

On the Trail of the Holy Grail of SDTM Implementation

Three Unique Case Studies

Ken Stoltzfus
Clinical Data Strategies
Octagon Research Solutions

PhUSE 2011



Unifying **Clinical Data** and **Submission Strategy** for the **Global Life Sciences Industry**

- Octagon Research Solutions
 - A development partnering organization that offers regulatory, clinical, process and IT solutions to the life sciences industry.
- Octagon experience on topic:
 - 600 studies converted to SDTM & ADaM (10,000+ domains) in support of over 54 regulatory submissions to the FDA
 - CDISC SDTM Co-authors
 - CDISC SDS Team Lead
 - Current CDISC team membership: SDS, ADaM, CDASH, SEND, SHARE, and Controlled Terminology
 - CDISC-authorized SDTM trainers

Agenda

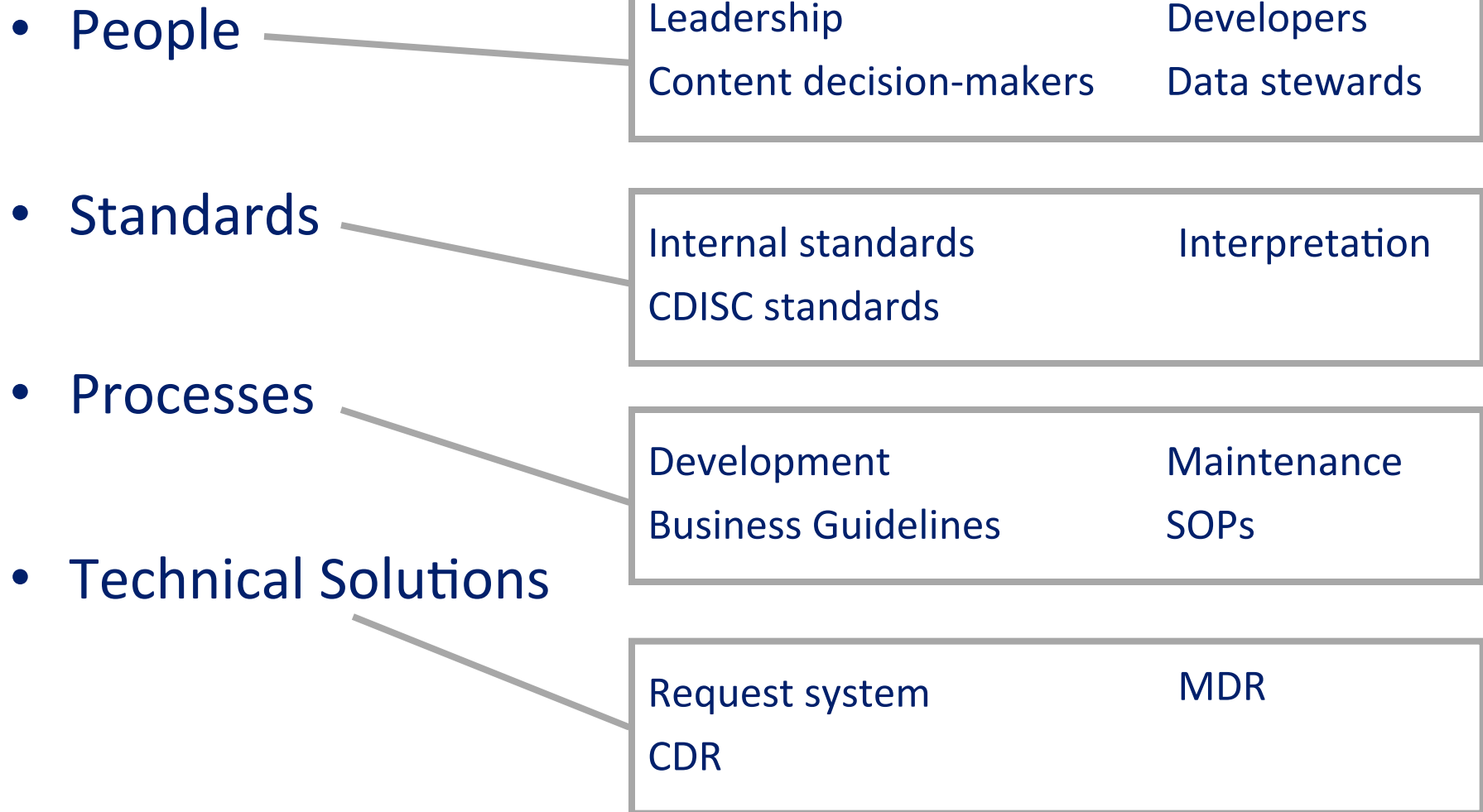
- Standards Governance
- Case Studies



Standards Governance

- What exactly is standards governance?
 - Oversight
 - Decision-making
 - Development
 - Maintenance
 - Compliance

Standards Governance



Ladies and gentlemen:

The case studies you are about to see are true.
Only the names have been changed to protect
the innocent.

Any resemblance to real CRFs, whether ongoing or
legacy, is purely coincidental.

Case Study 1 – Company Alpha

Snapshot of the Starting Point

Background

- Responding to questions from FDA reviewer
- Data mining difficult across unstandardized databases



Standards Governance

- None, although mandate issued to implement CDASH and SDTM
- No accompanying authorization for standards governance
- Standards development performed by focused group of SAS programmers, Biostatisticians, and EDC builders

Proposal 1: CE

The eCRF



StudyID

CA-027

Centre: 0010

Subject: 0006

Visit

USUBJID

CECAT =

Signs and Symptoms

VISITNUM

CESTDTC

Date of Assessment



SUPPCE

Date of Application



Time of Application

QNAM =

Application Site

CELOC

CESEV
Severity

RASHDM

Diameter

RASHDMU

CETERM = Rash

CEPRES = Y CETPT

Post-application 8 hr

mm

Post-application 16 hr

mm

Post-application 24 hr

mm

CEOCCUR = N
CESEV is null

CEOCCUR = U
CESEV is null

None
Mild
Moderate
Severe
Unknown

CEOCCUR = Y

Proposal 2: X1

The eCRF



Study ID
CA-027

Centre: 0010

Subject: 0006

Visit

USUBJID

X1CAT =

Signs and Symptoms

VISITNUM

X1DTC

Date of Assessment



SUPPX1

QNAM =

Date of Application



Time of Application

Application Site

X1LOC

X1TEST = Severity
X1ORRES = <value>

X1TEST = Diameter
X1ORRES = <value>

Rash

X1TPT

Severity

Diameter

X1ORRESU

Post-application 8 hr

mm

Post-application 16 hr

mm

Post-application 24 hr

mm

X1TEST =

Occurrence of Rash

X1ORRES = N

X1ORRES = U

None
Mild
Moderate
Severe
Unknown

X1ORRES = Y

Proposal 3: FA

The eCRF



StudyID
CA-027

Centre: 0010

Subject: 0006

Visit

USUBJID

FACAT =

Signs and Symptoms

VISITNUM

FADTC

Date of Assessment



SUPPFA

QNAM =

Date of Application



Time of Application

Application Site

FALOC

FATEST = Severity
FAORRES = <value>

FATEST = Diameter
FAORRES = <value>

FAOBJ = Rash

FATPT

Severity

Diameter

FAORRESU

Post-application 8 hr

mm

Post-application 16 hr

mm

Post-application 24 hr

mm

FATEST =
Occurrence

FAORRES = N

FAORRES = U

None
Mild
Moderate
Severe
Unknown

FAORRES = Y



The Discussion & The Decision

Proposal 1: CE

USUBJID	VISIT	CETPT	CETERM	CESTDTC	CESEV	CMOCCUR	CMPRESP
0010:0006	1	Post-application 8 hr	RASH	2010-03-22	MILD	Y	Y
0010:0006	1	Post-application 16 hr	RASH	2010-03-22	NONE	N	Y
0010:0006	1	Post-application 24 hr	RASH	2010-03-22	NONE	N	Y
0010:0006	2	Post-application 8 hr	RASH	2010-03-29	MILD	Y	Y
0010:0006	2	Post-application 16 hr	RASH	2010-03-29	MODERATE	Y	Y
0010:0006	2	Post-application 24 hr	RASH	2010-03-29	MODERATE	Y	Y

Proposal 2: X1

USUBJID	VISIT	X1TPT	X1TEST	X1DTC	X1ORRES	X1ORRESU
0010:0006	1	Post-application 8 hr	Occurrence of Rash	2010-03-22	Y	
0010:0006	1	Post-application 8 hr	Severity	2010-03-22	MILD	
0010:0006	1	Post-application 8hr	Diameter	2010-03-22	1	mm
0010:0006	1	Post-application 16 hr	Occurrence of Rash	2010-03-22	NONE	
0010:0006	1	Post-application 16 hr	Severity	2010-03-22		
0010:0006	1	Post-application 16 hr	Diameter	2010-03-22		mm

Proposal 3: FA

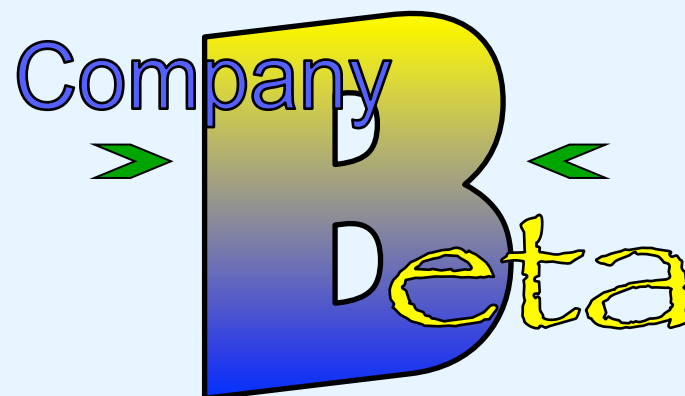
USUBJID	VISIT	FATPT	FATEST	FAOBJ	FADTC	FAORRES	FAORRESU
0010:0006	1	Post-application 8 hr	Occurrence	RASH	2010-03-22	Y	
0010:0006	1	Post-application 8 hr	Severity	RASH	2010-03-22	MILD	
0010:0006	1	Post-application 8hr	Diameter	RASH	2010-03-22	1	mm
0010:0006	1	Post-application 16 hr	Occurrence	RASH	2010-03-22	NONE	
0010:0006	1	Post-application 16 hr	Severity	RASH	2010-03-22		
0010:0006	1	Post-application 16 hr	Diameter	RASH	2010-03-22		mm

Case Study 2 – Company Beta

Snapshot of the Starting Point

Background

- Budget crisis
- Smarter use of resources
- Quicker study start-up
- CDISC standards



Standards Governance

- Small DM group managing company's collection standards
- Several internal resources with SDTM expertise from DM and SAS programming performed original SDTM mappings
- Eventual highly-visible, strong mandate from senior VP

Proposal 1: MH

The eCRF

Company  StudyID: CB-019 Centre: 0005 Subject: 0002 Visit: 
USUBJID
MHCAT = Cardiovascular Medical History
VISITNUM

Date Medical History Taken  SUPPMH

Evaluation of subject's medical history for:

MHTERM

MHOCUR

Hypertension

No Yes Unknown
☒ ☐ ☐

Ventricular arrhythmia

No Yes Unknown
☒ ☐ ☐

Myocardial infarction

No Yes Unknown
☒ ☐ ☐

Date of most recent MI

MIDAT



Number of MI

MINO



Coronary artery disease

No Yes Unknown
☒ ☐ ☐

Left ventricular hypertrophy

No Yes Unknown
☒ ☐ ☐

Date of most recent LVEF

LVEFDAT



Most recent LVEF

LVEFPCT

%

QNAM =

Proposal 2: MH + The FA

Company **Beta** StudyID **CB-019** Centre: 0005 USUBJID **0002** Subject: 0002 Visit **VISITUM**

MHCAT = Cardiovascular Medical History

MHDTC **FADTC**

Date Medical History Taken **FATEST = Date of most recent MH**
MHPRESP = Y **FAORRES = <date value>**

Evaluation of subject's medical history for:

MHTERM

Hypertension **MHOCCUR**
 No Yes Unknown
☒ ☐ ☐

Ventricular arrhythmia
 No Yes Unknown
☒ ☐ ☐

Myocardial infarction
 No Yes Unknown
☒ ☐ ☐

Coronary artery disease
 No Yes Unknown
☒ ☐ ☐

Left ventricular hypertrophy
 No Yes Unknown
☒ ☐ ☐

FAOBJ =

FATEST = Date of most recent LVEF
FAORRES = <date value>

FATEST = Most recent LVEF
FAORRES = <value>

Findings

Date of most recent MI **FATEST = Number of MI**
 Number of MI **FAORRES = <value>**

Date of most recent LVEF **FATEST =**
 Most recent LVEF % **FAORRES =**

The Discussion & The Decision

Proposal 1: MH

USUBJID	VISIT	MHTERM	MHDTC	CMOCCUR
0005:0002	1	Hypertension	2009-05-12	N
0005:0002	1	Ventricular arrhythmia	2009-05-12	N
0005:0002	1	Myocardial infarction	2009-05-12	Y
0005:0002	1	Coronary artery disease	2009-05-12	Y
0005:0002	1	Left ventricular hypertrophy	2009-05-12	Y

Proposal 2: FA (+ MH dataset above)

USUBJID	VISIT	FATEST	FAOBJ	FADTC	FAORRES	FAORRESU
0005:0002	1	Date of most recent MI	Myocardial infarction	2009-05-12	2008-10-14	
0005:0002	1	Number of MI	Myocardial infarction	2009-05-12	1	
0005:0002	1	Date of most recent LVEF	Left ventricular hypertrophy	2009-05-12	2008-11-07	
0005:0002	1	Most recent LVEF	RASH	2009-05-12	37	%

Case Study 3 – Company Gamma

Snapshot of the Starting Point

Background

- Implementation of a CDR
- Need for standard metadata for safety domains
- Foundation for TA domains



Standards Governance

- Lightly-supported group of clinicians and statisticians for purposes of centralized decision-making for SDTM mapping
- Standards governance group nearly paralyzed by workload
- Limited representation led to limited buy-in to standards

Proposal 1: CM

The eCRF



Study ID
CG-203
CMCAT

Centre: 0055

Subject: 0014
USUBJID

Visit
VISITNUM

Protocol-Restricted Medications

Date of Assessment

PRMDAT



SUPPCM

QNAM =

Did the subject take the following medications during the 24 hours prior to spirometry?

CMPRESP = Y

CMTRT

CMOCCUR

CMSTDTC

Short acting Beta 2-agonists

No ☒ Yes ☐ Unknown ☐

Date



Time

Long acting Beta 2-agonists

No ☒ Yes ☐ Unknown ☐

Date



Time

Anticholinergics

No ☒ Yes ☐ Unknown ☐

Date



Time

Inhaled corticosteroids

No ☒ Yes ☐ Unknown ☐

Date



Time

Proposal 2: DV

The eCRF



Study ID
CG-203
DVCAT

Centre: 0055

Subject: 0014

Visit

USUBJID

VISITNUM

Protocol-Restricted Medications

Date of Assessment

PRMDAT



SUPPDV

QNAM =

Did the subject take the following medications during the 24 hours prior to spirometry?

If PRM_NYU = Y

PRM_NYU

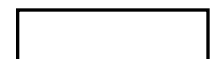
No Yes Unknown
☒ ☐ ☐

Short acting Beta 2-agonists

Date



Time



DVTERM = PRE-SPIROMETRY SHORT ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL

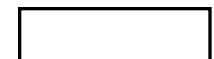
No Yes Unknown
☒ ☐ ☐

Long acting Beta 2-agonists

Date



Time

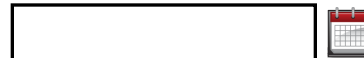


DVTERM = PRE-SPIROMETRY LONG ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL

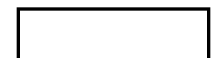
No Yes Unknown
☒ ☐ ☐

Anticholinergics

Date



Time



DVTERM = PRE-SPIROMETRY ANTICHOLINERGIC USAGE DIVERGENT FROM PROTOCOL

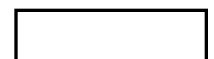
No Yes Unknown
☒ ☐ ☐

Inhaled corticosteroids

Date



Time



DVTERM = PRE-SPIROMETRY INHALED CORTICOSTEROID USAGE DIVERGENT FROM PROTOCOL

Proposal 3: XC

The eCRF



Study ID
CG-203
XCCAT

Centre: 0055

USUBJID

Subject: 0014

Visit

VISITNUM

Protocol-Restricted Medications

Date of Assessment

PRMDAT



SUPPXC

QNAM =

Did the subject take the following medications during the 24 hours prior to spirometry?

XCORRES

No Yes Unknown
☒ ☐ ☐

Short acting Beta 2-agonists

XCTEST = PRE-SPIROMETRY SHORT ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL

Date



Time

No Yes Unknown
☒ ☐ ☐

Long acting Beta 2-agonists

XCTEST = PRE-SPIROMETRY LONG ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL

Date



Time

No Yes Unknown
☒ ☐ ☐

Anticholinergics

XCTEST = PRE-SPIROMETRY ANTICHOLINERGIC USAGE DIVERGENT FROM PROTOCOL

Date



Time

No Yes Unknown
☒ ☐ ☐

Inhaled corticosteroids

XCTEST = PRE-SPIROMETRY INHALED CORTICOSTEROID USAGE DIVERGENT FROM PROTOCOL

Date



Time



The Discussion & The Decision

Proposal 1: CM

USUBJID	VISIT	CMTRT	CESTDTC	CMOCCUR	CMPRESP
0055:0014	1	Short acting Beta 2-agonists	2010-08-09T11:22	Y	Y
0055:0014	1	Long acting Beta 2-agonists		N	Y
0055:0014	1	Anticholinergics		N	Y
0055:0014	1	Inhaled corticosteroids	2010-08-09T21:01	Y	Y
0055:0014	2	Short acting Beta 2-agonists	2010-08-23T10:15	Y	Y
0055:0014	2	Long acting Beta 2-agonists		N	Y

Proposal 2: DV

USUBJID	VISIT	DVCAT	DVTERM	DVSTDTC
0055:0014	1	Protocol-Restricted Medications	PRE-SPIROMETRY SHORT ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL	2010-08-09T11:22
0055:0014	1	Protocol-Restricted Medications	PRE-SPIROMETRY INHALED CORTICOSTEROID USAGE DIVERGENT FROM PROTOCOL	2010-08-09T21:01
0055:0014	2	Protocol-Restricted Medications	PRE-SPIROMETRY SHORT ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL	2010-08-23T10:15

Proposal 3: XC

USUBJID	VISIT	XCTEST	XCDTC	XCORRES
0055:0014	1	PRE-SPIROMETRY SHORT ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL	2010-08-09T11:22	Y
0055:0014	1	PRE-SPIROMETRY LONG ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL		N
0055:0014	1	PRE-SPIROMETRY ANTICHOLINERGIC USAGE DIVERGENT FROM PROTOCOL		N
0055:0014	1	PRE-SPIROMETRY INHALED CORTICOSTEROID USAGE DIVERGENT FROM PROTOCOL	2010-08-09T21:01	Y
0055:0014	2	PRE-SPIROMETRY SHORT ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL	2010-08-23T10:15	Y
0055:0014	2	PRE-SPIROMETRY LONG ACTING BETA 2-AGONIST USAGE DIVERGENT FROM PROTOCOL		N

Summary

- SDTM implementation is complex, but ultimately achievable given the following:
 - Access to necessary expertise across functional areas
 - Thorough consideration of downstream analysis needs
 - Empowered standards governance
- No single perfect method

Acknowledgements

Barry Cohen

Dave Evans

Lex Jansen

Tore Haglund

Stephen Harrison

Harpreet Sahni

Contact Information

Ken Stoltzfus

Clinical Data Strategies

Octagon Research Solutions

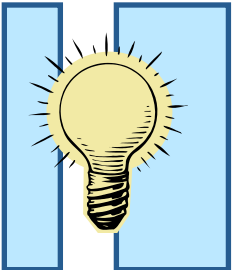
585 East Swedesford Road, Suite 200

Wayne, PA 19087

USA

Tel: 1-610-535-6500 (Ext. 5891)

kstoltzfus@octagonresearch.com



***Feel free to visit the Octagon booth for
more information on Octagon's solutions***

Questions

