X Corp APP System Validation Plan

Version 0.03

05-Dec-2004

Prepared By:

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System Validation Plan Approval

Signatures indicate agreement that this document meets its stated objectives and has been reviewed and approved by the signatories.

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Business Owner:

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Project Manager:

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Quality Assurance:

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1.0 Overview

This document provides the System Validation Plan for the X Corp APP System. The X Corp APP System is to be validated and used at X Corp Clinical Research and Drug Development Division for the analysis of clinical and other research data in the preparation of reports for submission to the FDA, for preparation of external publications, and for internal research and development. This document describes the validation approach, activities, responsibilities, and documentation necessary for the implementation of the X Corp APP System as described in the X Corp APP System Requirements Specification.

This document first provides a brief system description. Next is provided an outline of the validation approach, validation activities and associated documentation, and individual and company responsibilities necessary to ensure that the system is implemented and maintained as a validated system. The risk-based assement methodology to be used in the project is descrived in Appendix A of this document. The model presented there will serve as a analytic tool throughout the validation process.

At the conclusion of the activities outlined in this document a Validation Summary Report will be prepared. The Validation Summary Report will include the results of the plan given in this document, any deviations from expectations with description of the resolution, and references to supporting documentation.

2.0 System Description

The X Corp APP System is comprised of two components, the APP Server and the Client Workstations. The APP Server System is itself comprised of a number of component nodes, called "blades" which are to be used as a coherent dedicated resource. The Client Workstations will enable users to interact with applications hosted on the APP Server, securely transfer data and program files, and submit these items for analysis to applications hosted on the APP Server. The APP Server portion of this project is considered a closed system: access to the APP Server is limited to specific users autheticated as originating from specific Client Workstations. System-level (root) access will be restricted to specific individual X Corp Information Technology users needing access to the APP system for administrative purposes. The X Corp APP System is to be developed and maintained as a validated system, which will be installed and validated in accordance with the Risk-Based methodology employed (See Appendix A.).

The system Client Workstations are regarded as open systems, and will be installed and validated to a degree in accordance with the Risk-Based Assessment to be presented in Appendix A of this document.

2.1 Hardware and System Software

The APP Server System is comprised of a number of compute nodes, each of which is a commercially available "blade" component running the same single version of the operating system. The APP Server is a host-centric system, which includes a distributed file system and the requisite file-server software. The APP Server allows authenticated and secure connections with individual Client Workstations known to the system by a dedicated network address. Individual APP System users will

be restricted to using known, validated Client Workstations. All components of the APP Server will be located in the Computer Center of the X Corp Information Technology Department, located at 100 Lakeshore drive, Windwing Lake, Wisconsin. Client Workstations shall be located in facilities of X Corp Clinical Research and Drug Development Division located at 1 Research Park, Greatbury, Massachusetts.

2.2 Validation Scope

The sole business group to use the X Corp APP System is the Statistical Analysis and Programming Department of the Clinical Research and Drug Development Division located at 1 Research Park, Greatbury, Massachusetts.

"R" is the primary tool and programming language for data modelling and statistical analysis to be used on the X Corp APP Server System. We will validate the accuracy and suitability of the X Corp APP System implementation of R for production use as employed for data analysis, modeling and reporting purposes. In addition we will validate the installation of Client Workstations for their intended use.

Customized "glue" software used to make the multiple compute nodes of the APP Server work together to appear as a single server will be validated as an integral part of this validation.

Installation Qualification proceedures will include the testing of the component hardware, system software, application software and APP Server-to-Client Workstations communications. System software for the X Corp APP System will be qualified and tested for specific funtionality to a degree in accordance with the Risk-Based Assessment to be presented in Section 2.3 of this document.

Operational Qualification will demonstrate that the APP Server and Client Workstations function as expected, and that system applications produce the expected results.

Production Qualification demonstrates the functionality and acceptability for use of the X Corp APP System under typical daily usage conditions.

3.0 Definitions

Attribution of Data, The ability to trace data to individuals responsible for recording the data.

APP System, The interacting set of components described in the System Description section of this document.

Application, Software to be used directly by the business user, readily available as a named entity from a known source.

Business User, User of the APP System other than a System Administrator.

Custom Software, In-house developed or sponsored software that is created to fulfill business needs or system functions that are not fully met by features in available application software.

Installation Qualification (IQ), Demonstration that all important factors of the hardware and software installation adhere to supplier specifications and design parameters.

Operational Qualification (OQ), Functional Testing: Demonstration that components and

subsystems of assembled hardware equipment and software execute as expected with typical and atypical test operating data.

Production Qualification (PQ), Demonstration that the system performs properly, using production data and processes.

Production, Business use.

Requirements Traceability Matrix, A table that maps the elements of the Requirements Specification to their satisfaction by the Design Specification, Installation Qualification, Operational Qualification, and Production Qualification.

Risk-Based Assessment, Use of risk-analysis for prioritization of system requirements, assessment of design alternatives, determination of testing activities, and analysis of defect remediation and acceptance measures.

SDLC, System Development Lifecycle, the model used in this project as a framework for establishing the phases and content of system validation.

System Administrator, User having the responsibility and system-based authority for establishing and maintaining system users and monitoring the functioning of the X Corp APP System.

User, Individual carrying out any task on the X Corp APP System.

4.0 Responsibilities

4.1 Project Personnel

M. Chimmney, Director of Statistical Research,Business Owner. Provides business support for this project, input for Requirements Specification, reviews and approves all project-related documents. Responsible for issuing the System Acceptance/Release Memo.

Jon B. Dunn, X Corp. Manager, Statistical Analytics, Project Manager. Responsible for system design and project planning. Authors and reviews project documentation**.**

Frank Milkowski, X Corp, **IT Technical Manager**. Responsible for hardware/software system implementation, authoring and compilation of validation documents.

Tracy Jones-Smith, X Corp, **Technical Manager, Bioinformics**. Responsible for system business integration, authoring and compilation of validation documents.

Joan Hulldite, **X Corp, Quality Assurance Associate.** Regulatory representative for the project. Reviews and approves all project documents and provides regulatory guidance for implementing the system as a validated system. Assists in the execution of system validation and document preparation.

Millford Whiltorf, **X Corp. Project Administrator.** Attends all project meetings, responsible for meeting minutes. Compiles and maintains all project documents.

4.2 Qualifications

A copy of project personnel *Curricula vitae* as of the date of signing will be maintained with the validation documentation.

4.3 Validation Deliverables

One purpose of validation is to provide documented evidence that the system has been implemented properly: ie., implemented to meet all requirements defined in the Requirements Specification according to predefined validation procedures. The Project Administrator will maintain the signed deliverables during the course of the project. Upon completion of the project, all deliverables will be compiled as a formal Validation Package and will be appropriately archived at ...

A validation package will be completed at the conclusion of the validation effort, and will include the following documents:

- X Corp APP System Validation Plan
- X Corp APP System Requirements Specification
- X Corp APP System Design Specification
- X Corp APP System Client Workstation Installation Qualification Protocol
- X Corp APP System Server Installation Qualification Protocol
- X Corp APP System Operational Qualification Protocol (OQ)
- X Corp APP System Production Qualification Protocol (PQ)
- X Corp APP System Installation Qualification Summary Report
- X Corp APP System Operational Qualification Summary Report
- X Corp APP System Production Qualification Summary Report
- X Corp APP System Validation Summary Report
- X Corp APP System User Training Plan (including plan and materials)
- X Corp APP System Acceptance/Release Memo

5.0 Validation Activities

In order to comply with applicable FDA regulations and to prepare the X Corp APP System for production use, the validation will be carried out as a phased project modeled on a System Development Lifecycle (SDLC). There are four phases aimed toward system implementation: Development, Testing, Acceptance, and Production. A fifth phase, Retirement, brings the system out of production at some time to be decided by business management.

5.1 Development

The Development phase of the project encompasses and documents the following activities: the project System Requirements, Design Specification and Validation Plan.

5.1.1 System Requirements Specification

A System Requirements definition process produces the X Corp APP System Requirements Specification, which describes the features and characteristics of the proposed system seen as needed to satisfy the business need. The System Requirements Specification document is to be used as the basis for the system design and the development of the qualifications protocols (see below).

Hardware and software performance requirements shall be specified only as directly related to the system requirements. The System Requirements Specification will include software interface requirements (input and output), system business functions, system user roles, and security considerations. Each system requirement will be identified with a unique reference number (RID). RIDs will be tabulated to form the template Requirements Traceability Matrix, to be included as an appendix to the System Requirements Specification.

5.1.2 Design Specification

A System Design Specification will be produced to describe how the system will be constructed, configured, and installed to meet user performance and interface requirements, and to document any additional configuration or functional specifications required to support system operations (i.e., network response latency, security mechanisms, data backup parameters, etc.).

A security model shall be developed to serve as a blueprint for the security strategy and as the basis for implementation of security mechanisms.

Each system design feature should map to one or more RIDs documented in the Requirements Traceability Matrix.

5.1.3 Validation Plan

The X Corp APP System Validation Plan (this document) is developed to inform and guide all project and validation activities for implementation of the X Corp APP System. Any significant deviations from this plan during the course of the project that are not appropriately encompassed by the System Design Specifications, Installation Qualification, Operational Qualification, and Production Qualification will need to be recorded as an ammendment to this document.

5.2 Testing

Validation testing is comprised of three related activities: Installation Qualification, Operational Qualification, and Production Qualification. Each of these testing activities has a different focus in order to confirm that the system fully performs its required functions.

5.2.1 Installation Qualification (IQ)

The IQ demonstrates that the hardware, software, and configuration parameters associated with the assembly of the X Corp APP System components have been installed and configured properly, according to the Design Specification. Installation Qualification Protocol "IQ Action Cases" describe in detail how the IQ will be carried out for system components.

5.2.2 Operational Qualification (OQ)

The OQ tests the functionality of specific features of components in the system against the System Requirements. The OQ will establish that hardware and software components, interfaces and applications provided by the system are capable of consistently operating within the documented technical specifications and business requirements, producing the expected results.

The Operational Qualification Protocol shall specifiy how operational testing is to be be carried out. Detail of test case selection, testing methods, and deviation resolution will be layed-out in the OQ protocol. "OQ Test Cases" will describe in detail how the specific tests are to be carried out.

It may be possible to carry out Operational Qualification of certain components of the X Corp App System before other components of the system are fully Installation Qualified.

5.2.3 Production Qualification (PQ)

The Production Qualification phase commences after successful completion and sign-off of the Operational Qualification phase. The PQ will establish that the assembled X Corp APP System performs as documented and expected using typical production data and processes, prior to release of the system into production. Details of testing methodology will be presented in the PQ protocol.

5.2.4 Deviation Procedures

A deviation is defined as any instance where the observed and recorded result does not match the specified expected results. Examples of deviations could include an error or inconsistency in the test script, an application malfunction, or, an error or omission made by the tester during the execution of the test script. In the event a deviation is detected the problem must be documented, reviewed, analyzed and resolved. Detailed procedures for handling deviations will be provided in the Installation Qualification Protocol, the Operational Qualification Protocol and the Production Qualification Protocol. Resolution of all deviations will be tabulated in the Summary Report. In general the following proccess is followed in order to resolve deviations:

- Pertinent information is captured in writing on the Deviation Resolution Tracking Form. (see Appendix A). Any additional information, such as printouts or screen-shots can be attached to the form.

- All information collected is forwarded to the System Owner-authorized person responsible for review of test results.

- The reviewer confirms the status of the error.

- The reviewer proposes a course of action, documents the steps carried out, and passes the necessary information and documentation back to the tester to re-execute the test scripts.

At the successful conclusion of the retest, all documentation, including any documentation from failed testing, is passed to the reviewer for signature.

5.2.5 Validation Summary Report

A Summary Report will be produced to summarize the execution of each the three qualification activities described above. The Installation Qualification Summary Report and the Operational Qualification Summary Report must be reviewed and signed before commencement of Production Qualification testing.

The Validation Summary Report will summarize the results and the completion of all validation (IQ/OQ/PQ) activities according to this plan. It will include a compilation of the resolution of all deviations encountered during qualification testing. Approval of the Validation Summary Report will serve to place the X Corp APP System into production status, but the system will not be used in production until after the issuance of a System Acceptance/Release Memo.

5.3 Acceptance

After the signing of the Validation Summary Report, the System Acceptance/Release Memo should be produced to inform all affected persons of the completion of validation testing and of system availability to support production activities. Approval of the Validation Summary Report serves to place the X Corp APP System into production status, i.e. fit for use. However, the system is not to be used in production until the issuance of a System Acceptance/Release Memo.

The Validation Acceptance/Release memo documents that the X Corp APP System is accepted as a validated system meeting the users' needs and requirements according to specifications. Any deviations encountered during validation shall have been resolved according to deviation resolution procedues and risk-based assessment procedures to be defined as part of the validation process and in accord with company quality policies (see Appendix A).

The Production Phase for the X Corp APP System is entered once the system is released to the production via the System Acceptance/Release Memo.

5.4 Production

During the production phase, the system will be monitored in its operational state. Appropriate measures shall be taken to ensure that the system remains in a validated state during its operational use.

5.4.1 User Training

Only users who have received training will be allowed to log into the X Corp APP System. A Training Plan will be developed in order to detail the specific activities, roles, and responsibilities that require training for the new system. The Training Plan will include all application-level and process-level training necessary for users to utilize the new system in accordance with business goals and Standard Operating Procedures. All training will be documented.

5.4.2 SOPs

Production use of the X Corp APP System will be carried out according to Standard Operating Procedures (SOPs). The necessary SOPs will be in place prior to the release of the system for

production use. SOPs will address the following:

- Training
- Data Backup and Restore
- System Security Administration
- Disaster Recovery
- Change Control
- Problem Reporting and Management

5.5 Retirement

When it has been determined that the capabilities or features of the X Corp APP System are no longer fully adequate for business use, and that a new system should be implemented to perform new and/or existing functions, the X-Corp APP System will be retired from use. The objective of the retirement phase is to eliminate dependence on the system and to provide the orderly disposition for any cGxP-related data resident on the system. A Retirement Plan will be written and executed according to the specific characteristics of the system in place, regulatory requirements and business needs at that time.

6.0 Acceptance Critera

In order for validation of this system to be considered complete, all system requirements must be satisfied, and all required testing and documentation must be complete and accurate. Any deviations encountered during validation must be resolved according to the procedures outlined in this validation plan and in accord with company quality policies.

Appendix A

Risk-Based Assessment Methodology

1.0 Introduction

1.1 Background

Throughout the validation process various points recommend more-or-less formal use of risk assessment. We plan to employ a formal risk-analysis model at various points in the project: for prioritization of system requirements, assessment of design alternatives, determination of testing activities, and analysis of defect remediation and acceptance measures. Specific application of the risk-analysis model will be described in detail where employed.

The following section provides a description of the risk-analysis model which will be used for assessing requirement and design alternatives, testing activities, and acceptance measures carried out during validation and maintanence of the system. The approach employed is a "Top-Down" analysis, so that the risk analysis model presented here can be used throughout the project lifecycle.

1.2 Risk Assessment Documentation

Since many of the decisions and activities carried out during validation are will be based upon a risk-based analysis guided by the model presented here, the documentation of the use of the risk-analysis model during the validation process itself will serve to document the results of risk-based analysis.

2.0 Development of the Risk Model

Risk is seen here as the probability of an unwanted event to occur along with the severity the occurance brings. Using this conception, we find we can construct a graph of two dimensions, *severity* vs *probability*. Using this graph, each point of interest under consideration is ascribed a hypothetical risk-potential as related to consequences of designated severity. For illustration purposes we can consider the illumination source for an operating-room table: the point of intrest may be the replacement schedule for the light element. The risk-potential associated with a poorly designed replacement schedule is high, as the consequences of light-failure may be severe.

However, we further observe that the idea of a risk-potential for a point of interest is actually wider than noted so far. Sudden and infrequent disasters are often seen as different from gradual or far-removed influences, although each can result in hazardous failures with serious consequences.

The idea of "disaster" encompasses such things as sudden or uncontrollable natural events (such as earthquakes, storms, etc.), and semi-random, unforseeable human events (such as an electric-power company power blackout). Events in this arena of risk-potential are by definition difficult to control. For instance, a good light-element replacement schedule would have little to no effect on the ability to retain well-lit conditions in an operating room upon the occurance of an earthquake. The other area of risk-potential encompases various unwanted events which are common and predictable, (such as rust or mechanical wear) but are relatively easily controlled.

The essential difference between the first arena of risk-potential and the second is proximity of cause: events proximal to an adverse consequence are sudden, direct, and offer few points of control. Events that are more distial to a hazard are cumulative or slow-acting, and provide opportunities for systematic intervention. We view the two "areas" of risk descibed above as a continuous gradient,

and note that the causal proximity of an event prior to an adverse consequence can be distinguished from the probability of the occurance of the adverse event itself. Thus we find it useful, in the definition of a risk-analysis model, to divide the notion of Risk into three dimensions: “likelyhood” (the probability of an unwanted event), “proximity” (how many steps from the point of interest to occurance of a specified unwanted event), and “severity” (seriousness of the unwanted event).

The risk-analysis method used in the course of this project shall consist of two mappings which will then be combined: “severity vs likelyhood”, and “proximity vs likelyhood”. Since the likelyhood axis of the two mappings (graphs) is shared in common, placing the point of analytical interest on each of the two graphs and assessing the two graphs together will constitue a portion of our application of risk-analysis for that point of interest.

3.0 Application of the Risk Model

The acceptance of data derived from clinical trials forms the basis for FDA decisions regarding the safety and effectiveness of drugs meant for humans. Because these data have such broad and direct public health significance, the risk associated with use of these data is deemed to warrant measures to ensure that the data are “of the highest quality and integrity”(ref). Because the severity of risk assocated with failure of data correctness or integrity of data can be high, application of our analysis model in risk assessment must serve to minimize the likelyhood of corrupt data or failure of data integrity.

We plan to use risk-analysis at various points in validation for for prioritization of system requirements, assessment of design alternatives, determination of testing activities, and analysis of defect remediation and acceptance measures. System design should make use of risk assessment at various critical design points. During testing, any deviation between actual results obtained during testing and expected results for that operation must be resolved in some way. Deviation resolution may entail a risk assessment, especially in those cases where the resolution of particular error cases or deviations is not simple or obvious, or in those cases where remediation procedures are not well anticipated in the validation documents. Specification of the scope for descrepancy resolution or remediation activities, and the subsequent acceptance of these measures may be informed by subsequent additional risk-analysis; the specific procedures are to be described in the respective validation documents.

Appendix B

Deviation Resolution Tracking Form

APP System

Test Script ID/Test Number		**Test Step**	

Description of Deviation

Tester Signature	Date

Reviewer Comments

Reviewer's Signature	Date

Resolution Comments

Reviewer's Signature	Date