
Measuring the Benefits of Standards

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Gary Fleming & Michaela Jahn



Benefits of Standards - Overview

- It is a widely-held belief that standardization enhances efficiency
- There is not currently a great deal of evidence to support this
- An experimental design was developed to investigate this belief
- Focus on database setup role
- Different levels of standardization
- Results collected for specific, high-level tasks
- Conclusions drawn

Introduction

- Roche use Medidata Rave 5.6.3
- Roche “pRED Core Standards II” global library volume rolled out Q2 2010
- Uptake of standards use slower than expected
- Evidence required to prove the case that using standards increases efficiency
- Scope is specific to database setup

Methodology I – Test Plan

- A test plan was developed and independently reviewed to ensure no bias regarding the use/non-use of standards
- Test plan described the experimental design
 - Set up the safety components of a study using different levels of standards adoption
 - Measure the time taken for different tasks
- The test plan was made up of three different test scenarios:
 - 1) 100% use of “pRED Core Standards II” global library volume
 - 2) 50% use of “pRED Core Standards II” global library volume, 50% use of non-standard content
 - 3) No use of “pRED Core Standards II” global library volume: all non-standard

Methodology II – System Setup

- Clinical database system used: Medidata RAVE (version 5.6.3)
- Roche training URL utilized to allow controls for access and user role
- “pRED Core Standards II” global library volume copied to Roche training URL
- Three projects created in RAVE, as per test scenarios:
 - 1) CSIIEFF000: 100% sourced from “pRED Core Standards II” global library volume
 - 2) CSIIEFF050: Approximately 50% sourced from “pRED Core Standards II” global library volume
 - 3) CSIIEFF100: Nothing sourced from “pRED Core Standards II” global library volume

Methodology III - Testers

- Testers were recruited: three Clinical Database Programmers with comparable experience levels
- Each was randomly assigned to a test scenario
- Documentation and RAVE access provided to each tester

The study schedule and assessments were identical for all three test scenarios. The only difference was in the definition of these objects within the RAVE database for each test scenario.

Methodology IV – Documentation Provided

Several documents were provided (one of each per test scenario):

- Matrix Design Document (MDD) – schedule of assessments, sample numbers

CSII based MDD											
Period / Week	Form OID	Subject Level Forms	Screening	Period 1							
Day			D-28 to D-3	Day -2	Day -1						
Scheduled Time			notime	notime	predose equivalent	0.5	1	1.5	2	2.5	3
Assessments											
Visit Date	VISIT		X	X							X
Medical History	MH		X								
Demography (inc. Consent Date)	DM		X								
Subject Characteristics	SC		X								
Anthropometric measurements (hgt, wgt + BMI (derived))	VSA		X								
Anthropometric measurements (wgt + BMI (derived))	VSA										
Drugs of Abuse & Alcohol Tests	SU		X	X							
Single Vital Signs - supine (Sys, Dia, PR, Temp)	VS		X								
Single Vital Signs -supine (Sys, Dia, PR)	VS				X	X	X	X	X	X	X
Single 12-Lead ECG - supine (HR, RR, PR (PQ), QT, QTcF (derived), QRS, T-waves, U-waves, QTcB (derived))	EG		1001		1002	1003	1004	1005	1006	1007	1008

Methodology IV - Database Specification Document

- DSD (Database Specification Document) – validation checks, derivations, eCRF behaviours and source data verification marks

Required	Source	Check Description	Check Type	Edit Check Name	Folder	Form	Form English Description	Field	Query Message	Send Query to (Marking Group)
Yes	Global Library	'Birth date' must be answered.	Field	N/A	Any	DM	Demography	BRTH_DC	See instructions worksheet	1: Site from System
Yes	Global Library	'Birth date' cannot be a future date	Field	N/A	Any	DM	Demography	BRTH_DC	See instructions worksheet	1: Site from System
Yes	Global Library	'Consent date' must be answered.	Field	N/A	Any	DM	Demography	DSSTD_DC	See instructions worksheet	1: Site from System
No	Global Library	Ethnicity must be answered.	Field	N/A	Any	DM	Demography	ETHNIC	See instructions worksheet	1: Site from System
Yes	Global Library	'Race' must be answered.	Field	N/A	Any	DM	Demography	RACE	See instructions worksheet	1: Site from System
Yes	Global Library	'Sex' must be answered.	Field	N/A	Any	DM	Demography	SEX	See instructions worksheet	1: Site from System
Yes	Global Library	Age must be per protocol within specified age range (**18 to 65* years, inclusive). Use as Template: ** values to be updated per study	Edit	OQ_DM_AGE_RANGE	SCR	DM	Demography	BRTH_DC	Subject's age is out of range as specified by the protocol. Please confirm or correct the age.	1: Site from System
Yes	Global Library	Check that Date of consent is before or equal to screening visit.	Edit	OQ_DM_DSSTDDC_AFTER_SCR	SCR	DM	Demography	DSSTD_DC	Date of consent is after screening visit date. Please correct these dates.	1: Site from System
Yes	Global Library	If 'Race' is not answered OTHER, then 'Specify' should not be answered.	Edit	OQ_DM_RACE_NOTOTHER_RACESP_PRESENT	SCR	DM	Demography	RACE	'Race' is not answered OTHER but 'Specify' is answered. Please amend entry for 'Race' or delete entry for 'Specify'.	1: Site from System
									'Race' is not answered ASIAN but sub-category (Indian subcontinent or Other than	

Methodology IV - Clarifications Document

- Clarifications document – exact specifications of each variable to be built in the test scenario, grouped by eForm

2. Medical History – MHYN, MHTERM, MHACT

3. Personal Data (OID: DEMOG)

Consent Date: CONS_DC (dd MMM yyyy)

Date of Birth: BIRTH_DC (dd MMM yyyy)

Current Age: CUR_AGE (3)

Gender: GENDER(\$10) - Dictionary: GENDER

User Data String	Specify	Coded Data
Male	☐	M
Female	☐	F

Methodology IV – Background Information Document

- Background information document – information normally found within only a study protocol and not the MDD or DSD: For example - lab safety panel

Project Name: “A simple test study to examine the efficiency of using standard objects compared to using non-standard objects”

Most details for this study are in the MDD but there is also some further information in this document that would normally be listed in the protocol.

Subject status: In-patient, Outpatient, Healthy Volunteer or Other.

Lab tests (all lab results to be manually entered):

Biochemistry: Sodium, Potassium, Magnesium, Calcium, Chloride, Glucose, GGT, AST, ALT, LDH, Total Bilirubin, Urea, Creatinine, Protein, Albumin, Creatine Kinase.

Hematology: Hematocrit, Hemoglobin, RBC count, WBC count, Platelet count, WBC absolute differential count (neutrophils, eosinophils, basophils, lymphocytes, monocytes)

Coagulation: APTT, Prothrombin Time

Urinalysis: pH, Glucose, Blood, WBC, Protein

Pregnancy: Serum or Urine pregnancy test to be done at timepoints on MDD.

Methodology V – “CDP Time & Task Record”

- “CDP Task & Time Record” – to record time spent on each pre-defined task

CDP Name	
Task Description	Time Taken (hours)
Create fields, forms, folders, etc.	
Create and test eCRF behaviours	
DSD – create and unit test edit checks/custom functions	
DSD – fix user acceptance fails	

- “Create fields, forms, folders, etc.” consists of creation of data collection objects according to the protocol schedule of assessments
- “Create and test eCRF behaviours” consists of programming custom functions to add eForms, set visibility and default values as needed
- “DSD – create and unit test edit checks/custom functions” involves the creation of validation checks and custom functions within the database as well as updates to the DSD to confirm checks have been built and unit tested
- “DSD – fix user acceptance fails” is a post-UAT task where the CDP would review the DSD and fix any check fails before releasing for retesting

Results I - Overview

- Each tester was asked to record as accurately as possible the time taken for each of the tasks specified on the “CDP Task & Time Record”
- These tasks were chosen by the experimental designers to be the tasks expected to show the benefit of standards use within the experimental design
- Time taken for each task was measured in hours
- Following completion of the specified tasks, each tester returned their completed “CDP Time & Task Record” and DSD to the experimental designer

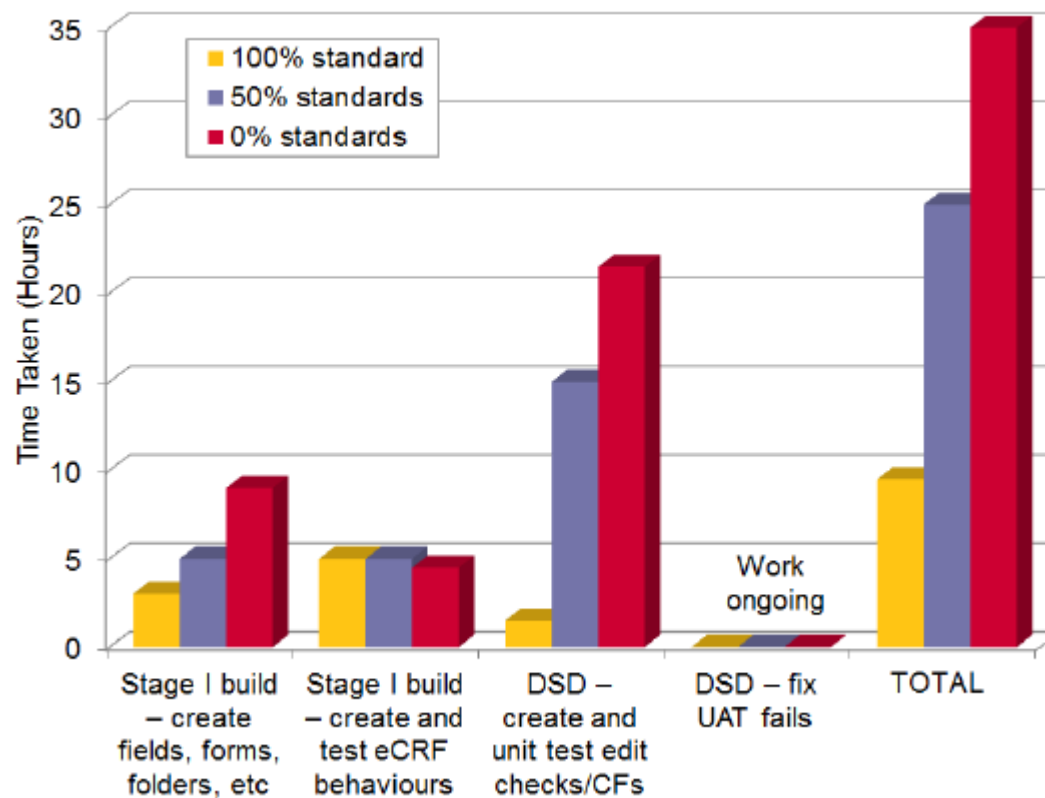
Results II – Tabulation

Task Description	100% use of standards	50% use of standards	No use of standards
Create fields, forms, folders, etc.	3	5	9
Create and test eCRF behaviours	5	5	4.5
DSD – create and unit test edit checks/custom functions	1.5	15	21.5
Total	9.5	25	35

- “Stage I Build – create fields, forms, folders, etc.” showed a strong benefit towards use of standards, however the task itself was not particularly time-intensive
- “Stage I Build – create and test eCRF behaviours” showed broadly similar time spent, which was expected because this task tends not to be heavily standardized, due to study-specific requirements
- “DSD – create and unit test edit checks/custom functions” showed a very strong efficiency gain for 100% use of standards

Results III – Graph

- Time taken (hours) by task, split by test scenario



Results IV – Totals and Summary of Results

- 100% use of standards was completed in 9.5 hours
- 50% use of standards was completed in 25 hours
- No use of standards was completed in 35 hours

- 100% use of standards was completed in **38%** of the time taken to complete the 50% use of standards
- 100% use of standards was completed in **27%** of the time taken to complete the no use of standards
- 50% use of standards was completed in **71%** of the time taken to complete the no use of standards.

- 50% result useful to highlight because a “real” study design would typically be set up using both standard and non-standard objects.

Conclusions

- There is a clear relationship between efficiency of database setup and use of standards. We propose that the belief that standardization enhances efficiency has been proved.
- The experimental design represented the extremes of standards usage and non-standards usage, therefore the test scenario where 50% of standards use was permitted can be considered to be a more realistic representation of a “real” study design.
- Therefore we also propose that the greater the use of standards within a study, the greater the benefits to the efficiency of the study database build.

Further Considerations

Benefits of standards demonstrated here within a precise scope, for certain tasks assigned to a single role (CDP).

Further benefits of standardization could be demonstrated for:

- Protocol design
- Study documentation creation (for example MDD, DSD)
- Data cleaning
- Data extraction including mapping of data to SDTM format
- Data visualization and analysis (for example with the Tibco Spotfire™ tool)

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