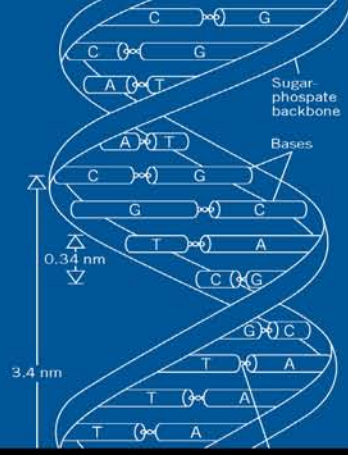


Roche

Experiences with the CFAST Diabetes Project

Petra Strücker, Senior Data Modeling Specialist (DMS), Hoffmann-La Roche Basel

Agenda (1)

1. Introduction to CFAST
2. Roche Participation in CFAST Diabetes Project
3. Standards Development Process
   - CDISC
   - CFAST Therapeutic Areas
4. CFAST Diabetes Project Team
   - Overview
   - Concept Developer Role

Agenda (2)

5. Concept Developer Responsibilities
   - Concept Maps
   - SHARE Metadata Display – Example Glucose
   - My Assignments
6. Learning so far
7. Suggestions for Future CFAST Projects

Introduction to CFAST

- Coalition for Accelerating Standards and Therapies
- Initiative supported by CDISC
- Has established a program to identify a core set of concepts and endpoints for targeted therapeutic areas (TAs) and translate them into CDISC standards along with
  - TransCelerate Biopharma Inc. (consists of pharmaceutical and biotechnology companies, Roche is one of those), C-Path FDA and National Cancer Institute Enterprise Vocabulary Services (NCI-EVS) which are sponsoring organizations for the program
  - Participation and input from many other organizations → for the diabetes project those ones are: Accenture, Takeda, Merck, Novartis, Novo Nordisk, Quintiles

Introduction to CFAST Program Overview Dec 2013

Roche

Approved Therapeutic Area Standards Projects

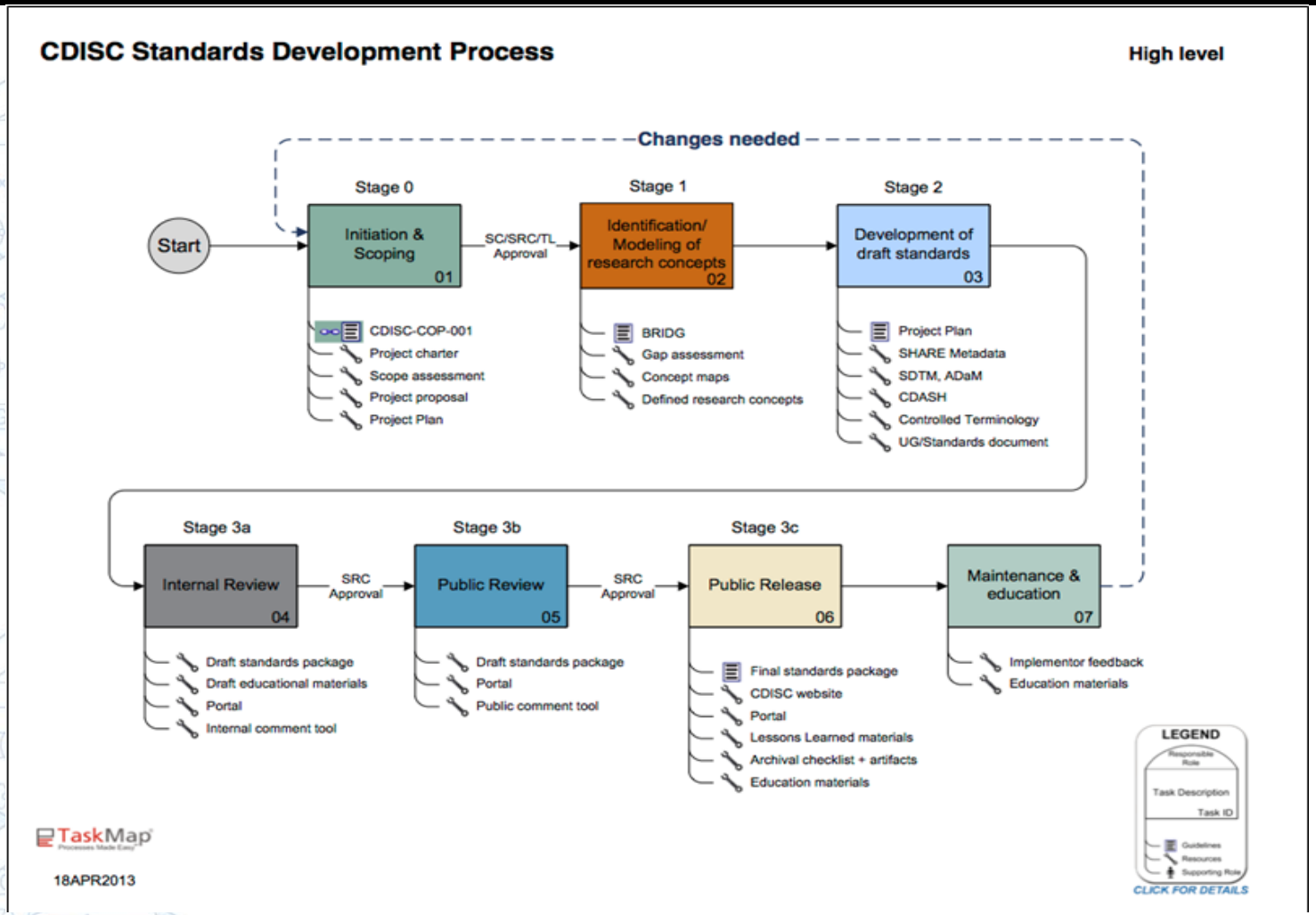
Therapeutic Area	Coordinating Organization(s) / Project Manager	Start Date	Stage 0 Scoping & Input	Stage 1 Concept Modeling	Stage 2 Standards Development	Stage 3a Internal Review	Stage 3b Public Review	Stage 3c Publication	Notes
Alzheimer's Disease v2	CPATH Jon Neville	Jan 13	Jan	Mar	Jun	Sep	Q4	*Q413*	Published December 2013
Asthma v1	CDISC Rhonda Facile	Nov 12	Jan	Mar	Jun	Jul	Q4	*Q413*	Published November 2013
Cardiovascular Endpoints v1	CDISC/DCRI Amy Palmer	Jun 13	Jul	Sep	Nov	*Q1*	*Q1*	*Q214*	
Multiple Sclerosis v1	CPATH Bess Leroy	Mar 13	May	*Oct*	Nov	*Q1*	*Q1*	*Q114*	
Diabetes v1	TCB Rachael Zirkle	Apr 13	May	Aug	Dec	*Jan*	*Q1*	*Q214*	
QT Studies v1	TCB John Owen	Aug 13	Oct	*Jan*	*Mar*			*Q214*	
Traumatic Brain Injury v1	CDISC Rhonda Facile	Oct 13	*Jan*	*Mar*				*2014*	
Hepatitis C v1	TCB John Owen	Nov 13	*Jan*	*Mar*				*Q414*	
Schizophrenia v1	CDISC/DCRI Amy Palmer	Nov 13	Jan	*Mar*				*Q414*	
Breast Cancer v1	TCB Sarah Davis	Jan 14	*Feb*	*Apr*				*2015*	
Influenza	C-PATH Jon Neville	Jan 14	*Feb*					*Q414*	
COPD v1	TCB TBD	Feb 14	*Apr*					*Q115*	

Key: | Stage completed | Stage ongoing | *Italics*=Projected | Months reflect when stage **completed**

Roche Participation in CFAST Diabetes Project

- Roche is a member of TransCelerate Biopharma, Inc.
- Our company looked for people to participate in the CFAST diabetes project
- As a Data Modeling Specialist (DMS) I have applied to this opportunity as
  - I have experience with diabetes trials, CDASH and SDTM
  - This is a great chance to contribute to the development of standards from data collection, data modeling and data management perspective
- The project team started its work in March 2013
- Publication of diabetes standards was originally planned for Q1/2014 but will now be Q2/2014 (see previous slide)

Standards Development Process CDISC



Standards Development Process CFAST Therapeutic Areas

Stage	Stage Description	CFAST Diabetes Project Status
0	Project Initiation and Scoping	Completed
1	Identification and Modeling of Research Concepts	Completed
2	Development of Draft Standards	Completed
3a	Internal Review	Internal review is completed and the project team currently assesses and incorporates the comments
3b	Public Review	Planned for Q1/2014
3c	Publication	Planned for Q2/2014

CFAST Diabetes Project Team Overview

- All members I work(ed) with are based in US
- Members and resource information:

Stages 0 and 1	Stages 2 to 3c
At least weekly project team TCs	Biweekly project team TCs
Project lead plus experts as needed	Project lead plus experts as needed
~6 concept modelers	3 concept modelers
0.2 FTE per concept modeler	0.4 FTE per concept modeler

CFAST Diabetes Project Team Concept Developer Role

- My role is called “Concept Developer”
- Main responsibilities are as follows:
  - Create concept maps
  - Work with clinical experts to ensure meaningfulness of proposed standards
  - Collaborate with standards experts to develop metadata
  - Develop CDASH and SDTM examples and ensure they are consistent with existing CDASH and SDTM standards
  - Convert input into Shared Health And Clinical Research Electronic Library (SHARE) metadata which results in mapping to Biomedical Research Integrated Domain Group (BRIDG), SDTM and controlled terminology

Concept Developer Responsibilities
Concept Maps

- Concept maps – sometimes called mind maps
- Explain clinical processes and research concepts
- Diagrams which include bubbles representing concepts, ideas and things
- Labeled arrows represent the relationships between the concepts, ideas and things

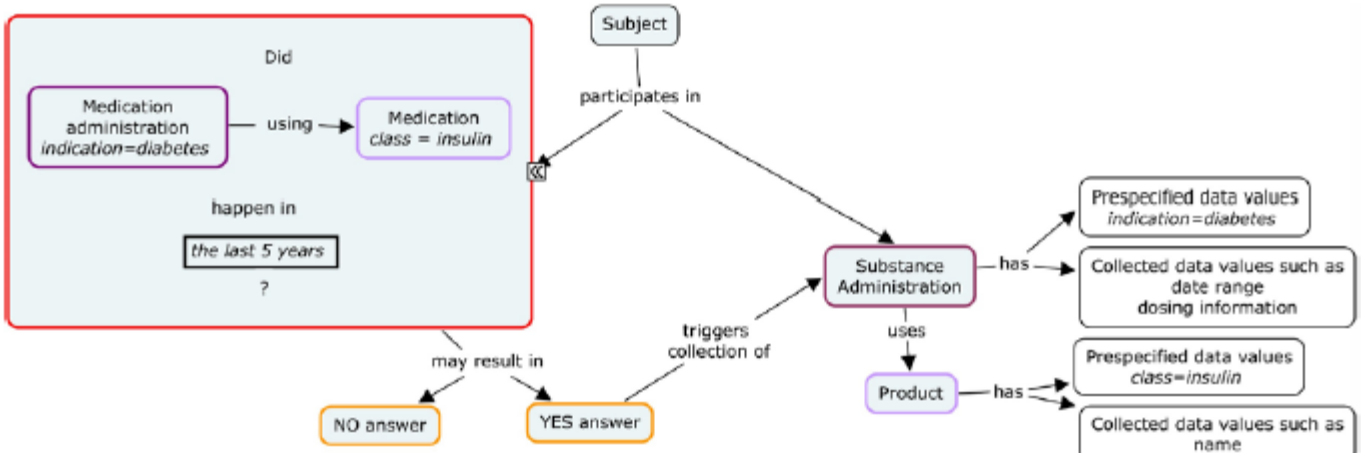


Diagram 3: Treatment Naive Query

Concept Modeler Responsibilities
SHARE Metadata Display

Concept: From CT for Glucose/GLUC			Domain: LB TEST: Glucose TESTCD: GLUC
BRIDG-based concept variable	**value(s)**	**Attribute**	**SDTM variable**
LabTest.DefinedObservation.methodCode.CD.code	Cxxxxx, C19340, Cxxxxx, C17156	Pre-specified method	METHOD
LabTest.DefinedObservation.methodCode.CD.displayName.value	Enzymatic Spectrophotometry; Reflectance Spectroscopy; Electrochemical; Mass Spectrometry		
LabTest.PerformedObservation.dateRange.IVL<TS>.low.value	*datetime*	Date of Test	
LabTest.PerformedObservation.studyDayRange.IVL<INT>.low.value	*integer*	Study Day of Test	
LabTest.PerformedObservation.negationIndicator.BL.value	TRUE, FALSE (SDTM NOT DONE, null)	Negation Indicato	LBSTAT
LabTest.PerformedObservation.negationReason.DSET<SC>.item.value	*free text*	Negation Reason	LBREASND
LabResult.PerformedClinicalResult.value.PQ.originalText.value	*free text*	Result Value	LBORRES, LBSTRESC, LBSTRESN
LabResult.PerformedClinicalResult.value.PQ.value	*decimal*		
LabResult.PerformedClinicalResult.value.PQ.unit.code	C64387;C42576;C67327; C67326;C67306;C48508; C67434	Result Unit	LBORRESU, LBSTRESU
LabResult.PerformedClinicalResult.value.PQ.unit.displayName.value	mmol/L; g/L; Null; ng/L; ng/dL; ug/L; umol/L; pmol/L		
LabResult.PerformedClinicalResult.baselineIndicator.BL.value	TRUE, FALSE (SDTM Y, null)	Baseline Indicato	LBBLFL
LabResult.PerformedClinicalResult.comment.ST.value	*free text*	Comment	COVAL
LabResult.PerformedClinicalResult.normalRangeComparisonCode.CD.code	C78727, C78800, C78801	Normal Range Comparison	LBNRIND
LabResult.PerformedClinicalResult.normalRangeComparisonCode.CD.displayName.value	NORMAL, HIGH, LOW		
LabNR.ReferenceResult.value.IVL<PQ>.low.value	*decimal*	Normal Range Lower Limit	LBORNRLO, LBSTNRLO
LabNR.ReferenceResult.value.IVL<PQ>.low.unit.code	C64387;C42576;C67327; C67326;C67306;C48508; C67434	Normal Range Lower Limit Unit	uses LBORRESU, LBSTRESU
LabNR.ReferenceResult.value.IVL<PQ>.low.unit.displayName.value	mmol/L; g/L; Null; ng/L; ng/dL; ug/L; umol/L; pmol/L		
LabNR.ReferenceResult.value.IVL<PQ>.high.value	*decimal*	Normal Range Upper Limit	LBORNRHI, LBSTNRHI
LabNR.ReferenceResult.value.IVL<PQ>.high.unit.code	C64387;C42576;C67327; C67326;C67306;C48508; C67434	Normal Range Upper Limit Unit	uses LBORRESU, LBSTRESU
LabNR.ReferenceResult.value.IVL<PQ>.high.unit.displayName.value	mmol/L; g/L; Null; ng/L; ng/dL; ug/L; umol/L; pmol/L		
Possible associated concepts			
Plasma	*Specimen*		Source of LBSPEC=PLASMA, LBSPCCND
Collection of the specimen on which the test was performed	*Specimen collection*		Source of LBDTC, LBDY
Serum	*Specimen*		Source of LBSPEC=SERUM, LBSPCCND
Collection of the specimen on which the test was performed	*Specimen collection*		Source of LBDTC, LBDY
Laboratory which performed the test	*Laboratory*		LBNAM

Example

Plasma/ Serum Glucose

Concept Developer Responsibilities My Assignments

- Lab tests
  - Identification of lab tests relevant for diabetes as disease is usually diagnosed by blood tests
  - Detailed description of each lab test and its role in diabetes
  - Specimen definition for each lab test
  - Work with clinical experts on scientific questions and phrasings
  - Collaborate with terminology experts for additions to CDISC CT
  - Define SHARE metadata for primary and secondary endpoints HbA1c and Glucose
- Self-Monitoring Blood Glucose Profile (SMBG)
  - Develop SDTM examples
- Section on FDA requirements for endpoints and covariates in diabetes

Learning so far (1)

- Being involved in the CFAST diabetes project gives me the chance to work with people from other pharmaceutical companies → opportunity to see how other companies handle data collection and tabulation for diabetes trials
- The project helps to understand how CDISC standards are developed for a complete TA in the context of
  - Data modeling
  - Data collection
  - Data transformation
  - Set-up of detailed user guidance

Learning so far (2)

- The project includes getting to know some details about FDA interactions and requirements
- The methodology and software used in the project team to create and present data models via concept maps were new for me
- It is the first time I got to know SHARE metadata concepts

→ *All interactions and processes are very useful when working in-house on the development and implementation of standards for any TA*

Suggestions for Future CFAST Projects (1)

- Clear training schedule for newcomers in order to
  - Reduce workload of experienced members
  - Increase project involvement and decision making of new members
- Increased knowledge exchange between project team members – even if there are time constraints
- Each concept modeler needs to be assigned with 0.4 FTE as otherwise it is hard to complete own tasks and to follow other members and thus the full project progress

Suggestions for Future CFAST Projects (2)

- More involvement and communication about final decisions
- Set-up, store and maintain centrally
  - Process documents (including Roles and Responsibilities)
  - Different types of templates (e.g. SDTM domain examples)
  - Different types of conventions, e.g. for
    - TA User Guide (e.g. terminology, usage of title case/ uppercase/ lowercase)
    - CDASH CRF examples (e.g. colours and annotations)
    - SDTM domain examples (e.g. table/ row descriptions, order of columns)