Using DataFax to Collect Product Stability Data

Chris Lemaire
Santarus, Inc.

What is Product Stability?

- **Stability:** The capacity of a drug substance or a drug product to remain within specifications established to ensure its identity, strength, quality, and purity throughout the retest period or expiration dating period, as appropriate.

- **Stability Profile:** The physical, chemical, biological, and microbiological behavior of a drug substance or drug product as a function of time when stored under the conditions of the Approved Stability Protocol.

Overview

- Product development was using a demonstration version of a commercially available Laboratory Information Management System (LIMS) to capture and analyze product stability data. The demonstration version was about to expire, and product development was not impressed with the software.

- Biostatistics and Data Management offered to find a solution to recording and analyzing product stability data by using available in-house database and data analysis software packages.

Project Planning and Feasibility
DataFax Advantages

- At the time this project was started, DataFax was the only CFR part 11 compliant and validated software in house.

- There were only 3 – 4 months before NDA submission and we had no time for software development.

Project Planning and Feasibility
DataFax Disadvantages

- DataFax has a simple key structure that may limit its ability to capture the data.

System Analysis, Requirements and Definition

- We reviewed the data being recorded and the resulting graphs produced during the analysis of the data. I concluded that we could in fact collect and organize the data using DataFax.

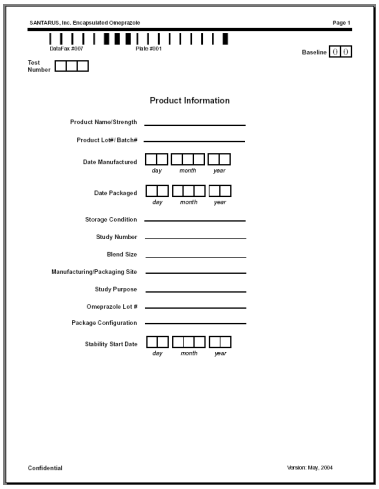
System Design

- The data could be collected using a concept similar to Case Report Forms (CRFs) used during clinical studies.
- Stability Analytical Data Logs (SADLs) could be used to record stability test results from the manufacture supplied test logs.
- However, we needed a method to uniquely identify the test conditions for the data being captured that would link all of the data points over time.

System Design (cont.)

- In order to uniquely identify and link data together we developed a Product Information SADL.
- The Product Information SADL identifies the storage conditions, lot and batch being tested.
- Each Product Information SADL has a unique test number assigned to it by an analytical associate which links all test, performed at specified time intervals, together.

System Design (cont.)
Product Information SADL



SANTARUS, Inc. Encapsulated Omeprazole Page 1

Data Fax: 8007 Plate #001

Baseline 0 0

Test Number

Product Information

Product Name/Strength

Product Lot# /Batch#

Date Manufactured day month year

Date Packaged day month year

Storage Condition

Study Number

Blend Size

Manufacturing/Packaging Site

Study Purpose

Omeprazole Lot #

Package Configuration

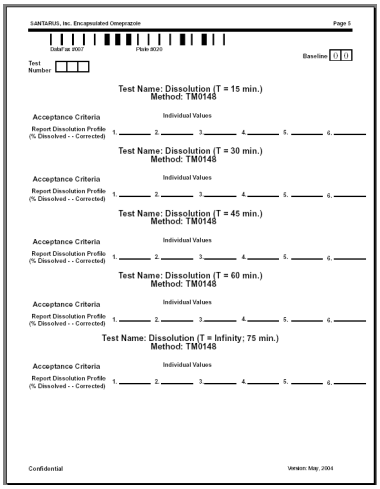
Stability Start Date day month year

Confidential Version: May, 2004

System Design (cont.)

- The design of the various SADLs to record the stability data was easy and straight forward, except when a re-test was performed for a specified test.
- A re-test section was created in the SADL binder using log pages similar to Adverse Events, Concomitant Medications or General Comments.

System Design (cont.)
On Schedule and Re-test SADLs


SANTARUS, Inc. Encapsulated Omeprazole Page 8

Test Name: Dissolution (T = 15 min.)
Method: TM0148

Acceptance Criteria | Individual Values

Report Dissolution Profile (% Dissolved - - Corrected)

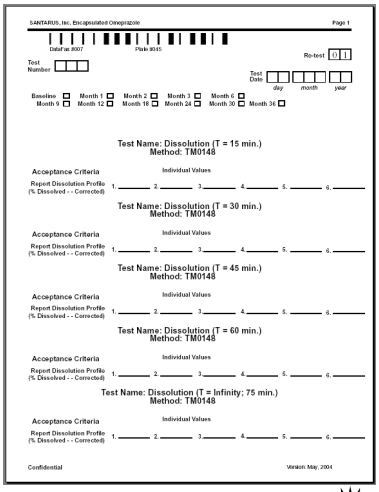
Test Name: Dissolution (T = 30 min.)
Method: TM0148

Test Name: Dissolution (T = 45 min.)
Method: TM0148

Test Name: Dissolution (T = 60 min.)
Method: TM0148

Test Name: Dissolution (T = Infinity; 75 min.)
Method: TM0148

Confidential Version: May, 2004


SANTARUS, Inc. Encapsulated Omeprazole Page 1

Test Name: Dissolution (T = 15 min.)
Method: TM0148

Test Name: Dissolution (T = 30 min.)
Method: TM0148

Test Name: Dissolution (T = 45 min.)
Method: TM0148

Test Name: Dissolution (T = 60 min.)
Method: TM0148

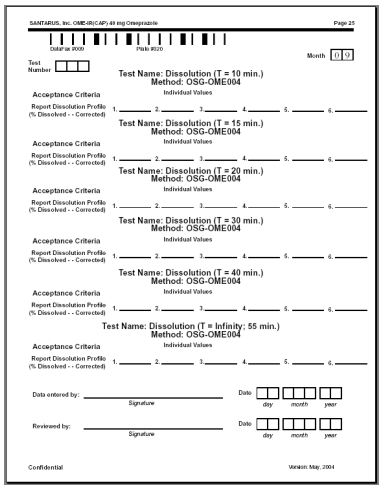
Test Name: Dissolution (T = Infinity; 75 min.)
Method: TM0148

Confidential Version: May, 2004

System Design (cont.)

- The test protocol may be amended requiring modification of test procedures or times.
- This can be achieved by creating a new SADL to reflect the protocol's modification.

System Design (cont.)



SANTARUS, Inc.-OME-IR(CAP)-40 mg Omeprazole Page 2/5

Stability# 9009 Plate #021

Month 0 9

Test Number

Test Name: Dissolution (T = 10 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 15 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 20 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 30 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 40 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = Infinity: 55 min.)
Method: OSG-OME004
Individual Values

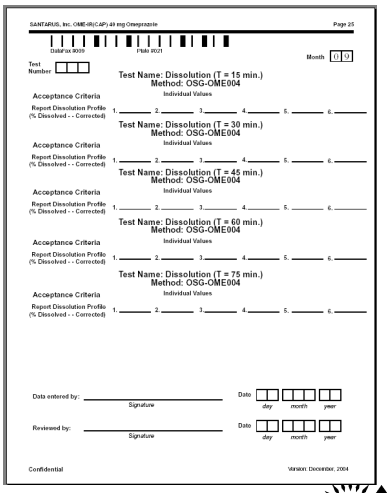
Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Data entered by: _____ Signature Date day month year

Reviewed by: _____ Signature Date day month year

Confidential Version: May, 2004



SANTARUS, Inc.-OME-IR(CAP)-40 mg Omeprazole Page 2/5

Stability# 9009 Plate #021

Month 0 9

Test Number

Test Name: Dissolution (T = 15 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 30 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 45 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 60 min.)
Method: OSG-OME004
Individual Values

Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Test Name: Dissolution (T = 75 min.)
Method: OSG-OME004
Individual Values

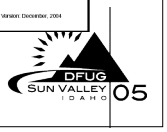
Acceptance Criteria

Report Dissolution Profile (% Dissolved - - Corrected) 1. 2. 3. 4. 5. 6.

Data entered by: _____ Signature Date day month year

Reviewed by: _____ Signature Date day month year

Confidential Version: December, 2004



Standard Operating Procedures

- Biostatistics and Data Mangement, Quality Assurance/Regulatory Affairs and Product Development worked together to create SOPs covering:

  1. SADL Development
  2. Database Design and Setup
  3. Data Entry and Data Validation

NDA Submission

- Biostatistics performed an analysis of the data and the results were included in our successful NDA submissions for the 20 and 40 mg formulations of Zegerid™.

Project Success/Return Business

- Product Development was happy with the results, and requested additional databases for new drug candidates.

Questions?