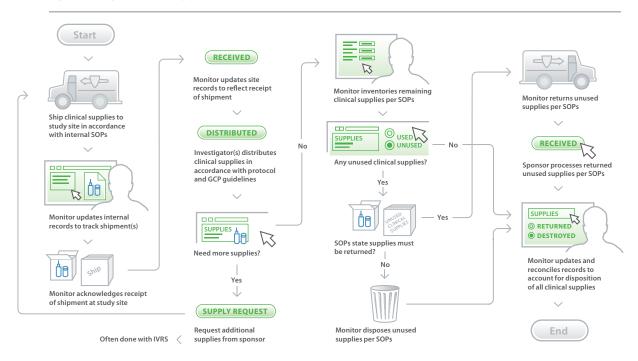
- Route the appropriate documents to the document management system (DMS) that stores the submission components and to update the DMS with the components and metadata of the IND amendment

- Update any in-house submission tracking database

For specifications concerning these integrations, see *www.adobe.com/devnet/livecycle/workflow/ articles/lc_workflow_qpac_overview.pdf.*

2.3 Shipping and managing clinical supplies

All records and documentation detailing the shipping, receipt, storage, handling, and disposition of investigational products are identified in the guidance as essential documents and must be maintained both by the investigator at the trial site and by the sponsor at its facilities. The procedures for managing clinical supplies and producing the supporting essential documents can be developed and implemented by each individual sponsor to meet the needs of the company. Each sponsor must document the procedures for managing all clinical supplies, and details of the procedures must be found in the individual protocols as well as the sponsor's SOPs. Although the initial shipment of clinical supplies is part of the study startup procedures, the drug accountability requirement is a process that runs throughout the trial. (The discussion on drug accountability contained in this roadmap assumes a monitored trial, which is illustrated in Figure 5.)

Figure 5. Drug accountability process

2.3.1 Shipping clinical supplies to study site in accordance with internal SOPs

The clinical monitor is responsible for ensuring the following drug accountability conditions are met:

- Storage times and conditions are acceptable, and supplies are sufficient throughout the trial.
- The investigational product is supplied only to subjects who are eligible to receive it and at the protocol specified dose.
- Subjects receive the necessary instruction on how to properly use, handle, store, and return the investigational product.
- The receipt, use, and return of the investigational product at the trial sites are controlled and documented adequately.
- The disposition of unused investigational product at the trial sites complies with applicable regulatory requirements and is in accordance with the sponsor's authorized procedures.

Before any clinical supplies are sent to an investigator's site, the monitor must complete a site investigation to ensure that the facilities are adequately prepared to accept, store, use, and distribute all supplies they will receive to support the study. Clinical supplies are then shipped to the site based on the number of subjects and the details of the protocol. The initial shipment is sent to the site in accordance with the defined procedures. The steps for sending the supplies are:

1. The monitor initiates a request for supplies to be sent to the site. This request can be an internal form that enables the monitor to fill in all the appropriate information concerning the shipment, or a web-based application that allows the monitor to fill out the request. The request may include, but is not limited to, the following:

- The protocol number and title
- The investigator's name, address, and site where the supplies are to be shipped
- Details concerning the supplies, such as number, strength, and packaging
- The date the supplies will be needed

- Any additional specific information that may be required for the shipment, such as temperature extremes, bio-hazard, or fragile materials warnings

- The monitor's signature, if required by the sponsor's SOPs

Note: Regardless of the mechanism for submitting the request, the request form must be produced as part of the essential documents in support of the study. Typically, the request would be filed in the appropriate section of the trial master file.

2. The request is sent to the sponsor's location that is responsible for fulfilling the request—typically a manufacturing facility responsible for manufacturing, packaging, and shipping clinical materials.

3. Once the request is received by the manufacturing facility, it is filled out and sent in accordance with the specifics of the request. Details of the shipment, including the expected date of arrival at the target site, are produced as an essential document and stored in the trial master file.

4. The monitor is notified that the shipment has been sent. The method for notifying the monitor is defined in the internal SOPs and/or protocol.

2.3.2 Updating internal records to track shipment
The monitor is responsible for ensuring that the internal essential documents are produced and stored in the appropriate location. In addition, once notified, the monitor tracks the status of the shipment.

2.3.3 Acknowledging receipt of shipment at study site
It is the monitor's responsibility to go to the study site once the shipment has arrived. The duties the monitor must perform include but are not limited to:

- Opening and inspecting the shipment, comparing the contents of the shipment with the details of the request

- Producing documentation that the contents of the shipment agree with the details of the request or document what is different from the request

- Ensuring that the documentation required by the SOPs and/or protocol are placed in the appropriate repositories at the investigator's site and the sponsor's facility

- Unpacking and storing the contents of the shipment in the appropriate location at the site

2.3.4 Distributing supplies in accordance with the protocol
As the study proceeds, the investigator uses the clinical supplies in accordance with the study procedures. As the supplies are depleted, additional supplies are requested from the sponsor. The monitor closely tracks the number of subjects being enrolled and randomized, the clinical supplies being distributed to the subjects, and the additional supplies being requested. As the study proceeds, the monitor is responsible for the following activities:

- Updating all documentation concerning the receipt and distribution of clinical supplies, including how many subjects are enrolled in the study and what supplies were distributed to each subject

- Ongoing supervision of the requests, shipments, and receipt of additional supplies

- Ensuring that all essential documents required by the protocol and/or SOPs are produced and properly placed in the appropriate repositories at the investigator's site and sponsor's facilities

2.3.5 Inventorying remaining supplies

Once the site has declared that the last patient has been seen for the last time and that there will be no further patients seen in connection with the study, the monitor inventories any remaining clinical supplies. The close-out process for drug accountability consists of:

1. Conducting an inventory to determine if any clinical supplies are still at the investigator's site

2. Disposing of the supplies in accordance with the details of the protocol and/or SOPs if supplies remain

3. Packing up supplies, clearly identifying the contents, and sending them back to the sponsor for disposal if clinical supplies must be returned to the sponsor

4. Disposing of any unused supplies of at the site, the monitor is responsible for disposal in accordance with the details of the SOPs and/or protocol if the SOPs state that any unused supplies should be disposed of at the site

2.3.6 Reconciling records to account for all clinical supplies

At the termination of the study, the monitor is responsible for:

- Ensuring that the drug accountability documentation accounts for all clinical supplies that were shipped to the site—documentation must exist detailing which clinical supplies were given to study subjects and which were returned to the sponsor or disposed of in accordance with the SOPs and/or protocol
- Ensuring that the essential documents are produced and placed in the appropriate repository at the investigator's site and the sponsor's facility

2.4 Streamlining the process of shipping and managing clinical supplies

As detailed earlier, the records and documentation produced in connection with shipping, receipt acknowledgement, storage, handling, and disposition of investigational products are identified in the guidance as essential documents and, as such, must be maintained both by the investigator at the trial site and by the sponsor at its facilities. Many companies have automated systems in place for electronic data capture in connection with the conduct of the study as well as systems for submitting requests for clinical supplies. Adobe technology provides tools to seamlessly automate and integrate multiple systems and processes—reducing the complexity of interfacing with many different systems. Some examples of how Adobe technology can be applied are outlined in the following sections.

2.4.1 Managing and tracking requests for clinical supplies

LiveCycle Process Management ES can be configured to:

- Monitor requests for supplies
- Ensure routing of requests to the appropriate individual for approval
- Route to the appropriate individual or system to fill the request
- Notify the clinical monitor that the request is being processed
- Notify the clinical monitor that the shipment has been sent

LiveCycle Process Management ES, along with LiveCycle ES Connectors for ECM, LiveCycle Forms ES, LiveCycle PDF Generator ES, and LiveCycle Content Services ES can be configured to:

- Interface with the appropriate systems to create the required documentation
- Interface with the appropriate repositories to ensure that the required documentation and metadata are put into the repositories

For more information about LiveCycle Process Management ES, visit *www.adobe.com/products/livecycle*. For detailed specifications concerning this implementation, refer to *www.adobe.com/devnet/livecycle/workflow/articles/lc_workflow_qpac_overview.pdf*.

2.4.2 Virtual site monitoring

Once the workflow has been defined, all the processes described in this guide can be automated by LiveCycle Business Activity Monitoring (BAM) ES to provide a dashboard view of the request from initiation to completion. In addition, implementations can be customized to use other Adobe tools, such as Adobe Flex® Builder™ and Acrobat Connect,™ to provide a rich, interactive platform for process management.

Adobe Flex Builder is an application development tool that can be used to create cross-platform rich internet applications that enable you to:

- View data from the clinical data collection system, such as number of patients randomized
- View data from the clinical supplies system, such as number of clinical supplies available at the study site
- Navigate the data up to and including the activities required to process a request for additional clinical supplies

A Flex application can be implemented across all therapeutic areas for monitoring drug accountability and can be expanded to include additional activities, including:

- Monitoring the repository of essential documents
- Monitoring the ongoing subject recruitment
- Monitoring the subject visits
- Monitoring questions and issues from the site

Another Adobe tool that can be used to streamline site monitoring is Acrobat Connect Professional, which is a rich web application for facilitating communication between geographically dispersed parties. The investigator's site and the clinical monitor can use Acrobat Connect to share documents and data in real time. This enables the monitor to address critical questions as they occur, instead of having the investigator's site compile questions and issues that are then addressed during a scheduled site visit. Such real-time communication over the web can reduce the time it takes to complete the study.

For more details about Adobe Flex and Flex Builder, visit *www.adobe.com/products/flex/productinfo/faq*. For more details about Acrobat Connect Professional, visit *www.adobe.com/products/acrobatconnect*. For more information about Adobe LiveCycle Business Activity Monitoring ES, visit *www.adobe.com/products/livecycle/bam.html*.

Section 3: References

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www.adobe.com/products/acrobatpro

Adobe LiveCycle Reader Extensions
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Adobe LiveCycle Process Management ES
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Enhanced Forms 1571 and 1572
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