HCL

Business Process Management for Life Sciences Industry

Optimizing Clinical Trials
for increasing ROI

WHITE PAPER

Table Of Contents

1 Introduction

Clinical trial supply chains (CTSCs) have historically focused on logistics and compliance, not excellence in execution. There is the clinical side of the business and then the operational side, with an iron curtain in the middle. Not surprisingly, only 23% of 107 pharmaceutical and biotech companies rate their CTSC processes as extremely effective, according to a recent AMR Research study.

Furthermore, a vast majority of companies rated their CTSC processes as under revision or slowly improving, at best. While not the sole driver of lengthy and expensive new product development cycles, inefficient CTSC processes certainly don't speed new drugs to market. Clinical trial supply chains require an infusion of end-to-end design, excellence in operations, and agility in execution.1

In life sciences industry, the accelerated pace of globalization and tighter regulatory regimes are rendering markets more interconnected, dynamic and competitive. In those circumstances organizations are required to make their business processes more integrated, flexible and transparent. Ubiquitous, commercial off-the-shelf enterprise application platforms are proving incapable of delivering the necessary level of business process agility required, thereby driving the demand for Business process management (BPM).

BPM has been a feature of the enterprise technology market for the last three decades. Today, BPM is more pertinent than ever. The global business environment is increasingly dynamic, pushing organizations to evaluate technologies that can help them respond to business challenges. By adopting BPM, enterprises can boost their ability to support key business processes and derive a palpable competitive advantage.2

BPM spans both business and technical domains and caters to a bewildering array of user scenarios. Consequently, BPM requires a finely-tuned go-to-market approach that depends on the choice of market channel, the customer constituency targeted, and enterprise maturity levels and, of course, the target industry. Never the less, BPM implementations have been shown to reduce the cost of application development up to tenfold and significantly lower the cost of process ownership.

HCL has worked with 10 of the top 15 pharmaceutical companies across the globe and has thus come up with a pre defined process to Optimize Clinical Trials for increasing business ROI. With doctors, clinical trial experts, statisticians, regulatory & validation experts, HCL combines domain excellence with IT services to provide business aligned solutions to revitalize Pharma enterprise.

1.1 Terminologies / Abbreviations used in this document

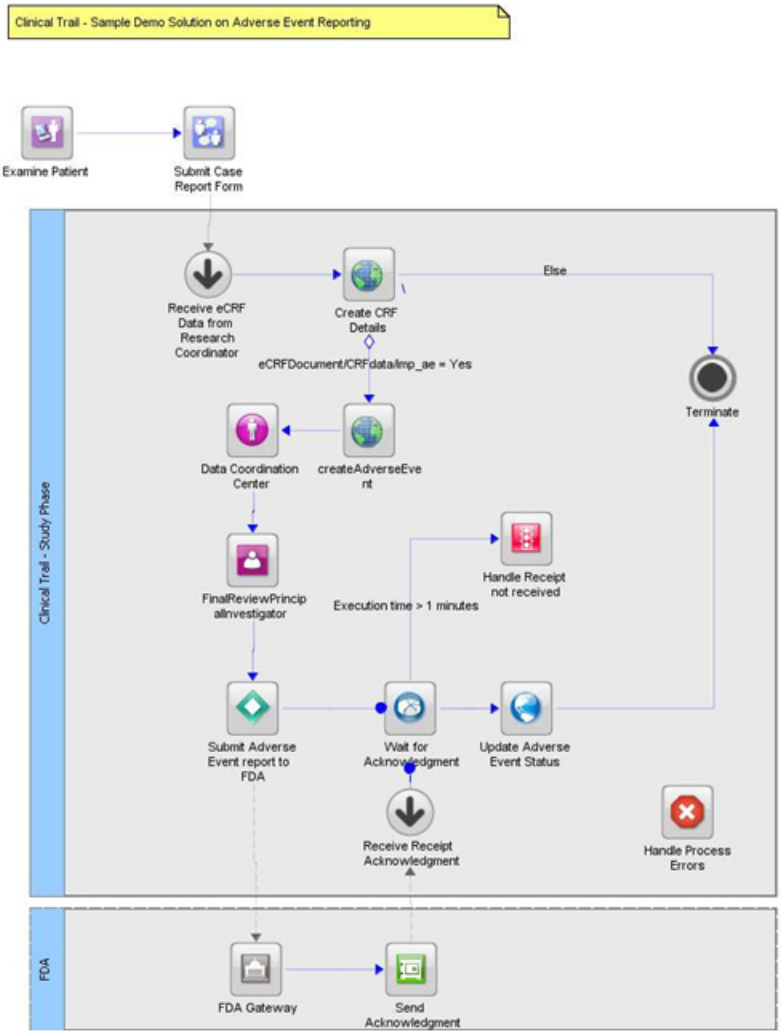
The Clinical Trial process involves complex workflow process involving different entities such as Principal Investigators, Patients, Clinical Project Manager, Clinical Research Associates/ Coordinators, Medical Advisor, Regulatory Officer, Safety Manager, Quality Assurance, Clinical Data Managers, Sites, Clinical Data Management Systems, Adverse Event Management System, Clinical Research Organization, Food and Drug Administration, Case Report Form with information flowing between all these entities and Clinical Research Organization across multiple systems.

Terminologies / Abbreviations	Description
BPM	Business Process Management
BAM	Business Activity Monitoring
B2B	Business-to-Business
Designer	Tool to design the business process
Task Engine	Engine which executes manual tasks
MWS	My webMethods Server, Common authorization for all the webMethods related components
ICSR	Individual Case Safety Report
FDA	Food and Drug Administration

2 Clinical Trial Process Overview

2.1 Process Flow Diagram

Even though products to automate clinical study processes have been available for many years, the market is by no means mature. By some estimates, there are more than 100 vendors that provide products that address some aspect of clinical development. In recent years, traditional products engineered to meet the needs of clinical study sponsors faced competition from newer, Web-based offerings that promised to simplify data entry, financial and study management processes for site investigators. 4 The diagram below depicts the business process flow for a typical Clinical Trial Process. The following code templates will help to understand the Bug Description and Waveform portions better:



2.2 Processing Steps

After understanding the typical process of clinical trials, HCL created a set of automated processes that enable the following steps:

- Investigators at sites examines the patient and Clinical Research Coordinator helps to enters these observations through a web based Case Report Form (CRF).
- If there are any adverse event noticed the overall interpretation is marked as "Abnormal and Clinically Significant" and the information regarding the adverse event is recorded in the web based form under Adverse Event Section.
- On submission of the eCRF information is stored in Clinical Data Management System (CDMS).
- If there is any adverse events following processing steps are carried out
  - Serious Adverse event information is persisted to the Adverse Event Management System.
  - Clinical Research coordinator at the Sites accesses the Adverse event information and check for the completeness and passes on this information to the Principal Investigator for an Final review.(Manual step)
  - The Principal Investigator performs an final review of event and takes necessary action and submits the data.(e.g Patient follow up to verify if the patient is taking up medications to rectify the adverse effects etc) (Manual step)
  - Once reviewed and identified as serious adverse event is sent to the Sponsor/CRO and FDA for regulatory compliance.
  - FDA sends an acknowledgment that the data has been received.
  - The business process then updates the Adverse event management system on the successful processing and reporting of the serious adverse event to FDA
  - In case acknowledgement is not received from FDA within a given period the system will notify the IT support person and terminate the process.
- If there are no serious adverse events the process terminates at this step.

3. Solution Detail

Components used

HCL implemented the above said business process in webMethods 7.1 suite by using the following components.

- webMethods Designer 7.1 – is used to design and configure the business process.
- webMethods Developer 7.1 – is used to implement the business logic
- My webMethods Server 7.1 – is used for BPM, BAM and also for integrating all the webMethods related components
- Task engine 7.1 – is used to execute manual tasks.
- Trading Networks 7.1- is used for integration with the FDA regulator body
- Optimize for Process 7.1 – is used to achieve BAM.

3.1 Prerequisites

- webMethods 7.1 suite with all the above mentioned products of webMethods need to be up and running.
- Custom tables need to be created in database
- Connection between the database and webMethods need to be established.
- Define User specific Roles for CT Investigator and CT Research Associates / Coordinator need to be created in MWS.
- Partner Profile: FDA (Regulatory body) and HCL (Trial Sponsor)what does this mean?

Partner Name	DUNS	Description
FDA	FDA	Food and Drug Authorities Regulatory body to which the Adverse Event data is to submitted
HCL	HCL	Trial Sponsor

Trial Note document Types :

Document Type	Description
ICSR Document	Individual Case Safety Report E2B XML format. The standard format for submitting Adverse event related information to FDA Gateway http://www.fda.gov/cder/aerssub/icsr-xml-v2.0.dtd
ICSR Acknowledgment Documentd	E2B XML Format in which the FDA acknowledges the receipt of ICSR. http://www.fda.gov/cder/aerssub /icsrack-xml--v1.0.dtd
EDIINT	The ICSR XML data is wrapped around EDIINT envelope and submitted to FDA
ICSR	Individual Case Safety Report
FDA	Food and Drug Administration

Processing Rules: The below processing rule is required as part of the simulation to act as FDA in generating the ICSR Acknowledgment.

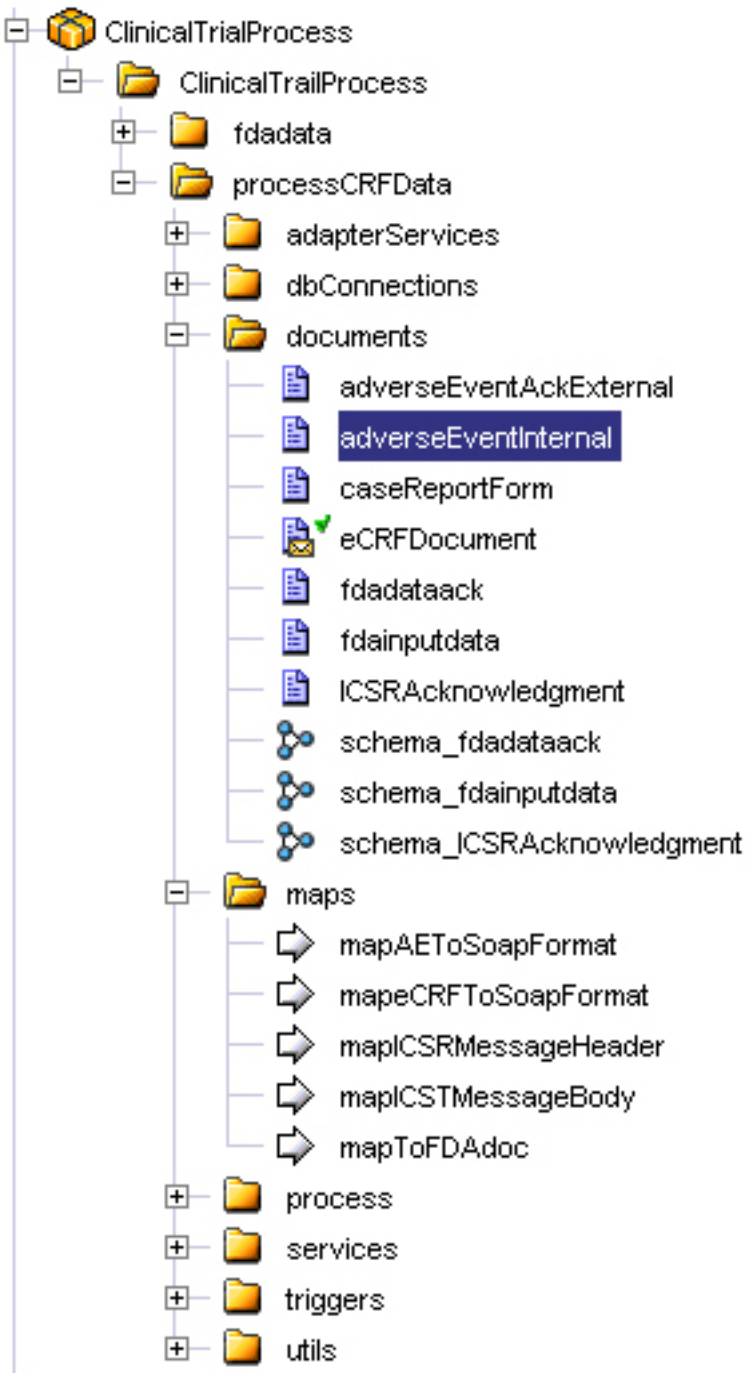
Processing Rule	Description
FDA Simulation	Processing rule to generate ICSR Acknowledgment when for ICSR Document type is submitted to TN. This will enact the role of FDA is generating the acknowledgements.

3.2 Package Structure

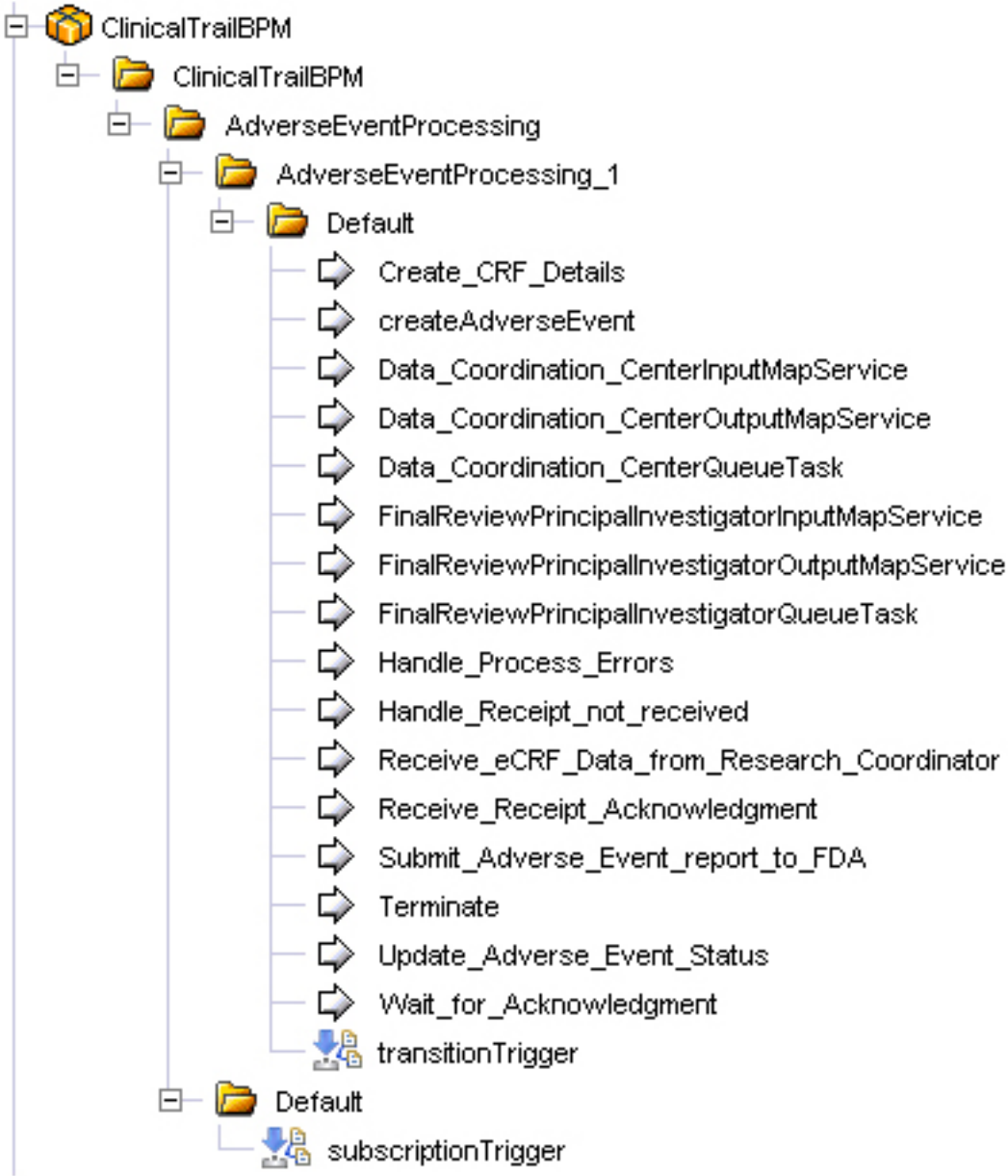
This section provides details related to the Package name and the structure of the folders with the package.

Following packages are utilized for implementing the business process.

- Clinical Trail Process
  - Contains the adapter connections, adapter services, document types, Web services and common services that are used to achieve the functionality


ClinicalTrialProcess
ClinicalTrailProcess
fdadata
processCRFData
adapterServices
dbConnections
documents
adverseEventAckExternal
adverseEventInternal
caseReportForm
eCRFDocument
fdadataack
fdainputdata
ICSRAcknowledgment
schema_fdadataack
schema_fdainputdata
schema_ICSRAcknowledgment
maps
mapAEToSoapFormat
mapeCRFToSoapFormat
mapICSRMessageHeader
mapICSTMessageBody
mapToFDAdoc
process
services
triggers
utils

- ClinicalTrailBPM
  - Contains the flow services related to Business Process



- HCLCaseStudyDemoUtil
  - Contains utility services that helps in web services invocation

3.3 Implementation Steps

The Clinical trail business process has been designed and orchestrated using Web services, Human Tasks implemented in Task engine, Trading networks and the integration server flow service.

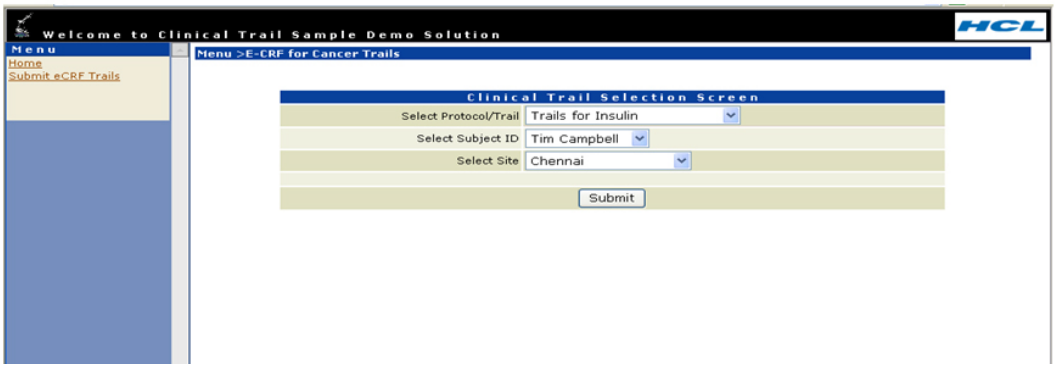
Following table provides the mapping of the functionality in the Business process to the implementation component and the consumer.

Functionality	Consumer/ User	Implementation Component	Description
eCRF submission form	Research Coordinator	DSP pages	A custom set of DSP pages have been created that can be utilized by the Clinical Research Coordinator to enter the Case Report Form information, It can be accessed through
Creating CRF details in CDMS System	webMethods Business process	Web Service	The interface to the CDMS system has implemented using JDBC adapter and exposed as a web service to the consumer.
Creating Adverse Event in AEMS	webMethods Business process	Web Service	The interface to the AEMS system has implemented using JDBC adapter and exposed as a web service to the consumer
Project Coordinator Manual Tasks of accessing Adverse events	Project Coordinator	Task Type (Access Adverse Event Data Center Coordination)	Implemented as Task in Task engine.
Final Review of Adverse Event by Principal	Principal Investigator	Task Type (Final Review ByPrincipal Investigator)	Implemented as Task in Task Investigator engine.
E2B XML data submission to FDA	webMethods Business process	Trading Networks	Implemented using the Trading network components and flow services

Processing Steps

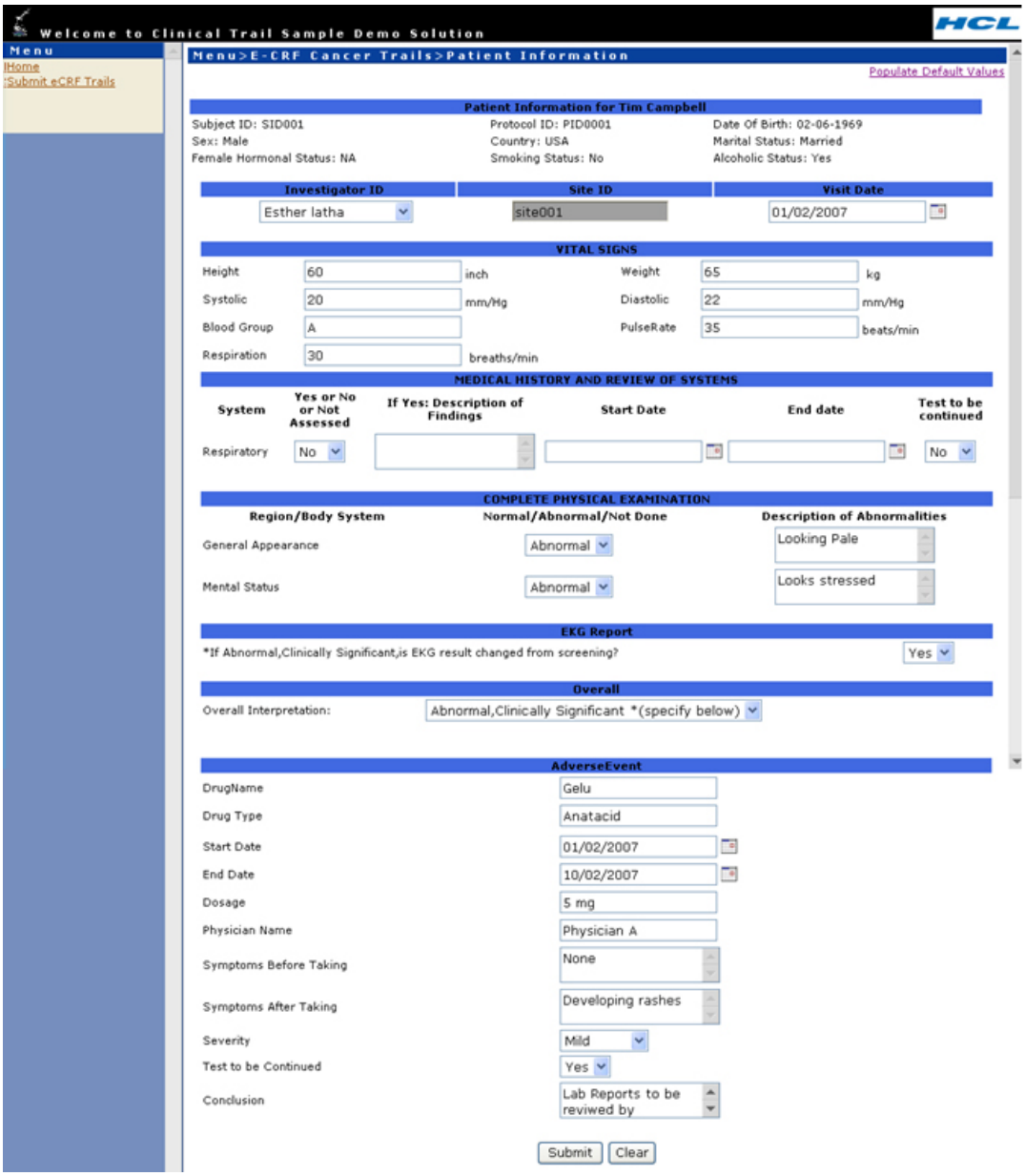
- A custom set of DSP pages have been created that can be utilized by the Clinical Research Coordinator to enter the Case Report Form information, It can be accessed through http://<server>:<port>/ClinicalTrialProcess/

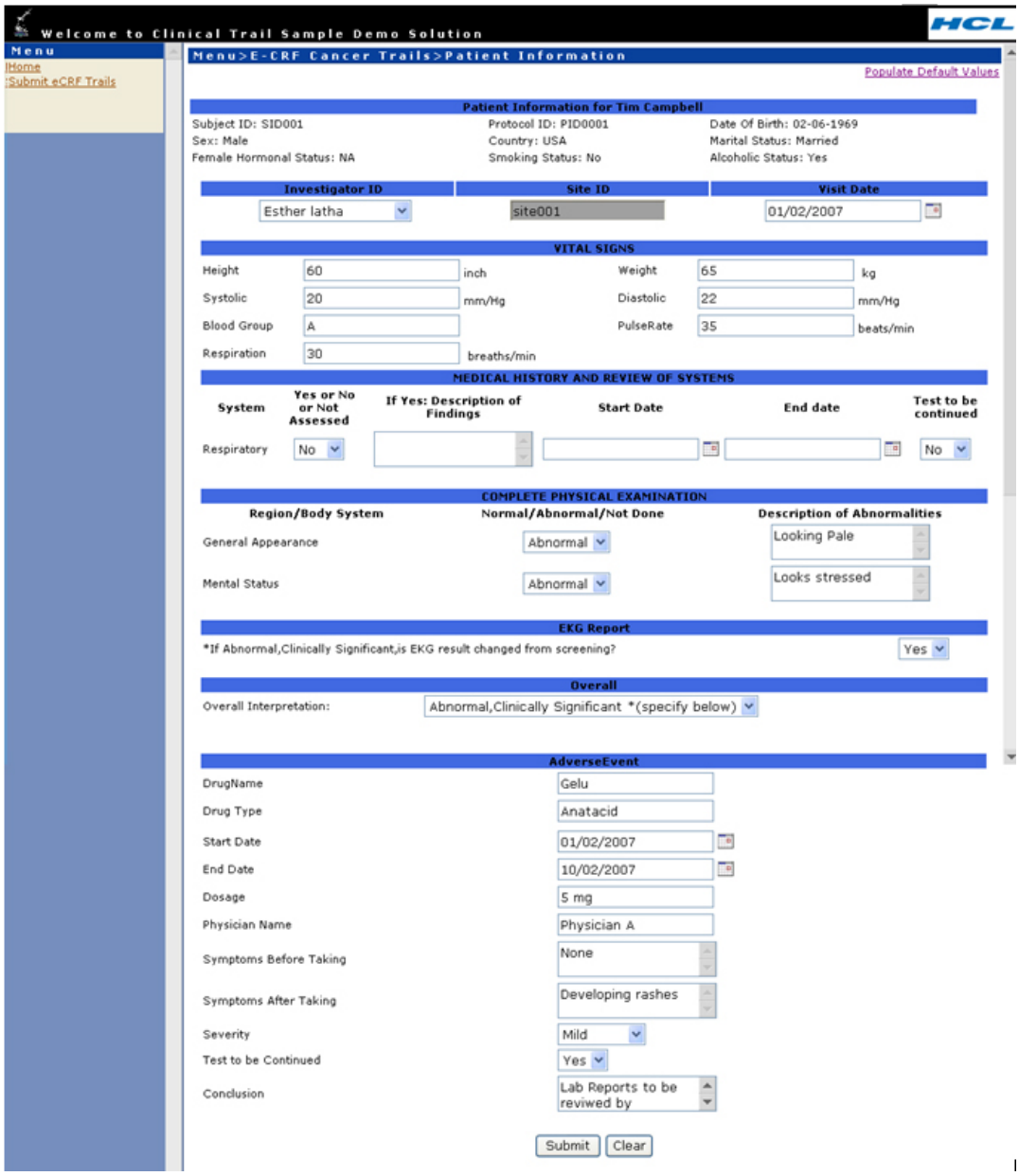
✍ Research Coordinator clicks on the 'Submit eCRF Trials' the web application displays Clinical Trail Selection screen for the user to select the Trail, Subject and the Investigation Site for which the eCRF requires to be submitted.



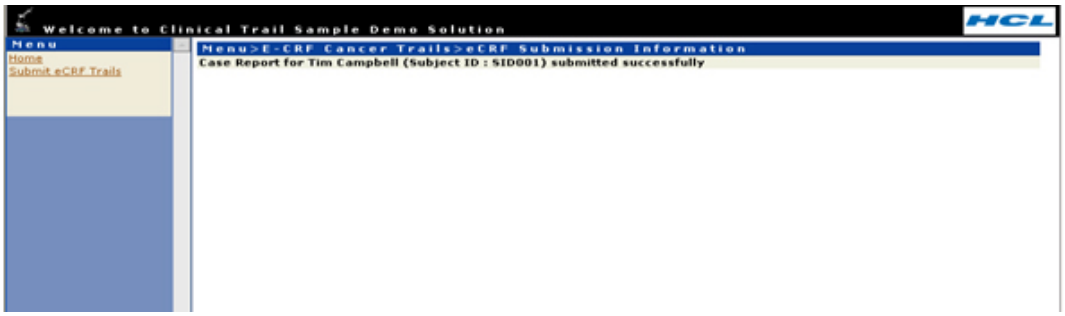
✍ On submission of the Trail, Subject and the Site the eCRF form is loaded and the page displays the information regarding the patient from the CDMS Patient table as shown below. The Research Coordinator fill in the patient examination details and submits the form.

Note : The Adverse event section of the form is displayed only when the Overall Interpretation field has an selection of "Abnormally Clinically Significant *(specify below). For all other user selection the adverse event section is hidden.

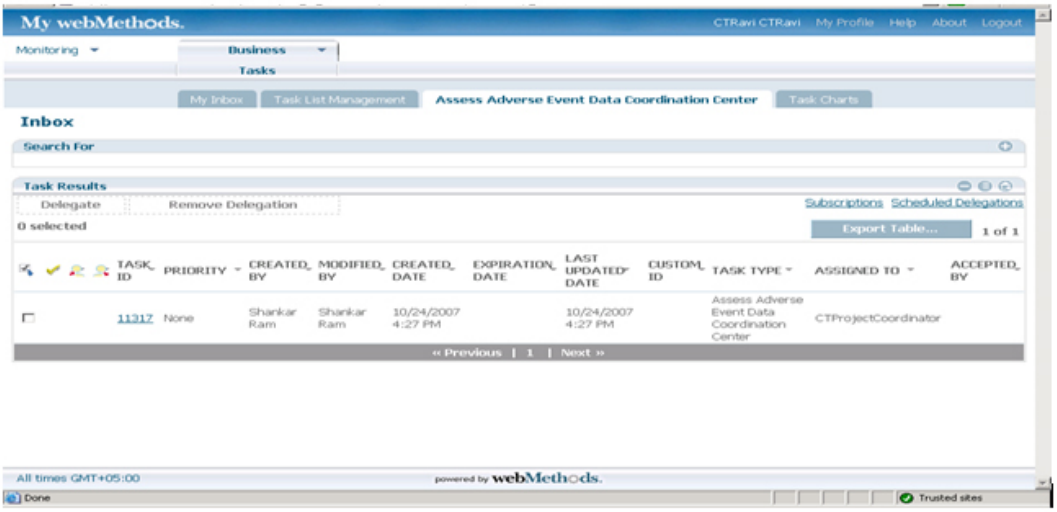

Welcome to Clinical Trail Sample Demo Solution
HCL
Menu
Home
Submit eCRF Trails
Menu>E-CRF Cancer Trails>Patient Information
Populate Default Values
Patient Information for Tim Campbell
Subject ID: SID001
Protocol ID: PID0001
Date Of Birth: 02-06-1969
Sex: Male
Country: USA
Marital Status: Married
Female Hormonal Status: NA
Smoking Status: No
Alcoholic Status: Yes
Investigator ID
Site ID
Visit Date
Esther latha
site001
01/02/2007
VITAL SIGNS
Height
60
inch
Weight
65
kg
Systolic
20
mm/Hg
Diastolic
22
mm/Hg
Blood Group
A
PulseRate
35
beats/min
Respiration
30
breaths/min
MEDICAL HISTORY AND REVIEW OF SYSTEMS
System
Yes or No or Not Assessed
If Yes: Description of Findings
Start Date
End date
Test to be continued
Respiratory
No
No
COMPLETE PHYSICAL EXAMINATION
Region/Body System
Normal/Abnormal/Not Done
Description of Abnormalities
General Appearance
Abnormal
Looking Pale
Mental Status
Abnormal
Looks stressed
EKG Report
*If Abnormal,Clinically Significant,is EKG result changed from screening?
Yes
Overall
Overall Interpretation:
Abnormal,Clinically Significant *(specify below)
AdverseEvent
DrugName
Gelu
Drug Type
Anatacid
Start Date
01/02/2007
End Date
10/02/2007
Dosage
5 mg
Physician Name
Physician A
Symptoms Before Taking
None
Symptoms After Taking
Developing rashes
Severity
Mild
Test to be Continued
Yes
Conclusion
Lab Reports to be reviwed by
Submit
Clear



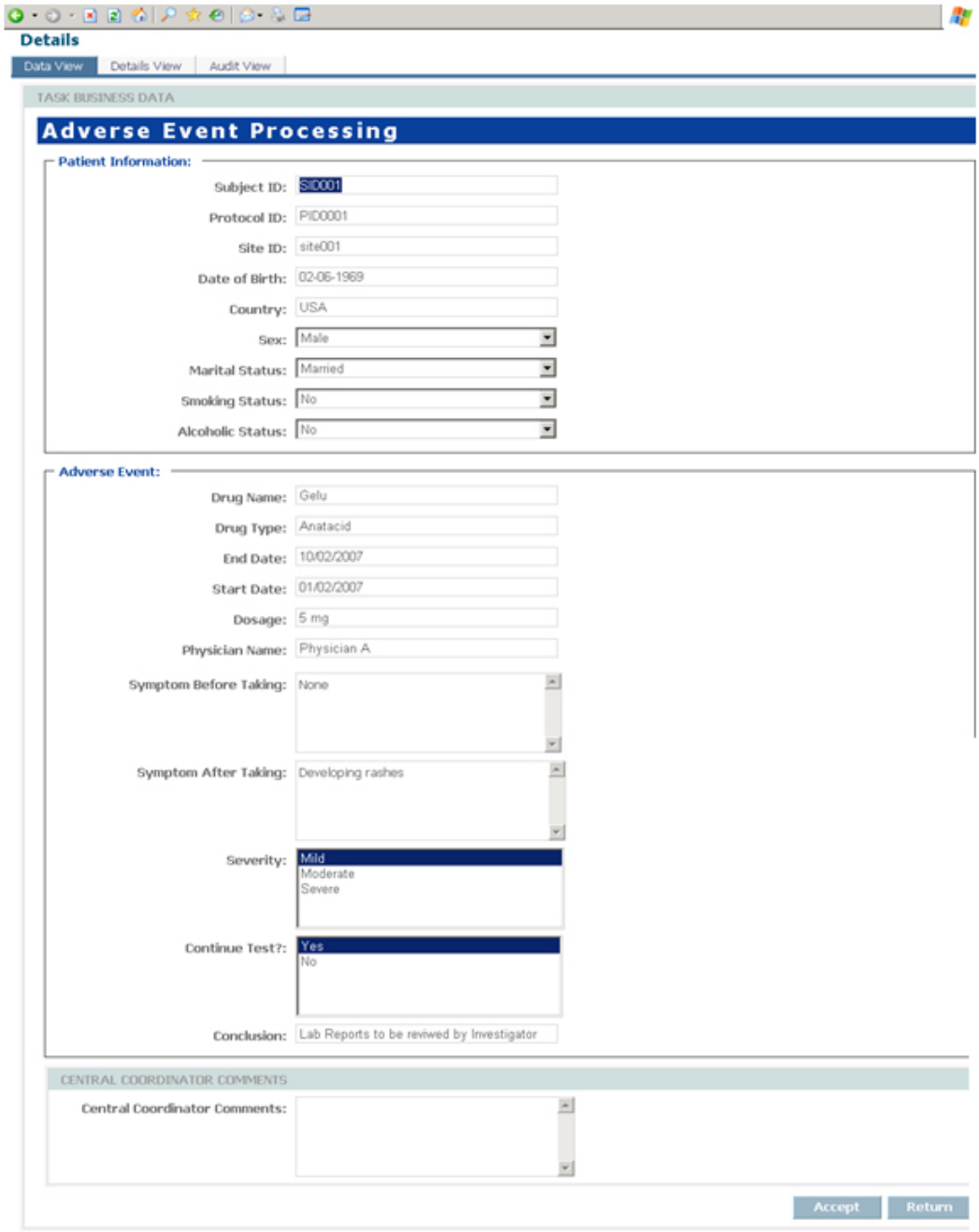
- Once the CRF data is submitted the web application acknowledges the successful submission. The receiveCRF flow service receives the submitted data maps to the eCRF Canonical document format and publishes it to the Broker. eCRF Canonical document is the entry level event for the Business process and is used to initiate the AdverseEventProcessing business process instance.



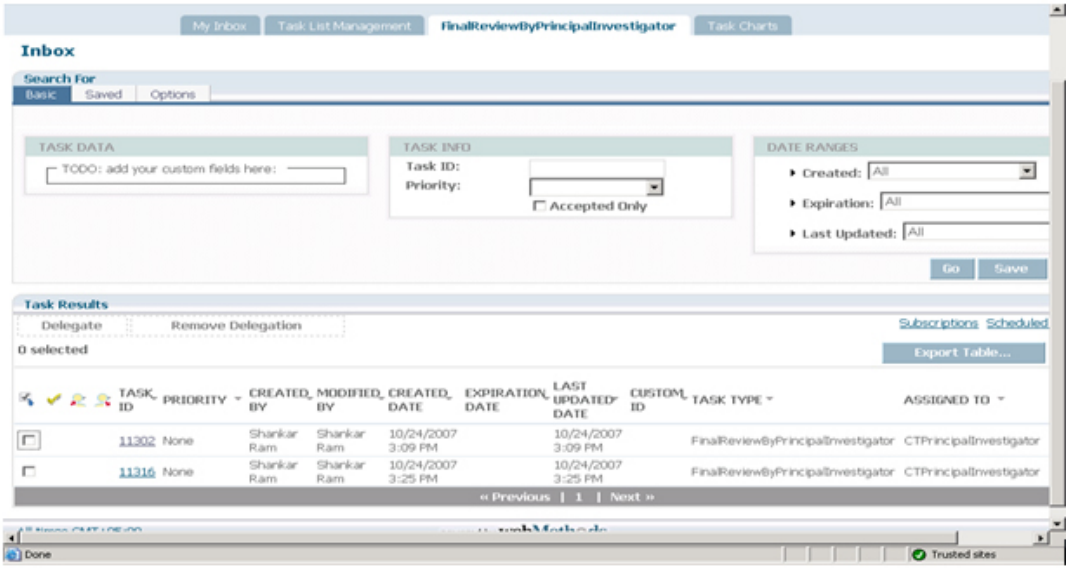
- Business process AdverseEventProcessing performs the following steps
  - Receives/Subscribes to the eCRF document and invokes the createCRFDetails webservice to populate the CRF details into the CDM system.
  - If the CRF data has an Adverse event the Business process performs the following operation
    - Invokes the createAdverseEvent Web Service to populate the Adverse event information into the AEMS
    - Creates a task for the Project Coordinator Inbox to access the adverse event. Project Coordinator logs into myWebMethods portal and access the "Assess Adverse Event Data Coordination Center" Task Inbox as shown below.



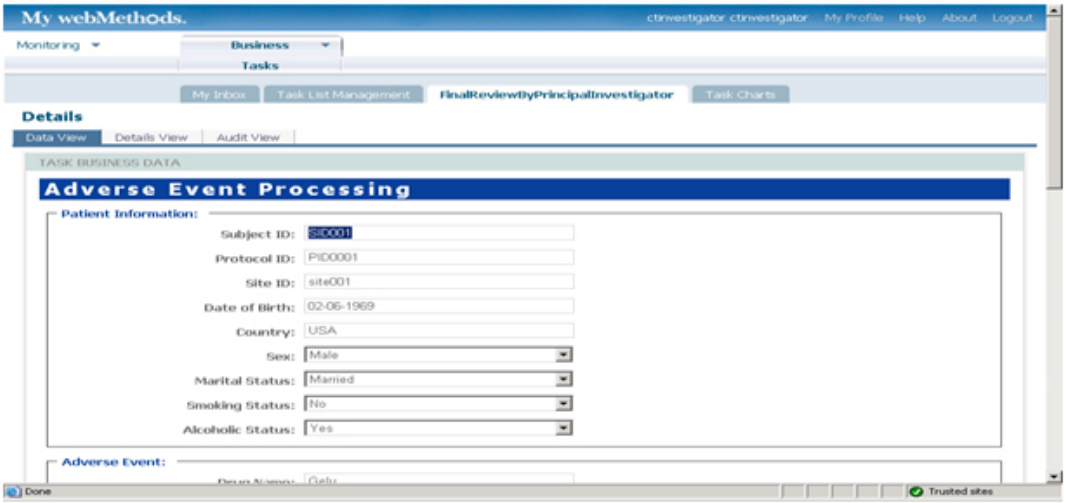
- Project Coordinator clicks on a particular task to view the Adverse Event details. The user fill in the Central Coordinator section with any comments relating to the Adverse event and clicks on Complete to submit his assessment.



- On completion of the assessment by Project Coordinator the Business process queues the Adverse Event task to the Principal Investigator inbox for Final review. Principal Investigator logs into myWebMethods portal and access the "FinalReviewByPrincipalInvestigator" Task Inbox as shown below.



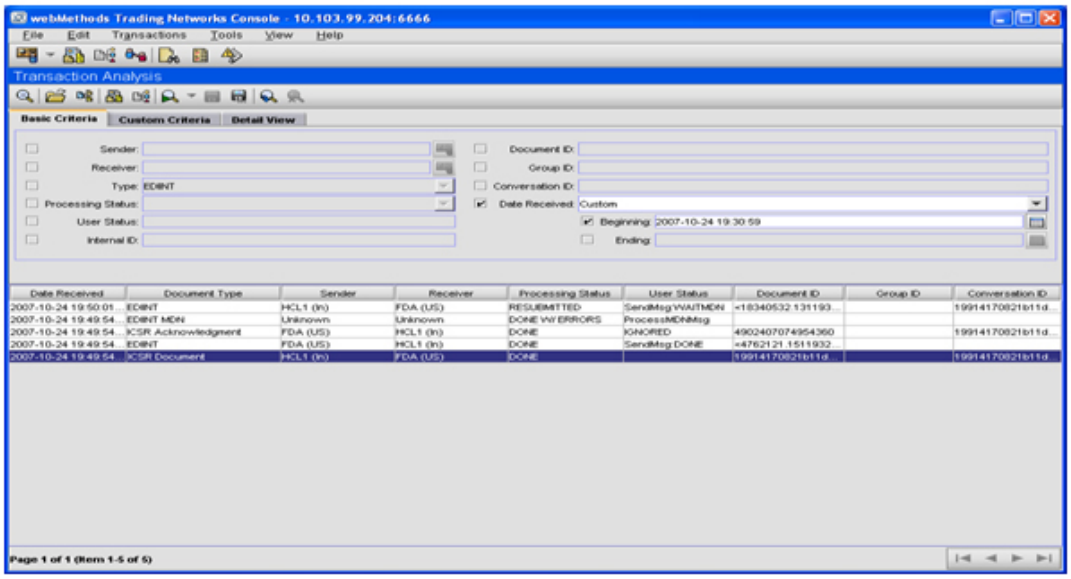
- Principal Investigator clicks on a particular task to view the Adverse Event details. The user fill in the Principal Investigator section with any comments relating to the Adverse event and clicks on Complete to submit his review.

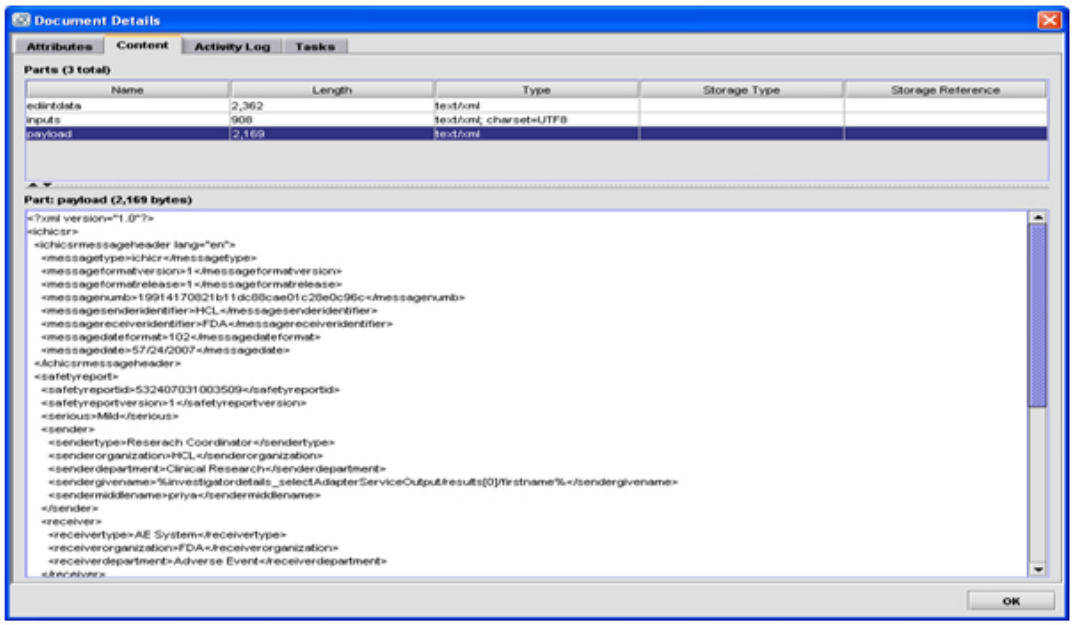


- Once the Principal Investigator completes the final review the, business process invokes the flow service to translate the Adverse Event data to E2B ICSR XML format and submit the data to FDA.
- The flow service translates the adverse event to ICSR xml format, wraps it as a payload in EDIINT and submits the data to TN for deliver the data using the Preferred Delivery method (Primary HTTP).

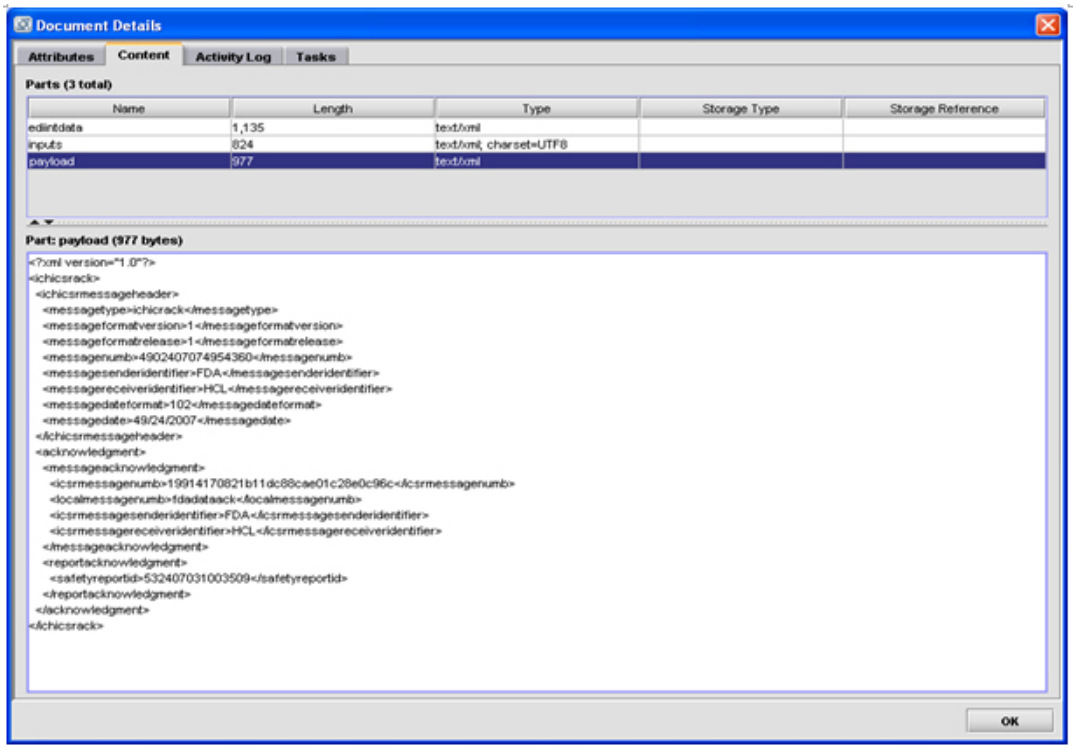
Note: The data is submitted to TN and the FDA is simulated using a flow service and processing rules on ICSR xml document to generate the acknowledgment

- ICSR XML wrapped with in EDIINT message submitted to FDA is shown below





- The Business process waits for the ICSR acknowledgement from FDA. ICSR Acknowledgment received in EDIINT from FDA is shown below



- Once the acknowledgement is received, in AEMS the status will be updated as Acknowledgment Received and the process is completed.
- In case the acknowledgment is not received within 1 minute of the submission the step times out and the error is handled.

3.4 Assumptions and Out of Scope

- The business process implemented is miniature process of actual adverse event processing. It does not take into consideration the other system such as LIMS (Lab Information management system) and the other entities (e.g other regulatory bodies)
- It is assumed that only one adverse event will be entered by the Research coordinator to keep this demo simple.
- It is assumed that there are only two levels of review of adverse event "Data Coordination Center" and "FinalReviewPrincipalInvestigator" to keep this demo simple and this may vary for different companies.
- Application Logging - Logging is done for each and every individual step at the process level and it can be tracked and monitored in my webmethods server.

4. Conclusion

Between now and 2010, the number of companies conducting more than 15 Phase 2 or Phase 3 clinical trials annually will increase by 40% or more, according to a recent AMR Research study. Increasingly, these trials will be conducted thousands of miles away from their traditional locations, with the percentage of clinical trials conducted in North America and Western Europe dropping from 55% to 38% as more clinical trials is conducted in India, China, the Middle East, Africa, and Eastern Europe.

In the future, the degree of CTM outsourcing will increase, with the focus shifting to services such as demand forecast planning. These services are more specialized than the CTM processes outsourced today, and therefore require a higher degree of talent and support from outsourcing partners. At the same time, companies must map architectures required to extend their infrastructures, business processes, and information visibility to contract manufacturers and service providers.3

The solution developed by HCL has enabled many leading Pharma companies to optimize their clinical trial throughput and thus enabled faster time to market. The solution also enables companies to design CTM processes from inside-out to ensure efficient and cost-effective clinical trial execution. The whole process thus gets balanced with focus on speed and cost effectiveness. Companies with more mature CTM processes can then measure and report assessment metrics, such as demand forecast accuracy, perfect order achievement, and supply chain costs.

5. References

- Clinical Trial Supply Chains: A Look Ahead, May 12, 2008 by Wayne McDonnell, Hussain Mooraj, AMR Research
- Business Process Management: Global Trends to 2013 (Strategic Focus), September 2008, Datamonitor
- Clinical Trials Are Moving Out, May 13, 2008 by Wayne McDonnell, Hussain Mooraj, AMR Research
- Clinical Study Automation and Management Application Market Definition, 2007 by Carol Rozwell, Gartner