PhUSE 2007

Paper RA06

MDMAP (Meta Data Management and Publishing) An application utilized in the management of clinical trial metadata

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ABSTRACT

The primary goal of the MDMAP (Meta Data Management and Publishing) application is the standardization and automation of the processes that Biostatistics used worldwide to capture, manage and maintain the clinical trial metadata when producing an electronic submission.

INTRODUCTION

After extensive development and validation, MDMAP was deployed to the users worldwide. This application, developed in SAS/IntrNet® and the J2EE® framework, has centralized the activity of collecting and managing clinical trial metadata. MDMAP implements a robust, scalable and secure enterprise solution that gives users complete functionality as they maintain and support their clinical metadata.

This paper will focus on the complex user requirements placed on the development team, and the improvements made since the launching of the application in order to follow the new recommendations and to make more user friendly the interface.

WHAT IS AN ELECTRONIC SUBMISSION?

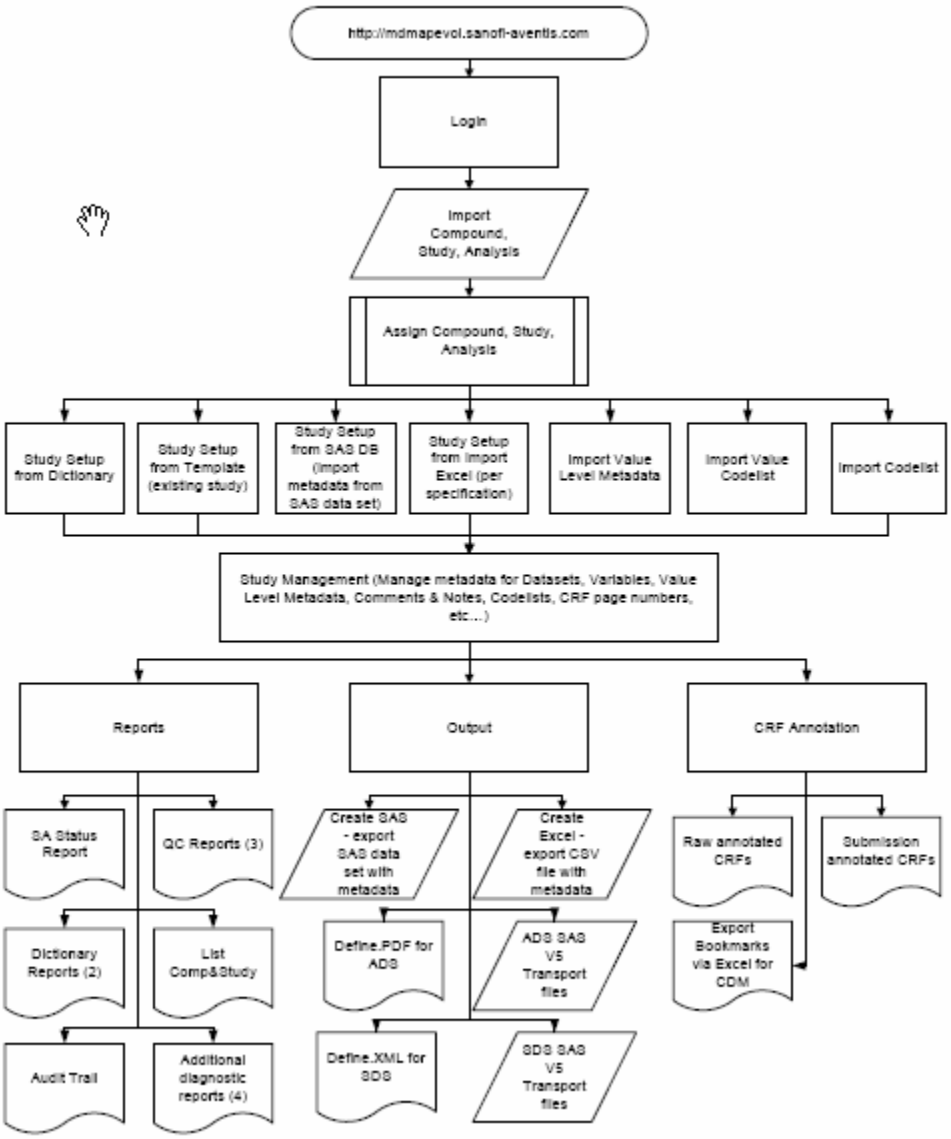
For those unfamiliar with deliverables for the Item 11 section of an electronic submission, it is perhaps best now to identify the required components of an ESUB package. In the eyes of Sanofi -Aventis, there are three key deliverables; DEFINE.PDF/DEFINE.XML, a blank study CRF annotated to the submission package and the actual submission database created in transport format. Additional deliverables such as patient profiles are outside the scope of MDMAP. Of the three components, DEFINE.PDF/DEFINE.XML is the most challenging and complex to manage. This document contains the metadata that supports the actual submission data. Some people often ask; what is metadata? Meta data is simply data describing data. Think of it as simply a SAS Proc Contents with additional key information added. Additional details on this key deliverable will be discussed later in the paper. The annotated CRF is key because this document allows FDA reviewers the ability to identify data collected during the clinical trial with data stored in the submission database. The production of this component has typically been an exhaustive manual effort by either statistical programming or clinical data management. The final key deliverable, creation of the transport files, is typically the most routine of all deliverables, however issues such as file size and audit trail can make this effort somewhat challenging.

APPLICATION REQUIREMENTS

From the beginning of the project, the working group assigned to MDMAP (Meta Data Management and Publishing) had an excellent understanding of the requirements of the project. This can be attributed to the fact that we had already successfully submitted several dossiers electronically. While those submissions were done manually, the requirements for each were identical and this attribute gave us a solid platform to base the MDMAP project. The primary objectives the working group had for the application were:

- Standardize and automate the process that Biostat and CMPK use worldwide to capture, manage and maintain the Clinical Trial Meta Data.
- Final Publishing capability (in define.pdf or define.xml format), including the capability of identifying selected datasets/variables in the output.
- Improve and streamline submission CRF annotation.
- Standardize and audit trail the creation of XPT submission transport files.
- Develop an application compliant with Sanofi-Aventis's interpretation of Regulatory Agency Guidance. (21CFR Part 11)
- Create components of item 11 of electronic submission in a secure environment ready for delivery to Regulatory Operations.

Figure 2 - MDMAP Evol - Internal Process Flow



APPLICATION FEATURES

MDMAP is an internally based, intranet product that has a web application feel to it, unlike other department tools developed in SAS with AF/Frame. Once launched and access has been approved and authorized, the user is prompted with a screen identifying five options. These options are the backbone of MDMAP.
They include:

ADMINISTRATION

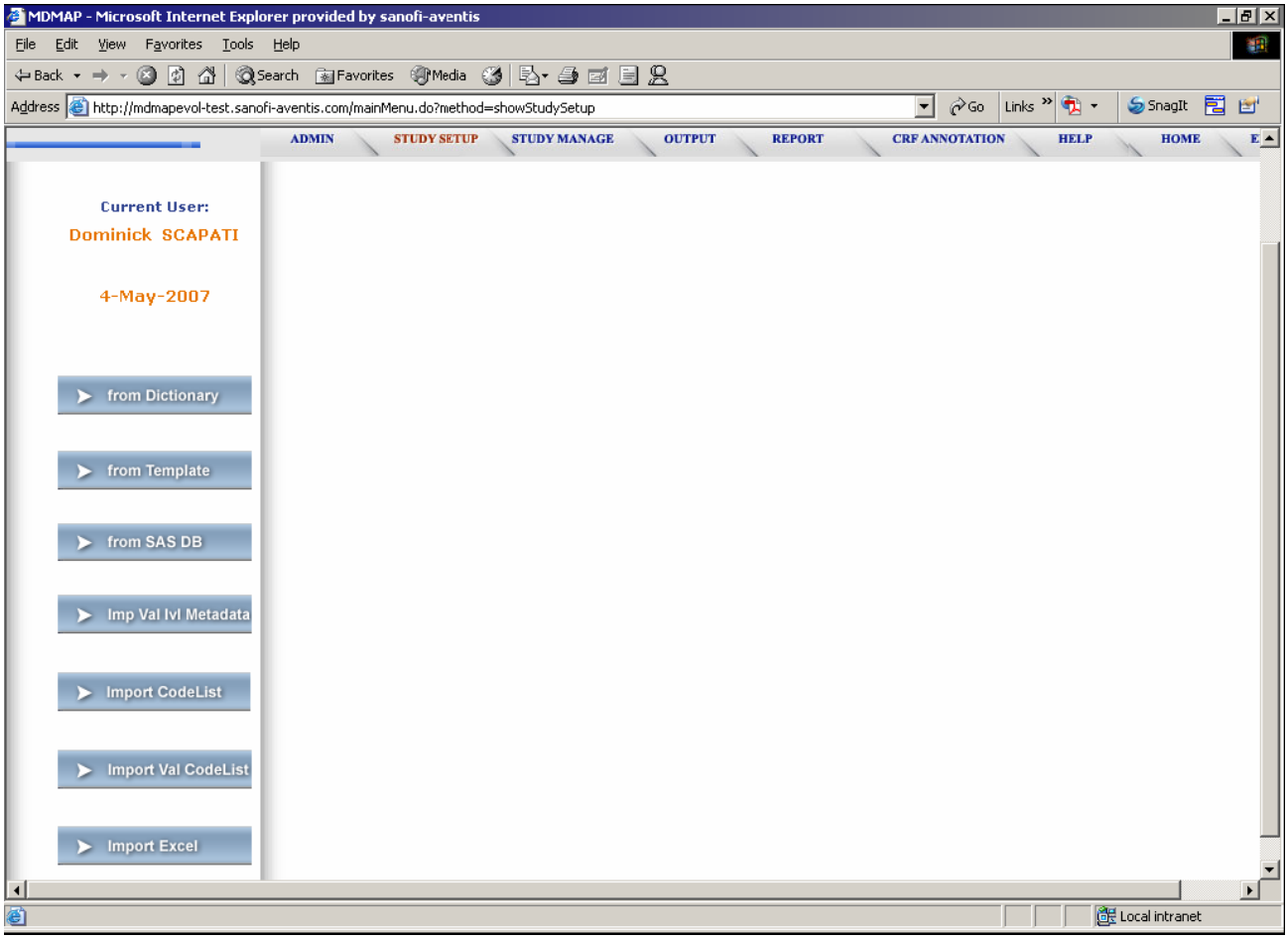
The administration option gives authorized users access to control admission to study metadata.
Another feature of the Administration option is the supervision of department dictionaries. Sanofi-Aventis adopted the CDISC philosophy of data standards and we keep and manage the metadata information for these dictionaries within MDMAP. Currently CDISC V2.6 and V3.1.1 standard are being maintained in the application.

STUDY SETUP

The primary feature of MDMAP is the ability to setup and manipulate study metadata. This is accomplished via the Study Setup

option. This selection has five options available:

- Import database design from Dictionary
- Import from Template of an existing MDMAP database
- Import database design from SAS DB
- Import from EXCEL
- Import Code list



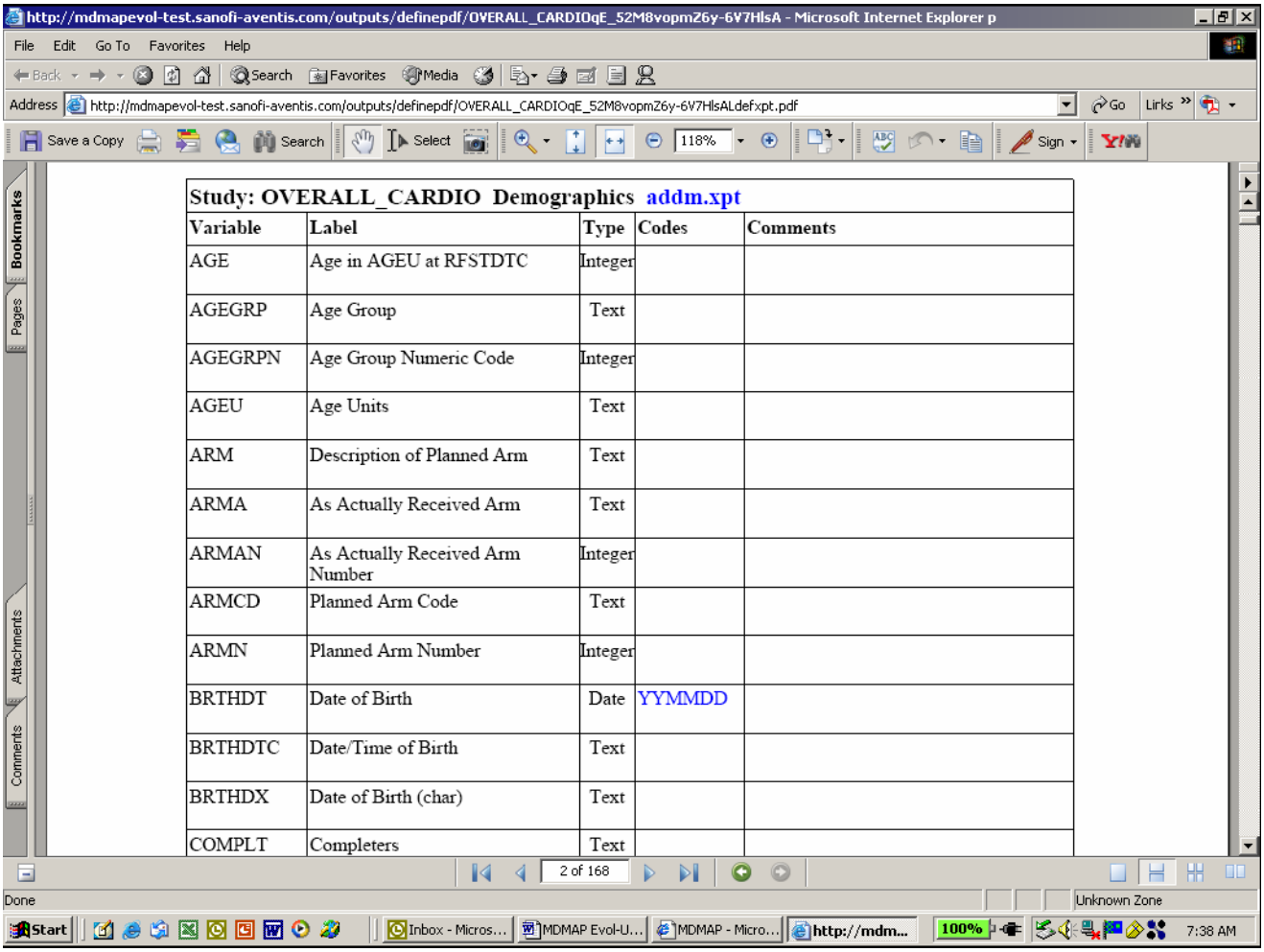
STUDY MANAGE

The most advanced and complex feature of MDMAP is the ability to create, edit and modify study metadata. It allows the user many helpful and advanced features such as the management of metadata for datasets, variables, comments, codelists, and value level metadata.

OUTPUT

The creation of metadata in either Excel or SAS file format and the creation of deliverables by Biostatistics for regulatory submissions in electronic format (eSub) is managed through the OUTPUT feature of MDMAP. The OUTPUT option allows the user the ability to:

- Create the DEFINE PDF
- Create the DEFINE XML
- Create the SAS Version 5 Transport (XPT) files
- Create Excel files
- Create SAS datasets
- Do the Final Publish



Study: OVERALL_CARDIO Demographics addm.xpt

Variable	Label	Type	Codes	Comments
AGE	Age in AGEU at RFSTDTC	Integer		
AGEGRP	Age Group	Text		
AGEGRPN	Age Group Numeric Code	Integer		
AGEU	Age Units	Text		
ARM	Description of Planned Arm	Text		
ARMA	As Actually Received Arm	Text		
ARMAN	As Actually Received Arm Number	Integer		
ARMCD	Planned Arm Code	Text		
ARMN	Planned Arm Number	Integer		
BRTHDT	Date of Birth	Date	YYMMDD	
BRTHDTC	Date/Time of Birth	Text		
BRTHDX	Date of Birth (char)	Text		
COMPLT	Completers	Text		

REPORTS

The MDMAP users can generate a wide report of standard reports for information and diagnostic purposes using the REPORT feature of MDMAP.

CRF ANNOTATION

MDMAP allows users the ability to annotate Case Report Forms for either items from a Clintrial panel or submission variables from SAS datasets based upon their respective profiles using the CRF ANNOTATION option.

TECHNICAL SOLUTIONS

The main objective of the MDMAP architecture design was to provide a robust, scalable and secure enterprise solution based on the already available infrastructure within the organization.

The advantages of a web-based architecture are many: minimal, if any, client side application footprint, quick and global access to multiple services residing on multiple remote systems, automatic software updates that do not require client side changes, multiple and concurrent access to these services, and interoperability when accessing differing services.

There are also disadvantages of web-based systems: network latency can affect the response time, and therefore the user experience when interacting with remote systems, unforeseen load by concurrent users can affect response times for all users, failover mechanisms need to be implemented to guarantee uninterrupted access to remote services, and schemes for data locking and simultaneous access have to be implemented.

CONCLUSION

MDMAP's goal was to be able to produce all electronic submission deliverables in a single package compliant within our comprehension of 21 CFR Part 11. In production since January 2005, we feel as though the application successfully automates the production of the required ESUB components in a secure environment. Users now do not need to have understanding of multiple technologies and processes when producing an electronic submission. Having a single application manage and publish

the ESUB delivery process provides users a consistent and validated environment from which to work.

CONTACT INFORMATION

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