The Evolution of SDTM

What’s new?
Agenda

1. FDA Submission Landscape
2. Evolution of CDISC Models
3. Development of Standards
4. CDISC SHARE
5. SDTM 3.1.4 Highlights
Agenda

1. FDA Submission Landscape
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The Food and Drug Administration (FDA) today announces the proposed rule making to require that data submitted for new drug applications (NDAs), biological license applications (BLAs), and abbreviated new drug applications (ANDAs) be provided in an electronic format that FDA can process, review, and archive. The proposal would also require the use of standardized data structure, terminology, and code sets contained in current FDA guidance (the Study Data Tabulation Model (SDTM), developed by the Clinical Data Interchange Standards Consortium) to allow for more efficient and comprehensive data review.
China’s SFDA Announces Major Reforms to Drug Regulatory Process

China’s State Food and Drug Administration (SFDA) has announced that it is implementing a series of reforms designed to improve the drug review and approval process, “and to promote the healthy development of China’s pharmaceutical industry.”

Wang Lifeng, director of the SFDA’s drug registration department, said the plan provides incentives for the research and development of innovative clinical drugs, adding that the approval process will be shortened for these drugs.

Project Scope
- Clinical reports & data from all clinical studies in Europe

Timelines
- Jan 2013 – Apr 2013: Advisory Groups
  - Patient Confidentiality
  - Clinical Data Formats
  - Rules of engagement
  - Good Analysis Practice
  - Legal Aspects
- June 2013: Draft Agency Policy
- Nov 2013: Final Agency Policy
- Jan 2014: Policy comes into force
SCIENTIFIC OPINION

Guidance for submission for food additive evaluations

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS)

European Food Safety Authority (EFSA), Parma, Italy

This Scientific Opinion, published on 16 August 2012, replaces the earlier version published on 18 July 2012.

ABSTRACT

This guidance document refers to the applications for authorisation of a new food additive or to a modification of an already authorised food additive, combining in a single document the description of the data requirements and their context, and also a description of the risk assessment paradigm applied. The document is arranged in four main sections: chemistry and specifications, existing authorisations and evaluations, proposed uses and exposure assessment, and toxicological studies. Assessment of the exposure to food additives is based on information on known or anticipated human exposure to the proposed additive or toxicologically relevant...
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1. FDA Submission Landscape
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Overview of CDISC Models  SEP 2013

**CDASH**
- CDASH v1.0 (OCT 2008)
- CDASH v1.1 (JAN 2011)
- CDASH UG v1.0 (APR 2012)
- CDASH v1.2 (DEC 2012 ?)
- CDASH E2B SAE IG (JUL 2013)
- CDASH v2.0 (APR 2014)

**SDTM**
- SDTM v1.0 + SDTM IG v3.1 (JUL 2004)
- SDTM v1.1 + SDTM IG v3.1.1 (AUG 2005)
- SDTM v1.2 + SDTM IG v3.1.2 (NOV 2008)
- SDTM IG v3.1.2 AMENDMENT 1 (DEC 2011)
- SDTM v1.3 + SDTM IG v3.1.3 (JUL 2012)

**ADaM**
- ADaM v2.0 (AUG 2006)
- ADaM v2.1 + ADaM IG v1.0 (DEC 2009)
- ADaM VALIDATION CHECKS v1.0 (SEP 2010)
- ADaM VALIDATION CHECKS v1.1 (JUL 2011)
- ADaM VALIDATION CHECKS v1.2 (JUL 2012)
- ADaM METADATA GUIDE (SEP 2013)
- ADaM IG v1.1 (OCT 2013)
- ADaM GENERAL OCCURRENCE MODEL v1.0 (FEB 2014)
- ADaM INTEGRATION IG v1.0 (MAR 2014)

**ODM**
- ODM v1.1 (APR 2002)
- ODM v1.2 (JAN 2004)
- ODM v1.2.1 (JAN 2005)
- ODM v1.3 (DEC 2006)
- ODM v1.3.1 (FEB 2012)
- EXTENDED ODM PRM XML SCHEMA (MAR 2014)

**THERAPEUTIC AREAS**
- ALZHEIMER v1.0 (SEP 2011)
- PAIN (JUN 2012)
- TUBERCULOSIS (JUN 2012)
- PARKINSON'S DISEASE (OCT 2012)
- VIROLOGY (NOV 2012)
- DEVICES (DEC 2012)
- PKD (FEB 2013)
- ALZHEIMER v1.1 (SEP 2013)
- ASTHMA (AUG 2013)
- MULTIPLE SCLEROSIS (JAN 2014)
- DIABETES (FEB 2014)
- THERAPEUTIC BRAIN INJURY (MAR 2014)
- SCHIZOPHRENIA (APR 2014)
- ONCOLOGY (JUN 2014)
- CARDIOVASCULAR (JUN 2014)
- VIROLOGY-HEPATITIS C (JUL 2014)

**SHARE**
- CDISC SHARE
- HEALTHCARE LINK
The Evolution of SDTM

- SDTM V1.1 and SDTM IG V3.1.1
  - Only for studies initiated prior to 13 Jun 2011
  - Date Support Ends 28 Jan 2015
- SDTM V1.2 and SDTM IG V3.1.2
  - Published Nov 2008
- SDTM V1.2 and SDTM IG V3.1.2 Am. 1
  - Published Dec 2011
- SDTM V1.3 and SDTM IG V3.1.3
  - Published Jul 2012
- SDTM V1.4 and SDTM IG V3.1.4
  - Expected end 2013
Data Standards Governance

DATA GOVERNANCE PROCESS

DEDICATED TEAM

DATA STANDARDS LIBRARY
- SDTM 1.3
- SDTM IG 3.1.3

THERAPEUTIC AREA STANDARDS

COMPANY STANDARDS

EXTERNAL
- FDA
- CDISC

INTERNAL
- NEW TA
- NEW STUDIES
- NEW DATA TYPE
CDISC Team Charters

- CDASH Team
- SDS Team
- Device team
- ADaM Team
- XML Technologies Team
- Terminology team
- BRIDG Team
- Questionnaire Team
- Protocol Team

#### CDISC Submission Data Standards (SDS) Team

**Team Charter**

**Team Mission**

To develop and maintain a consistent and comprehensive set of implementation guidance that support more efficient and effective integration, aggregation, and submission of metadata from human clinical trials to streamline FDA reviews and increase the value of collected research data.

**Scope**

- The SDS Team maintains the SDTM and SDTM IF and related documents, in alignment with the CDISC strategy, by organizing its constituent members into relevant sub-teams to deliver domain models that meet evolving data standardization needs of the FDA, as well as of key Therapeutic-focused Academic & Research Centers (e.g., DCEG, C-PATH, NIMH) and collaborative organizations such as TRANScelera BioPharma.

**2013 Product Goals**

- The SDS Team will implement its 2013 SDS Team - Project Delivery Plan, targeting delivery.
- An update to the Study Data Tabulation Model (SDTM) v1.1.
- An update to the Study Data Tabulation Model Implementation Guide (SDTMIG v1.1).
- The SDTM Implementation Guide: Pharmacokinetics/Pharmacodynamics (SDTMIG-Px v1.0).
- The SDTM Associated Persons Implementation Guide (SDTMAP v1.0).

**Other Major Projects**

- The SDS Team will begin a project to ship SDTM with SHARE in 2013, and will also initiate the creation and implementation of several new domains, enhancements, and/or corrections to previously published sections, and other incremental content targeted for inclusion on the next release of the SDTMIG (v 8.1.3). Domains may be released for review and provisional use prior to 8.1.5.

- These updates may be originated from previous existing plans, or as a direct result of Therapeutic Area project needs. Regardless, a call for volunteers will be issued to create the appropriate SDTM Development sub-teams.

**Collaborators**

- Full team is divided into sub-teams to deliver one or more components from the 2013 SDS Team - Project Delivery Plan to effectively maintain the SDTM and SDTM IF.
- Sub-teams set own meeting schedule, and mechanisms to report progress through their own SDTM Area Leads.
- SDS Area Leads ensure consistency across SDTM Sections domain under their care, and report on progress to each sub-team.
- SDS LT regularly meets with SDS Area Leads to share updates, review deliverable status and agreed 2013 SDS Team - Project Delivery Plan.
- Key meetings: Mondays 11am-12pm EDT
  - 1st & 4th Monday SDS LT
- Periodic meetings with extended SDS team including all volunteers.

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[Click here to download a zip file for all currently available team charters.](http://www.cdisc.org/team-charters)
CDISC Volunteers

New Volunteer Form

1. CDISC Project Teams and Sub-teams
2. Contact Information

CDISC depends on volunteers like you to develop, use, and maintain our open standards. The goal is to create a responsive community that can efficiently review and comment on draft standard documents as they become available as well as to build up membership on teams that develop new standards. Participating in the public review process is a necessary first step to becoming involved in CDISC team activities. Standards open for public review and new standards available for use are available on the CDISC website: www.cdisc.org.

What additional activities can you expect to be involved in as a CDISC volunteer? In addition to reviewing draft standards, you may be asked or decide to participate in any of the following:

- Actively participate during scheduled team teleconferences and task action items
- Evaluate and help resolve internal and external review comments on draft standards documents
- Participate in the development of new and updated standards documentation
- Help identify new versions of standards or new domains and align development with other standards teams
- Provide subject matter expertise and consultation
- Contribute to the development of team training materials

Click here to see the latest CDISC Technical Plan which shows major project deliverables for the year. For more information on Therapeutic Area standards, click here.

If you think you’re interested in contributing 8 or more hours a month to help, please fill out the form below and someone will follow up with you.

Thank you for considering volunteering for CDISC!

*Italics indicate team is not currently recruiting new volunteers.*

Please list where you would like to contribute to the CDISC mission (at least one selection is required):

- ADAM (Analysis Domain Model)
- BRIDG (Biomedical Research Integrated Domain Group)
- CDASH (Clinical Data Acquisition Standards Harmonization)
- Difine.XML (Difine Specifications)
- Healthcare Link
- ODM (Operational Data Model)

http://cdisc.wufoo.com/forms/m7p6r7/
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5. SDTM 3.1.4 Highlights
1. Oncology Domains – *Included in SDTMIG 3.1.3*

2. Alzheimer’s Disease V1 - *Final*

3. Pain V1 - *Provisional*

4. Parkinson’s Disease V1 - *Provisional*

5. Polycystic Kidney Disease V1 - *Provisional*

6. Tuberculosis V1 - *Provisional*

7. Virology V1 – *Provisional*

8. Asthma – *Open for public review*

* A CDISC provisional release is defined as a proposed standard that has completed a public review within the CDISC user community and is available for initial use; but subject to modification for some component parts still in process
CFAST Therapeutic Area Standards

CFAST
Coalition for the Advancement of Standards and Therapies

- Joint initiative of CDISC & C-Path
- Development of therapeutic area standards along with FDA and TransCelerate Biopharma, Inc.

http://www.cdisc.org/therapeutic
Therapeutic Area Standards Governance Model

CFAST Steering Committee

CFAST Scientific Advisory Comm.

CDISC Leadership

CFAST Program Manager(s)

TA Project Core Teams:
- Project Manager
- Clinical Lead
- Data Standards Lead
- Statistics Consultant
- Terminology Lead
- BRIDG Modeler
- Data Analyst
- Technical Writer

CFAST Support:
- IT
- Admin
- Communications

CDISC Foundational Standards Teams

Community and Process

FDA

CDISC

C-Path

TransCelerate BioPharma

© CDISC 2012
Enhanced Standards Development Process

1. Initiation & Scoping
   - SC/SRC/TL Approval
   - CDISC-COP-001
   - Project charter
   - Scope assessment
   - Project proposal
   - Project Plan

2. Identification/Modeling of research concepts
   - BRIDG
   - Gap assessment
   - Concept maps
   - Defined research concepts

3. Development of draft standards
   - Project Plan
   - SHARE Metadata
   - SDTM, ADaM
   - CDASH
   - Controlled Terminology
   - UG/Standards document

4. Internal Review
   - SRC Approval
   - Draft standards package
   - Draft educational materials
   - Portal
   - Internal comment tool

5. Public Review
   - SRC Approval
   - Draft standards package
   - Portal
   - Public comment tool

6. Public Release
   - Final standards package
   - CDISC website
   - Portal
   - Lessons Learned materials
   - Archival checklist + artifacts
   - Education materials

7. Maintenance & education
   - Implementor feedback
   - Education materials
# CFAST Program Overview July 2013

## Therapeutic Area Standards Under Development

<table>
<thead>
<tr>
<th>Therapeutic Area</th>
<th>Coordinating Organization(s)</th>
<th>Scoping &amp; Input</th>
<th>Concept Modeling</th>
<th>Standards Development</th>
<th>Internal Review</th>
<th>Public Review</th>
<th>Publication</th>
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</tbody>
</table>

**Issues**
- *Concept modeling done prior to standards development step.*
- *SAC working to define scope and deliverables.*

**Project Status:**
- Green = On track
- Yellow = At risk
- Red = Critical issues
- Light Blue = Stage ongoing
- Navy = Stage completed
- *Italicics = Projected*
CFAST Deliverables:

1. Mindmap visualization of disease area clinical concepts
2. Essential core data elements of the disease
3. Definitions
4. Data types (simple & ISO 21090)
5. BRIDG and SDTM mappings
6. SDTM domains and examples
7. Minimum value sets (from code lists) with definitions and C-Codes
8. User/Implementation Guide with permissions statement
9. Standard CDASH CRFs with SDTM annotations, as appropriate

Source: Cdisc Intrachange July 30 2013
Agenda

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What is CDISC SHARE?

http://www.cdisc.org/cdisc-share
CDISC SHARE

- Single, trusted, authoritative source for CDISC data standards
- Concepts, metadata, collections, relationships, value sets across the full spectrum of CDISC content
- Links research to healthcare concepts to support interoperability
- Aligned with NCI Semantic Systems

SHARE

- BRIDG, ISO21090
- Protocol, CDASH
- SDTM, ADaM
- Terminologies

Facilitates Data Exchange
- Access to data standards
- Source to target mapping & traceability
- Transformation logic

Adapted from Source by Sue Dubman, Sanofi-Aventis
Initial Release of CDISC SHARE is planned early 2014
What is the Potential Value of SHARE?

- Improves **data quality** based upon better definitions, change control
- Improves **data consistency**, encourages data re-use and facilitates aggregation of data and comparisons across organizations
- Improves **data exchange**, sharing, workflow and collaboration among multiple parties with clear, unambiguous standardised definitions
- Supports ability for 2 computers to understand information without direct human interpretation (**interoperability**)  
- Provides **reduction in costs** resulting from maintaining individual (and different) dictionaries within research organizations
- **Improves the speed** by which we develop new standards among all stakeholders with consistent, reliable governance
- Maintains version traceability, **change control** to allow impact analysis

Source: Cdisc Intrachange July 30 2013
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General Releases  SEP 2013

• Public Review Period ended
  – SDTM IG v3.1.4 Batch 1
  – SDTM IG v3.1.4 Batch 2
  – SDTM IG v3.1.4 Batch 3
Specifications for representing exposure data, Immunogenicity and Reproductive data

- EC - Exposure as Collected
- IS - Immunogenicity Assessments
- SR - Skin Response
- RD - Reproductive Details
• Specifications for representing morphology, histopathology and physiology data
  – MO - Morphology
  – MI - Microscopic Findings
  – CV - Cardiovascular Physiology
  – PR - Procedures
  – TD - Trial Disease Assessments
  – DD - Death Details
  – SS - Subject Status
• Draft SDTM Domain, SDTM Model Document and SDTMIG for AP
  - SDTM 1.4
  - SDTMIG for Associated Persons
  - HO - Healthcare Resource Utilization
**Therapeutic Areas**

- Oncology
- Alzheimer’s Disease
- Pain
- Parkinson’s Disease
- Polycystic Kidney Disease
- Tuberculosis
- Virology

**Therapeutic Areas**

- Alzheimer’s disease
- Assessment Scale – Cognitive (ADAS-Cog)
- Mini Mental Scale (MMSE)
- Audio Verbal Learning Test Version A (AVLTvA)
- Pain Intensity
- Brief Pain Inventory (BPI)
- EuroQol (EQ-5D)
- Karnofsky Performance Status Scale
- SF-36 Health Survey
- Hamilton Depression Scale
- Faces Pain Scale
- Mini Mental State Examination (MMSE)

**SDTMIG 3.1.3**

- TU – Tumor Identification
- TR – Tumor Results
- RS – Disease Response
- RELREC – Related Records

**SDTMIG 3.1.4**

- EC - Exposure as Collected
- IS - Immunogenicity Assessments
- SR - Skin Response
- RD - Reproductive Details
- MO - Morphology
- MI - Microscopic Findings
- CV - Cardiovascular Physiology
- PR - Procedures
- TD - Trial Disease Assessments
- DD - Death Details
- SS - Subject Status
- SDTM 1.4
- SDTMIG for Associated Persons
- HO - Healthcare Resource Utilization
Questions ?
Thank you for your attention